Letter to the editor

NAFLD: a sign of "early aging"?

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To te Editor,

Hamaguchi and colleagues very recently reported aging a risk factor for non-alcoholic fatty liver disease (NAFLD) in premenopausal women, independent of weight gain or influence of metabolic syndrome (1). On the other hand, Trian et al recently showed that oestradiol (E2) is a protective factor for non-alcoholic fatty liver disease in healthy men with an odds ratio of 0.954 (95% confidence interval: 0.946-0.967). In a group of men with NAFLD, total testosterone (TT) remained stable, free testosterone (FT) and E2 declined, and hepatic fat infiltration increased (P<0.001 for both). Testosterone (T) had no significant correlation with NAFLD (2).

The question is what other novel factor(s) mediate such a relation between aging and NAFLD?

It will be interesting to combine the results of these two studies (1;2) with a novel finding on Parkinson disease, as a very classic disease of aging. Loss of dopaminergic neurons and α-synuclein accumulation are the two major pathological hallmarks of Parkinson's disease. At present, the mechanisms governing depletion of dopamine content and α-synuclein accumulation are not well understood. Marwarha and colleagues very recently showed that the oxysterol 27-hydroxycholesterol (27-OHC) reduces the expression of tyrosine hydroxylase (TH), the rate-limiting enzyme in dopamine synthesis, and increases α-synuclein levels in SH-SY5Y cells, a human derived neuroblastoma cell line. They showed that 27-OHC regulates TH and α-synuclein expression levels through the estrogen receptors (ER) and LXR. They showed that inhibition of ERβ mediated 27-OHC-induced decrease in TH expression, an effect reversed by the ER agonist estradiol. They suggest that concomitant activation of ERβ and inhibition of LXRβ prevent 27-OHC effects and may reduce the progression of Parkinson's disease by precluding TH reduction and α-synuclein accumulation (3).

To the best of our knowledge, there is no study on a relation between dopamine with NAFLD, and this seems a hot area for investigation. We propose a hypothesis that changes/ands or loss of dopaminergic neurons; and changes in sex hormones, especially E2 in men and women over the time, and interactions between these factors with LXR might predispose to NAFLD. We suggest that clinical trials investigating sex hormones in NAFLD patients of any age, measure appropriate variables such as serum dopamine, E2, and 27-OHC change to yield preliminary data for future trials. We suggest that data from previous trials that have measured sex hormones and dopamine in NAFLD patients be re-analyzed retrospectively to attempt to find out any effect from routine hepatic measures such as hepatic enzymes, serum albumin, adiponectin, prothrombin time, cholinesterase, and other parameters of hepatic protein synthesis capacity and such as those. Such data would eventually be useful for hepatic rejuvenation in NAFLD patients in future.

References

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