UNIVERSITI TEKNOLOGI MARA

EFFECT OF EXOGENOUS LEPTIN AND EXERCISE ON BLOOD PRESSURE, RENAL SODIUM HANDLING AND EXPRESSION OF LEPTIN RECEPTOR IN NORMOTENSIVE SPRAGUE DAWLEY RATS

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Faculty of Medicine

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AUTHOR'S DECLARATION

I hereby declare that the work in this thesis was carried out in accordance with the regulations of Universiti Teknologi MARA. It is original and is the result of my own work, unless otherwise indicated or acknowledged as referenced work. This thesis has not been submitted to any other academic or non-academic institution for any other degree or qualification.

I also hereby acknowledge that I have been supplied with the Academic Rules and Regulations for Post Graduate Studies, Universiti Teknologi MARA, regulating the conduct of my study and research.

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ABSTRACT

Although leptin has been shown to increase blood pressure (BP), it is however unclear if this increase can be prevented by exercise. This study therefore investigated the effect of leptin treatment with concurrent exercise on blood pressure (BP), electrolytes output, creatinine clearance, urinary protein and albumin excretion, endothelin-1 (ET-1) and ICAM-1 levels and expression and localization of leptin receptor in normotensive rats. Ninety-four Male Sprague-Dawley rats weighing 250-270 g were divided into four groups consisting of a control group, leptin-treated, non-leptin-treated exercise group, and a leptin-treated exercise group. Leptin was given subcutaneously daily for 7, 14 and 42 days (60 µg/kg/day). Animals were exercised on a treadmill for 30 minutes at a speed of 0.5 m/s and at 5° incline four times per week. Measurement of systolic blood pressure (SBP) and collection of urine samples for estimation of electrolytes and creatinine was done once a week. Serum samples were collected at the end of the experiment for determination of electrolyte excretion, creatinine, ET-1 and ICAM-1 levels. Leptin receptor for gene expression and localization were determined from the rat's kidney. Data were analysed using ANOVA and post-hoc analysis and were presented as mean \pm S.E.M. Overall, when compared the treatment between 7, 14 and 42 days, mean SBP and serum ET-1 levels in the leptin-treated group was significantly higher than that in the control group whereas mean SBP and serum ET-1 level was significantly lower in the leptin-treated exercise group than those in leptin-treated and control groups. However, in 42 days treatment, SBP was decreased slowly after 21 days till up to 42 days of leptin treatment. Creatinine clearance, urinary sodium, potassium and calcium excretion, and urine output were not different between the four groups. Regular treadmill exercise prevents leptin- induced increases in SBP in rats, which might in part result from increased urinary sodium excretion in 14 days treatment and preventing the leptin-induced increases in serum ET-1 concentration. Although more studies are needed to elucidate the precise mechanism by which exercise prevents leptin-induced increases in blood pressure, it nevertheless suggests that exercise could be used as a modality in the prevention of rise in blood pressure in hyperleptinemic individuals, particularly those who are overweight.

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"Read! In the name of your Lord who created - Created the human from something which clings. Read! And your Lord is Most Bountiful- he who taught (the use of) the Pen, Taught the human that which he knew not"...Surah al-Alaq (1-5)

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