トレーニングが慢性腎臓病の進行に与える影響の解析

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Exercise Effect on Progression of Chronic Kidney Disease

by

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ABSTRACT

Chronic kidney disease（CKD）is a worldwide health burden that afflicts approximately 10,000,000 people even only in Japan. The unsolved issues around CKD lie not only in high, mainly cardiovascular, mortality of patients with end stage kidney disease but also in substantial expenditure for maintenance dialysis therapy. Unfortunately, effective remedies against CKD have not been well established although recent clinical trials casted light on several pharmaceutical agents for diabetes and hypertension such as renin-angiotensin-aldosterone（RAA）system inhibitors and sodium/glucose cotransporter 2（SGLT-2）inhibitors. Since aerobatic exercise benefit on CKD progression is controversial, we designed animal experiments in which two

different, immunologic and metabolic, renal injury models were conducted to mice which were concurrently subject to treadmill running test for 1 hour per day, 5 times per week. First, the exercise for 1 week prior to disease induction had no effect on albuminuria 8 hours after the induction, of mice with acute passive nephrotoxic serum induced glomerulonephritis. Secondly, we focused on diet-dependent renal injury and confirmed that high fat diet for only 8 weeks conferred to a significant amount of albuminuria in mice. Interestingly, the treadmill test for 8 weeks reduced albuminuria in mice fed with high fat diet as well as suppression of body weight gain. This result indicating that metabolic disorder based renal damage more than immunological renal damage may be able to receive benefits of the aerobatic exercise, raises a possibility that aerobatic exercise may prevent dyslipidemia-mediated CKD progression in a clinical setting. As to mechanistic process, in addition to improvement of systemic lipid and diabetic profile by skeletal activity, mitigation of renal lipotoxicity or enhancement of myokine action may also be contributory. Further study is needed to elucidate the underlying mechanism of the exercise effect on different animal CKD models.

要　旨

慢性腎臓病は国内患者数が約 1000 万人に達するともいわれる．進行例では心血管系合併症の危険が高まり生命予後が脅かされるのみならず，透析療法に係る経済負担が社会的課題となっている．慢性腎臓病に有効な治療は数少なく運動療法の意義も確立されていない．今回我々は，運動との関係性が検討されていないマウス腎臓病モデル（急性受動的腎毒性血清腎炎モデル及び高脂肪食負荷蛋白尿モデル）を用いて，トレッドミル運動（有酸素運動）1 時間週 5 回がアルブミン尿を軽減させるか検証した．前者の免疫学的モデルでは運動による改善効果は認められなかったが，後者の脂質代謝異常モデルでは 8 週間の継続的なトレッドミル運動が体重減少及びアルブミン尿減少に有用であることが分かった．以上より，腎臓病の成因によっては有酸素運動が有効である可能性がある．今後さらに分子機序を究明するとともに，他の腎臓病モデルでの運動の病態改善効果を検証する．