

EFFECTS OF BARIATRIC SURGERY ON NON-ALCOHOLIC FATTY LIVER DISEASE: THE ROLE OF MACROPHAGE-MEDIATED SYSTEMIC INFLAMMATION

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Background and Aims: Obesity is a pathologic condition that is characterized by a state of chronic low-grade systemic inflammation that contributes to development of comorbidities, including non-alcoholic fatty liver disease (NAFLD). The microenvironment generated by NAFLD in the liver tissue influences the proliferation and activation of a type of macrophages and the release of certain molecules that promote tissue damage. Macrophages play a major role in the immune system, specially because liver tissue homeostasis is maintained through an adequate balance of pro- and anti-inflammatory state. In order to identify potential therapeutic approaches, the aims of our study were to investigate how bariatric surgery modulates the inflammation and, in addition, whether this fact influences the pathogenesis of NAFLD.

Method: We carried out an observational, prospective, single-site and cross-sectional study with a pre-set duration of 1 year with patients who underwent bariatric surgery (n=120) as a model of obesity-induced NAFLD and lean healthy (n=50) as a control group. Liver biopsy and a blood collection were obtained immediately before bariatric surgery and after a 12-month period. We performed immunohistochemical, western blot and ELISA analysis to evaluate several inflammatory changes such as infiltration of macrophages (CD68) and expression/location of Chemokine (C-C motif) Ligand 2 (CCL2), Tumor Necrosis Factor alpha (TNF- alpha), Interleukin 10 (IL-10) and Galectin-3 (Gal-3).

Results: After bariatric surgery there was a significant improvement of liver tissue corresponding with a significant decrease in the presence of hepatic steatosis, acute inflammation and fibrosis after one year. These results contrasted with a significant profile change regarding the presence of macrophages in the liver, on the same line the alterations in the expression/secretion of CCL2-CCR2 axis, TNF- α , IL-10 and Gal-3. In addition, plasma levels of CCL2, TNF- α , IL-10 and Gal-3 showed significant differences after 12 months in patients who underwent bariatric surgery.

Conclusion: Bariatric surgery modulates the proliferation and activation of macrophages, specially, it modifies the secretion/release of molecules associated with the progression of NAFLD. Therefore, the

expression of CCL2, TNF- α , IL-10 and Gal-3 has been proposed as possible therapeutic targets and biological markers of the stages of NAFLD.

Figure:

