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ORIGINAL RESEARCH

High-fat liquid "Lieber-DeCarli" diet for an animal model of nonalcoholic steatohepatitis: does it really work?

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Abstract We could not reproduce the model described by Lieber et al for nonalcoholic steatohepatitis model in rats. In our trial the high fat liquid diet group of rats gained nearly 100 g or less weight compared to the mean weight gain stated in the original article. However, the fasting glucose level was statistically higher in this group as compared to the chow diet group. Some pathological abnormalities in the duodenum and jejunum samples were observed in the high fat liquid diet group. We do not know the exact reason for these changes. Overall, our study results arose some suspicions about the reproducibility of the model. Furthermore, to the best of our knowledge, no study using the proposed model has been published so far.

Keywords High-fat liquid diet · Lieber-DeCarli diet · Nonalcoholic steatohepatitis · Animal model

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Nonalcoholic steatohepatitis (NASH) is one of the most common diseases in the Western world. An ideal animal model that could let us unveil the pathophysiology of the disease and also test the potential treatment modalities does not exist yet. Lieber et al. proposed such a model for NASH in 2004 [1]. They claimed that with a high-fat liquid (LDC) diet (that derived 71% of energy from fat), a model could be established in 3 weeks and this would be successful in reflecting all the pathological aspects of NASH in humans. We aimed to perform a pilot study to ascertain the aforementioned model. Two groups of Sprague–Dawley rats—eight for the LDC diet group and eight for the control chow diet group—were used. Mean weight of the rats was 135 ± 2.5 g. All rats were allowed ad libitum type of eating and survived till the end of the trial. At the third week from the start of the study, the rats were decapitated. Samples of blood and liver tissues as well as stomach, duodenum, ileum, and colon tissues were obtained. The fasting glucose, aminotransferases, and other biochemical tests were carried out. After 3 weeks, mean weights of the rats were 211 ± 7.2 g in the LDC diet and 215 ± 8.3 g in the chow diet group, respectively ($P > 0.05$). The liver wet weights were 8.1 ± 0.3 g vs. 8.0 ± 0.4 g ($P > 0.05$). Other biochemical tests from the sera were as follows: ALT 61.5 vs. 54 U/L, AST 246 vs. 254 U/L, alkaline phosphatase 532 vs. 503 U/L, gamma glutamyl transferase 2.4 vs. 2.0 U/L, respectively (all $P > 0.05$). The only statistically significant difference was in fasting blood glucose, which was 319 mg/dL in the LDC diet group vs. 114 mg/dL in the controls ($P = 0.001$). Histopathological examination of the liver sections were normal in the chow diet group, and none of the LDC diet group of rats developed NASH—with the exception of 1–2% of microsteatosis observed in only two rats. The tissue samples from the stomach and colon were also normal in the LDC diet group. However, in the

samples from the duodenum and jejunum of the same group, an increased infiltration of inflammatory cells ($n = 3$), cryptitis ($n = 2$), superficial erosions ($n = 2$), focal but deep ulceration ($n = 1$), and diffuse and deep ulceration ($n = 1$) were reported.

In summary, we could not reproduce the model described by Lieber et al. In our trial, the LDC diet group of rats gained nearly 100 g or less weight compared to the reference [1]. However, the fasting glucose level was statistically higher in this group as compared to the chow diet group. Some pathological abnormalities in the duodenum and jejunum samples were observed in the LDC group. We do not know the exact reason for these changes. Furthermore, to the best of our knowledge, no study using the proposed model has been published so far. Our study results may indicate a problem of inconsistency of the LDC diet and there also arose some suspicions about the reproducibility of that model. The debate about consistency and reproducibility of the high-fat diets has been going for years in the literature. Some authors have demonstrated that when high-fat diets are given as ad libitum, normal rats become obese and develop hepatic steatosis [2–5]. But on the other hand, some other studies showed that it is difficult to induce obesity in normal rats with that type of feeding [6–8]. That inconsistency problem may be related to the self-limiting nature of ad libitum type of feeding.

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