

與近視及其他風險因素之長期研究

Long-term Study of Myopia and Other Risk Factors in Primary Open Angle Glaucoma among Chinese

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計畫主持人：洪伯廷

計畫參與人員：林隆光、施永豐、謝瑞玟、Harry Quigley、

邱春億、楊嶺、洪翠雙、黃玲瓏

執行單位：國立台灣大學醫學院眼科

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摘 要

近視為我國眼科學上或視覺健康上重大的問題，由於其流行病上的高頻度，加上高度近視，其世界上任何報告皆高，所以成為我國 45 歲以上視力障礙的主要原因。

近視伴有很多與隅角開放性青光眼相類似之病徵：(1) 眼軸的長度；(2) 視神經纖維與視神經乳頭凹陷以及有關變化；(3) 近視中開放性青光眼之頻度高，而反過來，開放性青光眼也具有高頻度的近視。兩者互相關係以及臨床上之分別，在預防失明上，即眼健康上具有其重要性，尤其在近視高頻度的台灣，將是應予深入研究之必要。

此次計畫獲得的結果件另表文獻，而其重要結論為：金山鄉中老年人的篩檢顯示網膜症為第二重要失明之原因，其中與近視或網膜退化有密切關係。另一重要進行的近視流行病學之再一次全國性 10,889 名學童近視篩檢也再度顯示了比起前次 1995 年之近視罹患率提高。為防止近視之繼續增加，其預防設施應再往下，即應要對更小之幼稚園年齡之小孩進行視力篩檢。

另一方面，對高度近視之視神經應用影像分析儀顯示近視之特徵為視神經盤之面積較健眼為大，並與眼軸長度有密切關係，但是與視神經盤內之凹陷或 rim 面積，則無特別有意義之分別。後者兩項視神經變化，可以作為開放性青光眼與近視之鑑別診斷。

最後，為對形成近視有密切關係之調節機能，則與美國 A&M 大學藥物毒物研究合作，研究 Dopamine 對抗劑在調節上之作用。

關鍵詞：原發性隅角開放性青光眼，近視，軸長，台大醫院

Conclusions of Project

(1) Current Issues in Myopia

Although myopia has been present in humans for a long time, the last few decades of the 20th century brought about an explosion in the prevalence of myopia worldwide, especially in developing Asian countries. Because of the rapidly increasing rates of this disease, it may be considered an epidemic of global proportions that warrants extensive research in the future. Therefore, myopia is equally important as a social issue of public health, as well as a problem that needs to be researched heavily on epidemiology, therapy as well as in advance etiological study.

Only recently we have begun to realize the importance of myopia in the impairment of visual function. Myopia affects the young and the old in their visual dysfunction, thereby greatly affecting a continuum in the community and its associated socioeconomic development. Thus, the solution to the problem of myopia requires much more than a simple corrective lens. As there is currently very little information available regarding the etiological molecular biology of myopia, it is essential for future research to focus on this field too.

In this presentation, the author shall briefly review the current status of myopia from an epidemiological standpoint, myopia and its relationship to visual impairment, and recent studies regarding a new therapeutic approach using multiple focal lenses along with topical medication.

(2) Epidemiologic Study of the Prevalence and Severity of Myopia Among Schoolchildren in Taiwan in 2000

A nationwide survey was performed in 2000 to determine the prevalence and severity of myopia among schoolchildren in Taiwan and to compare these findings with the results of the last survey performed in 1995.

We first divided the whole island into regions according to developmental grade scores and then sampled with the probability proportional to the size of the population within each stratum. A total of 10,889 students were enrolled.

The prevalence and severity of myopia in schoolchildren in Taiwan in 2000 increased compared to 1995, with the most severe increases occurring in younger age groups. Thus, preventing schoolchildren developing myopia at a young age may slow down the increase in severity of myopia in Taiwan.

(3) Visual Impairment Among the Middle-Aged and Elderly Population in Chin-Shan Township, Taipei County

To investigate the status and causes of visual impairment in middle-aged (40 to 65 years old) and elderly (>65 years old) people in Taiwan. Cataract was the most frequent cause of visual impairment and retinopathy was the second most frequent cause for the middle-aged and aged population of Chin-Shan Xiang, Taipei County, in 1992 and 1994.

(4) Evaluation of Optic Disc Changes in Severe Myopia

In glaucoma diagnosis, morphometry of the intra- and parapapillary structures can help to differentiate normal eyes with ocular hypertension from those with early glaucomatous optic nerve atrophy. However, these typical features are not valid in highly myopic eyes, where the optic disc has a distinctly different ophthalmoscopic appearance. The use of stereophotography with computerized planimetry to measure the size of the optic disc and neuroretinal rim has enhanced the assessment of the optic nerve in glaucoma.

(5) Effects of Dopamine Antagonists in Human Eye Accommodation

The purpose of this study was to evaluate the effects of dopamine antagonists in accommodation of the human eye. The dopamine antagonist drugs used in this experiment include 0.5% metoclopramide and 0.25% droperidol. Eighteen healthy subjects were enrolled; they were randomly assigned, in double-masked fashion, to receive topical administration of single drop of either 0.5% metoclopramide or 0.25% droperidol in one eye, with the fellow eye receiving isotonic saline as control. The accommodative abilities of both eyes were measured before instillation, and also at 3 and 6 hr after instillation of drugs, respectively. We studied the latency of reaction, the rate of accommodation, the average accommodative power, the rate of recovering and the total recovering time as the five parameters for evaluation the accommodative ability of each eye.

The results showed that there were significant changes in two parameters: the rate of accommodation and rate of recovering.

Keywords: POAG, myopia, axial length, NTUH

緣由與目的

青光眼現今廣被承認為引起失明及視力障礙之重要的眼疾,其在醫療上之重要性,乃是如果早期診斷並經適當的治療,大部分的病人,仍可維持「有用」「可用」的視力,具有預防醫學之特殊地位。根據 Quigley 之預估,在公元 2001 年後,在全球六十四億人口中,青光眼患者數目將達六千萬人以上,這將是帶給社會經濟一沉重負擔的疾病。

而另一方面台灣近視的流行病學,根據林隆光與陳建仁十年前後,對全國一百所學校中之一萬名學童之視力調查顯示,國小各年級之近視平均,在十年內由 33% 提升為 56%,國中生由 64% 提升為 76%,而高中生則由 75% 升高為 84%,而因網膜病變引起視力障礙之高度近視已達 19%。可見近視在台灣流行病學之嚴重性。

原發性隅角開放性青光眼,過去在台灣其發生雖然不如隅角閉鎖性青光眼嚴重,但由於近視人口之增加,隅角前房增大,將來原發性隅角開放性青光眼將步歐美人口,成為重要的國人青光眼。而這種青光眼中,據統計約有 14.6% 到 67% 罹患近視。反過來說,在近視病人中,則測出約 2.8% 到 28% 為原發性隅角開放性青光眼,這種青光眼病人中罹患近視。或相反地,近視中罹患青光眼之比率,各專家學者之研究結果相當不一,過去廣為爭論,例如研究對象選擇之水準,近視或青光眼判定水準之不一,未有良好之控制群等。而上述之各研究報告,都以白人為主,尚未有計畫周詳之國人實際結果。

眼壓為青光眼重要風險因子,現今已毋庸置疑。但是由於日本、美國方面,最近開始對所謂「正常眼壓青光眼」之流行頻率,陸續有重要訊息,使眼壓因素成為重要須重新檢討之題目。也就是說,有相當數目之青光眼病變之病人,其眼壓從未超過正常眼壓,但其視神經及視野仍然繼續惡化,而有些報告則指出長期追蹤這些病人,才能獲得是否真正的「正常眼壓」,或是血管因素所引發。這種正常眼壓,部分學者認為與近視有關,因此針對本群之眼壓血管變化加上近視之分析、追蹤,應可獲得相當程度之了解。

本計畫乃針對國人重要之兩眼疾,進行長期追蹤研究。一方面針對青光眼的風險因子—近視,以病案控制研究方法進行分析,一方面對以較確定之肯定因子—眼壓、年齡,以及家族性因子,作一深入之探討,同時對糖尿病等與近視同樣未確定之風險因子進行分析,而對較未能肯定因子,如血壓及血管因素,進行初步之資料收集與分析。

此外,根據本計畫收集病例之追蹤檢查,將對青光眼之進展與其他種種風

險因素之成長或存在,及其相關關係收集科學證據,例如近視程度與其進行相當關係分析,視野之變化關係,視神經盤陷凹出血,及視神經層厚度之意義,以施行問卷調查了解家族因素,偏頭痛,生活習慣(如閱讀時間,吸煙習慣)等之關係。

本計畫除由台大青光眼科及流行病學研究所生物統計參與外,也與馬偕醫學中心眼科,以及美國霍斯金大學 Dana 眼科預防中心進行合作研究。由於本計畫係有關中老年人之視力健康,及近視學童成人後之重要視力問題,期由本研究可對重要青光眼風險因子之證據,提供防盲政策重要之參考。

Effects of Dopamine Antagonists in Human Eye Accommodation

LING YEUNG,¹ POR T. HUNG,¹ LUKE L.L. LIN,¹ CHANG-HAO YANG,¹
and GEORGE C.Y. CHIOU²

¹*Department of Ophthalmology, National Taiwan University Hospital, College of Medicine,
National Taiwan University, Taipei, Taiwan, Republic of China*

²*Institute of Ocular Pharmacology and Department of Medical Pharmacology and Toxicology,
Texas A&M University System, Health Science Center, College Station, Texas*

ABSTRACT

The purpose of this study was to evaluate the effects of dopamine antagonists in accommodation of the human eye. The dopamine antagonist drugs used in this experiment include 0.5% metoclopramide and 0.25% droperidol. Eighteen healthy subjects were enrolled; they were randomly assigned, in double-masked fashion, to receive topical administration of a single drop of either 0.5% metoclopramide or 0.25% droperidol in one eye, with the fellow eye receiving isotonic saline as control. The accommodative abilities of both eyes were measured before instillation, and also at 3 and 6 hr after instillation of drugs, respectively. We studied the latency of reaction, the rate of accommodation, the average accommodative power, the rate of recovering and the total recovering time as the five parameters for evaluating the accommodative ability of each eye.

The results showed that there were significant changes in two parameters: the rate of accommodation and rate of recovering, whereas there were no significant changes in the other three parameters: latency of accommodation, average power of accommodation and total recovering time. In conclusion, the dopamine antagonists may have some effects on the rate of accommodation but not the degree of accommodation. Further studies with higher concentrations of these dopamine antagonists on dose-response relationships are needed before exact drug efficacy can be drawn.

INTRODUCTION

In the previous animal experiment, dopamine antagonists were found to have some therapeutic effect on reducing intraocular pressure (1). The presence of dopamine receptors in the ciliary bodies has also been confirmed in the rabbits (2). This effect has been studied in human clinical trials (3-5). In the clinical trials, we incidentally observed that the drugs seemed to have certain effects on the accommodation (6), so we conducted this trial to evaluate our observation. The drugs used in our experiment were metoclopramide and droperidol; both are potent dopamine antagonists. Metoclopramide is frequently used as a prokinetic agent to enhance gastrointestinal motility (5,7). It also has antiemetic

properties through a central dopamine antagonist effect (8). Droperidol is quite a safe neuroleptic agent (9), and it can be used in combination with fentanyl in neuroleptanesthesia (10). It also has an antiemetic effect (11). The safety of both drugs was assured in our previous experiment (6). If these dopamine antagonists really have any effect on accommodation, they will be potential drug candidates in the treatment of accommodative disorders, like myopia. In this experiment, we designed to analyze the accommodation ability in five different parameters, which represent the detailed part of accommodative processes of the human eye (12).

SUBJECTS AND METHODS

All subjects in this experiment were young healthy persons with ages between 20 and 30. None of them had any known systemic diseases or ocular diseases. Subjects with anisometropia of more than 2.0 diopters and high myopia of more than 8.0 diopters were excluded. There were a total of eighteen volunteers in this experiment; eight of them (4 male and 4 female) were enrolled in the test of metoclopramide, and ten of them (6 male and 4 female) were enrolled in the test of droperidol. They were randomly assigned, in double-masked fashion, to receive topical administration of a single drop of either 0.5% metoclopramide or 0.25% droperidol in one eye, with the fellow eye receiving isotonic saline as control. The accommodative abilities of both eyes were measured before instillation, at 3 and 6 hr after instillation of drugs.

During each measurement, a 3 diopters stimulation and a 5 diopters stimulation were given, then we recorded the response of each eye, respectively, and determined its accommodation ability. The degree of accommodation was recorded by an objective infrared optometer (AA-2000, Nidek, Aichi, Japan) and a Iriscorder (IC-1100, Nidek). They can simultaneously measure the accommodation and pupil response after a variable stimulation. The data were processed in a computer, and a graph of time versus degree of accommodation was obtained. Five parameters were taken from the graph, including the following: 1) The latency of reaction (seconds) is the length of period from starting stimulation to the initiation of response of the eye; 2) The rate of accommodation (diopters per second) is the upstroke slope in the graph; 3) The average accommodative power (diopters) represents the average degree of accommodation that can be made during the stimulation; 4) The rate of recovering (diopters per second) is the slope of the downward part in the graph; 5) The total recovering time (seconds) is the length of period from the end of stimulation to complete relaxation of the eye when

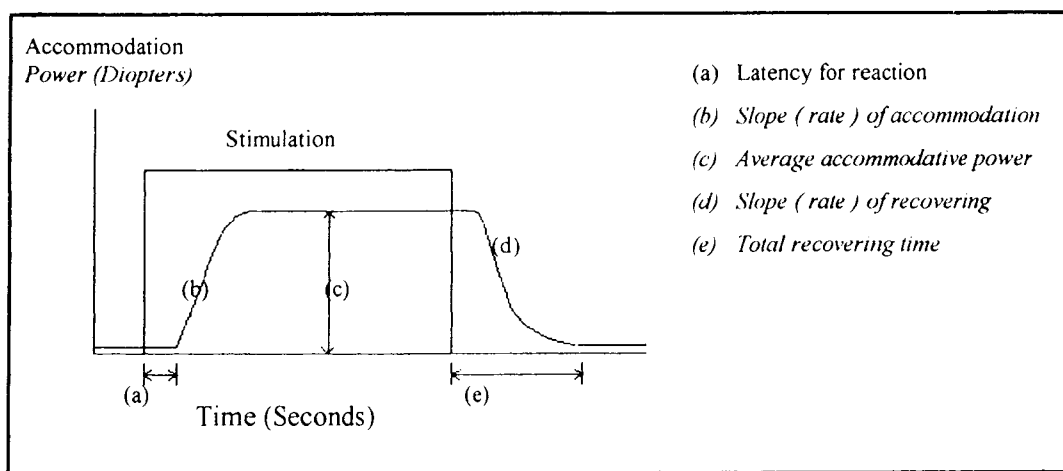


FIGURE 1. The Five Parameters to Evaluate the Accommodation Ability of Eyes.

the accommodative graph comes to baseline (Fig. 1). The pupil sizes prior and after medication were also measured. All data were analyzed and compared by SPSS using paired T-test, at 3 and 6 hr, respectively, with the initial values at 0 hr.

RESULTS

Ten volunteers received 0.25% droperidol, while eight received 0.5% metoclopramide. The results are summarized in Tables 1 to 5. There were statistically significant differences in the change of rate of accommodation and the rate of recovering (Table 2 and Table 4), while no statistically significant difference was noted in the other parameters.

In the study on the rate of accommodation (Table 2), when 3 diopters stimulation was given, the

TABLE 1.
The Change in Latency of Reaction after Instillation of
Metoclopramide (0.5%) or Droperidol (0.25%) in Healthy Volunteers

Drug Used	Stim.	0 hr.	3 hr			6 hr		
		Latency	Latency	Mean Change ($\pm$ SD)	P value	Latency	Mean Change ($\pm$ SD)	P value
Metoclopramide	3D	0.51	0.48	-0.04($\pm$ 0.05)	0.080	0.45	-0.06($\pm$ 0.07)	0.049*
	5D	0.49	0.48	-0.01($\pm$ 0.11)	0.763	0.46	-0.02($\pm$ 0.08)	0.451
Control Group	3D	0.48	0.43	-0.05($\pm$ 0.09)	0.170	0.43	-0.05($\pm$ 0.11)	0.227
	5D	0.46	0.44	-0.03($\pm$ 0.08)	0.451	0.41	-0.05($\pm$ 0.12)	0.275
Droperidol	3D	0.47	0.42	-0.05($\pm$ 0.11)	0.177	0.42	-0.05($\pm$ 0.11)	0.177
	5D	0.44	0.42	-0.02($\pm$ 0.06)	0.343	0.44	0.00($\pm$ 0.07)	1.000
Control Group	3D	0.43	0.41	-0.02($\pm$ 0.06)	0.343	0.43	0.00($\pm$ 0.11)	1.000
	5D	0.46	0.43	-0.03($\pm$ 0.09)	0.343	0.40	-0.06($\pm$ 0.08)	0.051

Unit of Latency of reaction is in Seconds

* $p < 0.05$ stands for statistically significant

Stim. stands for stimulation used in the experiment

($\pm$ SD) means standard deviation

"-" in Mean Change means shortening of the latency of reaction

TABLE 2.
The Change in Rate of Accommodation after Instillation of
Metoclopramide (0.5%) or Droperidol (0.25%) in Healthy Volunteers

Drug Used	Stim.	0 hr.	3 hr			6 hr		
		Rate	Rate	Mean Change ($\pm$ SD)	P value	Rate	Mean Change ($\pm$ SD)	P value
Metoclopramide	3D	0.99	1.50	0.51($\pm$ 0.60)	0.047*	2.20	1.22($\pm$ 0.58)	0.001*
	5D	1.62	1.89	0.27($\pm$ 0.64)	0.270	2.25	0.90($\pm$ 1.11)	0.056
Control Group	3D	1.36	1.59	0.23($\pm$ 0.45)	0.189	1.86	0.50($\pm$ 0.77)	0.110
	5D	1.91	1.74	-0.17($\pm$ 0.52)	0.391	2.52	0.61($\pm$ 0.10)	0.096
Droperidol	3D	1.60	2.32	0.72($\pm$ 0.64)	0.006*	2.24	0.65($\pm$ 0.72)	0.019*
	5D	2.36	2.53	0.17($\pm$ 0.76)	0.493	2.67	0.32($\pm$ 1.14)	0.403
Control Group	3D	1.79	2.22	0.43($\pm$ 0.99)	0.205	2.09	0.30($\pm$ 0.64)	0.178
	5D	2.04	2.30	0.26($\pm$ 0.75)	0.299	2.59	0.55($\pm$ 0.89)	0.081

Unit of Rate of Accommodation is in Diopters/Second

* $p < 0.05$ stands for statistically significant

Stim. stands for stimulation used in the experiment

($\pm$ SD) means standard deviation

"-" in Mean Change means the Rate of Accommodation became slower than before

TABLE 3.
The Change in Accommodative Power after Instillation of
Metoclopramide (0.5%) or Droperidol (0.25%) in Healthy Volunteers

Drug Used	Stim.	0 hr.	3 hr			6 hr		
		Ac.Pow.	Ac.Pow.	Mean Change (±SD)	P value	Ac.Pow.	Mean Change (±SD)	P value
Metoclopramide	3D	1.72	1.84	0.13(±0.38)	0.381	1.84	0.12(±0.45)	0.476
	5D	3.28	3.34	0.06(±0.42)	0.685	3.44	0.16(±0.50)	0.405
Control Group	3D	1.75	1.59	-0.16(±0.30)	0.180	1.59	-0.16(±0.27)	0.140
	5D	3.25	3.25	0.00(±0.38)	1.000	3.06	-0.19(±0.29)	1.111
Droperidol	3D	1.98	2.13	0.15(±0.29)	0.140	2.10	0.13(±0.34)	0.273
	5D	3.88	4.08	0.20(±0.33)	0.087	3.88	0.00(±0.35)	1.000
Control Group	3D	1.93	1.93	0.00(±0.26)	1.000	1.88	-0.05(±0.40)	0.705
	5D	3.75	3.75	0.00(±0.33)	1.000	3.75	0.00(±0.41)	1.000

Unit of Accommodative power is in Diopters

Stim. stands for stimulation used in the experiment

Ac.Pow. stands for Accommodative Power

(±SD) means standard deviation

"-" in Mean Change means decrease of the Accommodation Power

TABLE 4.
The Change in Rate (Slope) of Relaxation after Instillation of
Metoclopramide (0.5%) or Droperidol (0.25%) in Healthy Volunteers

Drug Used	Stim.	0 hr.	3 hr			6 hr		
		Slope	Slope	Mean Change (±SD)	P value	Slope	Mean Change (±SD)	P value
Metoclopramide	3D	-1.36	-2.36	-1.00(±1.11)	0.039*	-2.90	-1.53(±1.41)	0.018*
	5D	-2.67	-4.33	-1.66(±1.35)	0.010*	-5.11	-2.43(±1.43)	0.002*
Control Group	3D	-1.58	-2.61	-1.03(±1.89)	0.166	-2.70	-1.13(±1.78)	0.117
	5D	-2.66	-3.84	-1.19(±2.03)	0.141	-4.01	-1.36(±1.63)	0.051
Droperidol	3D	-1.93	-2.73	-0.81(±0.91)	0.020*	-2.61	-0.68(±0.77)	0.020*
	5D	-3.39	-5.07	-1.68(±3.15)	0.126	-4.30	-0.92(±1.55)	0.095
Control Group	3D	-2.58	-2.66	-0.08(±1.22)	0.834	-2.29	0.29(±1.57)	0.575
	5D	-4.34	-5.00	-0.66(±1.73)	0.256	-4.72	-0.38(±1.93)	0.545

Unit of Rate (Slope) of Relaxation is in Diopters/Second

Stim. stands for stimulation used in the experiment

* p < 0.05 stands for statistically significant

(±SD) means standard deviation

"-" in Mean Change means the slope of relaxation became more negative, that is faster in Rate of Relaxation

test eye had an increase in accommodation rate of 0.51 D/sec at 3 hr after instillation of metoclopramide and 1.22 D/sec at 6 hr. At the same time, the accommodation rate of control eyes increased by 0.23 D/sec and 0.50 D/sec only, respectively. In the group using topical droperidol, the test eye increased accommodation rate by 0.72 D/sec and 0.65 D/sec as compared with 0.43 D/sec and 0.30 D/sec in the control eye at 3 and 6 hr after instillation, so there were significant increases in rate of accommodation for both drugs. However, if 5 diopters stimulation was used instead of 3 D, neither of the drugs had significant change in accommodation rate.

As to the rate of recovering (Table 4), it showed a similar result as the rate of accommodation, with the addition of significant differences in the metoclopramide group when 5 D stimulation was given. The slope of recovering became more negative, implicating that the eyes were relaxing at a faster speed. The average increase in the rate of recovering of the metoclopramide group at 3 and 6

TABLE 5.
The Change in Total Recovering Time after Instillation of
Metoclopramide (0.5%) or Droperidol (0.25%) in Healthy Volunteers

Drug Used	Stim.	0 hr	3 hr			6 hr		
		Re.Time	Re.Time	Mean Change (±SD)	P value	Re.Time	Mean Change (±SD)	P value
Metoclopramide	3D	1.13	0.93	-0.20(±0.45)	0.249	1.15	-0.03(±0.51)	0.893
	5D	1.14	1.10	-0.31(±0.63)	0.206	1.04	-0.38(±0.60)	0.123
Control Group	3D	1.14	1.00	-0.14(±0.26)	0.173	1.00	-0.14(±0.25)	0.164
	5D	1.29	1.16	-0.13(±0.30)	0.272	1.09	-0.20(±0.35)	0.151
Droperidol	3D	1.08	1.10	0.02(±0.32)	0.847	0.96	-0.12(±0.38)	0.347
	5D	1.31	1.18	-0.13(±0.58)	0.496	1.13	-0.18(±0.55)	0.324
Control Group	3D	0.91	1.03	0.12(±0.17)	0.051	0.87	-0.04(±0.13)	0.343
	5D	1.03	1.25	0.22(±0.31)	0.053	1.23	-0.20(±0.41)	0.156

Unit of Recovering Time is in Seconds

Stim. stands for stimulation used in the experiment

Re.Time stands for Recovering Time

(±SD) means standard deviation

“-” in Mean Change means shortening of the Total Recovering Time

hr as 1.00 D/sec and 1.53 D/sec, respectively, when 3 diopters stimulation was given, while 1.66 D/sec at 3 hr and 2.43 D/sec at 6 hr when 5 diopters stimulation was given. On the other hand, in the droperidol group, significant difference only appeared when 3 diopters was used. Rate in test eyes increased 0.81 and 0.68 D/sec at 3 and 6 hr, as compared with decreased 0.08 and 0.29 D/sec in the control group. Therefore, both drugs significantly increased the rate of recovering at 3 D stimulation but no changes at 5 D stimulation in the droperidol group.

Although the average change in latency (Table 1) seemed significant ($p=0.049$) at 6 hr after instillation of metoclopramide when we used 3 D stimulation, it was not compatible with other results in the same parameter. Other parameters, such as the average accommodative power and the total recovering time, showed no statistically significant differences before and after instillation of drugs.

Apart from the accommodation ability, we also measured the pupil sizes prior and after medications. The pupil sizes did not show any significant change in either drug or control test groups, at 0, 3, and 6 hr during the experiment.

DISCUSSION

From this experiment, both dopamine antagonists implicated certain effects on the accommodative ability of the human eye. However as only the rate of accommodation and rate of recovering had significant changes, we confirmed that only these two components of accommodation process were affected. The other components, such as the latency of reaction, the average accommodative power and the total recovering time, either were not affected or their changes were too small to be detected in this experiment.

As seen in Tables 2 and 4, there were significant differences only when 3 diopters stimulation was given, except the rate of recovering in metoclopramide which had significant changes in 5 diopters stimulation. It may be assumed that most of our daily activity can be done smoothly and efficiently at the range of accommodation around 3 diopters. Therefore, it may be the most sensitive range when testing the accommodative ability. We rarely need to accommodate 5 diopters in our daily life, so it will be less sensitive to measure the changes in the accommodative ability in this range.

The rate of accommodation and recovering depend on the contractile process of the ciliary muscle. The results in this experiment give us a new hint when studying the receptors and regulating

processes in these smooth muscle cells. Do they have dopamine receptors or other receptors that can react with dopamine antagonists? What is the role of these dopamine antagonists in the contractile process? It warrants further study in the future. It is well known that accommodation disorders are closely related to the myopia development. However, apart from atropine, there is still no effective treatment for these patients (13). Atropine is a cholinergic antagonist, which causes the mydriasis and paralysis of ciliary muscle. Although it can be used to slow the progression of myopia (14), it has a lot of side effects (15), such as mydriasis or blurred near vision. Myopia is related to both the length of eyeball and the contraction-relaxation ability of ciliary muscles. Therefore, improvement of the contraction-relaxation ability is a promising way for the medical treatment of myopia.

In conclusion, the result of this experiment suggests that dopamine antagonists may play a certain role in the regulation of the contraction and relaxation of the ciliary muscle. Further study on their dose response effect with higher concentrations in a safe range to the eye may be interesting. Thus, they may provide us a new window in studying the regulation processes of ciliary muscle and may have potential in the treatment of myopia.

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REFERENCES

1. Hong, S.-J. and Chiou, G.C.Y. Effects of dopamine agonists and antagonists on pulsatile blood flow of ocular hypertensive rabbits. *J. Ocul. Pharmacol. Ther.* 9:117-124, 1993.
2. Mancino, R., Cerulli, L., Ricci, A., and Amenta, F. Direct demonstration of dopamine D1-like receptor sites in the ciliary body of the rabbit eye by light microscope autoradiography. *Naunyn Schmiedebergs Arch. Pharmacol.* 346:644-648, 1992.
3. Chiou, G.C. Treatment of open-angle glaucoma and ischemic retinopathy with dopamine antagonist. *J. Ocul. Pharmacol. Ther.* 10:371-377, 1994.
4. Chiou, G.C.Y. Recent advances in ocular pharmacology: Introductory remarks. *J. Ocul. Pharmacol. Ther.* 10:1-2, 1994.
5. Dowling, P.M. Prokinetic drugs: metoclopramide and cisapride. *Can. Vet. J.* 36:115-116, 1995.
6. Liao, S.L., Hung, P.T., Chen, Y.C., and Lan, W.L. Safety and ocular hypotensive efficacy of a single dose of metoclopramide or droperidol in healthy subjects. *J. Ocul. Pharmacol. Ther.* 15:117-121, 1999.
7. Reynolds, J.C. and Putnam, P.E. Prokinetic agents. *Gastroenterol. Clin. North Am.* 21:567-596, 1992.
8. DiPalma, J.R. Metoclopramide: a dopamine receptor antagonist. *Am. Fam. Physician* 41:919-924, 1990.
9. Chambers, R.A., and Druss, B.G. Droperidol: efficacy and side effects in psychiatric emergencies. *J. Clin. Psychiatry* 60:664-667, 1999.

10. Bissonnette, B., Swan, H., and Ravussin, P. Un V. Neuroleptanesthesia: current status. *Can. J. Anaesth.* 46:154-168, 1999.
11. Kaufmann, M.A., Rosow, C., Schnieper, P., and Schneider, M. Prophylactic antiemetic therapy with patient-controlled analgesia: a double-blind, placebo-controlled comparison of droperidol, metoclopramide, and tropisetron. *Anesth. Analg.* 78:988-994, 1994.
12. Kato, K. Accommodation function and its clinical evaluation. *Nippon Ganka Gakkai Zasshi* 98:1238-1255, 1994.
13. Wilson, D.R. and Keeney, A.H. Corrective measures for myopia. *Surv. Ophthalmol.* 34:294-304, 1990.
14. Hsiao, C.K., Chen, C.J., Shih, Y.F., Lin, L.L.K., Hung, P.T., Yao, T.C., Su, T.C., Lin, T.C., Tzeng, J.Y., and Chen, Y. Design and statistical analysis for the myopia intervention trial in Taiwan. *In* Myopia Updates II, Lin, L.L.K., Shih, Y.F., Hung, P.T., eds., Springer-Verlag, Tokyo, 2000, pp.161-164.
15. North, R.V. and Kelly, M.E. A review of the uses and adverse effects of topical administration of atropine. *Ophthalmic Physiol. Opt.* 7:109-114, 1987.

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Reprint Requests: Por T. Hung, M.D.
 Department of Ophthalmology
 National Taiwan University Hospital
 #7, Chung-Shan South Road
 Taipei, Taiwan, Republic of China
 Email: portying@ha.mc.ntu.edu.tw

Mitomycin-C in Glaucoma Filtering Surgery

PT Hung

Department of Ophthalmology, National Taiwan University Hospital, Taipei, Taiwan, Republic of China

Introduction

New concepts in glaucoma therapy have led to remarkable achievements in the 20th century. Recently-introduced drugs not only reduce intraocular pressure (IOP), but also aim to provide neuroprotection and increased retinal circulation. However, the practical approach remains the gold standard of glaucoma treatment, i.e. reduction of IOP by means of medication, laser surgery, or conventional surgery to obtain a safe target pressure. The surgical filtering procedure with adjunctive antimetabolites is still an excellent choice for reducing IOP in patients with advanced glaucoma.

A variety of antimetabolites, including mitomycin-C (MMC) and 5-fluorouracil (5-FU), are available for reducing IOP. Since MMC was first introduced for ophthalmologic use, and has been studied in-depth at the Department of Ophthalmology, at the National Taiwan University Hospital, this brief review will focus on MMC.

MMC was first developed in 1955 by Hata *et al.*, from *Streptomyces caespitosus*.¹ MMC inhibits cell mitosis by interrupting DNA synthesis, and probably also acts on the vascular endothelium. The late Kunitomo of the National Taiwan University first introduced this agent to

ophthalmology as a topical drop for prevention of recurrent pterygium.² In 1981, Chen, a former student of Kunitomo, was the first to use MMC intra-operatively for refractory glaucoma.³ This first patient had lost one eye in a traffic accident and had refractory high IOP in the remaining eye after cataract extraction, corneal transplant, and repeated filtering surgery (figure 1).

Adjunctive MMC application during filtering surgery has since been popularised for refractory glaucoma, and has been reported to maintain the filtering effect in patients with childhood glaucoma and secondary glaucoma, as well as when used in initial surgical approaches

for primary open angle glaucoma. However, such procedures are not without complications.

The first reported adverse effects of MMC were scleral changes, such as scleral melting in cases of pterygium excision. Complications may appear early, or as late as 15 to 20 years after MMC application (figure 2). MMC can also cause ocular complications and toxicity in glaucoma surgery. Eye surgeons must therefore exercise caution to avoid serious complications when performing MMC procedures.

Indications

In 1990, Chen *et al.* demonstrated that intra-operative MMC application is indicated for treatment of patients for whom filtering surgery carries a high risk of failure.⁴ Their study of MMC and fibroblast inhibition indicated that activated fibroblasts are one of the major factors leading to failed filtering surgery.

The indications for MMC set forth in their series included failure of previous filtering operations, previous intraocular



Figure 1. First application of adjunctive mitomycin-C in refractory glaucoma, 1981.³ Photograph reproduced courtesy of Professor Chen.

Because of the high prevalence of primary angle closure glaucoma in Asia, trabeculectomy with releasable sutures is probably safe for treatment of shallow anterior chamber glaucoma, with the goal of early restoration of the anterior chamber. Therefore, the concentration and duration of MMC application are also important in trabeculectomy for primary angle closure glaucoma. MMC application can also yield effective bleb formation after restoration of the chamber followed by releasing suture and digital pressure.

Subconjunctival Injection



With intra-operative application and washing techniques, the amount of MMC left in the eye is quite variable; it may also vary considerably among surgeons. Because of the potential adverse effects of MMC in pterygium surgery, as well as the possible cytotoxicity of MMC in the ciliary body, a variety of approaches have been tried to precisely control the MMC dose. Although drug carriers and controlled delivery implants have been used in an attempt to control the MMC dose more precisely, simple subconjunctival injection appears to be most practical and least invasive method.¹¹⁻¹³

In 1992, we first reported the use of simultaneous sclerostomy and subconjunctival MMC injection.¹¹ The sclerostomy was performed with a THC: YAG laser probe subconjunctivally in rabbits, and IOP and bleb survival were monitored. This procedure proved to be effective in enhancing bleb filtration. A similar rabbit experiment was reported in 1994 by Karp *et al.*¹³

Using the results of these animal studies as a starting point, we investigated the use of MMC subconjunctival

Figure 3. Subconjunctival mitomycin-C solution injection 24 hours prior to trabeculectomy.



injection prior to trabeculectomy in patients with refractory glaucoma in 1995.¹⁴ The total dose of MMC injection was 1 to 3 μ g (0.05 ml of a 0.02 mg/ml solution), 24 hours to 5 days prior to filtering surgery. The 27-gauge needle was inserted more than 1 cm away from the limbus to reach the planned trabeculectomy site, and the subconjunctival MMC solution was spread using the same needle (figure 3). During the follow-up period of more than 12 months, we observed significant IOP control and typical MMC blebs with diffuse, non-vascular appearance. Complications were minor.

The most important consideration in pre-operative subconjunctival MMC injection for filtering surgery is optimization of the MMC dose. Ando *et al.* showed that when 0.2 mg/ml MMC is injected subconjunctivally, followed by thorough washing 5 minutes later, approximately 3 μ g of MMC remains in the eye.¹⁵

Subconjunctival administration of MMC prior to filtering surgery appears to be a safe and easy procedure. Its advantages include exact control of the amount of MMC delivered, prevention

of back-flow of MMC intracamerally via a fistula during intra-operative use, and the fact that it improves the ease of the fornix-based conjunctival flap procedure. However, the procedure can be difficult in patients with a very thin conjunctiva or thick conjunctival scarring, and MMC can be difficult to place in the infrasceral lamella.

Conclusion



This brief review has described the background of intraoperative MMC application in ophthalmic procedures, as well as its indications and possible complications. Because of the potential complications, the concentration and duration of MMC application must be carefully controlled; a new approach, pre-operative subconjunctival injection, appears to have great advantage in this regard. The development of MMC and other antimetabolites has started a new era for glaucoma filtering surgery.¹⁶ However, the risk-benefit ratio for the patient should be carefully weighed prior to surgery using MMC or similar agents.

References

1. Hata T, Sugawara R, Kanamori K, *et al.* A new antibiotic from streptomycetes. *J Antibiotic* (Tokyo) 1956;Ser. A, 9: 141-146.
2. Kunitomo N, Mori S. Studies on pterygium, Report IV. A treatment of the pterygium by mitomycin-C. *Acta Soc Ophthalmol Jpn* 1963;67:601-607.
3. Chen CW. Medical innovation in the effect of fistulizing operation. *Proc Chin Med Assoc* (Taipei) 1983;30:15.
4. Chen CW, Huang HD, Bair JS, *et al.* Trabeculectomy with simultaneous topical application of mitomycin-C in refractory glaucoma. *J Ocular Pharmacol* 1990;6:175-182.
5. El-Rasheed S. Initial trabeculectomy with intraoperative mitomycin-C application in primary glaucoma. *Ophthalmic Surg Lasers* 1999;30: 360-366.
6. Rubinfeld RS, Pfister RR, Stein RM, *et al.* Serious complications of topical mitomycin-C after pterygium surgery. *Ophthalmology* 1992;9:1647-1654.
7. Ho TZ, Hung PT, Wang TH. Intraoperative application of mitomycin-C and stereoscopic fluorescein angiography study of hypotony. *Invest Ophthalmol Vis Sci* 1992;33 (Suppl. 4): 1271.
8. Liebmann JM, Sokol J, Ritch R. Management of chronic hypotony after glaucoma surgery. *J Glaucoma* 1996; 5:210-220.
9. Lee CH, Kim DC. Recurrence rate of pterygium with respect of mitomycin-C concentration in primary pterygium operation. *Invest Ophthalmol Vis Sci* 1999;40 (Suppl. 4):5913.
10. Singh K. Intraoperative 5-fluorouracil (5 FU) vs. mitomycin-C (MMC). The primary anti-metabolite study. *Invest Ophthalmol Vis Sci* 1999;40 (Suppl. 4): 84.
11. Wang TH, Hung PT, HO TC. THC:YAG laser sclerostomy with preoperative mitomycin-C subconjunctival injection in rabbits. *J Glaucoma* 1992;2:260-265.
12. Schwartz M, Yoles E, Solomon A. A potential treatment of glaucoma. *J Glaucoma* 1996;5:473-483.
13. Karp CL, Higginbotham EJ, Griffin EO. Adjunctive use of transconjunctival mitomycin-C in ab externo diode laser sclerostomy surgery in rabbits. *Ophthalmic Surg* 1994;25:22-27.
14. Hung PT, Lin LLK, Hsieh JW, Wang TH. Preoperative mitomycin-C subconjunctival injection and glaucoma filtering surgery. *J Ocular Pharmacol* 1995;11: 233-241.
15. Ando H, Kondom Y, Yamamoto T, Kitazawa Y. Intraoperative mitomycin-C uptake by the eye *in vivo* and contributory factors. *Invest Ophthalmol Vis Sci* 1994;35 (Suppl. 4):1426.
16. Loon SC, Chew PT. A major review of antimetabolites in glaucoma surgery. *Ophthalmologica* 1999;213:234-245.

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Address for correspondence:

Prof. PT Hung
Department of Ophthalmology
National Taiwan University Hospital
7 Chung-Shan South Road
Taipei
Taiwan
Republic of China

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1873 Rama 4 Road, Bangkok, Thailand

Tel: (66 2) 256 4423

Fax: (66 2) 252 8290

E-mail: rprin@chula.ac.th

The Efficacy of Brimonidine in Preventing Intraocular Pressure Elevation in the Provocative Test for Primary Angle-Closure Glaucoma

YUH-FANG CHEN,^{1,2} POR T. HUNG,¹ JUI-WEI HSIEH,¹
JEAN SHEIN,³ and CHUHSING K. HSIAO⁴

¹*Department of Ophthalmology, National Taiwan University Hospital, Taipei, Taiwan*

²*Department of Health, Taipei Hospital Capital Branch, Taipei, Taiwan*

³*New York University School of Medicine, New York, New York*

⁴*Division of Biostatistics, Institute of Epidemiology, National Taiwan University, Taipei, Taiwan*

ABSTRACT

The purpose of this study was to evaluate the efficacy of 0.2% brimonidine tartrate in preventing intraocular pressure (IOP) elevation in the dark-prone provocative test for primary angle-closure glaucoma (PACG). Twenty-two eyes from 22 patients with angle-closure glaucoma were enrolled in this study. Each of the selected eyes had previously tested positive in a recent dark-prone test. One drop of 0.2% brimonidine tartrate was then instilled in each eye 2 hours prior to a second dark-prone test. An IOP elevation of greater than 8 mmHg was regarded as a positive result. The IOP elevation in the first dark-prone test was 11.91 ± 5.17 (range: 5.7 – 27.3) mmHg, while the IOP only increased 5.70 ± 2.96 (range: 2.9 – 12.2) mmHg in the second dark-prone test that was pre-treated with 0.2% brimonidine tartrate ($p < 0.001$). A significant difference was also noted in the pre-test IOP (15.59 ± 3.86 mmHg vs. 13.33 ± 3.65 mmHg, $p = 0.008$) as well as in the post-test IOP (27.62 ± 7.27 mmHg vs. 19.03 ± 3.50 mmHg, $p < 0.001$) in the two sequential dark-prone tests. All but three of the initially positive dark-prone tests (86.46%) converted to negative tests after pre-treatment with brimonidine. There was a significant effect of 0.2% brimonidine tartrate in the prevention of IOP elevation in PACG patients previously found to test positive in the dark-prone provocative test.

INTRODUCTION

The incidence of primary angle-closure glaucoma (PACG) is higher in Asian populations, especially among the ethnic Chinese (1). Among these populations, PACG is more frequently chronic and

has few symptoms. It is also characterized by a gradual progression to angle-closure even after the pupillary-block mechanism has been eliminated by successful iridectomy (2). Therefore, the mechanisms of intraocular pressure (IOP) elevation in PACG are complicated, and it is important to investigate the pathogenesis of the mechanical forces leading to angle-closure. Since the pathophysiology of PACG is so different from primary open-angle glaucoma (POAG), the IOP measurements, optic nerve evaluations, and visual function tests generally accepted for POAG detection are not suitable for early detection of PACG.

On the other hand, the provocative test is an important technique that may allow clinicians to predict if an asymptomatic PACG patient with a normal IOP will develop angle-closure and IOP elevation. Since the pathophysiologies of POAG and PACG are different, the treatment modalities of these two entities of glaucoma also differ. For PACG, medications that can effectively prevent angle-closure and IOP elevation are more important than those for daily IOP control, which are required in POAG. Hung et al advocated that pilocarpine has a significant effect in preventing the rise of IOP after dark-prone tests in PACG (3). In this study, 0.2% brimonidine tartrate was used prior to a dark-prone test to evaluate its efficacy in preventing IOP elevation after provocation.

MATERIALS AND METHODS

We enrolled 22 angle-closure glaucoma patients who previously had at least one positive dark-prone test. They were classified into groups based on the morphology of their glaucoma. Diagnostic criteria for the acute glaucoma category included elevated IOP above 25 mmHg associated with angle closure. For chronic PACG, there should be an occludable angle with or without peripheral anterior synechiae, previous positive provocative tests, biometric evidence, and glaucomatous optic neuropathy. All eyes with chronic PACG were quiet and the IOP was below 20 mmHg prior to the dark-prone test. Patients who had persistently high IOPs in spite of patent iridectomies were classified as having post-iridectomy glaucoma (PIG). Plateau iris configuration was defined as the presence of an occludable angle in combination with a normal-depth anterior chamber (4).

The first modified dark-prone test was performed without pre-medication after washing out for previous medications. The patients remained in a sitting position with their faces down on the desk for 1.5 hours in a dark room. Darkness was enhanced with opaque goggles, and patients were instructed to keep both eyes open. An IOP elevation of more than 8 mmHg or a post-test IOP of more than 25 mmHg was considered positive. Those who had at least one positive test in one eye were enrolled in the study, and a subsequent dark-prone test was performed. For the subsequent test, one drop of 0.2% brimonidine was instilled in both eyes two hours prior to the test. A modified dark-prone test of the same duration was then performed again.

The eye with the positive result in the first dark-prone test was selected for study analysis. If both eyes were positive, the one with more elevated IOP was chosen. If both eyes had equal IOP elevation, the one with higher post-test IOP was analyzed. If post-test IOP was equal between two eyes, the right eye was defined as the study eye. The results were expressed as mean $\pm$ standard deviation. A paired student's t-test was used for the result analysis, and $p < 0.001$ was defined as being statistically significant.

RESULTS

Twenty-two eyes from 22 patients were analyzed. There were 3 eyes with acute PACG, 11 with chronic PACG, 5 with PIG, and 3 with plateau iris configuration. The patients consisted of 6 men and 16 women, and their average age was 58.55 ± 7.99 (range from 42 to 76) years old.

The results of the dark-prone tests are summarized in Table 1. The IOP elevation in the first, non-medicated dark-prone test was 11.91 ± 5.17 (range from 5.7 to 27.3) mmHg, while the IOP only

TABLE 1.
Results of Dark-prone Provocation Test

	No pretreat	Pretreat with brimonidine	P value
Pre-test IOP (mmHg)	15.59 ± 3.86 (7.5 – 25.8)	13.33 ± 3.65 (6.3 – 21.9)	0.0086
Post-test IOP (mmHg)	27.62 ± 7.27 (20.1 – 49.8)	19.03 ± 3.50 (14.3 – 25.8)	< 0.001
IOP elevation (mmHg)	11.91 ± 5.17 (5.7 – 27.3)	5.70 ± 2.96 (2.9 – 12.2)	< 0.001
Positive test (eye)	22	3	

increased 5.70 ± 2.96 (range from 2.9 to 12.2) mmHg in the dark-prone test with the 0.2% brimonidine pre-treatment ($p < 0.001$). A significant difference was also noted between the post-test IOP (27.62 ± 7.27 mmHg vs. 19.03 ± 3.50 mmHg, $p < 0.001$) in the two sequential dark-prone tests. The pre-test IOP was also lower when pre-treated with brimonidine; however, it did not reach the level of statistical significance ($p = 0.0086$). All but three of the initially positive dark-prone tests (86.46%) converted to negative tests after pre-treatment with brimonidine. The 95% confidence interval ranged from 0.72 to 1.00.

DISCUSSION

Brimonidine is a newly approved, highly selective alpha-2 adrenergic agonist. It decreases IOP by both suppressing aqueous humor inflow and increasing uveoscleral outflow (5). In a three-month study, mean peak IOPs with twice-daily dosing of 0.2% brimonidine were reduced by 24%, and the IOP reduction at trough was 15% in patients with ocular hypertension (6). Furthermore, 0.5% brimonidine has been proven to successfully prevent laser-induced acute IOP spikes and to reduce the mean IOP after argon trabeculoplasty (7). In this study, we reported a significant effect of 0.2% brimonidine tartrate in the prevention of IOP elevation in dark-prone provocation in patients with angle-closure glaucoma. Both the IOP elevation and post-dark-prone IOP were significantly decreased in the group pre-treated with 0.2% brimonidine tartrate ($p < 0.001$). Furthermore, 86.46% (19 in 22) of the PACG patients that initially tested positive in the dark-prone test later tested negative after using brimonidine.

Mechanisms of PACG can traditionally be classified as pupillary block and non-pupillary block types. However, it has been well recognized that in most instances these two types were mixed (8,9). Hung et al reported that 59.5% of 37 iridectomized eyes of PACG patients tested positive in the dark-prone provocative test. These eyes were previously assumed to be free from pupillary block (3). Such iridectomized eyes were labeled residual glaucoma or post-iridectomy glaucoma (PIG) (10). Mechanisms involved in non-pupillary block PACG or PIG include the plateau iris-like angle crowding mechanism, malignant glaucoma-like ciliary block mechanism, peripheral anterior synechiae, trabecular dysfunction, and/or lens factors (3). In the Chinese, a slow progression of angle-closure or the creeping angle is another important mechanism responsible for PIG (2).

Since mechanisms of PACG are different from those of POAG, parameters commonly used for the early detection of POAG, such as IOP, optic nerve assessment, and visual field changes, are not proper for the early detection of PACG. For this purpose, various provocative tests have been introduced. These include the dark-room, prone-position, dark-prone, and pharmacological pupillary dilation tests (11). The positive rates and predictive values of these tests are widely varied. However, generally speaking, negative results cannot exclude the possibility of PACG; only positive results are significant.

Aside from detecting PACG in its early stages, provocative tests also have an important role in evaluating the efficacy of PACG medications. Hung et al demonstrated that topical application of 1% pilocarpine prior to a dark-prone test significantly lowered rates of positive tests (15%) when compared to those pre-treated with 0.25% timolol (68%) or those without pre-treatment (100%) in 31 iridectomized PACG eyes. They also showed that after 1% pilocarpine pre-treatment in 8 previously positive dark-prone tests, only 3 (38%) remained positive (2). In our study, 86.46% of the positive dark-prone provocative tests converted into negative results after 0.2% brimonidine pre-treatment in 22 PACG eyes.

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REFERENCES

1. Hung, P.T. Angle-closure glaucoma. *J. Clin. Ophthalmol.* 8:27–31, 1990.
2. Hung, P.T. and Chen, Y.C. Medical therapy in primary angle-closure glaucoma: a model for evaluation of its efficacy. In *Glaucoma Update*, Krieglstein, G.K., ed., New York: Springer, 2000, pp. 169–172.
3. Hung, P.T. Provocation and medical treatment in post-iridectomy glaucoma. *J. Ocul. Pharmacol.* 6:279–283, 1990.
4. Hoskins, H.D. Jr. and Kass, M.A. Primary angle closure glaucoma without pupillary block (plateau iris). In *Diagnosis and Therapy of the Glaucoma*, 6th ed., Hoskins, H.D. Jr. and Kass, M.A., eds., St Louis: CV Mosby Co., 1989, pp. 241–242.
5. Toris, C.B., Gleason, M.L., Camras, C.B., and Yablonski, M.E. Effects of brimonidine on aqueous humor dynamics in human eyes. *Arch. Ophthalmol.* 113:1514–1517, 1995.
6. Serle, J.B. A comparison of the safety and efficacy of twice daily brimonidine 0.2% versus betaxolol 0.25% in subjects with elevated intraocular pressure. The brimonidine Study Group III. *Surv. Ophthalmol.* 41(Suppl 1):S39–S47, 1996.
7. Anonymous (The Brimonidine-ALT Study Group). Effect of brimonidine 0.5% on intraocular pressure spikes following 360° argon laser trabeculoplasty. *Ophthalmic Surg. Lasers* 26: 404–409, 1995.
8. Hung, P.T. and Chou, L.H. Provocation and mechanism of angle-closure glaucoma after iridectomy. *Arch. Ophthalmol.* 97:1862–1864, 1979.
9. Hoskins, H.D. Jr. and Kass, M.A. Introduction and classification of the glaucoma. In *Diagnosis and Therapy of the Glaucoma*, 6th ed., Hoskins, H.D. Jr. and Kass, M.A., eds., St Louis: CV Mosby Co., 1989, pp. 2–9.
10. Forbes, M. and Becker, B. Iridectomy in advanced angle closure glaucoma. *Am. J. Ophthalmol.* 57:57–62, 1964.
11. Hyams, S.W., Friedman, Z., and Meumann, E. Elevated pressure in the prone position. A new provocative test for angle-closure glaucoma. *Am. J. Ophthalmol.* 66:661–672, 1968.

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Reprint Requests: Por T. Hung, Ph.D.
 Department of Ophthalmology
 National Taiwan University Hospital
 No. 7, Chung-Shan South Rd.
 Taipei, Taiwan ROC
 E-mail: portying@ha.mc.ntu.edu.tw



Efficacy of Latanoprost in Reducing Intraocular Pressure in Patients with Primary Angle-Closure Glaucoma

Paul T.K. Chew, FRCS (Ed), FRCOphth,^{1,2} Por T. Hung, MD,³ and Tin Aung, FRCS (Ed), FRCOphth²

¹National University of Singapore, Singapore; ²Singapore National Eye Centre, Singapore; and ³Taiwan University Hospital, Taipei, Republic of Taiwan

Abstract. Two independent, prospective trials were recently conducted to assess the efficacy of latanoprost in reducing intraocular pressure (IOP) in patients with primary angle-closure glaucoma (PACG). The first study was a 2-week, randomized, double-masked comparison of latanoprost treatment and timolol treatment in patients with PACG. Patients were randomized to one of two parallel treatment groups, receiving either placebo in the morning and latanoprost 0.005% in the evening, or timolol 0.5% twice daily. The mean IOP reduction in latanoprost group was 8.8 ± 1.1 mm Hg (mean $\pm$ SEM, $p < 0.001$; 34.2%) from a mean baseline IOP of 25.7 ± 0.9 mm Hg, and the corresponding figures for the timolol group were 5.7 ± 0.9 mm Hg ($p < 0.001$; 22.6%) from a mean baseline IOP of 25.2 ± 1.1 mm Hg. A significantly greater IOP reduction of 3.1 ± 1.5 mm Hg (95% confidence interval: 0.1 to 6.0) was achieved in the latanoprost group compared to the timolol treatment group ($p = 0.04$). In the second study, latanoprost 0.005% once a day was added adjunctively to PACG patients with persistently elevated IOP after iridectomy, despite treatment with beta-blockers and pilocarpine. The IOP decreased by about 21% during the first 3 months, and showed a reduction of about 36% at the end of 1 year. At the 1-year follow-up, IOP was <20 mm Hg in all eyes. In both studies, latanoprost was well tolerated with few adverse events. These results demonstrate that latanoprost is effective in reducing IOP in patients with PACG. (*Surv Ophthalmol* 47(Suppl 1):S125-S128, 2002. © 2002 by Elsevier Science Inc. All rights reserved.)

Key words. angle-closure glaucoma • intraocular pressure • latanoprost • uveoscleral outflow

Glaucoma accounts for approximately 5.1 million of the blind people in the world, with nearly half of these residing in Asia.^{17,19} Primary angle-closure glaucoma (PACG) is the most frequently seen form of glaucoma in Eskimos, Mongolians, Chinese, and eastern Asian Mongoloid descendants,⁸⁻¹⁰ and it is probably the most common form of glaucoma in a global sense.³ A recent glaucoma prevalence study in a Caucasian population also indicated PACG is probably not as rare in Caucasians as had been previously believed.⁵

In PACG, gradual asymptomatic angle closure results in diminished aqueous outflow through the angles and a subsequent rise of the intraocular pressure (IOP). A peripheral iridotomy is usually performed to treat pupillary block in PACG; it has been accepted as the first choice of treatment. However, it is also recognized that iridectomy alone does not cure or reduce IOP sufficiently in all cases of PACG. There is a considerable number of patients who present with elevation of IOP even after success-

ful surgical or laser iridectomy, and this presentation has been termed residual PACG after iridectomy. This is a common entity in Asian patients with PACG, especially among the Chinese.¹⁵ Several non-pupillary block mechanisms cause such IOP elevation post-iridotomy, and these include lens factors; angle-iris crowding, such as from plateau iris; and damaged trabecular function.^{11,12,14,18} The elevation of IOP usually persists and requires further medical, laser, or surgical treatment. As there is insufficient information about treatment modalities or drug therapies for PACG, ophthalmologists empirically use topical beta-adrenergic receptor antagonists, or cholinergic agonists such as pilocarpine, to reduce IOP in patients with PACG.

Latanoprost, a prostaglandin $F_{2\alpha}$ -analog, has proven to be an effective ocular hypotensive drug in patients with primary open-angle glaucoma and ocular hypertension.^{1,2,6,7,16,21,22} Latanoprost has not been found to alter the aqueous humor production to a clinically significant extent,^{20,23} and its main mechanism for reducing IOP is an increase in the uveoscleral outflow.²⁰ In view of its novel mechanism of action, it is conceivable that latanoprost exerts its IOP-lowering effect in eyes with closed angles. Accordingly, two recent studies in Asia have investigated the efficacy of latanoprost in reducing IOP in patients with PACG.

Study 1

The first study was carried out in Singapore, and was designed as a 2-week, randomized, double-masked comparison of latanoprost treatment and timolol treatment in patients with PACG.⁴ PACG was defined as glaucomatous optic neuropathy with a compatible visual field defect and at least 6 clock hours of synechiae angle closure on gonioscopy. All patients had a previous peripheral iridotomy (PI), an IOP above 21 mm Hg after the PI, and current control with one or two pressure-reducing medications on two consecutive visits (retrospectively ascertained). The therapy was then withdrawn before the start of the study, and patients were required to complete a minimum wash-out period before randomization: 3 weeks for beta-adrenergic antagonists, 3 weeks for prostaglandins, 2 weeks for adrenergic agonists, 5 days for cholinergic agonists, and 5 days for carbonic anhydrase inhibitors. Patients were instructed to administer one drop of the allocated medication at 8 AM and 8 PM each day; on clinic visit days, the morning drop was administered at 7 AM before the visit. The IOP was measured at 9:00 AM and 5:00 PM, and the mean of the measurements used for the baseline and subsequent visits.

The patients were randomized to two parallel study groups (16 subjects each): one group was as-

signed to treatment with placebo in the morning and latanoprost 0.005% in the evening, and the other group received timolol 0.5% twice daily. Compared to baseline measurements, the IOP reduction at day 14 was statistically significant in both treatment groups ($p < 0.001$). In the latanoprost group the mean IOP reduction at day 14 was 8.8 ± 1.1 mm Hg (mean $\pm$ SEM, $p < 0.001$; 34.2%) from a mean IOP baseline of 25.7 ± 0.9 mm Hg, and the corresponding figures for the timolol group were 5.7 ± 0.9 mm Hg ($p < 0.001$; 22.6%) from a mean IOP baseline of 25.2 ± 1.1 mm Hg. The mean IOP at each measurement for the two treatment groups is presented in Table 1. A significantly greater IOP reduction of 3.1 ± 1.5 mm Hg (95% confidence interval: 0.1–6.0) was achieved in the latanoprost group compared to the timolol treatment group ($p = 0.04$). ANOVA analysis could not reveal any statistically significant relationship between degree of angle closure and IOP reduction, or between the number of previous medication and IOP reduction.

There were no serious adverse events, and the ocular and systemic adverse events found were reported as mild. The most common ocular adverse events in both groups were eye redness and irritation. There were two cases of mild anterior chamber cells in the latanoprost group, which resolved at the end of the study.

Study 2

The second study was carried out in Taiwan,¹³ and it evaluated the use of latanoprost 0.005% as an adjunct to medical therapy for residual angle-closure glaucoma after iridectomy. All 26 PACG patients (26 eyes) recruited into the study had failure of control of IOP with beta-blockers and pilocarpine, or even after further laser peripheral iridoplasty, and were therefore candidates for surgery. However, the addition of 0.005% latanoprost one drop daily was found to significantly reduce IOP. From a baseline IOP of 23.24 ± 4.31 mm Hg, the IOP was kept below 20 mm Hg throughout the study. IOP decreased by 21% from the pre-latanoprost therapy baseline IOP at the 3-month follow up, and by 36% at the end of 1 year,

TABLE 1

Intraocular Pressure (Mean $\pm$ SD, in mm Hg) in the Two Parallel Study Groups at Each Visit in the Singapore Study (Study 1)

Time	Latanoprost	Timolol
Baseline	25.7 ± 0.9	25.2 ± 1.1
Day 2	16.4 ± 3.7	21.2 ± 6.8
Day 7	16.0 ± 4.3	19.1 ± 3.0
Day 14	16.9 ± 5.2	19.4 ± 2.4

thus rendering further invasive procedures unnecessary. The long-term study also demonstrated another interesting observation that the IOP gradually decreased throughout the year of latanoprost therapy, indicating the effectiveness of latanoprost in reducing IOP in eyes with residual angle-closure glaucoma after iridectomy.

Discussion

These two studies were the first in the literature to have investigated the efficacy of latanoprost in reducing IOP in patients with PACG. In the first study, 2 weeks of treatment with latanoprost 0.005% once daily significantly reduced the IOP from the untreated baseline in patients with PACG, and the IOP reduction was significantly better than that of timolol. The mean IOP reduction found was 34% (8.8 ± 1.1 mm Hg) in the latanoprost group. In the second study of PACG patients concurrently treated with timolol and pilocarpine, the mean IOP dropped significantly by about 21% at the end of the first week of treatment, and by about 36% at the end of 1 year of therapy. Interestingly, the extent of the IOP reducing effect of latanoprost once daily found in these PACG patients was similar to that seen in POAG and ocular hypertension in other studies.^{2,6,7,21}

The second study also showed the effectiveness of latanoprost in reducing IOP in eyes with residual angle-closure glaucoma after iridectomy. There was an additive effect when latanoprost was used concurrently with pilocarpine and timolol. This is a useful finding as many patients with PACG in Asia are treated with these two medications.

The results of these two studies demonstrate that latanoprost exerts its pressure-reducing effect when the anterior chamber angles were partly closed. However, it could not be determined conclusively if latanoprost is effective in eyes with 360° of synechial angle closure. The mechanism of action of latanoprost in eyes with closed angles is not known. One possibility is that latanoprost enhances aqueous access to the ciliary body via the still-open part of the anterior chamber angle. Another possibility is that latanoprost facilitates aqueous flow through the peripheral anterior synechiae to the ciliary body.

Latanoprost was well tolerated in patients with PACG. Most of the adverse events were reported as mild. The most common ocular adverse events found were that of conjunctival hyperemia and ocular discomfort. There were 2 cases of mild anterior chamber cells in the Singapore study, which resolved at the end of the study. No eyelash change or iris pigmentation was noted after one year of treatment in the Taiwan study, and there were no systemic adverse events found.

In conclusion, latanoprost was found to reduce IOP in patients with PACG. A significantly greater IOP reduction was achieved with latanoprost 0.005% once daily than timolol 0.5% twice daily. Latanoprost was also effective in reducing IOP in PACG patients concurrently treated with timolol and pilocarpine. More extensive studies need to be performed to evaluate the long-term effect and in patients with different degrees of angle closure. The patient population in these studies was Asian, and it is not known if these results could be applied to other racial groups, as there may be differences in efficacy of latanoprost depending on race and iris color. However, these results suggest that latanoprost may be a therapeutic choice for the medical treatment of primary angle-closure glaucoma.

References

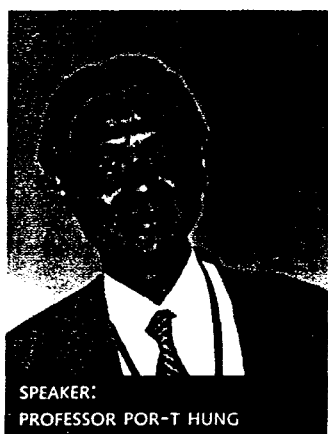
1. Alm A, Widengard I, Kjellgren D, et al: Latanoprost administered once daily caused a maintained reduction of intraocular pressure in glaucoma patients treated concomitantly with timolol. *Br J Ophthalmol* 79:12-6, 1995
2. Alm A, Stjernschantz J: Effects on intraocular pressure and side effects of 0.005% latanoprost applied once daily, evening or morning. A comparison with timolol. Scandinavian Latanoprost Study Group. *Ophthalmology* 102:1743-52, 1995
3. Alsbirk PH: Primary angle-closure glaucoma: oculometry, epidemiology, and genetics in a high-risk population. *Acta Ophthalmologica* 54(Suppl):5-31, 1976
4. Aung T, Wong HT, Yip CC, et al: Comparison of the intraocular pressure-lowering effect of latanoprost and timolol in patients with chronic angle closure glaucoma: a preliminary study. *Ophthalmology* 107:1178-83, 2000
5. Bonomi L, Marchini G, Marraffa M, et al: Epidemiology of angle-closure glaucoma: prevalence, clinical types, and association with peripheral anterior chamber depth in the Egna-Neumarkt Glaucoma Study. *Ophthalmology* 107:998-1003, 2000
6. Camras CB: Comparison of latanoprost and timolol in patients with ocular hypertension and glaucoma: a six-month masked, multicenter trial in the United States. The United States Latanoprost Study Group. *Ophthalmology* 103:138-47, 1996
7. Camras CB, Alm A, Watson P, Stjernschantz J: Latanoprost, a prostaglandin analog, for glaucoma therapy. Efficacy and safety after 1 year of treatment in 198 patients. Latanoprost Study Groups. *Ophthalmology* 103:1916-24, 1996
8. Congdon N, Wang F, Tielsch JM: Issues in the epidemiology and population-based screening of primary angle-closure glaucoma. *Surv Ophthalmol* 36:411-23, 1992
9. Foster PJ, Baasanhu J, Alsbirk PH, et al: Glaucoma in Mongolia. A population-based survey in Hovsgol province, northern Mongolia. *Arch Ophthalmol* 114:1235-41, 1996
10. Foster PJ, Oen FT, Machin D, et al: The prevalence of glaucoma in Chinese residents of Singapore: a cross-sectional population survey of the Tanjong Pagar district. *Arch Ophthalmol* 118:1105-11, 2000
11. Hung PT, Chou LH: Provocation and mechanism of angle-closure glaucoma after iridectomy. *Arch Ophthalmol* 97:1862-4, 1979
12. Hung PT: Provocation and medical treatment in post-iridectomy glaucoma. *J Ocul Pharmacol* 6:279-83, 1990
13. Hung PT, Hsieh JW, Chen YF, Wei T: Efficacy of latanoprost as an adjunct to medical therapy for residual angle-closure glaucoma after iridectomy. *J Ocul Pharmacol Ther* 16:43-7, 2000
14. Kim YY, Jung HR: Clarifying the nomenclature for primary angle-closure glaucoma. *Surv Ophthalmol* 42:125-36, 1997

15. Lowe RF: Persistent symptoms after peripheral iridectomy for angle-closure glaucoma. *Aust NZ J Ophthalmol* 15:83-7, 1987
16. Mishima HK, Masuda K, Kitazawa Y, et al: A comparison of latanoprost and timolol in primary open-angle glaucoma and ocular hypertension. A 12-week study. *Arch Ophthalmol* 114:929-32, 1996
17. Quigley HA: Number of people with glaucoma worldwide. *Br J Ophthalmol* 80:389-93, 1996
18. Ritch R, Lowe RF, Reyes A: Therapeutic overview of angle-closure glaucoma, in Ritch R, Shields MB, Krupin T (eds): *The Glaucomas*. St Louis, Mosby, 1989, pp 855-64
19. Thylefors B, Negrel AD, Pararajasegaram R, Dadzie KY: Global data on blindness. *Bull World Health Organ* 73:115-21, 1995
20. Toris CB, Camras CB, Yablonski ME: Effects of PhXA41, a new prostaglandin F2 alpha analog, on aqueous humor dynamics in human eyes. *Ophthalmology* 100:1297-304, 1993
21. Watson P, Sjerschantz J: A six-month, randomized, double-masked study comparing latanoprost with timolol in open-angle glaucoma and ocular hypertension. The Latanoprost Study Group. *Ophthalmology* 103:126-37, 1996
22. Watson PG: Latanoprost. Two years experience of its use in the United Kingdom. Latanoprost Study Group. *Ophthalmology* 105:82-7, 1998
23. Ziai N, Dolan JW, Kacere RD, Brubaker RF: The effects on aqueous dynamics of PhXA41, a new prostaglandin F2 alpha analogue, after topical application in normal and ocular hypertensive human eyes. *Arch Ophthalmol* 111:1351-8, 1993

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Reprint address: Prof Paul TK Chew, FRCS, Department of Ophthalmology, National University Hospital, 5 Lower Kent Ridge Road, Singapore 119074.

The Surgeon's Responsibility in Preserving Vision in Chronic Primary Angle Closure Glaucoma



SPEAKER:
PROFESSOR POR-T HUNG

PROFESSOR POR-T HUNG

DR JUI-WEN HSIEH

Department of Ophthalmology, Mackay
Memorial Hospital & National Taiwan
University
Taipei, TAIWAN

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Introduction and Epidemiology

Primary angle-closure glaucoma (PACG) is considered the most prevalent form of glaucoma as early as 1980s from Eskimo studies by Alsbirk.¹ In 1996, Quigley² reported his epidemiological approach and estimated that PACG patients comprise half to all glaucomas. The number of glaucoma patient was estimated to reach 66 million by the year 2000, with bilateral blindness from glaucoma estimated to affect 6.7 million people.

Studies on PACG has developed rapidly in the past few years, with studies in Taiwan in 1996³, Mongolia in 1997, Singapore in 2000 and Erga-Neumarket in 2000.

Recently, Foster⁴ preliminary estimated that 9.4 million people age more than 40 years old may have glaucomatous optic neuropathy in China alone. He suggested that PACG may be responsible for 91% of the 1.7 million of people with bilateral blindness, and 5.2 million of people with blindness in at least one eye.

According to our previous study, nearly two thirds of PACG were chronic and asymptomatic, with clinical

manifestation like that of primary open angle glaucoma (POAG). In developing countries, such asymptomatic glaucoma may be neglected until the patient is blind. Therefore, preventable glaucoma blindness from chronic PACG is an important public health challenge.⁵

In Asia, with economic progress, social transformation, improvement in general health care, an increasing geriatric population, increasing number of glaucoma patients can be expected in the future.

Chronic PACG

Chronic angle closure glaucoma (CACG) can be defined as a group of disease with common picture of a chronic course of glaucoma. Intraocular pressure elevation is related to angle closure, and acute elevation of IOP may develop during its chronic course. Some PACG may continue to progress as chronic PACG even after elimination of pupillary block mechanism by an iridectomy.

The current concept of PACG is a single or multiple mechanism of pupillary block working in the same eye

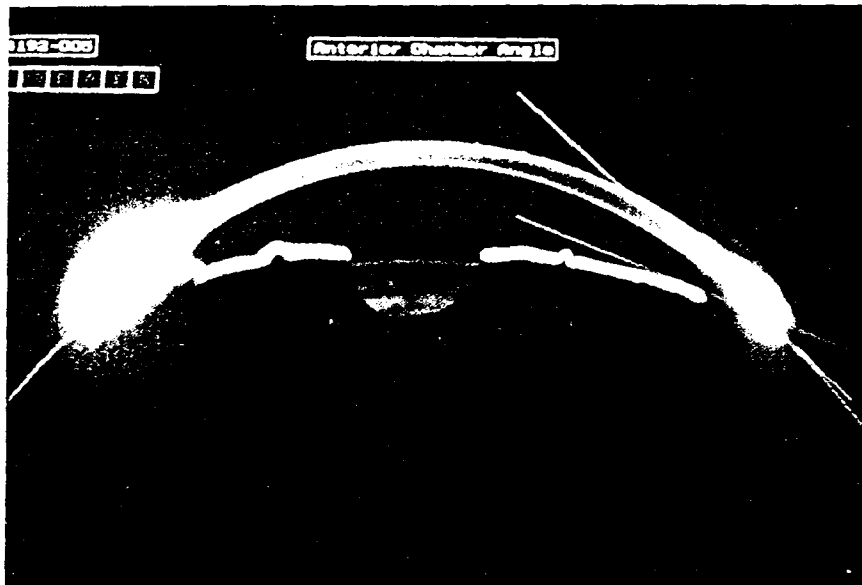


Figure 1
Scheimpflug image analyzer in a pupillary block primary angle-closure glaucoma. Chamber angle measurement, anterior chamber depth and iris bombe were known.



Figure 2
Ultrasound biomicroscopic picture in plateau iris syndrome showed the anterior rotation of ciliary process and narrowed angle.

Table 1

of chamber angle and optic nerve analyzer, may provide important information for early detection.⁶

Gonioscopy to see all quadrants of the angle is especially important for detection of PACG. In addition, repeated examination in suspicious case may be important, because narrowing of the chamber angle increases with advancing age. Ocular biometry can offer important information because of the smaller-than-average eye of PACG.

The pioneer work of Lowe in 1977 indicated that PACG is very rare if anterior chamber depth (ACD) is deeper than 2.5 mm, and more than 95% of PACG are less than 1.8 mm of ACD.⁷

Our study on acute glaucoma demonstrated that ACD less than 2.70 mm is the most sensitive (94%) and specific (94%) parameter to differentiate acute glaucoma from non-glaucoma.⁸ However, this data were derived from A-scan biometry, which although popular has limitations (e.g., measures cornea thickness).

Optic nerve study is another important parameter for management of chronic PACG and for follow up.

One such study involves slit lamp biomicroscopy or stereo disc photography. In our study, concentric steep enlargement of the optic disc cup was found, as well as peripupillary atrophy significantly larger in the PACG group than in control. The presence of a beta zone surrounding the disc is important.

(Figures 1 & 2). Probably iris crowding of different origin may also involve in different degree.

Forbes and Becker observed progressive IOP elevation in PACG even after an iridectomy, and called them post-iridectomy glaucoma or residual glaucoma. Such progressive PACG may develop even after an iridectomy, from angle pathology such as functional impairment of outflow by repeated attack, or from angle closure or peripheral anterior synechiae by creeping angle, chronic appositional closure, or plateau iris mechanism (Table 1).

The acute type of PACG or the chronic or subacute type of PACG can be interchangeable. For prevention of blindness, early detection and simple laser iridotomy prior to PACG are the most important methods, and is the responsibility of the eye surgeon.

Early Detection

The application of image analysis, such as A-scan ocular biometry, ultrasound biomicroscopy, Scheimpflug image study

Therapy

In the past, prophylactic iridectomy in the second eye of acute glaucoma was the rule, as there was a high risk of bilateral involvement in the second eye. In conjunction with improvement in ophthalmology research, the concept of PACG therapy is also changing.

Laser iridotomy to treat early stage of PACG from pupillary block mechanism has been accepted as safe and effective in opening and widening the anterior chamber angle. Image studies may provide important clues to the need to perform such procedures. However, it is well recognized that once PACG develop acutely raised intraocular pressure, chronic optic neuropathy, or angle damage, laser iridotomy may be less effective⁹ and the eye may proceed to develop poor outcomes. Thus, subsequent laser or surgery may be necessary. Nonetheless, although there are different

mechanisms involved in PACG, pupillary block mechanism is probably the most important and therefore, simple laser iridotomy should still be the first choice of treatment.

In addition, the most important factor in preserving the vision in PACG is to closely observe the therapeutic effect of laser and by long-term monitoring of the patients.

Conclusions

1. Chronic PACG is related to blindness and is probably the most important glaucoma in Asia.
2. Early detection with current image analysis of chronic PACG is important. Early laser iridotomy is the treatment of choice.
3. To preserve vision, eye surgeon is responsible to closely monitor chronic PACG cases for subsequent complications.

References

1. Alsirk PH. Limbal and axial chamber depth variations: a population study in Eskimos. *Acta Ophthalmol (Copenh)* 1987;64:593.
2. Quigley HA. Number of people with glaucoma worldwide. *Brit J Ophthalmol* 1996;80:389-93.
3. Congdon NC, Quigley HA, Hung PT, et al. Screen techniques for angle-closure glaucoma in rural Taiwan. *Acta Ophthalmol Scand* 1996;74:113-19.
4. Foster PJ, Johnson GJ. Glaucoma in China: how big is the problem? *Brit J Ophthalmol* 2001;85:1271-72.
5. Lim ASM, Lin HC. The challenge of close angle glaucoma. *Asia-Pacific J Ophthalmol* 2000;12:10-13.
6. Hung PT, Hou YC, Lan YL, et al. Chamber angle and biometric study in PACG and its lens. In *Glaucoma Update V*, Kriegstein GK ed. Kaden Verlag 1995;pp 309-15.
7. Lowe RF. Causes of shallow anterior chamber in primary angle-closure glaucoma: ultrasonic biometry of normal and angle-closure glaucoma eyes. *Am J Ophthalmol* 1969;67:87-95.
8. Lin YW, Wang TH, Hung PT. Biometric study of acute primary angle-closure glaucoma. *J formos Med Assoc* 1997;96:908-12.
9. Galin MA, Obstbaum SA, Hung PT. Rethinking prophylactic peripheral iridectomy. *Annals of Ophthalmol* 1976;11:1333.

Visual Impairment among the Middle-Aged and Elderly Population in Chin-Shan Township, Taipei County

Luke L-K Lin, Yung-Feng Shih, Tzyy-Chang Ho, Tsing-Hong Wang, Chien-Jen Chen¹, Por-Tying Hung

Department of Ophthalmology, National Taiwan University Hospital, Taipei, Taiwan; Institute of Epidemiology¹, National Taiwan University, Taipei, Taiwan

ABSTRACT

Objective: To investigate the status and causes of visual impairment in middle-aged (40 to 65 years old) and elderly (>65 years old) people in Taiwan. **Materials and Methods:** A total of 3901 residents of Chin-Shan Township, Taipei County, in 1992 and 2817 residents in 1994 received visual acuity and autorefractor examinations. If visual acuity was less than 20/50, further ocular examinations were performed. A total of 1210 subjects in 1992 and 884 subjects in 1994 received a complete ophthalmological exam, including slit-lamp examination, intraocular pressure, cycloplegic refraction, funduscopy examination, and biometric axial length. **Results:** The most frequent cause of low vision (corrected visual acuity between 20/50 and 20/200) for the middle-aged and aged population was cataract (70%) and related diseases. The second most frequent cause was retinopathy (15%). Corneal diseases, glaucoma and other factors comprised the remaining 15% of cases. Cataract was also the main cause of blindness (corrected visual acuity less than 20/200) in the middle-aged and aged population (60%). Retinopathy (20%) was the second most frequent cause of blindness in both groups. **Conclusions:** Cataract was the most frequent cause of visual impairment and retinopathy was the second most frequent cause for the middle-aged and aged population of Chin-Shan Xiang, Taipei County, in 1992 and 1994. (*Tzu Chi Med J* 2001; 13:75-79)

Key words: visual impairment, cataract, retinopathy, corneal disease, glaucoma

INTRODUCTION

The aging of populations is a global issue [1]. The proportion of elderly in both developed and developing countries is increasing and is forecast to continue to increase [2]. Not only is the proportion of the aged increasing, but the elderly population itself is getting older as people live longer, with an average life expectancy over 80 years of age for women in Japan. Both the increasing proportion of elderly and the aging of the elderly population have implications for the prevalence and incidence of eye diseases and the planning of eye care programs [3].

Although, there are almost always some older people whose health is as good as that of younger people, but

this number inevitably declines with age [4]. The major causes of visual impairment are age-related. Without preventive action, the prevalence of vision impairment is predicted to at least double. Precise data are needed for each country to plan specific preventive actions and provide for eye care needs. In 1995, WHO [5] estimated that there were 38 million blind persons globally and 110 million had low vision and were at great risk of becoming blind. This study investigated the status and causes of visual impairment among aging persons by analyzing population-based data from ocular examinations in 1992 and 1994 in the middle-aged (40 to 65 years old) and elderly residents (>65 years old) of Ching-Shan Township, Taipei County.

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Address reprint requests and correspondence to: Dr. Por-Tying Hung, Department of Ophthalmology, National Taiwan University Hospital, 7, Chung Shan South Road, Taipei, Taiwan

MATERIALS AND METHODS

Data from around residents over 40 years of age in Chin-Shan Township, Taipei County were included in this study. In 1992, this study included 44% of residents, and 31% were included in 1994. In 1992, a total of 3901 residents [middle-age (aged between 40 to 64 years) 2634, elderly (aged over 65 years) 1267] received best-corrected visual acuity and autorefractor examination (Topcon, RK-3000, Tokyo, Japan). Visual acuity was examined with a Landholt ring chart at 5 meters distance. Visual impairment was defined as visual acuity less than 20/50. If visual acuity was found less than 20/50, further ocular examinations were performed. A total of 1210 subjects (middle-aged 469, elderly 741) received a complete ophthalmologic examination, including slit-lamp examination, cycloplegic refraction, funduscopy examination, intraocular pressure examination (Tonopen), and biometric axial length (Sonomed, A-1500, Lake Success, USA). Three measurements were recorded for each procedure. Mean and standard deviations were calculated from three separate measurements. In 1994, a total of 2817 residents (middle-aged 1866, elderly 951) received best-corrected visual acuity and autorefractor examinations, and 884 of them (middle-aged 333, elderly 551) received further complete ophthalmologic examinations.

Data from all subjects were transferred from individual record sheets into a computer in the central office of the Department of Epidemiology of National Taiwan University. Visual impairment was categorized as "low vision" for moderate visual impairment and "blindness" for severe visual impairment. "Low vision" was defined as a best corrected visual acuity between 20/50 and 20/200, and "blindness" was defined as a best corrected visual acuity less than 20/200. The cause of visual impairment was divided into 5 categories: cataract, retinopathy, corneal diseases, glaucoma, and others. Cataract types included un-operated cataract, aphakia, and pseudophakia. Retinopathy types included myopic retinopathy, age-related retinopathy, and diabetic retinopathy. Corneal diseases included corneal scar and pannus. The "other" category of disease included trauma, optic nerve diseases, and strabismus. Analysis of variance and dependent or independent t-tests were per-

formed to evaluate the differences within groups.

RESULTS

Status of visual impairment

In this study, we found that approximately 12.0% of the middle-aged population had low vision in 1992, and 14.7% held this problem in 1994. However, the rate of low vision was 45.3% in elderly participants in 1992, and 38.7% in 1994. In the middle-age population 5.8% had blindness in 1992 and 3.1% in 1994. Of the elderly, 13.2% in 1992 and 19.3% in 1994 were blind (Table 1). There were no significant differences between groups in 1992 and 1994 ($p>0.05$).

Causes of visual impairment

Cataract and related diseases was the main cause of low vision for the middle-aged population (68.0%) and the elderly population (73.2%) in 1992. It occurred in 68.2% of the middle-aged population and 70.4% of the elderly population in 1994. The second most frequent cause of low vision was retinopathy (15.0%) both in middle-aged and elderly populations both in 1992 and 1994. Corneal diseases, glaucoma and other factors comprised the remaining 15.0% of cases (Table 2). The frequency of each cause of low vision was not significantly different between 1992 and 1994 ($p>0.1$).

Cataract was the main cause of blindness for the middle-aged population (62.0%) and elderly population (71.2%) in 1992. It was 64.4% in the middle-aged population and 68.3% in the elderly population in 1994. The second leading cause of blindness was retinopathy, with a frequency of 31.0% in the middle-aged group and 30.0% in the elderly group in 1992, and 12.0% in the middle-aged group and 28.0% in the elderly group in 1994 (Table 3). The frequency of each cause of blindness was not significantly different between 1992 and 1994 ($p>0.1$).

DISCUSSION

The median age of the population in the United States, most Western societies, and several non-Western societies is increasing [1,4]. Currently, approximately

Table 1. The Status of Visual Impairment among Middle-aged and Elderly Residents in 1992 and 1994

Best corrected visual acuity	$\geq 20/25$	20/50~20/25	20/200~20/50	$\leq 20/200$	Total
Middle-aged (1992)	1262 (47.9%)	903 (34.3%)	316 (12.0%)	153 (5.8%)	2634 (100%)
Elderly (1992)	105 (8.3%)	421 (33.2%)	574 (45.3%)	167 (13.2%)	1267 (100%)
Middle-aged (1994)	938 (50.3%)	595 (31.9%)	274 (14.7%)	59 (3.1%)	1866 (100%)
Elderly (1994)	104 (10.9%)	296 (31.1%)	368 (38.7%)	183 (19.3%)	951 (100%)

Table 2. The Causes of Low Vision among Middle-aged and Elderly Residents in 1992 and 1994

	Cataract	Retinopathy	Corneal diseases	Glaucoma	Others
Middle-aged (N)					
1992 (316)	68.0% (215)	15.8% (50)	4.7% (15)	4.7% (15)	6.6% (21)
1994 (274)	68.2% (187)	15.3% (42)	6.9% (19)	5.8% (16)	3.6% (10)
Elderly (N)					
1992 (574)	73.2% (420)	15.3% (88)	4.5% (26)	4.2% (24)	2.8% (16)
1994 (368)	70.4% (259)	14.9% (55)	6.5% (24)	5.4% (20)	2.7% (10)

Table 3. The Causes of Blindness among Middle-aged and Elderly Residents in 1992 and 1994

	Cataract	Retinopathy	Corneal diseases	Glaucoma	Others
Middle-aged (N)					
1992 (153)	62.0% (95)	20.3% (31)	8.5% (13)	3.3% (5)	5.9% (9)
1994 (59)	64.4% (38)	20.3% (12)	6.8% (4)	3.4% (2)	5.1% (3)
Elderly (N)					
1992 (167)	71.2% (119)	18.0% (30)	6.6% (11)	2.4% (4)	1.8% (3)
1994 (183)	68.3% (125)	15.3% (28)	7.6% (14)	4.4% (8)	4.4% (8)

12% of the population is over the age of 65 in the United States. By the year 2030, approximately 21% of population will be over the age of 65 [5]. In Taiwan, approximately 8% of the population was over the age of 65 in 1996.

In this study, we found that only 10% of elderly participants had a corrected visual acuity better than 20/25, 40% had low vision and 15% were blind. In contrast, only around 5% of the middle-aged population was blind. Around 12% in 1992 and 15% in 1994 of the middle-aged population had low vision. Most of this decrease in the percentage of individuals with maximum acuity and the greater variability in the best-corrected acuity was due to the effects of degeneration or disease conditions.

Cataract is usually the leading cause of blindness in underdeveloped and developing countries. In Thailand, cataract is the most common cause (74.65%) of blindness [6]; followed by corneal blindness (4.93%) and phthisis bulbi and glaucoma (3.52%). This study also found that the highest prevalence rates of low vision were seen in cataract (78.55%), refractive errors (5.63%), and macular degeneration (3.49%). Cataract is also the leading cause of blindness in Malaysia [7].

Our study found that cataract was the main cause of blindness in both the middle-aged and aged population. The second most frequent cause of blindness was retinopathy. Our results are similar to a study from Korea [8], in which the leading causes of blindness among an elderly population were un-operated senile cataract

(53.2%), macular degeneration (12.5%), corneal scar (8.3%), vascular retinopathy (6.5%), and glaucoma (1.7%). Corneal scar appears to be more common in Korea than Taiwan. However, because trachoma was a very common disease in Taiwan 40 years ago, many patients developed pannus and trichiasis that led to corneal scarring.

Our results are dissimilar to those of some developed countries in the West [9,10] and in Japan [11]. In the West, age-related macular degeneration (20.7%-26.0%), senile cataract (12.0%-23.0%), glaucoma (10.0%-12.0%), and diabetic retinopathy (7.0%-11.0%) are the leading causes of vision loss among the elderly. The Japan National Society for the Prevention of Blindness (JNSPB) conducted a survey of acquired blindness and found that diabetic retinopathy was the leading cause of blindness, comprising about 18.0% of cases followed by glaucoma at 15.0%. Cataract occurred in 16.0% of cases, but simple cataract was not the problem.

Senile cataract was the most common cause of blindness among the elderly in this study. The number of cataract operations financially supported by the government has increased and cataract surgery and rehabilitation of patients have dramatically improved in recent years. The economy is growing and improvements in the standard of living have increased the incidence of diabetic and hypertensive retinopathy. However, laser surgery and other surgical modalities are now able to minimize the risk of severe visual loss and restore useful vision in some cases. These treatments may affect the statistics

on the leading causes of blindness in Taiwan. Therefore, frequent surveys of the causes and prevalence of blindness in the middle-aged and elderly population should be performed.

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REFERENCES

1. Steel K, Maggi S: Ageing as a global issue. *Age Aging* 1993; **22**:236-239.
2. Martin LG: Population aging policies in east Asia and the United State. *Science* 1991; **251**:527-531.
3. Manton KG: The dynamics of population aging: Demography and policy analysis. *Milbank Mem Fund Q* 1991; **69**:309-338.
4. World Health Organization: Health of Elderly. Report on a WHO Expert Committee. WHO Technical Report Series 779, Geneva, 1989.
5. Thylefors B, Negrel AD, Pararajasegaram R, Dadzie KY: Global Data on Blindness. WHO/PBL/94.40 Geneva, 1994.
6. Wongwetsawat S: Epidemiology of blindness and low vision in Thailand 1994. In: Jenchitr W, ed. Report of the prevention of blindness and control of visual impairment programme in Thailand, 1st ed., Lampang: Kijserree printing, 1997, pp 27-49.
7. Selvarajah S: Rehabilitation of the visually handicapped in Malaysia: In: Current Aspects in Ophthalmology Vol. 1, Amsterdam: Elsevier Science Publishers 1992, pp 155-158.
8. Kim WS, Kim IS, Hu JU, et al: Community-based eye health survey in area of Buan-Kun and Dobong-Ku in Korea. *Korean J Ophthalmol* 1990; **4**:103-108.
9. Becker MR: Serving the needs of the visually impaired elderly. In: Kwitko ML, Weinstock FJ, eds. *Geriatric Ophthalmology*, 1st ed., London: Grune and tratton, 1985, pp 15-29.
10. Tielsh JM, Sommer A, Witt K, et al: Blindness and visual impairment in an American urban population: The Baltimore Eye Survey. *Arch Ophthalmol* 1990; **108**:286-290.
11. Nakae R, Kogure F, Nagaya Y, et al: Guideline of health and welfare. Report of Research on Ministry of Health and Welfare of Japan 1991; **38**:13-22.

台北縣金山鄉中老年人視力障礙狀態之調查

林隆光 施永豐 何子昌 王清泓 陳建仁¹ 洪伯廷

國立台灣大學附設醫院眼科部 國立台灣大學流行病學研究所¹

摘要

目的：為了觀察台灣中年(40至65歲)及老年人(超過65歲)視力障礙之狀態及其原因。**材料與方法：**共計在1992年有3901位居民及在1994年有2817位居民接受視力及電腦驗光檢查。如果視力低於0.4，則作更進一步之檢查。全部在1992年有1210位及1994年有884位接受完整的眼科檢查，包括裂隙燈、眼壓、睫狀肌麻痺後屈光、眼底檢查及眼軸長之測定。**結果：**中老年人低視力(最佳矯正視力介於0.1至0.4)之主要原因是白內障及其相關疾病(70%)，其次是視網膜疾患(15%)。另外15%為角膜疾患、青光眼及其他原因。中老年人失明(最佳矯正視力低於0.1)之主要原因仍是白內障及其相關疾病(60%)。視網膜疾患依然是第二失明原因(20%)。**結論：**白內障是1992及1994年中老年人視力障礙之主要原因，而視網膜疾患是第二原因。(慈濟醫學 2001; 13:75-79)

關鍵語：視力障礙，白內障，視網膜疾患，角膜疾患，青光眼

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EPIDEMIOLOGIC STUDY OF THE PREVALENCE
AND SEVERITY OF MYOPIA AMONG
SCHOOLCHILDREN IN TAIWAN IN 2000

L.L.K. Lin, Y.F. Shih, C.K. Hsiao, C.J. Chen, L.A. Lee, P.T. Hung



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EPIDEMIOLOGIC STUDY OF THE PREVALENCE AND SEVERITY OF MYOPIA AMONG SCHOOLCHILDREN IN TAIWAN IN 2000

Luke L-K Lin, Yung-Feng Shih, C. Kate Hsiao,¹ Chien-Jen Chen,¹ Loung-An Lee,² and
Por-Tying Hung

Background and Purpose: A nationwide survey was performed in 2000 to determine the prevalence and severity of myopia among schoolchildren in Taiwan and to compare these findings with the results of the last survey performed in 1995.

Methods: We first divided the whole island into regions according to developmental grade scores and then sampled with the probability proportional to the size of the population within each stratum. A total of 10,889 students were enrolled, including 5,664 boys and 5,225 girls, with ages ranging from 7 to 18 years. The refractive status and corneal radius of each student were measured with an autorefractometer under cycloplegia and checked with retinoscopy. Axial length was measured using biometric ultrasound.

Results: The myopia rate increased from 20% at 7 years, to 61% at 12 years, and 81% at 15 years. A myopic rate of 84% was found for schoolchildren aged 16 years through 18 years. The mean refractive index reached myopic status at the age of 8, and increased to -4.12 D in girls and -3.15 D in boys at the age of 18 years. The prevalence of high myopia (> -6.0D) at the age of 18 years was 24% in girls and 18% in boys. The increase in axial length corresponded with the progression of myopia. The anterior chamber depth was slightly deeper from 7 years to 13 years and then remained stable. The lens thickness decreased from 7 years to 11 years. After age 15, further thickening of the lens was correlated with both age and severity of myopia. However, the corneal curvature was not related to age or severity of myopia. Girls had a higher prevalence and more severe degree of myopia than boys. Children in urban areas had a higher prevalence and more severe degree of myopia than children in rural areas.

Conclusion: The prevalence and severity of myopia in schoolchildren in Taiwan in 2000 increased compared to 1995, with the most severe increases occurring in younger age groups. Thus, preventing schoolchildren developing myopia at a young age may slow down the increase in severity of myopia in Taiwan.

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Key words:

myopia
prevalence
axial length
corneal curvature

Taiwan has developed rapidly within the past two decades, not only economically but also in educational standards. Goldschmidt studied the prevalence of myopia among individuals in different occupational categories grouped according to the expected level of close-work performed, and found that college students had a higher prevalence of myopia [1]. During their school years, more than 70% of children in Taiwan become myopic [2]. Our previous study showed that the prevalence of myopia among chil-

dren of purely aboriginal ancestry was lower than that among children of Chinese ancestry, and rural children had a lower prevalence than urban children [3]. Rapid economic development in Taiwan may have impacted the prevalence of myopia. This study aimed to determine the prevalence of myopia among schoolchildren in Taiwan in 2000. Nationwide surveys of myopia in schoolchildren have been performed every 5 years since 1983. The last survey was performed in 1995, and found that the preva-

Department of Ophthalmology, College of Medicine and Hospital, ¹Institute of Epidemiology, College of Public Health, National Taiwan University, and ²Institute of Statistical Science, Academia Sinica, Taipei.

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Reprint requests and correspondence to: Dr. Yung-Feng Shih, Department of Ophthalmology, National Taiwan University Hospital, 7 Chung-Shan South Road, Taipei, Taiwan.

lence of myopia ranged from 12% at 7 years old to 56% at 12 years old, and more than 76% at 15 years old[4]. In senior high and vocational schools (16–18 yr old), the prevalence reached a striking 84%. The myopia rates approached 50% among rural children compared to 70% among children in urban areas.

Most investigations have used cross-sectional methods to determine the refraction of large samples. Large sample studies have used different definitions of myopia [5, 6]. To facilitate appropriate comparisons of the prevalence of myopia as well as secondary trends across different populations, studies should have similar definitions of myopia, refract children under cycloplegia, and report findings by age. Nationwide surveys of the prevalence of myopia in schoolchildren in Taiwan have been performed four times since 1983, using the same sampling scheme with probability proportional to population size. All schools were stratified first based on the developmental grade of the areas where the school is located. Cycloplegic refractions and ocular components were measured and analyzed. The techniques used for refraction and the definition of myopia were the same as in our previous surveys.

Materials and Methods

Sampling methods

In Taiwan, students attend primary school (age 7–12 yr), then junior high school (age 13–15 yr), and senior high school (age 16–18 yr) before entering university. In addition, Taiwan has many vocational schools for students aged 15 years to 18 years. After completion of elementary education, about 80% of children enter either senior high school or vocational schools.

This study used a survey method based on a grading of the developmental status of cities. Areas were first stratified based on the developmental grade and then sampled with a probability proportional to their population size. The total population for the regions surveyed in this study included nearly 4 million schoolchildren in elementary, junior high, senior high, and vocational schools in Taiwan. The multistage stratified sampling method was used to select random samples of schoolchildren for this national survey. In the sampling of schoolchildren, the 361 administrative areas in Taiwan were first grouped into 10 strata according to their urbanization status. They included Taipei City, Kaohsiung City, and eight strata of other areas. Various numbers of townships were further selected from each stratum based on the sampling probabilities proportional to their population sizes. A total of 18 administrative areas were selected for inclusion in this study. Elementary, junior high, senior high, and voca-

tional schools within these areas were next selected with a probability proportional to the student size. A total of 41 primary schools, 39 junior high schools, 13 senior high schools, nine vocational schools, and four colleges were selected from these 18 administrative areas. Students in these schools were then randomly selected based on their grade and sex. A total of 11,995 students were selected and 10,889 (91%) participated in the study, including 5,664 boys and 5,225 girls with ages ranging from 7 to 18 years.

Examination

Corneal radius and refractive status were measured with an autorefractor (RK-3000, Topcon, Tokyo, Japan). Cycloplegic refraction was measured 30 minutes after the last instillation of three drops of 1% tropicamide at 5-minute intervals. All values of refractive status were rechecked with a retinoscope by one of two senior ophthalmologists. The biometric axial length (including anterior chamber depth [ACD], lens thickness, and total axial length) was measured by A-scan ultrasonography (A-1500, Sonomed, Lake Success, NY, USA). Three measurements were recorded for each procedure, and mean and standard deviations (SDs) were calculated from these measurements.

Calculation and statistics

Data from the right eye only were used to determine the prevalence of myopia and the distribution of refractive errors and ocular components in the population. Mean values of spherical equivalents of refractive status and corneal radii from the autorefractometer were used for calculation. Emmetropia was defined as a mean spherical equivalent of between -0.25 D and $+0.5$ D. Myopia was defined as a mean spherical equivalent of -0.25 D or more. Astigmatism was not assessed in this study.

Data were entered into the computer of the central office in the Department of Epidemiology of National Taiwan University. Due to the omission of some unclear data, the total numbers for each measurement showed some difference. To avoid data entry errors, double-entry of data was performed by two independent groups plus a third person for adjudication. Results for ocular components are given as mean $\pm$ SD. Regression analysis was used to test for trends with respect to age. Analysis of variance and multiple comparisons were performed to evaluate the differences within groups or between boys and girls.

Results

Prevalence

The prevalence of myopia increased from 20% at 7 years old to 61% at 12 years old, and 81% at 15 years old.

The increasing trend was statistically significant ($p < 0.01$). The prevalence of myopia was approximately 84% among schoolchildren aged 16 to 18 years (Fig. 1). The overall prevalence of myopia in this sample was around 64% for girls and 59% for boys.

The prevalence of high myopia (> -6.0 D) was around 8.2% in girls and 6% in boys among all students surveyed. It increased with age in girls from 0.2% at 7 years old to 3.4% at 12 years old, and 13.0% at 15 years old. It also increased with age in boys from 0.2% at 7 years old to 1.5% at 12 years old, and 13.0% at 15 years old. Between the ages of 16 and 18 years old, it increased from 19% to 24% in girls and from 13 to 18% in boys (Fig. 2). Both increases were significant ($p < 0.001$) with respect to age.

The overall prevalence of anisometropia (> -2.0 D) was approximately 2.8% in girls and 2.6% in boys. It increased with age from 0.2% at 7 years old to 2.3% at 12 years old in girls, and from 0.6% to 2.7% in boys. At the age of 15 years old, the prevalence of anisometropia was 5.5% in girls and 2.9% in boys ($p < 0.001$). The prevalence of anisometropia was even higher at the age of 18 years (6.6% in girls and 5.3% in boys; Fig. 3).

Severity

Table 1 shows the mean refractive status within each age group for boys and girls. The mean ocular refraction was nearly emmetropic at 7 years old. It became myopic at 8 years old, with -0.2 D for girls and -0.1 D for boys. The severity of myopia gradually increased with age and educational level. Students in high schools had a higher degree of myopia than younger students ($p < 0.001$). The mean spherical equivalent at the age of 12 years was -1.64 D in girls and -1.26 D in boys, then progressed to -2.99 D in girls and -2.79 D in boys at the age of 15 years, and further progressed to -4.12 D in girls and -3.15 D in boys at the age of 18 years. There was a significant trend between the mean refractive status and age for both boys and girls (both $p = 0.0001$).

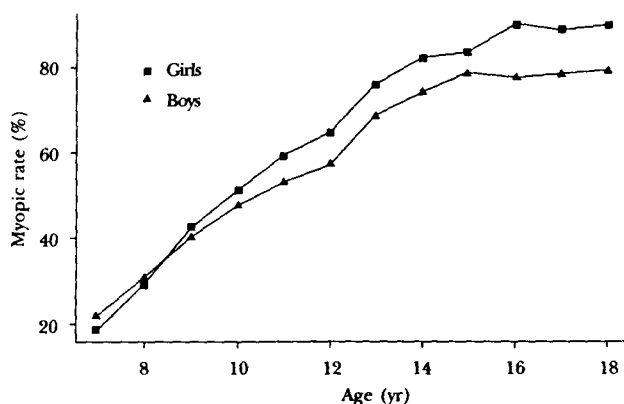


Fig. 1. Prevalence of myopia among schoolchildren in Taiwan.

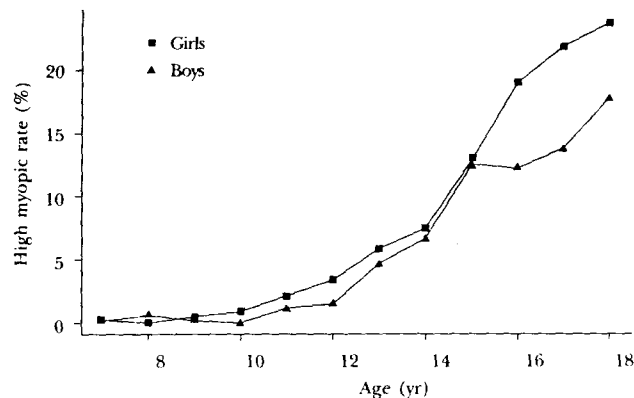


Fig. 2. Prevalence of high myopia (> -6.0 D) among schoolchildren.

For all students, mean deviation in refractive status in girls (-2.0 D $\pm$ 2.61) was significantly greater than that in boys (-1.57 D $\pm$ 2.36; $p < 0.0001$).

Corneal curvature

The corneal radius remained almost unchanged with increasing age and was not significantly different for girls and boys ($p > 0.05$; Table 2). Corneal curvature in boys (7.85 ± 0.26 mm) was significantly flatter than that in girls (7.72 ± 0.25 mm; $p < 0.0001$).

Axial length

Axial length gradually increased with age and, thus, the severity of myopia increased with age for both boys and girls (both $p = 0.0001$). At 7 years old, the mean axial length was 22.55 mm in girls and 23.02 mm in boys. At 8 years old, when the mean refractive index started to become myopic, it was 22.86 mm in girls and 23.38 mm in boys. At 9 years old, the mean axial length was 23.12 mm in girls and 23.68 mm in boys, and increased to 23.79 mm in girls and 24.17 mm in boys at the age of

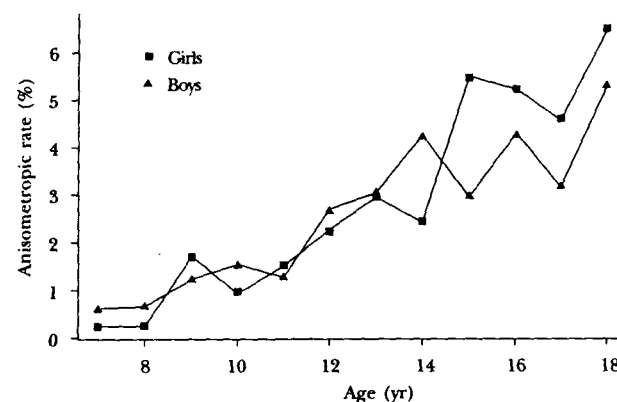


Fig. 3. Prevalence of anisometropia (> -2.0 D) among schoolchildren.

Table 1. Refractive status (D) among male and female schoolchildren in each age group (right eye only)

Age (yr)	Boys			Girls		
	n	Mean ($\pm$ SD)	95% CI	n	Mean ($\pm$ SD)	95% CI
7	494	+0.11 $\pm$ 1.01	+0.02 to +0.20	430	+0.22 $\pm$ 1.12	+0.11 to +0.32
8	455	-0.19 $\pm$ 1.40	-0.32 to -0.06	460	-0.10 $\pm$ 1.19	-0.21 to +0.01
9	486	-0.52 $\pm$ 1.37	-0.64 to -0.40	404	-0.65 $\pm$ 1.57	-0.80 to -0.49
10	518	-0.67 $\pm$ 1.57	-0.81 to -0.54	427	-0.87 $\pm$ 1.94	-1.05 to -0.68
11	478	-1.05 $\pm$ 1.82	-1.22 to -0.89	466	-1.35 $\pm$ 2.04	-1.54 to -1.17
12	480	-1.26 $\pm$ 1.93	-1.44 to -1.09	440	-1.64 $\pm$ 2.11	-1.84 to -1.44
13	528	-1.91 $\pm$ 2.26	-2.10 to -1.71	441	-2.31 $\pm$ 2.32	-2.53 to -2.10
14	543	-2.33 $\pm$ 2.36	-2.53 to -2.14	417	-2.55 $\pm$ 2.39	-2.78 to -2.32
15	480	-2.79 $\pm$ 2.63	-3.03 to -2.55	457	-2.99 $\pm$ 2.63	-3.23 to -2.75
16	420	-2.76 $\pm$ 2.71	-3.04 to -2.52	462	-3.83 $\pm$ 2.64	-4.07 to -3.59
17	382	-2.91 $\pm$ 2.59	-3.17 to -2.65	420	-3.89 $\pm$ 2.73	-4.15 to -3.63
18	394	-3.15 $\pm$ 2.83	-3.43 to -2.87	396	-4.12 $\pm$ 2.77	-4.39 to -3.84
Total	5658	-1.57 $\pm$ 2.36	-1.63 to -1.51	5220	-2.00 $\pm$ 2.61	-2.07 to -1.92
<i>p</i> -value		0.0001			0.0001	

p-value based on test of age trend.

12 years. At 15 years old, the mean axial length further increased to 24.42 mm in girls and 24.96 mm in boys, and at the age of 18 years was 24.97 mm in girls and 25.26 mm in boys (Table 3). Axial length in boys (24.26 ± 1.30 mm) was significantly greater than that in girls (23.91 ± 1.35 mm; $p < 0.0001$).

Anterior chamber depth

The ACD increased slightly with age and severity of myopia for both boys and girls (both $p = 0.0001$). At 7 years old, the ACD was 3.45 mm in girls and 3.54 mm in boys, and increased to 3.51 mm in girls and 3.59 mm in boys at 8 years old, when the mean refractive status

became myopic. At 9 years old, the ACD was 3.57 mm in girls and 3.66 mm in boys. It increased continuously with age and the progression of myopia. At 13 years old, the ACD was 3.68 mm in girls and 3.78 mm in boys. It remained stable from the age of 13 to 18 years, around 3.69 mm in girls and 3.78 mm in boys (Table 4). ACD in boys (3.71 ± 0.28 mm) was slightly greater than that in girls (3.63 ± 0.27 mm; $p < 0.0001$).

Lens thickness

The mean lens thickness decreased between 7 and 11 years old. At 7 years old, it was 3.57 mm in girls and 3.55 mm in boys. At 8 years old, it was 3.5 mm in both

Table 2. Corneal curvature radius (mm) among male and female schoolchildren in each age group (right eye only)

Age (yr)	Boys			Girls		
	n	Mean ($\pm$ SD)	95% CI	n	Mean ($\pm$ SD)	95% CI
7	469	7.82 $\pm$ 0.26	7.80 to 7.84	408	7.70 $\pm$ 0.26	7.68 to 7.73
8	442	7.86 $\pm$ 0.26	7.83 to 7.88	440	7.71 $\pm$ 0.25	7.69 to 7.74
9	473	7.87 $\pm$ 0.26	7.84 to 7.89	389	7.70 $\pm$ 0.25	7.68 to 7.72
10	505	7.83 $\pm$ 0.26	7.81 to 7.86	414	7.74 $\pm$ 0.25	7.72 to 7.77
11	464	7.82 $\pm$ 0.26	7.80 to 7.85	455	7.71 $\pm$ 0.26	7.69 to 7.74
12	464	7.85 $\pm$ 0.25	7.82 to 7.87	425	7.69 $\pm$ 0.24	7.67 to 7.72
13	480	7.86 $\pm$ 0.24	7.84 to 7.88	403	7.73 $\pm$ 0.24	7.70 to 7.75
14	497	7.85 $\pm$ 0.26	7.82 to 7.87	384	7.73 $\pm$ 0.25	7.71 to 7.76
15	438	7.86 $\pm$ 0.25	7.84 to 7.88	421	7.73 $\pm$ 0.24	7.71 to 7.76
16	346	7.86 $\pm$ 0.23	7.83 to 7.88	435	7.73 $\pm$ 0.25	7.70 to 7.75
17	319	7.85 $\pm$ 0.25	7.82 to 7.87	405	7.72 $\pm$ 0.25	7.69 to 7.74
18	309	7.88 $\pm$ 0.29	7.85 to 7.91	375	7.71 $\pm$ 0.23	7.68 to 7.73
Total	5206	7.85 $\pm$ 0.26	7.84 to 7.86	4954	7.72 $\pm$ 0.25	7.71 to 7.72
<i>p</i> -value		0.0237			0.1985	

p-value based on test of age trend.

Table 3. Axial length (mm) among male and female schoolchildren in each age group (right eye only)

Age (yr)	Boys			Girls		
	n	Mean ($\pm$ SD)	95% CI	n	Mean ($\pm$ SD)	95% CI
7	470	23.02 $\pm$ 0.72	22.95 to 23.08	412	22.55 $\pm$ 0.73	22.48 to 22.62
8	441	23.38 $\pm$ 0.85	23.30 to 23.46	441	22.86 $\pm$ 0.80	22.78 to 22.93
9	473	23.68 $\pm$ 0.89	23.60 to 23.76	389	23.12 $\pm$ 0.94	23.03 to 23.21
10	504	23.75 $\pm$ 0.98	23.67 to 23.84	414	23.42 $\pm$ 1.04	23.32 to 23.52
11	466	23.99 $\pm$ 1.03	23.91 to 24.09	457	23.65 $\pm$ 1.07	23.55 to 23.74
12	464	24.17 $\pm$ 1.07	24.08 to 24.27	426	23.79 $\pm$ 1.20	23.67 to 23.90
13	496	24.56 $\pm$ 1.17	24.46 to 24.66	428	24.16 $\pm$ 1.29	24.03 to 24.28
14	519	24.68 $\pm$ 1.20	24.58 to 24.79	406	24.21 $\pm$ 1.15	24.10 to 24.33
15	453	24.96 $\pm$ 1.26	24.84 to 25.08	442	24.42 $\pm$ 1.27	24.31 to 24.55
16	420	24.95 $\pm$ 1.30	24.82 to 25.07	459	24.86 $\pm$ 1.12	24.76 to 24.97
17	383	25.01 $\pm$ 1.34	24.88 to 25.15	419	24.92 $\pm$ 1.26	24.80 to 25.04
18	394	25.26 $\pm$ 1.41	25.12 to 25.40	394	24.97 $\pm$ 1.21	24.85 to 25.08
Total	5483	24.26 $\pm$ 1.30	24.22 to 24.29	5087	23.91 $\pm$ 1.35	23.88 to 24.23
p-value		0.0001			0.0001	

p-value based on test of age trend.

Table 4. Anterior chamber depth (mm) among male and female schoolchildren in each age group (right eye only)

Age (yr)	Boys			Girls		
	n	Mean ($\pm$ SD)	95% CI	n	Mean ($\pm$ SD)	95% CI
7	470	3.54 $\pm$ 0.25	3.51 to 3.56	412	3.45 $\pm$ 0.25	3.43 to 3.48
8	441	3.59 $\pm$ 0.27	3.56 to 3.62	441	3.51 $\pm$ 0.25	3.49 to 3.53
9	473	3.66 $\pm$ 0.27	3.63 to 3.68	389	3.57 $\pm$ 0.27	3.55 to 3.60
10	504	3.67 $\pm$ 0.27	3.64 to 3.69	414	3.59 $\pm$ 0.27	3.57 to 3.62
11	466	3.71 $\pm$ 0.28	3.69 to 3.74	457	3.65 $\pm$ 0.25	3.63 to 3.67
12	464	3.72 $\pm$ 0.28	3.70 to 3.75	425	3.66 $\pm$ 0.26	3.63 to 3.68
13	496	3.78 $\pm$ 0.28	3.75 to 3.81	428	3.68 $\pm$ 0.28	3.66 to 3.71
14	518	3.78 $\pm$ 0.26	3.75 to 3.80	406	3.67 $\pm$ 0.27	3.64 to 3.69
15	453	3.81 $\pm$ 0.28	3.78 to 3.83	442	3.67 $\pm$ 0.26	3.64 to 3.69
16	420	3.75 $\pm$ 0.28	3.73 to 3.78	459	3.70 $\pm$ 0.24	3.68 to 3.73
17	382	3.76 $\pm$ 0.28	3.73 to 3.79	419	3.69 $\pm$ 0.26	3.67 to 3.72
18	394	3.77 $\pm$ 0.28	3.74 to 3.79	394	3.69 $\pm$ 0.28	3.66 to 3.72
Total	5481	3.71 $\pm$ 0.28	3.70 to 3.72	5086	3.63 $\pm$ 0.27	3.62 to 3.64
p-value		0.0001			0.0001	

p-value: based on test of age trend.

girls and boys. Thereafter, the lens thickness continuously decreased with increasing age and severity of myopia to 11 years old, and then remained unchanged until age 15 years. However, lens thickness increased after age 15 years. It was 3.52 mm in girls and 3.51 mm in boys at the age of 18 years. Lens thickness at each age was not significantly different between boys and girls (boys, 3.46 $\pm$ 0.21 mm; girls, 3.47 $\pm$ 0.20 mm; $p > 0.05$; Table 5).

Differences between cities and villages

There were significant differences in the prevalence and severity of myopia between students in cities and

villages. Boys (Taipei City, 49.2%) and girls (provincial cities, 52.1%) in metropolitan primary schools had a higher prevalence of myopia than children in remote (boys, 22.1%) and aboriginal (girls, 27.8%) areas. The prevalences of myopia in junior high schools of aboriginal and remote areas were 31.8% and 44.4% for boys, and 61.9% and 73.3% for girls, respectively. The highest prevalence of myopia was among schoolchildren aged from 13 to 15 years old in Kaohsiung City (boys, 81.1%) and provincial cities (girls, 88.3%). Table 6 shows the mean ocular refraction in schoolchildren aged 7 through 15 years old with respect to the 10 developmental gradings of urbanization. The ANOVA

Table 5. Lens thickness (mm) among male and female schoolchildren in each age group (right eye only)

Age (yr)	Boys			Girls		
	n	Mean ($\pm$ SD)	95% CI	n	Mean ($\pm$ SD)	95% CI
7	470	3.55 $\pm$ 0.22	3.53 to 3.57	412	3.57 $\pm$ 0.19	3.55 to 3.59
8	441	3.50 $\pm$ 0.20	3.48 to 3.52	441	3.49 $\pm$ 0.22	3.47 to 3.51
9	473	3.47 $\pm$ 0.20	3.45 to 3.49	389	3.47 $\pm$ 0.21	3.45 to 3.49
10	504	3.43 $\pm$ 0.19	3.41 to 3.45	414	3.44 $\pm$ 0.20	3.42 to 3.46
11	466	3.43 $\pm$ 0.20	3.41 to 3.44	457	3.42 $\pm$ 0.18	3.40 to 3.43
12	464	3.44 $\pm$ 0.18	3.42 to 3.45	425	3.44 $\pm$ 0.20	3.42 to 3.46
13	496	3.41 $\pm$ 0.20	3.40 to 3.43	428	3.44 $\pm$ 0.21	3.42 to 3.46
14	519	3.43 $\pm$ 0.19	3.41 to 3.45	406	3.47 $\pm$ 0.20	3.45 to 3.49
15	453	3.42 $\pm$ 0.20	3.40 to 3.44	442	3.45 $\pm$ 0.20	3.43 to 3.47
16	420	3.49 $\pm$ 0.21	3.47 to 3.51	459	3.46 $\pm$ 0.19	3.45 to 3.48
17	382	3.51 $\pm$ 0.21	3.49 to 3.53	419	3.48 $\pm$ 0.19	3.47 to 3.50
18	394	3.51 $\pm$ 0.21	3.49 to 3.53	394	3.52 $\pm$ 0.19	3.50 to 3.54
Total	5482	3.46 $\pm$ 0.21	3.46 to 3.47	5086	3.47 $\pm$ 0.20	3.46 to 3.47
p-value		0.0950			0.0535	

p-value: based on test of age trend.

Table 6. Refractive status (D) of schoolchildren in developmental strata (right eye only)

	Boys		Girls	
	Primary school Mean $\pm$ SD (n)	Junior high school Mean $\pm$ SD (n)	Primary school Mean $\pm$ SD (n)	Junior high school Mean $\pm$ SD (n)
Developing area	-0.52 $\pm$ 1.58 (694)	-2.44 $\pm$ 2.41 (307)	-0.62 $\pm$ 1.77 (618)	-2.53 $\pm$ 2.65 (246)
Aboriginal area	0.02 $\pm$ 1.75 (24)	-0.22 $\pm$ 1.52 (22)	-0.41 $\pm$ 1.35 (18)	-1.36 $\pm$ 1.87 (21)
Industrial area	-0.64 $\pm$ 1.73 (566)	-2.13 $\pm$ 2.35 (177)	-0.76 $\pm$ 2.10 (510)	-2.29 $\pm$ 2.34 (185)
Hilly area	-0.75 $\pm$ 1.63 (54)	-1.11 $\pm$ 2.13 (27)	-0.38 $\pm$ 1.21 (46)	-2.31 $\pm$ 2.76 (30)
Remote area	0.09 $\pm$ 1.16 (104)	-1.83 $\pm$ 2.20 (111)	-0.47 $\pm$ 1.94 (108)	-2.28 $\pm$ 1.97 (103)
Service business area	-0.59 $\pm$ 1.42 (304)	-1.75 $\pm$ 2.33 (100)	-0.74 $\pm$ 1.60 (258)	-2.30 $\pm$ 2.26 (89)
Combination area	-0.30 $\pm$ 1.36 (218)	-1.65 $\pm$ 2.18 (127)	-0.48 $\pm$ 1.40 (195)	-2.16 $\pm$ 2.10 (138)
Taipei city	-0.88 $\pm$ 1.85 (325)	-2.48 $\pm$ 2.43 (197)	-1.03 $\pm$ 2.03 (321)	-3.12 $\pm$ 2.67 (222)
Kaohsiung city	-0.66 $\pm$ 1.58 (163)	-2.92 $\pm$ 2.48 (106)	-0.92 $\pm$ 1.87 (156)	-2.81 $\pm$ 2.33 (84)
Provincial cities	-0.76 $\pm$ 1.60 (459)	-2.83 $\pm$ 2.54 (377)	-0.85 $\pm$ 1.70 (397)	-3.23 $\pm$ 2.54 (197)

ANOVA test, $p < 0.0001$.

test and multiple comparisons test between separate strata or groups also demonstrated significant differences in mean refractive status among schoolchildren in cities, towns, and villages.

Discussion

In this nationwide survey of schoolchildren, we found that the prevalence of myopia was higher than in our previous study in 1995 [4]. At 7 years old, the prevalence of myopia had increased from 12% in 1995 to 20% in 2000; at 12 years old, it had increased from 56% to 61%; at 15 years old, it had increased from 76% to 81%; at the age of 16 to 18 years, the rate remained

unchanged at around 84% in both 1995 and 2000. One possible reason for the increasing prevalence of myopia in Taiwan is the increased workload from formal education. Epidemiologic surveys have consistently found a higher prevalence of myopia in academically based populations that was related to the level of education [7–11]. Although we did not directly investigate whether there was a causal relationship between myopia and the type of schooling or educational environment, it is clear that myopia typically develops in children of young age and gradually increases in prevalence, as well as in severity, from grade school through graduate school.

Studies from Singapore [12] and Japan [13, 14] have also found an increase in the prevalence of myopia over the past several decades. Most schoolchildren

in these countries are in stringent academic programs [15–17]. Taiwan's rapid development within the past two decades, stressful lifestyle, and small and crowded living environments might all be factors contributing to the high prevalence of myopia.

In this study, schoolchildren in Taiwan were found to have not only an increased prevalence of myopia but increased dioptric power as well. The severity of myopia was higher than in our previous study in 1995 [4]. At 12 years old, myopic refraction increased from -1.10 D to -1.64 D in girls and from -0.98 D to -1.26 D in boys. At the age of 18 years, it increased from -3.92 D to -4.12 D in girls and from -2.71 D to -3.15 D in boys. The prevalence of high myopia was also greater than in our previous study in 1995 [4], at 24% compared to 20% in girls and 18% compared to 12% in boys at age 18 years. One reason for the high prevalence of high myopia in Taiwanese may be the young age at the onset of myopia. Myopia is commonly classified into early-onset myopia (myopia developing prior to the age of 15 yr) and late-onset myopia (myopia developing after the age of 15 yr) [1]. In Taiwan, the prevalence of myopia at 7 years old increased from 4% in 1986 to 12% in 1995, then to 20% in 2000. A study of Finnish schoolchildren found that myopia progressed faster in children with an earlier age of onset of myopia, and in children who had more severe myopia at initial examination [18]. Our 1995 study found that the mean ocular refraction became myopic at 9 years old, while in this study in 2000, myopic status developed at 8 years old. These findings indicate that the prevalence and severity of myopia are increasing in Taiwan.

Ocular components may change considerably with age and the progression of myopia. Newborns are usually hyperopic. In subsequent years, the ocular axis elongates with thinning of the lens and flattening of the cornea, which leads to emmetropia in children between the ages of 8 and 10 years [13]. In our study, the axial length showed close correspondence with the ocular refraction. The mean axial length at 9 years old was close to the values of emmetropic adult eyes in Taiwan [19]. Thereafter, the axial length increased with age and severity of myopia. The ACD became slightly deeper with increasing age. At 9 years old, the ACD was 3.57 mm in girls and 3.66 mm in boys. The ACD continuously increased with age and the progression of myopia. The mean ACD at the age of 12 years was 3.66 mm in girls and 3.72 mm in boys. It remained stable from the age of 13 to 18 years, around 3.69 mm in girls and 3.77 mm in boys. The mean lens thickness decreased from 3.57 mm in girls and 3.55 mm in boys at 7 years old to 3.42 mm in girls and 3.43 mm in boys at the age of 11 years. It remained unchanged from 11 to 15 years old, but increased after the age of 15 years. In contrast, no change was found in the corneal radius with increasing age or severity of myopia.

Gender could affect the distribution and severity of myopia. Our study found that the prevalence of myopia and the mean refractive status were higher in girls than in boys. The prevalence of high myopia was also greater in girls, especially after puberty. The NHANES data show that the prevalence of myopia is higher in females than in males [6]. The study in Finnish schoolchildren also found that myopia progressed faster in girls than in boys [1], and several other studies found similar results [12, 20]. However, the prevalence of anisometropia (> -2.0 D) in our study was not different between girls and boys, and also increased with age and the severity of myopia. A previous study found differences in ocular components between girls and boys [21]. In our study, the mean axial length in boys was greater than that in girls, while the mean refractive status was less myopic in boys. This may be due to the fact that boys are taller than girls. Eye size may be linked to body stature, with taller individuals having longer axial length [7]. The mean ACD in boys was slightly greater than that in girls, although the lens thickness in boys and girls was similar. The mean corneal curvature in boys was significantly flatter than that in girls in our study.

Taiwan is a rapidly developing urban country, and the schooling system is highly competitive. In this survey, we found that the prevalence and severity of myopia among students in cities were much higher than in remote and aboriginal areas. This finding suggests that environmental influences may play a role in the prevalence and extent of myopia. School systems in cities are more competitive than those in rural areas. Many children in cities also attend extracurricular classes after school hours or use computers at home at a very early age. Previous epidemiologic studies have suggested that close-work activity, such as reading, writing, and computer use, may be related to myopia development [22–26].

In summary, our findings demonstrate that the prevalence of myopia and high myopia has continued to increase over the past 15 years in Taiwan [2, 4]. In addition, the age of onset of myopia decreased from 12 years old in 1983 to 8 years old in 2000. At 7 years old, the mean prevalence of myopia in 2000 was 20%. The mean refractive status became myopic at 8 years old. The prevalence and severity of myopia in girls were greater than those in boys. Boys had a longer mean axial length, greater ACD, and flatter cornea than girls. The prevalence and severity of myopia continuously progressed with education level and age. The increase in axial length was correlated with the progression of myopia. However, corneal curvature remained unchanged during the progression of myopia. The role of minor changes in lens thickness and ACD in the progression of myopia needs further investigation.

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References

1. Goldschmidt E: On the etiology of myopia. *Acta Ophthalmol Suppl* 1968;98:1-171.
2. Lin LLK, Chen CJ, Hung PT, et al: Nation-wide survey of myopia among schoolchildren in Taiwan, 1986. *Acta Ophthalmol Suppl* 1988;185:29-33.
3. Lin LLK, Hung PT, Ko LS, et al: Study on myopia among aboriginal school children in Taiwan. *Acta Ophthalmol Suppl* 1988;185:34-6.
4. Lin LLK, Shih YF, Tsai CB, et al: Epidemiologic study of ocular refraction among schoolchildren in Taiwan in 1995. *Optom Vis Sci* 1999;76:275-81.
5. Cohn H: *Hygiene of the Eye*. London: Simpkin, Marshall & Co, 1886.
6. Sperduto RD, Siegel D, Roberts J, et al: Prevalence of myopia in the United States. *Arch Ophthalmol* 1983;101:405-7.
7. Teasdale TW, Goldschmidt E: Myopia and its relationship to education, intelligence and height: preliminary results from an on-going study of Danish draftees. *Acta Ophthalmol Suppl* 1988;185:41-3.
8. Rosner M, Belkin M: Intelligence, education, and myopia in males. *Arch Ophthalmol* 1987;105:1508-11.
9. Angle J, Wissmann DA: Age, reading, and myopia. *Am J Optom Physiol Opt* 1978;55:302-8.
10. Parssinen TO: Relation between refraction, education, occupation, and age among 26- and 46-year-old Finns. *Am J Optom Physiol Opt* 1987;64:136-43.
11. Baldwin WR: A review of statistical studies of relations between myopia and ethnic, behavioral, and physiological characteristics. *Am J Optom Physiol Opt* 1981;58:516-27.
12. Rajan U, Tan FT, Chan TK, et al: Increasing prevalence of myopia in Singapore school children. In: Chew SJ, Weintraub J, eds. *Proceedings of the Fifth International Conference on Myopia, Toronto, Ontario, Canada, June 22-24, 1994*. New York, NY: Myopia International Research Foundation, 1995:41-6.
13. Hosaka A: The growth of the eye and its components: Japanese studies. *Acta Ophthalmol Suppl* 1988;185:65-8.
14. Hosaka A: Population studies — myopia experience in Japan. *Acta Ophthalmol Suppl* 1988;185:37-40.
15. Ling SL, Chen AJ, Rajan U, et al: Myopia in ten year old children — a case-control study. *Singapore Med J* 1987;28:288-92.
16. Chow YC, Dhillon B, Chew PT, et al: Refractive errors in Singapore medical students. *Singapore Med J* 1990;31:472-3.
17. Law NW, Chew SJ, Ritch R, et al: Survey of refraction in a Chinese population shows that myopia severity can be predicted from its age of onset. *Invest Ophthalmol Vis Sci* 1992;33:709. [abstract]
18. Parssinen O, Lyyra AL: Myopia and myopic progression among schoolchildren: a three-year follow-up study. *Invest Ophthalmol Vis Sci* 1993;34:2794-802.
19. Hsu WM: Axial length and lens thickness in normal adult eye. *J Formos Med Assoc* 1983;82:1170-4.
20. Rasmussen OD: Incidence of myopia in China. *Br J Ophthalmol* 1936;20:350-60.
21. Curtin BJ: *The Myopias: Basic and Clinical Management*. Philadelphia: Harper & Row, 1985:51-2.
22. Angle J, Wissmann DA: The epidemiology of myopia. *Am J Epidemiol* 1980;111:220-8.
23. Richler A, Bear JC: Refraction, near work and education. A population study in Newfoundland. *Acta Ophthalmol (Copenh)* 1980;58:468-78.
24. Bear JC, Richler A, Burke G: Nearwork and familial resemblances in ocular refraction: a population study in Newfoundland. *Clin Genet* 1981;19:462-72.
25. Wong L, Coggan D, Cruddas M, et al: Education, reading, and familial tendency as risk factors for myopia in Hong Kong fishermen. *J Epidemiol Community Health* 1993;47:50-3.
26. Zylbermann R, Landau D, Berson D: The influence of study habits on myopia in Jewish teenagers. *J Pediatr Ophthalmol Strabismus* 1993;30:319-22.

EVALUATION OF OPTIC DISC CHANGES IN SEVERE MYOPIA

Tsing-Hong Wang, Szu-Yuan Lin, Yung-Feng Shih, Jau-Kang Huang, Luke L-K Lin,
and Por T. Hung

Purpose: To evaluate the changes in the optic nerve head in highly myopic subjects by means of confocal laser scanning ophthalmoscope.

Methods: Using laser scanning and a three-dimensional image analysis system, we studied 114 young (21.4 ± 1.4 years), highly myopic subjects with refractive errors greater than -8.0 D and a control group of 29 subjects (18.9 ± 1.2 years) with myopia of -3.0 D or less. Measurements included cycloplegic refraction, corneal curvature, biometric axial length, and morphometric values of the optic disc obtained with a laser scanning disc analyzer.

Results: The optic disc area in highly myopic eyes was similar to that in mildly myopic eyes. However, regression analysis revealed that the optic disc area increased with axial length in subjects with severe myopia. The cup/disc ratio, the disc depth, the neuroretinal rim area, and the tilting of the disc were not significantly different between the severe and mild myopia groups.

Conclusions: These findings may be useful in further investigations of myopic progression and of the mechanisms responsible for the development of myopic complications.

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Key words:

axial length
myopia
optic disc
neuroretinal rim
laser scanning ophthalmoscopy

Taiwan has a large population of school children with myopia [1]. A nationwide survey in 1999 found a prevalence rate of myopia among senior high school students of around 84%, and 16% were highly myopic with a refractive error of -6 D or more [2]. The potential complications associated with severe myopia, such as retinal detachment, macular degeneration, and glaucoma, are therefore of great concern.

Previous studies have reported that the nerve fibers of myopic eyes are susceptible to glaucomatous damage [3-5]. In glaucoma diagnosis, morphometry of the intra- and parapapillary structures can help to differentiate normal eyes with ocular hypertension from those with early glaucomatous optic nerve atrophy [6-10]. However, these typical features are not valid in highly myopic eyes, where the optic disc has a distinctly different ophthalmoscopic appearance [11, 12]. The use of stereophotography with computerized planimetry to measure the size of the optic disc and neuroretinal rim has enhanced the assessment of the optic nerve in glaucoma [13-15].

The purpose of this study was to measure the size and the form of the optic disc and parapapillary region in highly myopic eyes, and to determine the characteristic changes associated with myopia.

Subjects and Methods

Subjects were selected from the freshman class of the School of Medicine of National Taiwan University in 1996. Only those without any ocular diseases or previous ocular surgery were eligible. Informed consent was obtained from all subjects prior to enrollment. A total of 114 highly myopic subjects (72 women and 42 men) with a mean age of 18.9 ± 1.2 years (18-24 years) and a mean refractive error of -9.78 ± 2.18 D (-8 to -17 D), and 29 control subjects (20 women and 9 men) with a mean age of 21.4 ± 1.3 years (19-24 years) and a mean refractive error of -1.67 ± 1.22 D ($+2.5$ to -3.0 D) were enrolled in the study.

Department of Ophthalmology, National Taiwan University Hospital, Taipei.

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Reprint requests and correspondence to: Dr. Yung-Feng Shih, Department of Ophthalmology, National Taiwan University Hospital, 7 Chung-Shan South Road, Taipei, Taiwan.

All subjects underwent a series of ophthalmic examinations, including cycloplegic refraction and corneal curvature measurement with an autorefractometer (RK-3000, Topcon, Tokyo, Japan), slit lamp biomicroscopy, intraocular pressure (IOP) measurement with a Goldmann tonometer, biometry by A-scan ultrasonography (A-1500, Sonomed, Lake Success, NY, USA), and extended fundus examination with indirect ophthalmoscopy after pupil dilation. Disc topographic values were assessed with a confocal laser scanning ophthalmoscope (TopSS, Laser Diagnostic Technologies, San Diego, CA, USA) and stereophotography (TRC-SS2, Topcon) after pupil dilation. For each eye, three 10° confocal laser tomographic scanning images were obtained and the mean values of the three images were analyzed by the software version 2.2 (TopSS, Laser Diagnostic Technologies). The border of the optic disc was outlined with the help of stereophotographs. To reduce the variance in defining the reference plane, one skilled technician performed all imaging procedures and parameter calculations. The TopSS system acquires 32 sectional images (taken within a 1–3 mm depth range) in 0.9 seconds and pupil dilation is generally not needed. The photographic magnification in this system was corrected automatically, taking into account only the anterior corneal curvature and refraction as previously described [16, 17].

Various optic disc variables were measured, including horizontal and vertical diameters, total area, degree of tilting, height variation, average depth, and maximum depth. The cup volume and cup/disc ratio were also determined, as well as the area of the neuroretinal rim. The reference cap, which is defined as the imaginary cap that is placed over the user-defined disc contour, was used for volumetric calculations. For contour tilt, a positive value indicated tilt of the contour line downward toward the nasal side, and a negative value indicated tilt to the temporal side. An offset surface distance 100 μ m below the reference cap was used to define the top surface of the cup. Height variation was calculated as the difference between the maximum and minimum heights along the perimeter of the area of interest. The cup area was considered to lie 100 μ m below the cap of the area of interest. Cup volume was defined as the volume of the open space below the effective area. Maximum depth was calculated as the difference between that height and the corresponding heights of the same pixels at the cup. The neuroretinal rim area was defined as the difference between the total disc area and cup area. Only the right eye of each patient was used for data analysis. Data are presented as the mean $\pm$ standard deviation. Two-sample *t*-tests were used to evaluate differences between various subgroups. Regression analysis was used to examine the relationship between

optic disc and axial length. A *p* value of less than 0.05 was considered statistically significant.

Results

The age difference between the control group and the highly myopic group was not significant, while obvious differences were found in the refractive errors and axial lengths between the two groups (Table 1). IOP in the two groups ranged from 10 to 21 mm Hg.

The horizontal and vertical diameters and the total area of the disc were similar in the highly myopic and mildly myopic groups (Table 2). The disc size showed a similar pattern of distribution in the two groups (Fig. 1). However, the disc size correlated significantly with the axial length in the highly myopic group ($r = 0.43$, $p < 0.01$), with the optic disc area tending to be larger in eyes with greater axial length (Fig. 2). However, the disc size was not significantly correlated with the axial length in the mildly myopic group ($r = 0.15$) (Fig. 3). The disc area was greater than 3.0 mm² in 14 cases (12.2%) in the highly myopic group, but in only two cases (6%) in the mildly myopic group (Fig. 1). The two subjects in the control group with the largest disc size (2.98 mm² and 2.78 mm²) also had relatively long axial lengths, of 25.62 and 25.58 mm, respectively.

The cup/disc ratio was not significantly different in the highly myopic and mildly myopic groups. Both groups had similar grades of contour tilt and height variation to the temporal side, but the volume of the cup in the highly myopic group was significantly smaller than that in the mildly myopic group (Table 2). The average and maximum depths of the cup were also significantly lower in the highly myopic group. The neuroretinal rim, which contains the nerve fibers from the ganglion cells of the retina, was not significantly different in the two groups ($p = 0.06$) (Table 2).

Table 1. Baseline characteristics of the highly myopic and control groups

	Highly myopic group	Control group	<i>p</i> -value*
No. of eyes	114	34	
Age (years)	18.8 $\pm$ 1.2	21.4 $\pm$ 1.4	0.55
Refraction (D)	-9.78 $\pm$ 2.18	-1.67 $\pm$ 1.22	< 0.001
Axial length (mm)	27.17 $\pm$ 0.78	23.68 $\pm$ 0.89	< 0.001

Mean $\pm$ standard deviation. * Two-sample *t*-test.

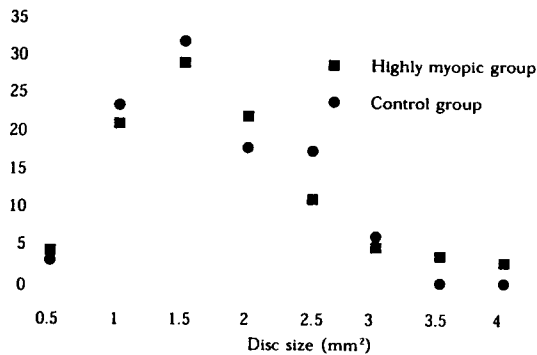


Fig. 1. Distribution of disc size in the highly myopic ($n = 114$ eyes) and control ($n = 34$ eyes) groups.

Discussion

In highly myopic eyes, the scleral canal usually takes an oblique course toward the nasal aspect of the orbit, and an oblique insertion of the optic disc has been reported to be more common [18]. Therefore, it is difficult to identify and monitor glaucomatous optic changes in these eyes. Confocal laser scanning systems provide a three-dimensional view of the optic disc, and a quantitative method for measuring its actual shape. In this study, we used the TopSS confocal laser scanning system to evaluate the differences in disc variables between highly myopic and mildly myopic subjects. We found that the optic disc area in highly myopic eyes was similar to that in mildly myopic eyes; however, regression analysis revealed that optic disc area increased with axial length in subjects with severe myopia. The cup/disc ratio, the disc depth, the neuroretinal rim area,

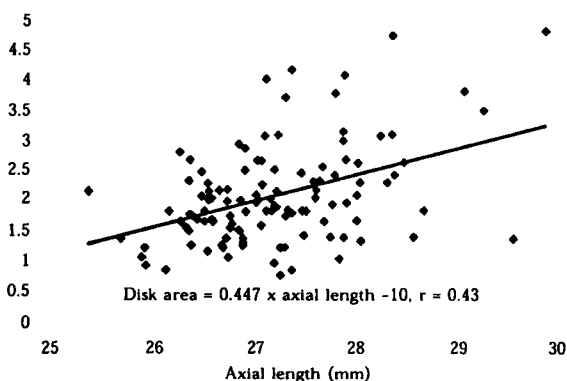


Fig. 2. Relationship of axial length and disc area in the highly myopic group ($n = 114$ eyes).

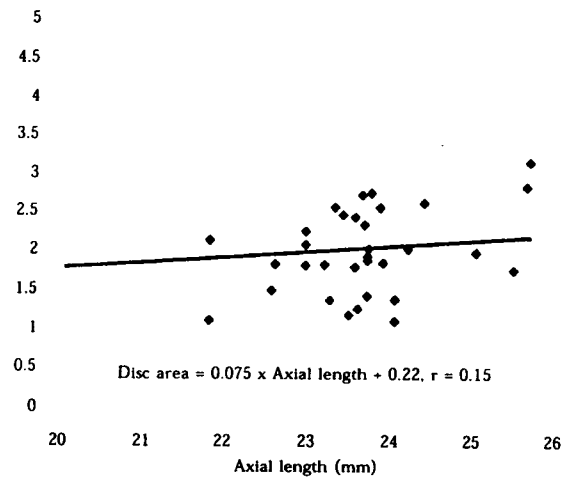


Fig. 3. Relationship of axial length and disc area in the control ($n = 34$ eyes) group.

and tilting of the disc were not significantly different between the two groups.

Size of the optic disc

The optic disc area is not constant among individuals, varying by a factor of about 1:7 [19, 20]. Thus, variability in disc diameter among eyes might influence the clinical appearance of the disc. This variability is pathogenetically and morphogenetically important. Some reports have indicated a poor relationship between disc size and myopia [21, 22], but other studies have found a positive correlation between optic disc size and axial length [18, 23]. In the present study, highly myopic subjects with refractive errors of more than -8.0 D did not have a significantly larger optic disc than mildly myopic subjects; however, the disc size was positively correlated with the axial length. The disc area of subjects in the highly myopic group (mean, $2.07 \pm 0.81 \text{ mm}^2$) was also no greater than that of normal eyes ($2.69 \pm 0.70 \text{ mm}^2$; range, 0.86–5.86 mm^2) reported in the literature [20].

Similarly, Britton et al found no relationship between eye length and disc diameter in normal adults [24]. The refractive error and disc diameter are also unrelated. These findings may be attributed to several factors. The most important factor is the number of tilted discs, which was included in our study. Several studies revealed that the optic discs of highly myopic eyes are oval, with rotation of the longer axis of the disc on the anterior-posterior axis [11, 12]. This disc tilting from the oblique insertion of the optic disc and the long axial length of the eyeball not only caused exposure of the anterior aspect of the posterior scleral canal but also decreased the disc area. Another important factor

Table 2. Disc parameter data of the highly myopic and control groups

Variable	Highly myopic group (n = 114 eyes)	Control group (n = 34 eyes)	p value*
H diameter (mm)	1.49 ± 0.25	1.47 ± 0.27	0.83
V diameter (mm)	1.71 ± 0.29	1.68 ± 0.19	0.60
Neuroretinal rim area (mm ²)	1.42 ± 0.60	1.20 ± 0.24	0.06
Total area (mm ²)	2.07 ± 0.81	1.98 ± 0.54	0.58
Cup/disc ratio	0.30 ± 0.15	0.36 ± 0.17	0.07
Tilt (°)	-13.45 ± 9.41	-14.20 ± 6.57	0.68
Height variation	0.45 ± 0.18	0.41 ± 0.11	0.29
Cup volume (mm ³)	-0.099 ± 0.094	-0.218 ± 0.197	< 0.001
Average depth	-0.144 ± 0.165	-0.225 ± 0.109	0.013
Maximum depth (mm)	-0.292 ± 0.161	-0.512 ± 0.266	< 0.001

Data are mean ± standard deviation; H = horizontal; V = vertical. * Two-sample *t*-test.

is the number of subjects with congenital myopia included in the study. We found that highly myopic subjects with larger discs (> 3.0 mm) were more myopic and had longer axial lengths. Jonas et al found discs to be larger and more ovaly configured in highly myopic subjects [11], and Papastathopoulos et al demonstrated that larger human donor eyes had larger optic discs [19]. A large optic disc may be related to early-onset myopia or may be congenital in origin.

The control subjects in this study were not emmetropic or non-myopic; fewer than 10% of college students in Taiwan are non-myopic [25], which made recruiting volunteers for the control group difficult. Although control group subjects had axial lengths of less than 25.0 mm, there was no significant difference in disc size between the two groups. In addition, the magnification factors used to calculate the disc size from clinical photographs might have been inaccurate. A similar situation may arise in scanning laser tomography, because the axial length is determined on the basis of keratometry and refractive error, and is not really incorporated into a correction factor for magnification. This finding suggests that the size of the optic disc might be genetically determined, and that increased severity of myopia might contribute to the increased disc diameter.

Shape of the optic disc (tilt and cup/disc ratio)

Enlargement of the cup is one of the early signs of glaucomatous damage to the optic nerve. Several studies have reported that the mean cup/disc ratio in normal eyes is 0.25 [26, 27]. The areas of the optic disc and optic cup are related, with a larger optic disc associated with a larger optic cup. If the increasing disc size is correlated with increasing axial length, the highly myopic group should have had larger optic cups. Although some studies have reported an association of myopia with a large cup/

disc ratio, others did not find this phenomenon [23, 26]. Fledelius found a weak association between cup size and refraction (and axial length), with larger cups associated with myopia [28]. The lack of a significant difference in cup/disc ratio between highly myopic and mildly myopic subjects in the current study is similar to most previous studies [21–23, 26]. However, Tomlinson and Phillips found a significant correlation between cup/disc ratio and the axial length of the eye [29]. This discrepancy might be due to the difficulty in defining the disc margin and in evaluating the cup/disc ratio in highly myopic subjects. In this study, highly myopic subjects with larger discs showed less tilting and less contour variation to the temporal side.

Neuroretinal rim

Previous studies have shown that the neuroretinal rim area is highly variable interindividually and is independent of age, sex, and right or left eye [13, 23, 24, 30, 31]. Like the optic disc and cup, the neuroretinal rim area was suggested to be correlated with the optic disc area. However, Varma et al were unable to find any relationship between refractive error and the optic disc area, neural rim area, or optic cup size [23]. Bengtsson noted that the linear width of the neuroretinal rim is independent of the diameter of the disc and is more likely to be clinically useful [17]. Britton et al also confirmed the great variability in disc sizes and the lack of a relationship between the linear disc diameter and the linear neuroretinal rim width [24]. In this study, we found that the neuroretinal rim area was not significantly different in highly and mildly myopic subjects.

In conclusion, the optic disc size did not differ significantly between subjects with severe myopia and those with mild or no myopia in our study. However, the disc size correlated with the axial length. In addition,

highly myopic subjects with larger discs (> 3.0 mm) had a higher grade of myopia and longer axial length, which might have been early-onset or congenital in origin. No significant differences were noted in cup/disc ratio and the neuroretinal rim area between severe and mild myopia. Therefore, we propose that the optic disc size and glaucoma susceptibility may be independently determined, and further longitudinal studies to assess the relationship among optic disc variables in severe myopia is necessary.

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References

1. Lin LLK, Chen CJ, Hung PT, et al: Nation-wide survey of myopia among schoolchildren in Taiwan, 1986. *Acta Ophthalmol* 1988;66:29-33.
2. Lin LLK, Shih YF, Tsai CB, et al: Epidemiological study of ocular refractions among school children (aged 6 through 18) in Taiwan. *Optom Vis Sci* 1999;76:275-81.
3. Phelps CD: Effect of myopia on prognosis in treated primary open-angle glaucoma. *Am J Ophthalmol* 1982;93:622-8.
4. Daubs JE, Crick RP: Effect of refractive error on the risk of ocular hypertension and open-angle glaucoma. *Trans Ophthalmol Soc UK* 1981;101:121-6.
5. Perkins ES, Phelps CD: Open angle glaucoma, ocular hypertension, low-tension glaucoma, and refraction. *Arch Ophthalmol* 1982;100:1464-7.
6. Sommer A, Miller NR, Pollack I, et al: The nerve fiber layer in the diagnosis of glaucoma. *Arch Ophthalmol* 1977;95:2149-56.
7. Quigley HA, Miller NR, George T: Clinical evaluation of nerve fiber atrophy as indicator of glaucomatous optic nerve damage. *Arch Ophthalmol* 1980;98:1564-71.
8. Airaksinen PJ, Drance SM: Neuroretinal rim area and retinal nerve fiber layer in glaucoma. *Arch Ophthalmol* 1985;103:203-4.
9. Jonas JB, Frenandez MC, Naumann GOH: Parapapillary atrophy and retinal vessel caliber in nonglaucomatous optic nerve damage. *Invest Ophthalmol Vis Sci* 1991;32:2942-7.
10. Weder J, Dannheim F, Dannheim D: The topographic relationship between optic disc and visual field in glaucoma. *Acta Ophthalmol* 1990;68:568-74.
11. Jonas JB, Gusek GC, Naumann GOH: Optic disk morphometry in high myopia. *Graefe's Arch Clin Exp Ophthalmol* 1988;226:587-90.
12. Hyung S-M, Kim DM, Hong C, et al: Optic disc of the myopic eye: relationship between refractive error and morphometric characteristics. *Korean Journal of Ophthalmology* 1992;6:32-5.
13. Caprioli J, Miller JM: Videographic measurements of optic nerve topography in glaucoma. *Invest Ophthalmol Vis Sci* 1988;29:1294-8.
14. Dreher AW, Tso PC, Weinreb RN: Reproducibility of topographic measurements of the normal and glaucomatous optic nerve head with the laser tomographic scanner. *Am J Ophthalmol* 1991;111:221-9.
15. Dreher AW, Weinreb RN: Accuracy of topographic measurements in a model eye with the laser tomographic scanner. *Invest Ophthalmol Vis Sci* 1991;32:2992-6.
16. Bengtsson B, Krakau CET: Correction of optic disc measurements on fundus photographs. *Graefe's Arch Clin Exp Ophthalmol* 1992;230:24-6.
17. Bengtsson B: The variation and covariation of cup and disc diameters. *Acta Ophthalmol* 1976;54:804-18.
18. Quigley HA, Brown AE, Morrison JD, et al: The size and shape of the optic disc in normal human eyes. *Am J Ophthalmol* 1990;108:51-7.
19. Papastathopoulos KI, Jonas JB, Panda-Jonas S: Large optic discs in large eyes, small optic discs in small eyes. *Exp Eye Res* 1995;60:459-61.
20. Jonas JB, Gusek GC, Guggenmoos-Holzmann I, et al: Size of the optic nerve scleral canal and comparison with intravital determination of optic disc dimensions. *Graefe's Arch Clin Exp Ophthalmol* 1988;226:213-5.
21. Miglior S, Brigatti L, Velati P, et al: Relationship between morphometric optic disc parameters, sex and axial length. *Curr Eye Res* 1993;13:119-24.
22. Chihara E, Chihara K: Covariation of optic disc measurements and ocular parameters in the healthy eye. *Graefe's Arch Clin Exp Ophthalmol* 1994;232:265-71.
23. Varma R, Tielsch JM, Quigley HA, et al: Race-, age-, gender-, and refractive error-related difference in the normal optic disc. *Arch Ophthalmol* 1994;112:1068-76.
24. Britton RJ, Drance SM, Schulzer M, et al: The area of the neuroretinal rim of the optic nerve in normal eyes. *Am J Ophthalmol* 1987;103:497-504.
25. Lin LLK, Wang TH, Jan JH, et al: Survey of the ocular refraction with its optical components among freshmen in National Taiwan University. *Acta Soc Ophthalmol Sinicae* 1991;30:597-604.
26. Erkkila H, Laatikainen L: Characteristics of optic disc in healthy school children. *Acta Ophthalmol* 1979;57:914-21.
27. Jonas JB, Gusek GC, Naumann GOH: Optic disc, cup, and neuroretinal rim size, configuration and correlations in normal eyes. *Invest Ophthalmol Vis Sci* 1988;29:1151-8.
28. Fledelius HC: Refraction and eye size in the elderly: a review based on literature, including own results. *Acta Ophthalmol* 1988;66:241-8.
29. Tomlinson A, Phillips CI: Ratio of optic cup to optic disc in relation to axial length of the eyeball. *Br J Ophthalmol* 1969;53:765-7.
30. Chi T, Ritch R, Stickler D, et al: Racial difference in optic nerve head parameters. *Arch Ophthalmol* 1989;107:836-9.
31. Caprioli J, Miller JM: Optic disc rim area is related to disc size in normal subjects. *Arch Ophthalmol* 1987;105:1683-5.

**Current Issues in Myopia:
Epidemiology, Visual Impairment and Intervention
with HOYA Multifocal Lenses**

Por T. Hung¹, Yung-Feng Shih¹, Luke L-K Lin¹, C. Kate Hsiao², Chein-Jen Chen², Jean Shein¹

¹Department of Ophthalmology, National Taiwan University Hospital, Taiwan

²Division of Biostatistics, Institute of Epidemiology, College of Public Health, National Taiwan University, Taiwan

Correspondence to: Por T. Hung, M.D.

Department of Ophthalmology, National Taiwan University Hospital, Taiwan

No. 7, Chung-Shan S. Rd., Taipei, Taiwan

Tel: 886-2-23123456 ext. 5186

Fax: 886-2-2341-2634

Introduction

Although myopia has been present in humans for a long time, the last few decades of the 20th century brought about an explosion in the prevalence of myopia worldwide, especially in developing Asian countries. Because of the rapidly increasing rates of this disease, it may be considered an epidemic of global proportions that warrants extensive research in the future. Therefore, myopia is equally important as a social issue of public health, as well as a problem that needs to be researched heavily on epidemiology, therapy as well as in advance etiological study.

Only recently we have began to realized the importance of myopia in the impairment of visual function. Myopia affects the young and the old in their visual dysfunction, thereby greatly affecting a continuum in the community and its associated socioeconomic development. Thus, the solution to the problem of myopia requires much more than a simple corrective lens. As there is currently very little information available regarding the etiological molecular biology of myopia, it is essential for future research to focus on this field too.

In this presentation, the author shall briefly review the current status of myopia from an epidemiological standpoint, myopia and its relationship to visual impairment, and recent studies regarding a new therapeutic approach using multiple focal lenses along with topical medication.

Epidemiology

World Blindness

Cataracts, glaucoma and infectious ocular disorders are still considered the major causes of blindness in many parts of world. Previously, it was accepted that technologically advanced societies had different etiologies and rates of blindness with respect to under-developed nations. However, recent economic and social transformations in under-developed countries have gradually transformed this former discrepancy in the prevalence of blindness. Also, ocular diseases that were previously seen only in more advanced societies are now being found in the still-developing countries. For example, the major retinal etiologies of blindness are now seen in patients from developing countries, especially in Asia. One of the end results of severe myopia is retinochoroidal change. Seen more frequently in the geriatric population and in high myopes, such retinal disorders have recently become the third major cause of blindness in some developing countries. In this

respect, myopia may be considered the third most prevalent cause of blindness and visual impairment in the world, following cataracts and glaucoma.

Review of Epidemiology

An epidemiological study is the first step in understanding a disease's prevalence and/or incidence and the extent to which race, sex, genetics and other related factors increase the likelihood of developing that disease. It can be approached using a cross-sectional method, as well as a longitudinal study with long-term follow-up. The former cross-sectional study would offer an overview of the general current status of myopia, while the longitudinal follow-up study would have the advantage of providing information regarding the course of development of myopia and its relationship to aging or another long-term risk factor.

The difficulties of an epidemiological study on myopia lie in finding willing subjects within an eligible population. The study group chosen in the screening should reasonably represent the general population being studied. Other factors for screening that require serious consideration include the method of refraction used, such as cycloplegic retinoscopy or automated refraction, and the environmental factors, such as daily activities.

One of the important issues in any epidemiological study is how to define the disease that is being studied. In this study, patients had to fulfill certain criteria that ruled them in as having myopia. It is important to unify research in this field in order to strengthen the interpretation of results. Zadnick et al collected recently published reports on myopia, and reviewed the criteria for having myopia as defined by each author, as well as the method of measuring the refractive error in each study. The criteria for the classification of myopia ranged from at least -0.25 D to at least -0.75 D, spherical equivalent to horizontal only, and the different methods of examination included retinoscopy, autorefraction, and subjective refraction.

Except in the United States, Australia, Taiwan, and some East Asian countries, there are only a few well-designed representative or population-based studies on the prevalence of myopia. It is thought that both genetic and environmental factors constitute major etiologies in the development of myopia. The environmental factors include socioeconomic trends, academic pressures, familial influences, and near work demands. There are several studies on the prevalence of myopia, but few of these reports emphasize the importance of environmental factors.

The prevalence of myopia in each of the earlier reports was quite variable. Although the prevalence ranged anywhere from 1.4% to 9.1% according to different samples, most of the

reports had a common trend, demonstrating an increased prevalence with age and an increasing prevalence in successive studies within the same age group. The highest rate reported thus far was seen in a study done in university freshmen. In 1988, Lin found 91% of this population to be myopic. The prevalence of myopia is steadily increasing in Asia, especially in the ethnic Chinese. Reports from Singapore, Hong Kong, Mainland China, Japan, and Taiwan confirm this alarming trend.

Epidemiological Studies in Taiwan

Myopia studies in Taiwan have been done for more than 60 years, originally researched by the late Professor Motegi in the aboriginal population and the late Professor Yang in the Tong Mon primary school population.

In Taiwan, there are about 250,000 aboriginal people of Polynesian descent. From the early 1944, Motegi performed a series of eye screening surveys among the Taiwanese aborigines, which demonstrated that over 80% of the subjects studied were emmetropic. Fifteen years later in 1959, a more well-designed myopia study was carried out by Ko among the Tong Mon primary school children in Taipei, and it was found that only 5.31% were myopic.

The trends comparing the urban and the provincial prevalence rates are quite significant. In 1982, Chung executed a study of refractive error in a population of 227 aboriginal students from the Ping-Tung mountain region. Among this population, he reported that 2.3% were myopic, 38.3% were emmetropic and 59.3% were hyperopic. These numbers indicate a much lower rate of myopia in the aboriginal population. Also in 1988, Lin demonstrated that while only 13% of the aboriginal junior high school children were myopic, 30% of the children of Taiwanese and Chinese origin from the same school were considered near-sighted.

In 1980, the myopic prevalence was 20.8% in Taipei primary school children, but it increased to 22.2% in 1983, and then dramatically rose to 36.2% in 1988. Thereafter, the national myopic project was carried out until the year 2000. During each study period, the stratified samples numbered from 100,000 to 350,000, and they underwent the same procedures at each evaluation. The only alteration in protocol occurred in 1990, when assessment with ultrasound biometry was added to the study regimen. The results of these screening projects indicate that the prevalence of myopia is steadily increasing year by year, and the age of onset of myopia is getting younger and younger. Additionally, the prevalence of high myopia, defined as refractive error greater than -6.0 D, is also increasing in all age groups.

Current Taiwan's Epidemiology Study

From 1983 until 2000, we proposed a large-scale longitudinal study on myopia. we performed nationwide surveys on more than 2000 stratified samples of randomly selected school children every two to four years. The school children were between the ages of 7 and 15 and were stratified according to the geographical area in which they lived. The children were separated into urban and suburban categories, and the total numbers of children in each group ultimately matched the proportions in the overall population of school children living in urban and suburban settings in Taiwan. A total number of 10878, including 5664 boys and 5225 girls, were enrolled in 2000. The refractive status and corneal radius of each student were studied with retinoscopy and by autorefractometer under cycloplegia. Axial length was measured with biometric ultrasound. The results demonstrated that the rate of myopia was 20% at the age of 7, jumped to 61% at the age of 12, then rose to 80% at the age of 15. The prevalence in 16-year-old school children was 83%, and it was found to be 85% at age 18. The mean refractive status demonstrated that the average age of onset of myopia was at the age of 8, and it increased to -4.12 D in girls and -3.27 D in boys by the age of 18. At the age of 18, the prevalence of high myopia, which was defined as refractive error over -6.0 D, was found to be 24% in girls and 19% in boys.

Ocular measurements apart from refractive error were also recorded. An increase in axial length is known to correspond with the progression of myopia. By age 9, the subjects' average axial length had already reached an adult length of more than 23 mm. The 9-year-old male student had an average axial length of 23.68 mm, and his female counterpart measured 23.12 mm. The anterior chamber depth was slightly deeper from age 7 to age 12 and then remained stable at 3.77 mm in boys and 3.69 mm in girls. The lens thickness was found to be thinner from age 7 to age 11; it became thicker after age of 15. However, the corneal curvature remained unchanged in spite of aging and the severity of myopia.

Generalized statements can be made about myopia, given the data collected in this study. The prevalence and degree of myopia in girls was found to be more severe than in boys. As per previous reports, this study reflected that the prevalence of myopia in Taiwan has been increasing year by year. In addition, the severity of myopia and prevalence of high myopia is also steadily on the rise, due to the development of myopia at earlier ages.

Visual Impairment in Myopia

Non-pathological myopia can be somewhat inconvenient in daily life, but currently adequate means of refractive correction provide remarkable visual restoration without

hindering myopes from fully participating in their daily activities.

However, the visual impairment from myopic retinochoroidal changes, or other associated ophthalmological lesions, may induce irreversible visual deficits, even with the latest optical lens or refractive surgical techniques. Such incidents of myopia-induced visual distortion are mostly seen in cases of high myopia. Unfortunately, as was previously mentioned, high myopia has consistently increased in prevalence in recent times, especially in Taiwan.

In a 30-year follow-up of 29 high myopes, Goldschmidt noticed that ocular complications related to visual impairment began accumulating over the course of the last 10 years of follow-up. In a study of 1601 eyes of 811 high myopes, Lin correlated the severity of maculopathy with the degree of myopia, the axial length and the age of the patient. In another study, Shih postulated that the size of the optic disc crescent was related to myopic maculopathy, and this was seen in 73% of 736 high myopes. Adachi also reported that mean sensitivity loss in blue on yellow perimetry correlated with the severity of myopia, even in young patients.

Considering the global increase in the prevalence of myopia, along with the increasing population of high myopes, secondary visual functional impairment is an important issue. As a result, serious problems in aging myopes can be expected.

Therapeutic Approach

Main goals in the treatment of myopia

Means of correcting myopia have evolved over a long period of time. From the original simple glass lens, to the introduction of the multifocal lens and the contact lens, to the advent of refractive surgery, the end objective of myopic therapy was always to improve visual acuity for the myope and to temporarily reduce the progression of the disease. However, as the ways of refractive correction become increasingly complex, there is a proportional increase in the risks and complications associated with each technique. Although the aforementioned modalities can achieve satisfactory visual improvements, they still fall short in eliminating the pathological ocular changes seen in myopia. Long-standing or severe myopia may lead to retinochoroidal or structural changes in the eye, and may subsequently cause visual distortion.

In another words, with increasing rates of global myopia and high myopia, both of which can cause rather severe visual impairment, the current goals in myopia therapy should

aim to prevent the myopia-associated pathological changes of the eyes.

Myopia Therapy

There have been many proposals for alternative therapies for myopia. Traditionally, suggestions have included ocular exercise and Qi-Qong exercise.

On a more scientific level, medical therapy with a mydriatic has also been used to treat myopia. The thought is that the mydriatic agent would reduce accommodation and hence stall the development of myopia. The search for medical therapy to treat myopia is still ongoing but the results may be equivocal. Early studies looked at the application of parasympatholytic agents such as atropine and cyclogyl, parasympathomimetic agents such as pilocarpine and vagostigmine, and other sympathomimetic or sympatholytic drugs.

Recently, a long-term experiment has proven that the instillation of one drop 1% atropine in the eyes of school children before bedtime inhibits the progression of myopia after a one-year follow-up. The disadvantage for school children on such a regime is that they suffer from photophobia and difficulties in performing near work because of a dilated pupil. Fortunately, with long-term observation, we found that the photophobia component was overcome by most of the school children. In order to compensate for the paralytic accommodative status, a simple near glass lens or a multiple focal lens was prescribed.

After further evaluation, the concentration of atropine was adjusted to 0.5%. Therefore, three groups of patients were studied in our clinical trial, each with a different myopic therapy: (a) 0.5% atropine eyedrops with HOYA multifocal lenses; (b) HOYA multifocal lenses only; (c) single glass lenses only. This study followed a double-blind randomized design with a long-term follow-up.

Each group consisted of students between the ages of 6 and 13. Our observations demonstrated that the combination of a HOYA multifocal lens and a 0.5% atropine eye drop once a day at bed time significantly reduced the progression of myopia and its secondary effects on ocular structure. As one of the first paper to document such findings, this well-designed study relies on its sound scientific basis to report the promising combination of medical and optic lens therapy as an effective treatment for myopia.

Conclusion

The development of myopia relies upon genetic as well as environmental factors. It is recommended that future study designs consider both etiologies on a molecular level, researching topics such as the growth factors of myopic sclera. In the future, long-term

follow-up studies using various combinations of therapies will be the norm in evaluating definitive treatments for myopia.

References

- Chou AC, Shih YF, Ho TC, Lin LLK. The effectiveness of 0.5% atropine in controlling high myopia in children. *J Ocul Pharmacol Ther* 1997;13(1):61-67.
- Curtin B. Topics to be considered when establishing standards for clinical myopia studies. *Acta Ophthalmologica, Suppl* 1988;65:61.
- Goldschmidt E. Epidemiology of myopia: Scandinavian and Hong Kong experiences. In *Myopia Update*, Tokoro T ed Springer-Verlag Tokyo, 1998 page 3.
- Hirai H, Saishin M and Yamamoto K. Longitudinal and cross-sectional study of refractive changes in pupil from 3 to 7 year of age. In *myopia Updates*, Tokoro T ed Springer-Verlag Tokyo, 1998 page 81.
- Hu FR, Tan CY, Chang SW, Chang HW. Analysis of corneal topography after excimer laser photorefractive keratectomy. *J Formos Med Assoc* 1998;97:159-164.
- Hung PT. Studies on myopia – Epidemiology, Pathogenesis and Therapeutic approach. In *HOYA Vision Care*, Mishima S edi 1998 page 62-67.
- Hsu WM. Axial length and lens thickness in normal adult eye. *J Formos Med Assoc* 1983;82:1170-1174.
- Lin LLK, Chen CJ, Hung PT, Ko LS. Nationwide survey of myopia among schoolchildren in Taiwan, 1986. *Acta Ophthalmol* 1988;Suppl 185:29-33.
- Lin LLK, Hung PT, Ko LS, Hou PK. Study of myopia among aboriginal school children in Taiwan. *Acta Ophthalmol* 1988;Suppl 185:34-36.
- Lin LLK, Shih YF, et al. 1996 National Health Report. Report on epidemiological study of 12000 myopia among age 6 to 18 in Taiwan 1996. National Health Department Executive Yuan.
- Lin LLK, Shih TF, Hsiao CK, Chen, CJ, Lee LA, Hung PT. Epidemiological study of ocular refracton among schoolchildren in Taiwan, 2000. *J Formos Med Assoc* (In press).
- Lin LLK, Shih YF, Lee YC, Hung PT, Hou PK. Changes in ocular refraction and its components among medical students – A 5-year longitudinal study. *Optom Vis Sci* 1996;73(7)495-498.
- Lin SY, Shih YF, Lin JC, Lin LLK, Hung PT, Hou PK. Familial and environmental factors

- of highly and mildly myopic university students. *Tzu Chi Med J* 1998;10:19-27.
- Lin SY, Shih YF, Lin LLK, Jan JH, Chen CJ. Familial correlation of the optical components between myopic children. *Trans Soc Ophthalmol Sinicae* 1998;37:235-240.
- Motegi et al. Survey of the refractive status among Taiwanese aborigines I. *J. Formosan Med Assoc* 1944;43(11):778-790.
- Reiner A, Shih YF, Fitzgerald MEC. The relationship of choroidal blood flow and accommodation to the control of ocular growth. *Vision Res* 1995;35(9):1227-1245.
- Shih YF, Chen CH, Chou AC, Ho TC, Lin LLK, Hung PT. Effect of different concentrations of atropine on controlling myopia in myopic children. *J Ocul Pharmacol Ther* 1999;15:85-90.
- Shih YF, Chen MS, Hwang JK, Lin LLK, Hung PT, Hou PK. The blood-aqueous barrier in anisometropia and high myopia. *Ophthalmic Research* 1996;28:137-140.
- Shih YF, Ho TC, Lin SY, Lin LLK, Hung PT, Hou PK. The relationship between the size of optic disc crescent and myopic retinopathy. *Tzu Chi Med Journal* 1996;8:205-211.
- Shih YF, Hsiao CK, Chen CJ, Chang CW, Hung PT, Lin LLK. An intervention trial on efficacy of atropine and multifocal glasses in controlling myopic progression. *Acta Ophthalmologica* (In press)
- Shih YF, Lin SY, Huang JK, Jian SW, Lin LLK, Hung PT. The choroidal blood flow response after flicker stimulation in chicks. *J Ocul Pharmacol Ther* 1997;13(3):213-218.
- Shih YF, Wang AH, Ko LS. Refractive status of medical students in National Taiwan University. *Trans Soc Ophthalmol Sinicae* 1989;28:53-58.
- Tokoro T, Shih YF. Correlation between myopic macular chorioretinal atrophy and refractive error, axial length and age. Presented at XXVI International Congress of Ophthalmology, Singapore, 1990.
- Wong LC, Lue YF, Shih YF. Accommodation and pupillary response in early onset myopic schoolchildren. *Optom Vis Sci* 1998;75(8):611-616.
- Yen MY, Hou K, Liu JH. Contrast sensitivity in high myopia. *Trans Soc Ophthalmol Sinicae* 1990;29:21-24.
- Zadnik K and Mutti DM. Let's define myopia: A need for consensus? In *Myopia 2000, Proceedings of the VIII International Conference on Myopia, Conference on Myopia 2000 Inc. Boston USA, 2000* page 320-324.

Table 1 The Importance of Myopia

Blindness of Myopia
Epidemic with Civilization
Global increasing prevalence
Increasing high myopia
Pathophysiological Change
Structural
expansion glaucoma?
growth signal?
Physiological change
convergence and muscle
accommodation
Pathological change
retinochoroidal
optic nerve?
others?

Table 2 Epidemiology of Myopia

Mode of Myopia Development
Increasing prevalence
Myopia and high myopia
Increasing early onset of myopia
The earlier, the higher degree of myopia
Longitudinal study
Increasing rate in same age group yearly
Increasing rate and degree of myopia in same age group yearly
Intense academic pressure or near work profession

Table 3 Myopia Therapies

-
1. Traditional ocular exercise, etc.
 2. Ordinary glass
 3. Multifocal lenses
 4. Contract lens
 - Ortho-keratomelium
 5. Corneal surgery
 6. Medical Thearpy
-