ABSTRACT

THE MECHANISM OF FOLICULOGENESIS DISORDER ON *MUS MUSCULUS* MICE EXPOSED TO CIGARETTE SMOKE

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Background: The cause of female infertility, according to WHO, is ovulation disorders, amounting to 33%. Disorders of ovulation process are usually caused by hypothalamic-pituitary, ovarian, and endometrial disorders. Therefore, it causes disruption of the follicular maturation process and impaired implantation. One of the triggers of oocyte maturation process disruption is the presence of Reactive Oxygen Species (ROS) which can affect the occurrence of oxidative stress, one of which is caused by substances contained in cigarette smoke. Based on the reality of society, the reality in the community, smoking habit remains difficult to stop, even though health workers and media have often socialized about the dangers of cigarette smoke.

Material and Methods: This study utilized a true experimental design with a post-test control group. The subjects used in this study were 20 female Balb/c mice (*Mus musculus*) aging approximately 8-10 weeks, weighing 25-30 grams. The independent variable was the exposure to cigarette smoke, while the intermediate variables include MDA level, GnRH level, HSP70 expression, Smad3 expression, GDF9 expression, theca cell apoptosis index, oocyte cell apoptosis index, and the dependent variable was the number of follicles. Data analysis uses independent t-test or Mann Whitney's test.

Results: The results show that cigarette smoke increased the MDA level ($p = 0.001$), decreased the GnRH level ($p = 0.000$), decreased HSP 70 expression in theca cells ($p = 0.002$), decreased Smad 3 expression ($p = 0.000$), decreased GDF 9 expression ($p = 0.000$), and increased the theca cell apoptosis index ($p = 0.000$). However, cigarette smoke did not affect the oocyte apoptosis index ($p = 1$) and increased follicular disorder ($p = 0.000$).

Conclusions: The mechanism of folliculogenesis disorders due to the exposure to cigarette smoke goes through theca cell pathway, resulting on MDA level increase, GnRH level and HSP 70 expression decrease, and apoptosis increase in theca cells, there by increasing folliculogenesis disorders. Besides, cigarette smoke affects granulosa cells through the decrease of Smad3 and GDF9 expressions through the necrosis pathway in oocytes, there by reducing the number of follicles in the ovary.

Keywords: MDA, GnRH, folliculogenesis, cigarette smoke, mice.