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Alcohol-Induced Pathological Changes of Femur and Liver in the Castrated Rats

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Introduction

Osteoporosis is usually considered a disease of older women reported the rate, pattern and determinants of bone loss, far less information is available for men although it is also common in men [1,2]. The three major causes of osteoporosis in men are excessive alcohol intake, long-term glucocorticoid therapy, and hypogonadism [3,4]. In process of bone resorption, type I collagen crosslinking molecules, pyridinoline (PYD) are released into the circulation and cleared by the kidney. ^2H_2O as a tracer has been applied to measure synthesis rates of slow-turnover proteins and successfully applied to bone collagen synthesis, skeletal muscle and cardiac muscle in rat. The objective of this study was to examine osteoporosis and alcohol-induced changes of femur and liver in post-menopausal males using the developed method.

Materials and Methods

Ten-week-old male rats were divided into the following four treatment groups: (1) sham-operated control rats receiving tap water *ad libitum* (Sham+tap group, n=6), (2) sham-operated rats receiving alcohol (Merck KGaA, Darmastadt, Germany) *ad libitum* at a concentration of 15% (Sham+alcohol group, n=6), (3) bilaterally castrated rats receiving tap water *ad libitum* (CX+tap group, n=8), and (4) bilaterally castrated rats receiving 15% alcohol *ad libitum* (CX+alcohol group, n=8). Rats were sacrificed at week 9, 15 and analyzed by histopathological study, serum PYD assay (Metra™ Serum PYD EIA kit; Quidel Corporation, Sandiego, CA), ^2H_2O labeling (Cambridge Isotope Labs, Andover, MA), and proteome analysis.

Results

Serum PYD concentration increases were observed in Sham + alcohol group, CX + tap group, and CX + alcohol group compared with Sham + tap group. CX group revealed marked changes by alcohol ingestion. It was also observed that castration was contributed to decrease of bone collagen synthesis rates in comparison with Sham group and alcohol administration of post-menopausal stage accelerated the degradation of bone. Meanwhile, the rates of collagen synthesis in liver were negative relation to bone collagen synthesis rates. Liver collagen synthesis rates were increased in alcohol ingestion group and castration group. On histopathological findings revealed the same results except the change of liver. Castration and alcohol administration were no significant effects on histopathological features of liver in comparison with sham- and tap-group.

Discussion

This study demonstrated for the first time that early change of femur and liver in post-menopausal male individuals influenced on alcohol through histopathological study, serum PYD assay, ^2H_2O labeling, and proteom analysis. We observed serum PYD was competitive enzyme immunoassay in the osteoporosis and the unique features of ^2H_2O labeling to measure collagen synthesis rates were excellent marker of bone degradation, aging and alcohol-induced early change of liver. It represented an interesting and specific biochemical marker of collagen breakdown and alcohol-induced changes on bone were more serious in post-menopausal individuals. Besides, it was observed collagen synthesis rates relation to hepatic fibrosis/cirrhosis of liver were markedly increased in post-menopausal individuals due to aging and alcohol effects, which was not detected through histopathological findings because of it's a early stage change with not a distinguishable feature. The further study of up and down regulated protein revealed in proteome analysis are needed to understand function of these proteins and protect the changes from aging and alcohol abuse.

References

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