

論 文 要 旨

The administration of hepatocyte growth factor prevents total parenteral nutrition-induced hepatocellular injury in a rat model

ラットモデルに対する肝細胞増殖因子投与は、
完全静脈栄養関連肝障害を予防する。

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Abstract

Purpose: The pediatric patients with gastrointestinal disorders which cause intestinal failure such as Hirschsprung's disease, midgut volvulus, necrotizing enterocolitis and inflammatory bowel disease require long term total parenteral nutrition (TPN) and fasting. However, TPN leads to parenteral nutrition-associated liver disease (PNALD). Hepatocyte growth factor (HGF) is the polypeptide as potent hepatocyte mitogen. It has also multifunction such as anti-inflammation and antioxidant action. However, the effect of HGF for PNALD is not clear. The aim of this study is to evaluate the effect of HGF for PNALD in a TPN and fasting rat model. **Methods:** Using Sprague-Dawley rat, a catheter was placed in the right jugular vein received 7-day continuous TPN and fasting. All rats were divided into 3 groups (each group: n = 8): TPN-alone [TPN group], TPN plus intravenously administration of HGF at 0.3mg/kg/day [TPN+HGF(Low) group], and TPN plus HGF at 1.0mg/kg/day [TPN/HGF(High) group]. Final TPN composition was glucose 12.5 g, amino acids 2.0 g, fat 2.1 g. On day 7, the rats were euthanized, and the liver specimens harvested. The liver tissue was histologically analyzed, and in the pathological evaluation, the nonalcoholic fatty liver disease (NAFLD) score was used for quantitative analysis. **Results:** Histologically, hepatic steatosis and infiltration of inflammatory cells in all groups were observed, but TPN+HGF(Low) group and TPN+HGF(High) group revealed less findings of hepatic steatosis and inflammation compared with TPN group (Figure 1). In the pathological findings using NAFLD score, both steatosis and lobular inflammation score in the TPN+HGF(Low) group and the TPN+HGF(High) group were significantly lower compared with those in the TPN group [Steatosis: 1.13 ± 0.64 vs. 2.75 ± 0.46 ($p < 0.01$), 0.88 ± 0.64 vs. 2.75 ± 0.46 ($p < 0.01$), respectively], [Lobular inflammation: 1.38 ± 0.74 vs. 2.87 ± 0.35 ($p < 0.01$), 1.13 ± 0.64 vs. 2.87 ± 0.35 ($p < 0.01$), respectively]. NAFLD activity score in the TPN/HGF(Low) group and the TPN/HGF(High) group were significantly lower compared with that in the TPN group [3.13 ± 1.96 vs. 6.88 ± 1.13 ($p < 0.01$), 2.25 ± 1.75 vs. 6.88 ± 1.13 ($p < 0.01$), respectively.] (Figure 2). **Conclusion:** The intravenously administration of HGF in a TPN and fasting rat model attenuates hepatic steatosis and inflammation dose-dependently. HGF would be effective for PNALD.

Fig. 1 Representative histological findings of the liver tissue specimens

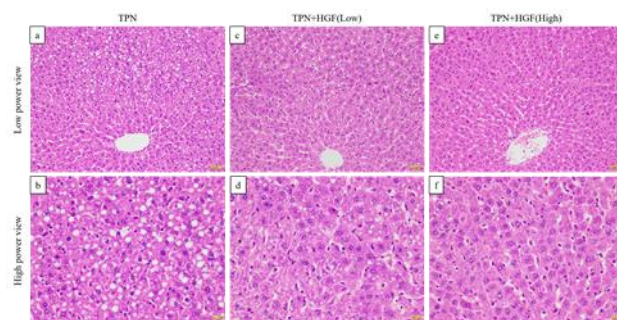
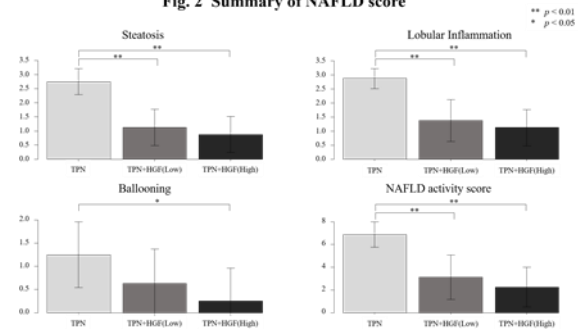


Fig. 2 Summary of NAFLD score



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