

**Effects of Testosterone and Oxandrolone on the mRNA Expression of
SARS-Cov2 virus-Entry Genes in the Lung of Mice**

By

Dana Ismail Lutfi ALNajjar

Supervisor

Dr. Yazun Jarrar

Al-Zaytoonah University of Jordan, 2021

Abstract

Introduction: There are different opinions on the incidence of COVID-19 between males and females, and on how do testosterone and oxandrolone affect the entry of the coronavirus.

Aims: This study aimed to find out the effect of testosterone and oxandrolone on mRNA expression of the SARS-Cov2 entry genes: *ace2*, *tmprss2*, and *cathepsin* genes.

Methods: Twenty-eight balb/c mice were divided into 4 groups and were administrated separately with the vehicle, testosterone, oxandrolone, and the untreated female group in clinically equivalent doses for 21 days. Then, the expression of SARS-Cov2 entry genes *ace2*, *tmprss2*, and *cathepsin* were analyzed using a real-time PCR assay. In addition, the testosterone level in the blood was analyzed and the total body weight of the mice was measured before and after administration of the drugs.

Results: It was found that the mice in both testosterone and oxandrolone administrated groups showed a significant increase in the total body weight by 3.5 and 8.1 Kg, respectively. In addition,

the mRNA expression of the *ace2* gene was upregulated significantly (P value < 0.05) in the mice's lungs of the testosterone-administrated group by 2.5 folds and it was higher in the female group by 3.41 folds. The *tmprss2* gene expression was upregulated significantly (P value < 0.05) in the oxandrolone-administrated group by 6.6 folds and it was higher in the female group by 3 folds. However, the mRNA expression of the *cathepsin l* was higher significantly (P value < 0.05) in the female group by 2.6 folds, but the upregulation of the cathepsin after administrated of the testosterone and the oxandrolone failed to reach the statistical significance (P value > 0.05). Additionally, the administration of testosterone and oxandrolone caused pathohistological alterations, where both drugs induced inflammation and oxidative stress in the lungs of the administrated mice.

Conclusion: It was found that there are significant differences in the mRNA expression of SARS-Cov2 entry genes in the lungs between male and female mice. Administration of testosterone and oxandrolone drugs to the male mice upregulated significantly the mRNA expression of *ace2* and *tmprss2*, respectively, in the mouse lungs. These results can increase our understanding of the molecular mechanism of the sexual hormones on the mRNA expression of SARS-Cov2 entry genes and can explain, at least in part, the difference in the incidence of SARS-Cov2 infection between males and females.

Keywords: Testosterone, Oxandrolone, gene expression, lung, SARS-Cov2.