UNIVERSITI TEKNOLOGI MARA

ADVERSE EFFECTS OF NICOTINE ON DECIDUALIZATION, PREGNANCY AND PARTURITION

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AUTHOR'S DECLARATION

I 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 institutions or non-academic institution for any other degree of qualification.

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

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ABSTRACT

Nicotine was shown to adversely affect female reproduction, however the mechanism of nicotine action remains unclear. One of the possibility is the altered reproductive endocrine profile. This study was designed to investigate the effects of nicotine on several female reproductive processes and the corresponding endocrine profile. Different nicotine dose administration and treatment duration on estrous cycle, decidualization and pregnancy outcome were carried out. Nicotine tartrate 7.5 mg/kg/day administered sc for five days following unilateral ovariectomy was shown to prolong the estrous cycle duration ($p<0.001$) with no change seen in the number of ova flushed and no alteration in endocrine profile was demonstrated. Administration of 5.0 mg/kg/day nicotine tartrate failed to demonstrate attenuation in decidualization, however nicotine tartrate 7.5 mg/kg/day was found to increase the adrenal glands weight following treatment for nine days ($p<0.01$) in pseudopregnant rats. The degree of decidualization in animals receiving 7.5 mg/kg/day nicotine tartrate was significantly attenuated in all the treatment schedules and was more pronounced in animals receiving longer nicotine treatment ($p<0.001$). The level of plasma estrogen was significantly higher ($p<0.05$) and the plasma progesterone was significantly lower ($p<0.001$) in animals receiving longer nicotine treatment. Exogenous progesterone administration (2mg/day) failed to completely reverse the deleterious effect of nicotine on decidualization. In pregnant rats, administration of nicotine tartrate 7.5 mg/kg/day for nine days significantly increased the number of fetal loss by 2.86 times on day 16 of pregnancy compared with control. The weight of the feto-placental unit was also significantly reduced ($p<0.001$). The estrogen level was significantly higher ($p<0.01$) and progesterone was significantly lower ($p<0.05$) on day 16 of pregnancy when compared with control. During parturition, there was an increase in fetal loss when compared with the blastocyst implantation sites on day 10 of pregnancy. This was seen when nicotine was given for nine days ($p<0.001$) or from day 5 through day 9 of pregnancy ($p<0.001$). The birth weight of the pups was also significantly reduced in nicotine-treated groups however the weight was normalized after a few days. The persistent endocrine profile seen with an increase in estrogen and a decrease in progesterone may play a role in derangement of the reproductive process following nicotine administration. However, administration of exogenous progesterone failed to completely reverse this derangement point to other possibilities of reproductive dysfunction apart from sex hormones profile. In conclusion, nicotine-induced reproductive dysfunction is possibly mediated through multiple mechanisms.

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