The Protective Role of Metformin against Oxandrolone-Induced Mood Depression and Infertility in Rats

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ABSTRACT

Background: Oxandrolone is a synthetic testosterone analogue that preserves or restores muscle mass and is widely used among bodybuilders and athletes. Oxandrolone is associated with many different side effects, such as hepatic impairment, sexual dysfunction and mood depression. On other hand, the antidiabetic metformin is known to reduce the infertility in diabetic patients .

Aim: The aim of this study is to investigate the protective role of metformin against oxandrolone induced mood depression and infertility.

Methods: Twenty eight rats were divided into 4 groups, each group consisted of 7 rats. The first group received the vehicle dimethyl sulfoxide, second received 0.28 mg/kg oxandrolone, third group was administrated 0.28 mg/kg oxandrolone plus 70 mg/kg metformin, and the last group received 70 mg/kg metformin. The administration was for continuous 14 days in doses equivalent to the doses used clinically. During drug administration, the alterations in the mood were examined using sucrose intolerance and

Swimming Force test. After rat's scarification, testes and livers were isolated from the rats for analysis of the morphological, histological, biochemical and gene expression analysis.

Result: It was revealed that oxandrolone significantly (ANOVA, *P* value < 0.05) reduced the relative weights of testes, while metformin attenuated significantly this reduction in the relative testes weights. The sperm count was decreased significantly (*P* value < 0.05) in rats treated with oxandrolone by 82%, while metformin normalized the sperm count to reach to reach 51% of the sperm count of the control group. In addition, metformin prevented significantly (ANOVA, *P* value < 0.05) the sharp decline in serum testosterone levels induced by oxandrolone. CYP11A1 was downregulated significantly (ANOVA, *P* value < 0.05) in the testes of oxandrolone-treated rats. Whereas, co-administration of metformin with oxandrolone ameliorated significantly (ANOVA, *P* value < 0.05) the doweregulated associated with oxandrolone treated group. Regarding the mood alterations, the results of the Swimming. Force test showed that oxandrolone significantly (ANOVA, *P* value < 0.05) reduced the time spent in swimming (0.6 min), but the time was significantly (ANOVA, *P* value < 0.05) longer (5 min) in rats which were treated with oxandrolone plus metformin. In Sucrose test, our results revealed that rats which were treated with only oxandrolone; consumed only 2% of the total volume of sucrose solution. However, co-administration of metformin with oxandrolone increased significantly (ANOVA, *P* value < 0.05) the sucrose consumption to 29.5%. There were no significant differences in the levels of hepatic enzymes, ALT and AST, in the blood and relative liver weights among all rat groups. In addition, the histological examination showed that neither oxandrolone nor metformin have an influenced on the liver of oxandrolone- and metformin-treated rats.

Conclusion: The present study concluded that metformin has a protective effect against oxandrolone induced mood depression and infertility. Metformin can be introduced as a protective agent against oxandrolone-induced harmful effects in athletes. Further clinical studies are needed to confirm the protective effect of metformin against oxandrolone-induced harmful side effects among human athletes.

Keywords: Oxandrolone, metformin, infertility, depression