BACKGROUND/AIMS: Intestinal bacteria induce endogenous signals that play a pathogenic role in hepatic insulin resistance and non-alcoholic fatty liver disease. Probiotics could modulate the gut flora and could influence the gut-liver axis. We aimed to investigate the preventive effect of two probiotic mixtures on the methionine choline-deficient diet-induced non-alcoholic steatohepatitis model in rats.

METHODS: Two studies, short-term (2 weeks) and long-term (6 weeks), were carried out using 60 male Wistar rats. The 2-week study included six groups. Rats were fed with methionine choline-deficient diet or pair-fed control diet and were given a placebo or one of two probiotic mixtures (Pro-1 and Pro-2) by orogastric gavage. In the 6-week study, rats were allocated into four groups and were fed with methionine choline-deficient diet or pair-fed control diet and given a placebo or Pro-2. At the end of the 2- and 6-week periods, blood samples were obtained, the animals were sacrificed, and liver tissues were removed. Serum alanine aminotransferase activity was determined; histologic and immunohistochemical analysis was performed for steatosis, inflammation, protein expression of tumor necrosis factor-?, and apoptosis markers.

RESULTS: In both studies, methionine choline-deficient diet caused an elevation of serum alanine aminotransferase activity, which was slightly reduced by Pro-1 and Pro-2. In the 2- and 6-week studies, feeding with methionine choline-deficient diet resulted in steatosis and inflammation, but not fibrosis, in all rats. In the 2-week study, in rats fed with methionine choline-deficient diet and given Pro-1, steatosis and inflammation were present in 2 of 6 rats. In rats fed with methionine choline-deficient diet and given Pro-2, steatosis was detected in 3 of 6 rats, while inflammation was present in 2 of 6 rats. In the 6-week study, in rats fed with methionine choline-deficient diet and given Pro-2, steatosis and inflammation were present in 3 of 6 rat livers. In both the 2- and 6-week studies, methionine choline-deficient diet resulted in tumor necrosis factor-?, proapoptotic Bax, caspase 3, caspase 8, and anti-apoptotic Bcl-2 expression in all rat livers. Pro-1 and Pro-2 treatment influenced protein expression involved in apoptosis and tumor necrosis factor-? in varying degrees.

CONCLUSIONS: Pro-1 and Pro-2 decrease methionine choline-deficient diet-induced steatohepatitis in rats. The preventive effect of probiotics may be due, in part, to modulation of apoptosis and their anti-inflammatory activity.

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