CB1 protein expression in high-Cd accumulated liver in local rodent (bank voles)

(การแสดงออกของโปรตีน CB1 ในตับของหนูท้องนาที่มีแคดเมียมสะสมอยู่ในปริมาณสูง)

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Abstract

Introduction: The endocannabinoid (EC) sytem composes of two specific G-protein coupled receptor; cannabinoid receptor 1(CB1) and cannabinoid receptor 2 (CB2), the endogenous lipidic ligand (endocannabinoids) and the enzymes involved in synthesizing and metabolizing endocannabinoids. The pathogenesis of liver fibrosis is associated with the upregulation of endocannabinoids and their receptor, CB1. A toxic heavy metal, cadmium (Cd) causes an adversely effects on various organs especially liver which is a main target organ of Cd toxicity. Cd can be detoxified after association with metallothionein (MT). Then, MT is known as a biomarker of tissue Cd retention. However, the CB1 expression in high-Cd liver has not been reported.

Objective: This study was to localize and investigate the CB1 protein expression in liver of bank voles that contained a high level of Cd. The level of CB1 expression was compared between high- and low-Cd livers.

Methodology: 5 bank voles from Kalasin province and another 3 bank voles from three sub-districts of Tak province, where has been reported as a high-Cd accumulated area, were used and collected their liver tissues. *MT1A* expression was used as a marker for Cd accumulated level in liver. The *MT1A* level in all liver tissues was analyzed by RT-PCR. The CB1 protein expression was studied by immunohistochemical staining. Moreover, the histopathology of all livers was also observed by H&E staining.

Result: The liver of bank voles taken from Tak province showed a high level of *MT1A* expression then, we classified as a high-Cd group. Whereas the MT1A level was low in liver of bank voles from Kalasin province which was named as low-Cd group. By H&E staining, we found a swelling hepatocytes and likely large sinusoids in liver tissue of high-Cd group. The immunoreactivity of CB1 was localized in the cytoplasm of hepatocyte of low-Cd group. Whereas CB1 immunoreactivity was predominantly expressed in cytoplasm of double nucleated hepatocyte and hepatic satellite cell (HSC).

Conclusion: Our results showed the expression of CB1 was highly detected in double nucleated hepatocyte and HSC of high-Cd liver. It has been reported that Cd exposure activated the releasing of inflammatory and cytotoxic mediators from Kupffer cell that can directly

damaged hepatocytes. The inflammatory progression induces fibrogenic process, which involves the HSC activation and hepatic myofibroblasts to the injured area, where they synthesize a various factors such as fibrogenic cytokines, and inhibitors of matrix degradation. Moreover, CB1 can mediate liver fibrosis through the effects on apoptosis and has been found in HSC of cirrhotic liver. Taken together, we suggest that Cd possibly enhances the liver inflammation, fibrogenic process and activates HSC function that can detect by CB1 upregulation.

Keyword CB1, cadmium, liver, bank voles