UNIVERSITI TEKNOLOGI MARA

EFFECT OF EXOGENOUS LEPTIN ON BLOOD PRESSURE, URINARY PROTEIN EXCRESION, ENDOTHELIAL ACTIVATION AND ACE2 EXPRESSION DURING PREGNANCY IN THE RAT

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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

Raised leptin levels have been reported in placentae and serum of women with elevated blood pressure and proteinuria during pregnancy. The role of leptin in this however remains unclear. ACE2 is a new member in RAAS, which is reported to have hypotensive and anti-inflammatory effect and its suppression leads to increased blood pressure and endothelial activation. Therefore, this study investigated the effect of leptin and xanthenone (ACE2 activator) administration on systolic blood pressure (SBP), proteinuria and serum markers of endothelial activation during pregnancy in Sprague-Dawley rats. Eighty female Sprague-Dawley rats, aged 12-13 weeks were randomised into 10 groups, Group 1 acted as a control non-pregnant group and given saline (NSNP). Group 2, control pregnant rats, was given saline (NSP), group 3 was given 60 μg / kg /day of leptin starting from the 1st day of pregnancy (LD1-60), group 4, was given 60 μg / kg /day of leptin starting from the 10th day of pregnancy (LD10), group 5, given leptin from day 16 of pregnancy (LD16). Group 6 (L14D-60), given leptin approximately 14 days before pregnancy, Group 7 was non-pregnant rats receiving leptin for a period of 20 days (LNP). Group 8, given 60 μg / kg /day of leptin with 600 μg / kg /day of xanthenone (XNT), an ACE2 stimulant from day 1 of pregnancy (L+ACE2a), while group 9 was given 600 μg / kg /day of XNT alone starting from day 1 of pregnancy (ACE2a). Group 10 was given 120 μg / kg /day of Leptin starting from day 1 of pregnancy (LD1-120). SBP, serum ACE, ACE2, endothelin-1, E-selectin and ICAM-1 levels were estimated. ACE2, endothelin-1, E-selectin and ICAM-1 gene expressions were determined in the kidney and aorta. Data were analysed using ANOVA and post-hoc analysis, data are presented as mean ± S.E.M. Compared to group 1, SBP was higher in the leptin only treated group ($P<0.001$) and lower in rats treated with xanthenone alone ($P< 0.01$). ACE2 activity and expression were lower in leptin only treated rats ($P<0.05$). Urine protein excretion, serum endothelin-1, serum E-selectin, and ICAM-1 levels were significantly higher than controls in leptin only treated rats ($P<0.05$) but not in the others. It seems, leptin administration during pregnancy significantly increases SBP, urinary protein excretion, levels and expression of markers of endothelial activation, but decreases the level and expression of ACE2. These effects are prevented by xanthenone, implicating the role of ACE2 in leptin-induced raised blood pressure and proteinuria during pregnancy. However, further studies are required to examine the underlying mechanism responsible for this and its relevance to preeclampsia in humans.

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