

ラット心臓アデニンヌクレオチドおよびミトコンドリア酸化リン酸化反応に及ぼすアドレノクロムの効果

G.M.L. Taam*, 竹尾 聡, A. Ziegelhoffer*, P.K. Singal*,
R.E. Beamish*, N.S. Dhalla*

Canadian Journal of Cardiology 2(2) 88-93 (1986)

Effect of adrenochrome on adenine nucleotides and mitochondrial oxidative phosphorylation in rat heart

Gina M.L. TAAM*, Satoshi TAKEO, Attila ZIEGELHOFFER*, Pawan K. SINGAL*,
Robert E. BEAMISH*, and Naranjan S. DHALLA*

ABSTRACT: Effects of adrenochrome, an oxidation product of epinephrine, on myocardial energy production were investigated by studying changes in adenine nucleotide content and mitochondrial oxidative phosphorylation activities in the isolated rat heart. Perfusion of the heart with 50 mg/L adrenochrome induced a marked decline in contractile force within 5 min and this was associated with a rapid decline in the myocardial ATP/AMP ratio. A significant decrease in ATP and ATP/ADP ratio as well as a significant increase in ADP and AMP content was observed at 10 min of perfusion with adrenochrome. Furthermore, mitochondrial oxidative phosphorylation activities were unchanged except that an increase in state 4 respiration and a decrease in RCI value were seen in the heart perfused with adrenochrome for 10 min. Autoradiography of the sections from hearts perfused with ¹⁴C-adrenochrome revealed the localization of a significant amount of radioactivity on mitochondria. Adrenochrome at concentrations of 20 mg/L or higher was found to inhibit the oxidative phosphorylation activities of heart mitochondria under in vitro conditions. The depressant effects of adrenochrome on mitochondrial oxidative phosphorylation were additive to those seen with calcium. These data suggest that adrenochrome in the presence of excess calcium in the myocardial cell may impair the process of energy production in mitochondria and this may result in contractile failure of hearts exposed to this cardiotoxic metabolite of epinephrine .

抄録 エピネフリン酸化生成体であるアドレノクロムのラット摘出心臓におけるアデニンヌ

クレオチドとミトコンドリア酸化的リン酸化活性に及ぼす効果を検討した。50mg/l アドレノクロムで灌流した摘出ラット心臓における ATP, ATP/ADP 比は減少し、ADP, AMP は増加した。ミトコンドリアの state4 と RCI 値は減少した。¹⁴C-アドレノクロムを灌流した組織オートラジオグラフィーによればアドレノクロムがミトコンドリア膜に局在化していることがわかった。In vitro における酸化的リン酸化能はアドレノクロムと Ca²⁺ とが共存すると阻害された。これらのデータは心臓が Ca 過負荷状態でアドレノクロムの作用を受けると心機能不全に陥いる可能性を示唆した。

* Faculty of Medicine, University of Manitoba, マニトバ大学医学部