

行政院國家科學委員會專題研究計畫 成果報告

Thalidomide 對鼠部份肝切除後肝臟再生及血管增生相關生長因子之影響

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國科會 91 年研究計畫成果報告

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ABSTRACT:

Angiogenesis plays important roles in the cancer growth of many kinds, including hepatocellular carcinoma (HCC). It is an important step in the tumorogenesis and tumor metastasis. Some antibodies to the vascular growth factor and some naturally occurring anti-angiogenesis molecules are used now in the management of cancer treatment to those refractory cancers that are unresponsive to traditional treatment modalities. Promising effects are reported in these kinds of animal and clinical experiments. Thalidomide, a sedative with anti-angiogenesis activity, which was abandoned due to its teratogenesis to fetus, is now revised because of its anti-angiogenesis activity. As important as in tumorogenesis, angiogenesis is also an important step in the regeneration of liver after partial hepatectomy. In the treatment of HCC, thalidomide shows some promising effect in the control of tumor growth. On the other hand, whether thalidomide will interfere with liver regeneration after partial hepatectomy is an interesting topic to clinicians. In this experiment, we study the effect of thalidomide on liver regeneration after hepatectomy in a rat model. The effect of Thalidomide on the healing of surgical wound will be evaluated during the same experiment.

METHODS:

Experiment animal: male Balb/c mouse of weight 20 gm

Stratification: Control group:

C0: x10, sacrificed at day 0 of partial hepatectomy

C1: x10, sacrificed at day 1 after hepatectomy

C2: x10, sacrificed at day 2 after hepatectomy

C5: x10, sacrificed at day 5 after hepatectomy

C7: x10, sacrificed at day 2 after hepatectomy

Experiment group:

Intraperitoneal injection of thalidomide 50mg/kg/day for 7 days

T0: x10, sacrificed at day 0 of partial hepatectomy

T1: x10, sacrificed at day 1 after hepatectomy

T2: x10, sacrificed at day 2 after hepatectomy

T5: x10, sacrificed at day 5 after hepatectomy

T7: x10, sacrificed at day 2 after hepatectomy

The liver weight gm per 10gm BW were measured.

The percentage of liver weight over estimated whole liver weight was calculated.

The VEGF, HGF, IGF-2 concentrations in the blood samples were determined.

RESULTS:

The standardized liver weight of experiment group at time Day0 was significantly heavier than that of control group, 0.761 vs 0.564 gm, $p < 0.0001$. The body weight of each control and experiment groups were not significantly different. In the control group, the percentage of liver regeneration a Day 1, 2, 5, and 7 were 68.7%, 81.4% , 90.1% and 97.3% respectively. The standardized liver weight had significant increment among groups along with time. But in the experiment group, the percentage of liver regeneration at Day 1, 2, 5, and 7 were 56.7%, 78.4%, 77.7%, and 68.3% respectively. There were no significant increments of liver weight along with time. As to the change of VEGF, HGF and IGF-2 concentration, they are still in progress.

CONCLUSION:

Thalidomide, through an unknown mechanism increases the intact liver weight after 7 days of intraperitoneal injection. But thalidomide will interfere the regeneration of liver after partial hepatectomy. This might be through the inhibition of some growth factors, and the factors involved in the mechanism is still under investigation by using the materials collected during this experiment.