β-胡蘿蔔素對於大白鼠酒精性肝臟疾病之影響

Effect of β-Carotene on Alcoholic Liver Disease in Rats

中文摘要

本研究利用體外及體內實驗，針對β-胡蘿蔔素與酒精性肝臟疾病之關聯性作有系統之探討。體外實驗部分，以含有粉末酒精之飼料飼養酒精組大白鼠，誘發大白鼠形成酒精性肝臟疾病，並以不含酒精之飼料飼養對照組大白鼠。10 週後，酒精組血漿中肝功能指數 GOT 與 GPT 的活性分別較對照組提高 24%以及 61%，顯示酒精組肝臟受損的情形較對照組嚴重。同時由肝臟病理切片圖可以明顯觀察到酒精組的肝臟有脂質堆積的情形。確定酒精組大白鼠形成酒精性脂肪肝後，開始進行初代肝細胞培養實驗。由對照組大白鼠所取出之初代肝細胞，依培養液中無添加或有添加β-胡蘿蔔素，分為 HC 組和 HC+B 組。同樣地，酒精組大白鼠所取出之肝細胞，依培養液中無添加或有添加β-胡蘿蔔素，分為 HE 組和 HE+B 組，並進行培養 24 小時。由初代肝細胞培養實驗之結果顯示，HE 組肝細胞生存力顯著較 HC 組降低 68%，而添加β-胡蘿蔔素後，HE+B 則是顯著較 HE 提高 42%。抗氧化酵素活性方面，HE 組之麩胱甘　過氧化　(GPX)與過氧化氫　(CAT)之活性分別顯著較 HC 組降低 54%與 31%，添加β-胡蘿蔔素後，HE+B 組之 CAT 活性則是顯著較 HE 組提高 61%。至於麩胱甘　還原　(GRD)與超氧化物岐化　(SOD)之活性，各組間無顯著差異。另外，麩胱甘　(GSH)濃度方面，HC 組與 HE 組無顯著差異，添加β-胡蘿蔔素後，HC+B 組與 HE+B 組顯著較 HC 組與 HE 組各增加 156%與 143%。脂質過氧化產物 MDA 濃度方面，各組間無顯著差異。另外，肝細胞中及培養液中β-胡蘿蔔素與維生素 A 之濃度均顯著增加。結論，添加β-胡蘿蔔素能夠使酒精性肝臟疾病大白鼠之初代肝細胞中 GSH、β-胡蘿蔔素以及維生素 A 的量增加，並提高抗氧化酵素 CAT 的活性，因而降低酒精對肝細胞所造成的傷害，提高肝細胞存活率。

體內實驗部分，以雄性 SD 大白鼠 24 隻為實驗動物，依肝功能指標 GOT、GPT 分成三組：控制組(C)、酒精組(E)及酒精補充β-胡蘿蔔素組(E+B)，每組 8 隻，實驗期為 10 週。以含有 58%粉末酒精(佐藤食品工業，日本)飼料飼養 E 組，以添加β-胡蘿蔔素之粉末酒精飼料飼養 E+B 組，對照組則是利用等熱量之方式以不含粉末酒精飼料飼養。結果顯示，與 C 組相比較，E 組的 GOT、GPT 分別顯著提高 25%與 27%，而與 E 組比較之下，E+B 組的 GOT、GPT 則分別顯著降低 12%及 15%。抗氧化能力方面，紅血球中四種抗氧化酵素活性，各組間均無顯著的變化。而肝臟中抗氧化酵素活性方面，E 組 GPX 活性顯著較 C 組下降 21%，另外，E 組 CAT 活性則是顯著較 C 組提高 27%，而補充β-胡蘿蔔素後，E+B 組 CAT 活性則是顯著較 E 組降低 20%，至於 GRD 與 SOD 活性，各組間則是無顯著之差異。GSH 濃度方面，E 組紅血球與肝臟中 GSH 含量分別顯著較 C 組減少 15%與 23%，補充β-胡蘿蔔素後，E+B 組紅血球與肝臟中 GSH 含量則是分別顯

著較 E 組增加 43%與 27%。至於血漿與肝臟中 MDA 之濃度，各組間均無顯著差異。另外，E+B 組大白鼠肝臟中有測得β-胡蘿蔔素，並同時觀察到維生素 A 含量較 E 組顯著增加 51%。在脂質代謝方面，E 組血中三酸甘油酯(TG)濃度顯著較 C 組增加 96%，而 E+B 組的 TG 則是顯著較 E 組減少 40%，高密度脂蛋白膽固醇(HDL-C)也顯著較 E 組增加 13%。至於肝中 TG 與 TC 含量，E 組較 C 組分別顯著增加 73%與 33%，E+B 組則是較 E 組分別顯著減少 38%以及 20%。血中尿酸濃度方面，E 組較 C 組顯著增加 50%，E+B 組則是較 E 組顯著減少 30%。最後，由肝臟組織病理切片觀察顯示，E 組大白鼠肝臟中有脂質堆積的現象，而 E+B 組大白鼠則無此現象。由以上結果可知，補充β-胡蘿蔔素可以抑制因長期酒精攝取所造成之抗氧化物質 GSH 的減少，並預防酒精性高脂血症、脂肪肝及高尿酸血症的形成，進而減少酒精對肝臟的傷害。

關鍵字：β-胡蘿蔔素、酒精性肝臟疾病、初代肝細胞、大白鼠

英文摘要

The purpose of this study was to investigate the effects of β-carotene on alcoholic liver diseases in rats. In vitro study was to evaluate the effects of β-carotene on the cell viability and antioxidant enzymes activities in hepatocytes from rats with alcoholic liver disease (ALD). Rats in ethanol group were given ethanol-containing diet (powdered- ethanol 58g per 100g diet), and rats in control group were fed isocaloric diet without ethanol. After 10 weeks, rats in ethanol group showed a significant increase in plasma GOT and GPT activities by 24% and 61%, respectively. Furthermore, the apparent accumulation of fat within hepatocytes was observed in ethanol group. Then, the hepatocytes were taken out and cultured for 24 hrs. Hepatocytes from control group were cultured in the medium without (HC) or with b-carotene (HC+B), and from ethanol group were also cultured in the medium without (HE) or with β-carotene (HE+B). Results showed that lactate dehydrogenase leakage (LDH leakage), which is the index of cell viability, was significantly increased by 68% in HE than in HC, but reduced by 42% in HE+B than in HE. When compared to HC, the activities of glutathione peroxidase (GPX) and catalase (CAT) in HE were significantly decreased by 54% and 31%, respectively. CAT activity in HE+B group was significantly increased by 61% than in HE. However, the activities of glutathione reductase (GRD) and superoxide dismutase (SOD) showed no difference in each group. The levels of glutathione (GSH) in HC+B and HE+B groups were significantly increased 155% and 143% than in HC and HE, respectively. The concentration of lipid peroxidation products malondialdehyde (MDA), showed no difference in each group. On the other hand, the cellular levels of β-carotene and retinol were significantly increased in HC+B and HE+B. And the levels of b-carotene and retinol

in medium increased in HC+B and HE+B. These results demonstrate that β-carotene can increase cell viability, CAT activities, GSH, β-carotene and retinol concentrations in cultured hepatocytes from rats with ALD.

In vivo study was to investigate the effects of β-carotene on antioxidant enzyme activities, lipid metabolism, and hyperuricemia in rats with ALD. Rats were divided into three groups, such as control (C), ethanol (E) and ethanol with β-carotene (E+B) groups. Rats in E group were given ethanol-containing diet (58%), in E+B group rats were fed ethanol-containing diet with β-carotene, and rats in C group were fed isoenergetic diet without ethanol or b-carotene. After 10 weeks, results revealed that plasma GOT and GPT activities in E group were significantly increased by 25% and 27% respectively than in C group. When compared to E group, plasma GOT and GPT activities in E+B group were significantly decreased by 12% and 15% respectively. The activities of erythrocyte GPX, GRD, SOD and CAT showed no difference in each group. Additionally, hepatic GPX activity in E group was significantly decreased by 21% than in C group. Hepatic CAT activity in E group was significantly increased by 27% than in C group, whereas it was significantly decreased by 20% in E+B group than in C group. The activities of GRD and SOD in liver showed no difference in each group. When compared with C group, the concentration of GSH was significantly decreased by 15% in erythrocyte and 23% in liver of E group. In E+B group, GSH content in erythrocyte and liver were significantly increased by 43% and 27% respectively than in E group. The level of MDA in erythrocyte and liver showed no difference in each group. β-carotene storage was detected in liver of E+B group. The hepatic retinol content was significantly increased by 51% in E+B group than in E group. Plasma triglyceride (TG) concentration in E group was significantly increased by 27% and 96% respectively than in C group. And the hepatic TG and total cholesterol (TC) contents in E group were significantly increased by 73% and 33% respectively than in C group. However, in E+B group, plasma TG and hepatic TG, TC levels were significantly lowered 40% and 38%, 20% respectively than in E group. Besides, both plasma TC and high-density lipoprotein cholesterol (HDL-C) concentrations were significantly increased 13% in E+B group than in E group. The level of plasma uric acid in E group was significantly increased by 50% than in C group, but it was significantly decreased by 30% in E+B group than in E group. Furthermore, the apparent accumulation of fat within hepatocytes was observed in ethanol group. Results demonstrate that b-carotene supplementation could prevent alcoholic liver diseases formation by enhancing antioxidant capacity, decreasing the plasma TG concentration, and inhibiting the accumulation of TC and TG in liver.

Key words： β-carotene、alcoholic liver diseases、hepatocytes、rats.