Leptin and Non-Alcoholic Fatty Liver Disease: Hints From Preliminary Clinical Studies

Leptin acts through LepRs, which belong to the cytokine receptor class I family. Regarding LepR, lower circulating LepRb, the predominant subunit of LepR in NAFLD patients than controls were reported [5]. The soluble LepR (sLepR), which is considered as the carrier for leptin is also found to be decreased in NAFLD patients [6]. In both studies, the circulating LepR levels were inversely correlated with leptin levels, indicating the possibility that any positive or adverse consequences of the increasing leptin. However, not all studies get the same conclusion, some other investigators reported no association of sLepR levels with NAFLD, while still others presented sLepR levels were positively correlated with the stage of hepatic fibrosis [7, 8]. These controversial results might be attributed to differences in populations (age, race, BMI, et al), inclusion criteria (staging and grading of the disease, co-morbidity et al). Another important issue is the complex in defining NASH, even if graded or staged with the same histological system, it might be not reflect the severity of disease. Furthermore, the levels of circulating leptin can be affected by BMI, while the change of BMI is not that consistent with the severity of NAFLD. Finally, leptin may act on the liver through autocrine or paracrine, therefore, the levels of circulating leptin may insufficiently reflect the diseases.

As for the leptin and leptin receptor gene expression evaluation in NAFLD populations, a small size study that based on immunohistochemistry technique has revealed higher hepatic leptin expression in NAFLD patients [9], while another two studies found no leptin gene expression in the liver [10, 11]. In a single nucleotide polymorphisms (SNPs) network analysis study, carriers of the G allele of patatin-like phospholipase domain-containing 3 (PNPLA3) SNP rs738409 showed lower peripheral LEP expression, together with higher rates of hepatic steatosis compared with CC genotype. Another SNP study showed GG homozygous showed...
73% higher hepatic fat content as compared with CC homozygous, and also the risk of progressive inflammatory and fibrosis is also significant increased [12]. Even these results are attracting, the data need to be carefully interpreted, since the studies are observational, no cause-effect mode can be established. On the other hand, large sample size studies are deficient in SNP studies because of the lack resource of getting liver tissues, the data attained may not achieve statistical power.

The aforementioned clinical data from cross-sectional studies need to be cautiously interpreted, and the results may need further verification. However, these preliminary studies indicate leptin is an active player in the development of NAFLD, and the change of leptin is differ in different stages of NAFLD, thus clarifying the mechanism of leptin in NAFLD may help to guide strategy making in phase treatment on NAFLD patients.
References


