Latin American Journal of Pharmacy
(formerly *Acta Farmacéutica Bonaerense*)
Lat. Am. J. Pharm. **41** (10): 2027-33 (2022)

Received: June 21, 2022
Accepted: July 26, 2022

Molecular Mechanism and Pathogenesis-Oriented Treatment of Antipsychotic Drug-Induced Infertility in Female Rats

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SUMMARY. **Typical and atypical antipsychotics may cause subfertility through oxidative stress in reproductive cells and endocrine axis. This experimental study was designed to determine the effects of adenosine triphosphate (ATP) treatment on oxidative stress markers and hyperprolactinemia in subfertility due to antipsychotics. A total of 54 Albino Wistar female rats were divided into nine groups as the healthy (HG), haloperidol (HPL), olanzapine (OLZ), clozapine (CLZ), aripiprazole (ARZ), ATP+haloperidol (ATP+HPL), ATP+olanzapine(ATP+OLZ), ATP+clozapine (ATP+CLZ) and ATP+aripiprazole (ATP+ARZ) groups. ATP was injected intraperitoneally (ip) at a dose of 25 mg/kg to animals in ATP+HPL, ATP+OLZ, ATP+CLZ, and ATP+ARZ groups. HG, HPL, OLZ, CLZ, and ARZ groups were given the same volume of distilled water via ip. One hour after administration of drugs and solvent, haloperidol (2 mg/kg) for ATP+HPL and HPL groups, olanzapine (2 mg/kg) for ATP+OLZ and OLZ groups, clozapine (20 mg/kg) for ATP+CLZ and CLZ groups and aripiprazole (3 mg/kg) for ATP+ARZ and ARZ groups was given orally to by gavage. This procedure was repeated once a day for 15 days. After this period, blood samples were taken for oxidant, antioxidant and prolactin measurement and the animals were kept with mature male rats for one month for breeding. The degree of oxidative stress, hyperprolactinemia and subfertility caused by antipsychotics were found to be haloperidol, olanzapine, clozapine, aripiprazole, in order of frequency. ATP administration reversed the increase in oxidants markers and the decrease of antioxidants significantly. ATP administration prevents subfertility due to antipsychotic drugs.**

RESUMEN. Los antipsicóticos típicos y atípicos pueden causar subfertilidad a través del estrés oxidativo en las células reproductivas y el eje endocrino. Este estudio experimental fue diseñado para determinar los efectos del tratamiento con trifosfato de adenosina (ATP) sobre los marcadores de estrés oxidativo y la hiperprolactinemia en la subfertilidad debida a antipsicóticos. Un total de 54 ratas hembras Albino Wistar se dividieron en nueve grupos como sanas (HG), haloperidol (HPL), olanzapina (OLZ), clozapina (CLZ), aripiprazol (ARZ), ATP+haloperidol (ATP+HPL), ATP grupos +olanzapina (ATP+OLZ), ATP+clozapina (ATP+CLZ) y ATP+aripiprazol (ATP+ARZ). Se inyectó ATP por vía intraperitoneal (ip) a una dosis de 25 mg/kg a animales en los grupos ATP+HPL, ATP+OLZ, ATP+CLZ y ATP+ARZ. Los grupos HG, HPL, OLZ, CLZ y ARZ recibieron el mismo volumen de agua destilada vía ip. Una hora después de la administración de fármacos y disolvente, haloperidol (2 mg/kg) para grupos ATP+HPL y HPL, olanzapina (2 mg/kg) para grupos ATP+OLZ y OLZ, clozapina (20 mg/kg) para ATP+CLZ y CLZ y aripiprazol (3 mg/kg) para los grupos ATP+ARZ y ARZ por vía oral por sonda. Este procedimiento se repitió una vez al día durante 15 días. Después de este período, se tomaron muestras de sangre para la medición de oxidantes, antioxidantes y prolactina y los animales se mantuvieron con ratas macho maduras durante un mes para la reproducción. El grado de estrés oxidativo, hiperprolactinemia y subfertilidad causado por los antipsicóticos resultó ser haloperidol, olanzapina, clozapina, aripiprazol, en orden de frecuencia. La administración de ATP revirtió significativamente el aumento de los marcadores de oxidantes y la disminución de los antioxidantes. La administración de ATP previene la subfertilidad debida a los fármacos antipsicóticos.

KEY WORDS: adenosine triphosphate, antipsychotics drug, infertility, rat.

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ISSN 0326 2383 (printed ed.)
ISSN 2362-3853 (on line ed.)