Antihypertensive therapy improves insulin resistance and serum levels of interleukin-6 and -10 in spontaneously hypertensive rats with steatohepatitis

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ファイル（説明）	博士論文全文 博士論文要旨 最終試験結果の要旨 論文審査の要旨
別言語のタイトル	降圧療法は,脂肪肝炎を誘導した高血圧モデルラットのインスリン抵抗性,および血清中のIL-6とIL-10濃度を改善する
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論 文 要 旨

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【Introduction】Metabolic syndrome based on insulin resistance (IR) and hypertension is risk factors for both advanced liver disease and cardiovascular disease in patients with nonalcoholic steatohepatitis (NASH). We investigated the effects of severe hypertension induced by a high-salt (HS) diet and antihypertensive therapy on the pathophysiological condition of spontaneously hypertensive rats (SHRs) with steatohepatitis. Steatohepatitis was induced by a choline-deficient, L-amino acid–defined diet (CDAA).

【Methods】Seven-week-old male SHRs were randomly divided into five groups: those receiving six weeks of standard chow with normal-salt concentration, followed by an additional 8 weeks of a standard chow or CDAA with normal-salt (control and CDAA groups, respectively); and those receiving six weeks of standard chow with HS, followed by a CDAA containing HS for an additional 8 weeks with or without the anti-hypertensive agents amlodipine or hydralazine.

【Results】In the CDAA and CDAA+HS groups, blood pressure was significantly correlated with serum levels of insulin, fasting blood glucose, and homeostasis model assessment-IR (HOMA-IR). Antihypertensive therapy ameliorated elevated glucose, insulin, and HOMA-IR. Furthermore, increased serum interleukin (IL)-6 levels following the CDAA+HS diet were attenuated by antihypertensive therapy. Additionally, serum IL-10 levels were increased by antihypertensive therapy, and the decreased proportion of splenic CD4+CD25+Foxp3+ T cells observed following a CDAA+HS diet tended to be restored by amlodipine.

【Conclusions】Antihypertensive therapy improved glucose metabolism and imbalances of cytokine expression in a rat model of hypertension with steatohepatitis, suggesting that antihypertensive therapy acting through immunological factors may be beneficial for patients with metabolic syndrome–associated NASH.