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# Effect of Olanzapine on Mean Arterial Blood Pressure: An Experimental Study

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***Abstract:***
***Introduction:*** *Schizophrenia or psychosis, a major group of CNS disorders which results in serious distortion of one's capacity to recognize reality, affects approximately 1 % of world population. Olanzapine is an atypical antipsychotic which is efficacious in the treatment of schizophrenia. Orthostatic hypotension is commonly reported as compared to hypotension itself. Thus we propose this study to evaluate hypotensive effect of olanzapine and to delineate its probable mechanism.*
***Materials and methods:*** *Adult albino wistar rats (200–250mg) of either sex were grouped into six groups each containing six animals. Groups 1 received 10ml/kg normal saline, groups 2, 3, 4 received olanzapine (0.5, 1.5, 5mg/kg respectively), groups 5, 6 received prazosin (0.5, 1.5mg/kg respectively) intraperitoneally and blood pressure was measured after 0, 30, 60 &120 minute by using non invasive blood pressure (NIBP) measurement method .*
***Results:*** *Administration of low dose of olanzapine caused no significant change in blood pressure but in higher doses (1.5, 5 mg/ kg) there was significant fall in BP. These effects were similar to prazosin 0.5 & 1.5mg/kg.*
***Conclusion:*** *Olanzapine in human dose equivalent (1.5 & 5mg/kg) produces significant fall in BP in rats, which is similar to that seen with prazosin.*
***Keywords:*** *Atypical antipsychotics, Hypotension, NIBP, Schizophrenia.*

## I. Introduction

Schizophrenia is a chronic debilitating mental illness with a lifetime prevalence of 1%, characterized by perturbations of cognition and behavior and by abnormal or limited display of emotion.[1] Because of severity of symptoms and chronic pattern of the disease, patients often have significant disability with serious physical, social, and economic consequences.[2, 3] The first generation antipsychotics are notably associated with movement disorders and approximately one third of patients of schizophrenia do not respond to these drugs.[3] So now the second generation antipsychotic drugs represent the preferred choice of pharmacological treatment for schizophrenia. Although atypical antipsychotics are thought to be safer than typical antipsychotics, they still have severe side effects including increased risk of stroke, sudden cardiac death, blood clots, diabetes and weight gain. Patients with schizophrenia have an increased risk of sudden death and are 2–4 times more likely to die prematurely compared to the general population.[1] The second generation antipsychotics (SGAs) being associated with cardiovascular side effects can have serious consequences to patients. An important cardiovascular side effect of first generation antipsychotics is orthostatic hypotension with rates up to 77% compared to 15% with placebo.[3] This side effect is very rare with the atypical drugs, and the effect of these drugs on mean blood pressure is not well studied.As there is paucity of published data regarding the effect of atypical antipsychotics on blood pressure it was felt pertinent to study the effect of olanzapine, the prototypical antipsychotic, on the mean blood pressure in animal model.

## II. Materials And Methods

### *2.1. Animals used*

Adult albino rats of wistar strain of either sex weighing approximately 200-250 gm were used to monitor their mean blood pressure using non invasive blood pressure instrument using the tail-cuff method. The animals were housed in the Departmental Animal House in polypropylene cages that was well ventilated temperature regulated with air cooling and 12 hour light and dark cycle in standard laboratory conditions and fed with standard animal feed and water *ad libitum.* They were allowed to acclimatize to the laboratory conditions for a period of one week. They were randomly distributed into groups containing six animals in each group. The experimental protocol was approved by the Institutional Animal Ethics Committee.

### *2.2. Drugs used*

Olanzapine was obtained from Sun Pharmaceutical Industries Ltd., Baroda, India.Prazosin was procured from Sun Pharmaceutical Industries Ltd., Baroda, India.All the drugs were freshly dissolved in distilled water and given intraperitoneally in a volume not exceeding 1ml /l00 g body weight. Before drug administration, animals were deprived of food for 5 hour allowing water available *ad libitum.*
The drugs were administered in the following manner,Animals in group 1 was provided with normal saline10 ml/kg i.p, group 2 olanzapine 0.5mg/kg i.p, group 3 olanzapine 1.5mg/kg i.p, group 4 olanzepine 5 mg/kg i.p, group 5 prazosin 0.5mg/kg i.p, group 6 prazosin 1.5mg/kg i.p followed by 0, 30, 60, 120 min observation period.

### *2.3. Instrument used*

Non invasive blood pressure (NIBP) measurement by tail cuff method – It is non invasive blood pressure measurement system that is based on the principle of volume pressure recording. An occlusion tail cuff is inflated to impede blood flow to tail. The occlusion cuff is slowly deflated and the second tail cuff is inflated containing volume pressure recording (VPR) sensor, measures physiological characteristics of returning blood flow. As the blood flow returns to tail, the VPR sensor cuff measures tail swelling as a result of arterial pulsations from blood flow. The system provides high degree of accuracy, high sensitivity and reproducibility. The rat is placed in a chamber at $37^0$ C for 10 min, and then restrained in acrylic restrainer and put on heating pad to maintain body temperature. Tail cuff and pulse sensor is inserted in the tail of rat and connected to a cylinder of compressed air through an arrangement of inlet and outlet valves that permit inflation and deflation of the cuff at a constant rate. The tail cuff pressure is continuously recorded with a solid state pressure sensor. For each indirect blood pressure determination the inflation and deflation readings are always recorded, with the compression interval. Basal blood pressure was measured in all rats prior to experiment and was compared with post drug blood pressure.

### *2.4. Statistical analysis*

The results of tail flick method were expressed as mean ± standard error of mean; Analysis of one way variance (ANOVA) with Post hoc Tukey`s test was done. Paired Student's "*t*" test was employed for comparison between the two means as a measure of significance. *P* value of <0.05 was regarded as a statistically significant.

## III. Results

At 30min, normal saline and the lowest dose of olanzapine (0.5mg/kg) did not produce any change in blood pressure. But all others doses the drug produced significant fall in blood pressure in comparison to negative control (NS) group. The effects produced by the two higher doses of olanzapine were similar ($p<0.05$) to the lower dose of prazosin. The effect produced by olanzapine was dose dependent. Results are shown in Table 1.At 60 min, all the drugs produced fall in blood pressure in comparison to the negative control (NS) group. The hypotensive effect produced by olanzapine lowest dose (0.5mg/kg) and moderate dose (1.5mg/kg) were lesser than olanzapine 5mg/kg and prazosin 0.5 & 1.5mg/kg. Olanzapine 5mg/kg produces similar effects to prazosin 0.5mg/kg which is significantly lesser than prazosin 1.5mg/kg as shown in Table 1. Prazosin produced fall in blood pressure in dose dependent manner. At 120 min, effect produced by olanzapine 5mg/kg was equal to prazosin 0.5 & 1.5mg/kg which were similar.

**Table 1:** Effect of different doses of olanzapine & prazosin on mean arterial blood pressure

| Group | Drug | Dose in mg/kg | Mean Blood Pressure ± SEM | | | |
|---|---|---|---|---|---|---|
| | | | 0min | 30min | 60min | 120min |
| 1. | Normal Saline | 10ml/kg | 111.83±1.51 | 111.84 ±1.03 | 111.68 ±1.14 | 111.33±1.51 |
| 2. | Olanzapine | 0.5mg/kg | 108.16±1.88 | 107.28±0.65 | 99.54±1.25* | 93.39±0.77** |
| 3. | Olanzapine | 1.5mg/kg | 110.65±1.32 | 100.02±0.53* | 97.52±0.84*** | 80.55±1.02*** |
| 4. | Olanzapine | 5mg/kg | 112.02±1.44 | 97.78±0.98*** | 84.56±1.82*** | 71.94±1.36*** |
| 5. | Prazosin | 0.5mg/kg | 111.29±1.22 | 100.91±0.91*** | 83.6±0.86*** | 71.04±1.32*** |
| 6. | Prazosin | 1.5mg/kg | 114.26±1.11 | 91.98±0.93*** | 71.64±1.27*** | 67.47±1.45*** |

Paired t-test – * $p<0.05$, ** $p<0.01$, *** $p<0.001$

## IV. Discussion

Major treatment goals of schizophrenia are to maintain symptom relief, decrease relapses, increase functioning, and improve quality of life. Second generation antipsychotics are widely used for the treatment and management of schizophrenia and other psychiatric disorders.[4, 5, 6] The second generation antipsychotic drugs have lower side effect profile, so now- a- days, they are preferred drug of choice. Among the second generation antipsychotics olanzapine is one of the most commonly used antipsychotic drug. Olanzapine has a higher

affinity for 5-$HT_{2A}$ serotonin receptors than $D_2$ receptors, which is a common property of all atypical antipsychotics. [4, 5, 6] Apart from that it acts as antagonist to all subtypes of $\alpha_1$ & $\alpha_2$ adrenergic receptors.

Olanzapine is known to cause orthostatic hypotension although less frequently but have been noted and mechanism underlying is suggested as alpha adrenergic blockade action along with several other mechanisms such as calcium blockade, inhibition of centrally mediated pressor reflexes, and negative ionotropic effects, have also been proposed for its adverse effects.[7] Additionally, olanzapine also exhibits a relatively low affinity for serotonin 5-$HT_1$, $GABA_A$, beta-adrenergic receptors, and benzodiazepine binding sites. There is paucity of studies showing hypotensive side effect due to olanzapine. But the result of our study correlates with the findings of Jana et al. [8]

## V. Conclusion

In the present experiment, olanzapine showed significant fall in mean arterial blood pressure in rats at human dose equivalent. Above this, further clinical and experimental studies are needed to prove the same.

## References

[1]. Perälä J, Suvisaari J, Saarni SI, Kuoppasalmi K, Isometsä E, Pirkola S et al. Lifetime prevalence of psychotic and bipolar I disorders in a general population. Arch Gen Psychiatry 2007; 64:19-28.
[2]. Wu EQ, Birnbaum HG, Shi L, Ball DE, Kessler RC, Moulis M et al. The economic burden of schizophrenia in the United States in 2002. J Clin Psychiatry 2005; 66(9):1122-9.
[3]. Buckley PR: Treatment of schizophrenia: let's talk dollars and sense. Am J Manag Care 1998; 4:369-83.
[4]. Procyshyn RM, Honer WG, Wu TK, Ko RW, McIsaac SA, et al. Persistent antipsychotic polypharmacy and excessive dosing in the community psychiatric treatment setting: a review of medication profiles in 435 Canadian outpatients. J Clin Psychiatry 2010; 71: 566–73.
[5]. Gohlke JM, Dhurandhar EJ, Correll CU, Morrato EH, Newcomer JW, et al. Recent advances in understanding and mitigating adipogenic and metabolic effects of antipsychotic drugs. Front Psychiatry 2012; 3: 62.
[6]. Procyshyn RM, Wasan KM, Thornton AE, Barr AM, Chen EY, et al. Changes in serum lipids, independent of weight, are associated with changes in symptoms during long-term clozapine treatment. J Psychiatry Neurosci 2007; 32: 331–8.
[7]. Fayek M, Kingsbury SJ, Zada J, Simpson GM. Cardiac effects of antipsychotic medications. Psychiatr Serv 2001; 52: 607-9.
[8]. Jana AK, Praharaj SK, Roy N. Olanzapine- induced orthostatic hypotension. Clinical Psychopharmacol and Neurosci 2015; 13(1):113-4.