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行政院國家科學委員會補助專題研究計畫成果報告

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Safety of Early Discontinuation of Prophylaxis Against *Pneumocystis carinii* Pneumonia in Patients with Advanced Stage of HIV-1 Infection: A Prospective Study

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ABSTRACT

From June 1999 to June 2002, 156 HIV-1-infected patients, 142 males, with a median age of 36 years (range, 23-73 years) who had an initial CD4+ cell count<100 x 10^6/L (median CD4+, 25 x 10^6/L; range, 0-93 x 10^6/L) and plasma viral load (PVL) of 382,000 copies/ml (RT-PCR) were enrolled in a prospective observational study aiming to ascertain if primary and secondary prophylaxis could be discontinued earlier than what is now recommended by the USPHS/IDSA guidelines for prevention of opportunistic infections, that is, CD4+≥200 x 10^6/L on two occasions with an interval of 3 months. As of October 31, 2002, at least 107 patients had discontinued PCP prophylaxis after HAART when their median CD4+ increased to 104 x 10^6/L (range, 2-586 x 10^6/L) and median PVL decreased to <400 copies/ml after a median observation duration of 14 months (range, 4-40 months). Of the 107 patients, 61 had CD4+≥100 x 10^6/L and 68 PVL<400 copies/ml. Bacterial infections developed in 17 patients (7 pneumonia or bronchitis) and new opportunistic infections in 27 patients (31 episodes), including 1 toxoplasmosis and 3 PCP. The three patients who developed PCP had virologic and immunologic failure despite HAART. We conclude that in HIV-1-infected patients who had initial CD4+ count<100 x 10^6/L, earlier discontinuation of PCP prophylaxis when CD4+ increases to≥100 x 10^6/L is safe if they respond favorably to HAART.

Key Words: *Pneumocystis carinii* pneumonia; HIV-1 infection; highly active antiretroviral therapy; trimethoprim-sulfamethoxazole; prophylaxis

BACKGROUND

Pneumocystis carinii pneumonia remains the most common cause of AIDS-defining opportunistic infections in HIV-1-infected patients who had CD4+ count<200 x 10^6/L. In order to prevent development of PCP, the expert panel of USPHS and IDSA recommend prophylaxis be given to patients with CD4<200 x 10^6/L.

With introduction of highly active antiretroviral therapy (HAART), morbidity and mortality of patients with HIV-1 infection has dramatically declined. Restoration of immunity after plasma viral load is suppressed become possible. Since 1999, several investigators have found that primary and secondary prophylaxis may be safely discontinued if patient's CD4+count has increased to ≥200 x 10^6/L on two occasions with an interval of 3 months. However, discontinuation of prophylaxis in several patients with CD4+<200 x 10^6/L did not bring with it PCP as long as patients continue to receive HAART, regardless PVL in one study. Therefore, we hypothesize

that prophylaxis against PCP can be safely discontinued when CD4+ increases to ≥100 x 10^6/L.

OBJECTIVES

This prospective observational study aimed to ascertain if prophylaxis against PCP can be safely discontinued when CD4+ increases to ≥100 x 10^6/L in 156 consecutive HIV-1-infected patients (142 males) with a median age of 36 years (range, 23-73 years) enrolled from June 1999 to June 2002 who had an initial CD4+ cell count<100 x 10^6/L (median CD4+, 25 x 10^6/L; range, 0-93 x 10^6/L) and plasma viral load (PVL) of 382,000 copies/ml (RT-PCR). The secondary end point was development of bacterial infections or new opportunistic infections other than PCP.

RESULTS

As of October 31, 2002, at least 107 patients had discontinued PCP prophylaxis after HAART when their median CD4+ increased to 104 x 10^6/L (range, 2-586 x 10^6/L) and median PVL decreased to <400 copies/ml after a median observation duration of 14 months (range, 4-40 months). Of the 107 patients, 61 had CD4+≥100 x 10^6/L and 68 PVL<400 copies/ml. 41 patients discontinued prophylaxis before CD4+ increase to≥100 x 10^6/L because of adverse effects (27 patients) and loss to follow-up (14). Over the median observation duration of 14 months (range, 4-40 months), bacterial infections developed in 17 patients (7 pneumonia or bronchitis) and new opportunistic infections in 27 patients (31 episodes), including 1 toxoplasmosis and 3 PCP. The most common new OI was herpes zoster (11 episodes), followed by NTM/MAC infection (5), CMV disease (4) and TB (3). The three patients who developed PCP had virologic and immunologic failure despite HAART because of poor adherence. We conclude that in HIV-1-infected patients who had initial CD4+ count<100 x 10^6/L, earlier discontinuation of PCP prophylaxis is afe if the patients continued to receive HAART and adhere to HIV care provided.

DISCUSSION

Our study aimed to assess the feasibility and safety of early discontinuation of primary and secondary prophylaxis. The rationale of this study was that nearly one-third of the patients developed adverse effects, especially allergic reactions, to the prophylactic regimens prescribed, most commonly, trimethoprim-sulfamethoxazole. A substantial proportion of the patients with adverse effects could not tolerate rechallenge or switch to other regimens. Therefore, if our results are confirmed by other investigators, the recommendations of preventing PCP can be revised.

The findings of our study showed that no episodes of PCP developed in patients who continued to receive HAART and adhered to HIV care which should be reassuring to the clinicians caring for HIV-infected patients at advanced stage of HIV infection who initiate HART and are intolerant of the prophylaxis regimens. Moreover, early discontinuation of antimicrobial therapy may reduce the risk for emergence of bacterial antimicrobial resistance, reduce pill burden and risk of complicated drug-drug interactions, and may have positive psychologic impact on the patients.

SELF-ASSESSMENT

The study was well conducted and the results may have a great impact on HIV care if the results are confirmed. The limitations are shorter observation duration, small case number, and not a randomized placebo control study.

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