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Evaluation of Convulsive Potential of Some Fluoroquinolones in Albino Rats

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ABSTRACT: Fluoroquinolones are broad-spectrum antimicrobials with central nervous system (CNS) adverse effects like dizziness, anxiety, and seizures. There is little comparative data available concerning the convulsant activity of the individual fluoroquinolones.

This study aimed to compare the proconvulsant activity of Ciprofloxacin, Pefloxacin, Sparfloxacin and Lomefloxacin in rats by determining the maximal electroshock seizure (MES) and minimal electroshock threshold (MET) models.

Ciprofloxacin 100 mg/kg, i.p. and pefloxacin, sparfloxacin, and lomefloxacin 60 mg/kg, i.p. were administered 1 hour prior to testing to adult albino rats. The tonic extensor phase was regarded as proconvulsant activity in the MES model. A decrease in seizure threshold of 3 mA was regarded as a positive response in MET model. Student's unpaired t-test and Fisher's exact test were used for data analysis.

All fluoroquinolones had proconvulsant effects. In the MES model, pefloxacin produced the greatest increase in tonic extensor duration (28.16 ± 1.26 s; $p < 0.001$), followed by ciprofloxacin (19.50 ± 1.14 s; $p < 0.01$). The smaller but significant effects ($p<0.05$) were observed for sparfloxacin and lomefloxacin. Ciprofloxacin (5/6 animals) and pefloxacin (4/6 animals) significantly reduced seizure threshold in the MET model, while sparfloxacin and lomefloxacin did not.

All the fluoroquinolones tested exhibited proconvulsant effects, with pefloxacin and ciprofloxacin exhibiting the highest proconvulsant effects. These results help to justify the use of fluoroquinolones with caution in patients with epilepsy or seizure disorder.

INTRODUCTION

Fluoroquinolones are one of the most commonly used antimicrobial drugs in the world, are active against both Gram-positive and Gram-negative bacteria, have excellent oral bioavailability and excellent tissue penetration (1). They are used on a regular basis for the treatment of UTI, CAP, intraabdominal infections, and more and more as empirical therapy for MDROs (2). Fluoroquinolone therapy is known to have central nervous system (CNS) adverse effects (3). The overall rate of CNS adverse reactions is from 0.9% to 2.1% and the mild CNS effects include headache, dizziness, insomnia, and anxiety (4). Less common but clinically significant are more severe effects like psychosis, hallucinations, tonic clonic seizures etc. especially in vulnerable population. Fluoroquinolones have been reported to be proconvulsant, due in large part to inhibition of gamma-aminobutyric acid type A (GABA-A) receptor binding that decreases inhibitory neurotransmission and increases neuronal excitability (5).

Besides, the participation of the N-methyl-D-aspartate (NMDA) receptor system and change in CNS lipophilicity have been suggested as contributing mechanisms (6). The relative contribution of these pathways may vary across the different fluoroquinolone drugs because of the structural differences in the side chains and physicochemical properties of these drugs (7). Several fluoroquinolones have been pulled from the world market due to safety issues (8). Haemolysis, renal failure and hypoglycaemia led to the withdrawal of temafloxacin, hepatotoxicity of trovafloxacin, cardiac arrhythmias (torsades de pointes) of grepafloxacin and phototoxicity and cardiac effects of sparfloxacin (9). These events have highlighted the need for thorough preclinical safety testing of the fluoroquinolones, including evaluation of central nervous system (CNS) effects. There are continuing reports of CNS adverse effects associated with newer fluoroquinolones (10).

Regulatory agencies such as the US Food and Drug Administration (FDA) have released new black-box warnings for the fluoroquinolone class of antibiotics due to reports of fluoroquinolone-associated disability (FQAD) that includes peripheral neuropathy and CNS disturbances (11). Recent studies have linked the use of fluoroquinolones to psychiatric side effects, to exacerbation of seizures and to the risk of neurological complications in susceptible patients (12). There is increasing literature pertaining to neurotoxic effects of fluoroquinolones but there is limited comparative experimental information on the proconvulsant efficacy of individual agents available from standardised animal seizure models (especially agents employed in the Indian subcontinent) (13).

The majority of existing studies have focused on single medications, and there have been few direct comparisons of the seizure modifying effects of various fluoroquinolones under similar conditions. Therefore, the current study was designed to compare the proconvulsant activity of the four fluoroquinolones, namely ciprofloxacin, pefloxacin, sparfloxacin and lomefloxacin, in two validated preclinical seizure models; the maximal electroshock seizure (MES) test that reflects generalised tonic-clonic seizure susceptibility, and the minimal electroshock threshold (MET) test that reflects seizure threshold. The purpose was: (1) To determine the relative proconvulsant potencies of these agents; and (2) To obtain experimental data pertinent to the safe clinical use of these agents, especially in patients who might be susceptible to seizures.

Aim and Objectives of the Study

Aim

To assess and compare the proconvulsant activity of some fluoroquinolones in albinos rats by experimental seizure models .

Objectives

1. To evaluate the effect of ciprofloxacin, pefloxacin, sparfloxacin and lomefloxacin on maximal electroshock seizures (MES) in albino rats.
2. To assess the effect of these fluoroquinolones on the seizure threshold by the minimal electroshock threshold (MET) test.
3. To determine the relative proconvulsant activity of the four fluoroquinolones.
4. To characterise the differences in convulsant activity between the MES and MET models and to discuss these differences with regards to the known neuropharmacological properties of fluoroquinolones.

MATERIAL AND METHODS

Animals

For all experiments, adult albino rats (8-12 weeks old, 150-200 g) of both sexes were used. Animals were obtained from a registered animal facility and kept in groups of 5-6 animals per cage in standard polypropylene laboratory cages with stainless steel wire mesh tops. Animals were kept under controlled environmental conditions with ambient temperature of 22 ± 2°C, relative humidity of 50–60%, and a 12 hours light-dark cycle (lights on at 07:00 hours). The standard rodent diet (Amrut Rat and Mice Feed, Pranav Agro Industries, Sangli, India) was fed in pellet form and filtered drinking water was available ad libitum. For 30 minutes prior to experimentation, the food was removed. All experiments were performed during the same time window (between 10:00 and 16:00 hours), to reduce the effect of circadian variation.

Drugs and Drug Preparation

Ciprofloxacin hydrochloride (Zim Laboratories, Nagpur), pefloxacin mesylate (Wockhardt Ltd., Aurangabad), sparfloxacin (Wockhardt Ltd., Aurangabad) and lomefloxacin hydrochloride (IPCA Laboratories, Mumbai) were supplied as gift samples by the manufacturers. All drugs were freshly prepared on the day of each experiment. Ciprofloxacin and pefloxacin were prepared in sterile distilled water. The poorly water soluble drugs, Sparfloxacin and lomefloxacin were dissolved in distilled water added with a small quantity of 0.1 N of sodium hydroxide (NaOH). The dose of the drug was optimised so that the volume of injection was not to exceed 0.1 mL/100 g body weight in all groups. Drugs were given by the intraperitoneal (i.p.) route.

Dose Selection

The doses were derived by converting the standard single clinical therapeutic dose in man to rat dose by the body surface area normalization method (Nair and Jacob, 2016). Ciprofloxacin was given (i.p.) at 100 mg/kg (500 mg in human). Pefloxacin, sparfloxacin and lomefloxacin were given at 60 mg/kg i.p. which equates to there respective standard single doses per orally administered in adults. These doses are within the range of doses reported in previous experimental studies of fluoroquinolone neurotoxicity.

Experimental Groups

Thirty six rats were randomly divided into six groups of 6 rats per group. Group I received sterile distilled water (1 mL/kg, i.p.) and was used as the vehicle control for the ciprofloxacin and pefloxacin. For the vehicle control (sparfloxacin and lomefloxacin), group II was given distilled water (0.1 N NaOH, i.p., 1 mL/kg). Ciprofloxacin (100mg/kg, i.p.) was administered to Group III. Pefloxacin (60 mg/kg, i.p.) was given to group IV. Sparfloxacin (60 mg/kg, i.p.) was given to Group V. Lomefloxacin (60 mg/kg, i.p.) was administered to group VI. Animals were then given a seizure model 1 hour after drug or vehicle administration.

Maximal Electroshock Seizure (MES) Test

Generalised tonic-clonic seizures were obtained with a convulsiometer (Techno Electronics, Lucknow, India) applied to the ear-clip electrodes which gives 150 mA of 0.2 seconds for 150 times. The characteristic seizure components observed were tonic flexion, tonic extension, clonic convulsions and post ictal depression in the following order. A stopwatch was used to measure the time of the hind-limb tonic extensor phase, in seconds. The duration of tonic extensor phase, compared with the vehicle control was used as an index of proconvulsant activity, as described by Turner (1965).

Minimal Electroshock Threshold (MET) Test

Seizure threshold was determined by using a Techno Electronics, Lucknow, India, electroconvulsiometer which supplies a current of 0.2 s duration. In the absence of experimental stage a threshold of minimal seizures was determined by the control group by increasing the amplitude in steps starting from 6 mA and using a minimal inter-stimulus interval of 48 hours between determinations.Minimal seizure" that occurred was defined as facial clonus ten seconds or more without loss of righting reflex. This protocol was used to determine the seizure threshold of 27 mA. One hour after drug or vehicle administration, each animal was given a sub-threshold stimulus of 24 mA (three mA below the threshold). The presence of a response (facial clonus for ≥10 seconds) at this sub-threshold current was interpreted as a proconvulsant response, as in Swinyard's (1949) method.

Statistical Analysis

Data from the MES test are reported as mean ± SEM. An unpaired Student's t-test was used for the analysis of between group differences. Significance of Groups III and IV was calculated in comparison with Group I while significance of Groups V and VI was calculated in comparison with Group II. Differences in number of animals responding positively in treatment and control groups for the MET test were analysed by Fisher's exact test. A p value < 0.05 was deemed to be statistically significant. All analyses were carried out with standard statistical software.

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RESULTS

Maximal electroshock seizure

The difference in the duration of the tonic extension phase in different groups of animals was calculated. Mean duration of tonic extensor phase in control group (Distilled water) was 12.33±1.14.

Mean duration of tonic extensor phase in control (distileed water + drop of 0.1 N NAOH) group was 12.22 ±1.17 . Pefloxacin increased the duration of this phase to 28.16±1.26 ($p < 0.001$) which is highly significant. Similarly Ciprofloxacin too prolonged duration of tonic extensor phase to 19.50 ±1.14 ($p< 0.01$) which is also highly significant. Sparfloxacin and lomefloxacin also significantly increased the duration of tonic extensor phase to 17.11±1.14 and 16.55±1.00 respectively ($P<0.05$).

Table No 1 : Effect of test drugs on maximal electroshock seizures in rats

Group N=6	**Pre-treatment**	**Dose mg/Kg IP**	**Duration of Tonic Extensor phase (sec) Mean ± SEM**
I	Distilled water	1ml/ Kg	12.33±1.14
II	Distilled water +Drop of NAOH	1ml/Kg	12.22±1.17
III	Ciprofloxacin	100mg/Kg	19.50±1.14**
IV	pefloxacin	60 mg/Kg	28.16±1.26***
V	Sparfloxacin	60 Mg/Kg	17.11±1.14*
VI	Lomefloxacin	60Mg /Kg	16.55±1.00*

Significance of group III & IV calculated in comparison with Group I

Significance of group V &VI calculated in comparison with Group II

*P <0.05,**p<0.01, ***P<0.001

Statistical analysis by Students Unpaired t test

Minimal Electroshock Threshold

The difference in seizure threshold was calculated in different group of animals. In both control groups none of the animals tested positive for facial clonus at 24 mA. But after ciprofloxacin administration 5 animals tested positive for facial clonus ($P<0.01$) which is highly significant. After Pefloxacin administration 4 animals tested positive for facial clonus ($P<0.05$) which is statistically significant. After both sparfloxacin and lomefloxacin administration 3 animals tested positive for facial clonus however the difference was not significant .

Table No 1 : Effect of test drugs on Minimal Electroshock Threshold in rats

Group N=6	**Pretreatment**	**Dose mg/Kg IP**	**No of animals showing positive response ie facial clonus**
I	Distilled water	1ml/ Kg	O
II	Distilled water +Drop of NAOH	1ml/Kg	O
III	Ciprofloxacin	100mg/Kg	5**

IV	pefloxacin	60 mg/Kg	4*
V	Sparfloxacin	60 Mg/Kg	3N S
VI	Lomefloxacin	60Mg /Kg	3N S

Significance of group III & IV calculated in comparison with Group I

Significance of group V &VI calculated in comparison with Group II

*P <0.05,**p<0.01,

Statistical analysis by Fischer exact test

DISCUSSION

The results of the present study were generally similar to those of Gopalakrishna et al. (14) who showed that there was proconvulsant activity in experimental seizure models with varying degrees of activity of fluoroquinolones. However, pefloxacin had the most proconvulsant activity followed by ciprofloxacin and sparfloxacin and lomefloxacin had comparatively weak activity in the present study. In contrast, Gopalakrishna et al. reported that levofloxacin exerted very little effect on seizure activity and ofloxacin unexpectedly produced anticonvulsant activity with significant reductions of the duration of tonic hind limb extension.One of the advantages of the present study was the introduction of the Minimal Electroshock Threshold (MET) model which demonstrated that both ciprofloxacin and pefloxacin had a significant effect on lowering the threshold for seizures, confirming epileptogenic activity. Some of these variations between individual fluoroquinolones could be associated with varying degrees of GABA-A receptor antagonism, lipophilicity and NMDA receptor-mediated excitatory activity. The results from the present study corroborate with previous evidence showing that fluoroquinolones have effects other than antimicrobial activity.

In the present study, the proconvulsant activity of ciprofloxacin, pefloxacin, sparfloxacin and lomefloxacin has been investigated in MES or MET models, while the effects of these drugs on oxidative stress, biochemical parameters and immunotoxicity have been investigated by Erdemli et al. (15)Ciprofloxacin had significant side effects in both studies. In the present study, the tonic extensor phase was prolonged and the seizure threshold was decreased after ciprofloxacin treatment, reflecting its marked proconvulsant properties; Erdemli et al. reported significant changes in biochemical and oxidative stress markers after treatment with ciprofloxacin. In the present study, pefloxacin was also found to be the most effective proconvulsant agent followed by comparatively less effective sparfloxacin and lomefloxacin.Combined, these findings indicate a complex mechanism of toxic action for fluoroquinolones that is different for each compound, and may encompass CNS excitation as well as oxidative stress. Therefore, selection of fluoroquinolones is justified, especially in patients who are at higher risk for neurological side effects.

The data obtained in the present study can be compared to the data obtained by Gupta et al. (2020) (16) who assessed the dysglycemic properties of fluoroquinolones in rats. In the present study, the proconvulsant action of ciprofloxacin, pefloxacin, sparfloxacin, and lomefloxacin was evaluated using MES and MET models while Gupta et al. examined the changes in blood glucose after administration of these four drugs. In both studies, adverse effects were shown to be different among each of the individual fluoroquinolones. Both studies demonstrated that ciprofloxacin has significant adverse effects; in Gupta et al.'s study it caused substantial hypoglycemia and in the present study it displayed significant proconvulsant effects. Gupta et al also concluded that ofloxacin showed the lowest effect on blood glucose level indicating that it has less adverse effect profile compared to others, while the present study revealed that sparfloxacin and lomefloxacin had less proconvulsant effect than ciprofloxacin and pefloxacin.The findings of both studies emphasize the differences in the toxicities of fluoroquinolones and the different mechanisms by which these adverse effects can occur, including glucose homeostasis and central nervous system excitability. Hence, the use of fluoroquinolones should be carefully considered, especially in patients with a history of seizures and/or glucose intolerance.

LIMITATION

Some restrictions in this study need to be noted. First, the sample size of six animals per group was in line with the generally accepted pharmacological screening procedure, but the number is small, thus reducing the statistical power and the

generalisability of the results. Second, only two models of seizures were used; the use of chemoconvulsant models (e.g., pentylenetetrazol, bicuculline) may give a fuller characterization of the proconvulsant profile. Thirdly, plasma and brain concentrations of drugs were not determined and definitive conclusions about the relationshsip of pharmacokinetics and pharmacodynamic effects could not be drawn. Fourth, the mechanism of differential activity in the two models was not directly explored, and binding studies with the receptors as well as electrophysiology experiments would be required to validate the proposed mechanisms. Last, the use of older fluoroquinolones in this study should be compared to newer agents (moxifloxacin, levofloxacin and gemifloxacin) using new experimental paradigms to determine proconvulsant potential.

CONCLUSION

The present study reveals that all four fluoroquinolones, namely, ciprofloxacin, pefloxacin, sparfloxacin and lomefloxacin exhibited proconvulsant effects in experimental models of seizures in albino rats. In the maximal electroshock seizure (MES) model, pefloxacin had the highest proconvulsant effect followed by ciprofloxacin, while sparfloxacin and lomefloxacin had less effect. In the minimal electroshock threshold (MET) model, ciprofloxacin and pefloxacin significantly decreased the threshold for seizures, suggesting a higher likelihood of inducing seizures. There are apparent differences between the fluoroquinolones in theconvulsant effects, which could be mediated by the differences in GABA-A receptor antagonism, lipophilicity, and/or interactions with other excitatory neurotransmitter systems like the NMDA receptor.

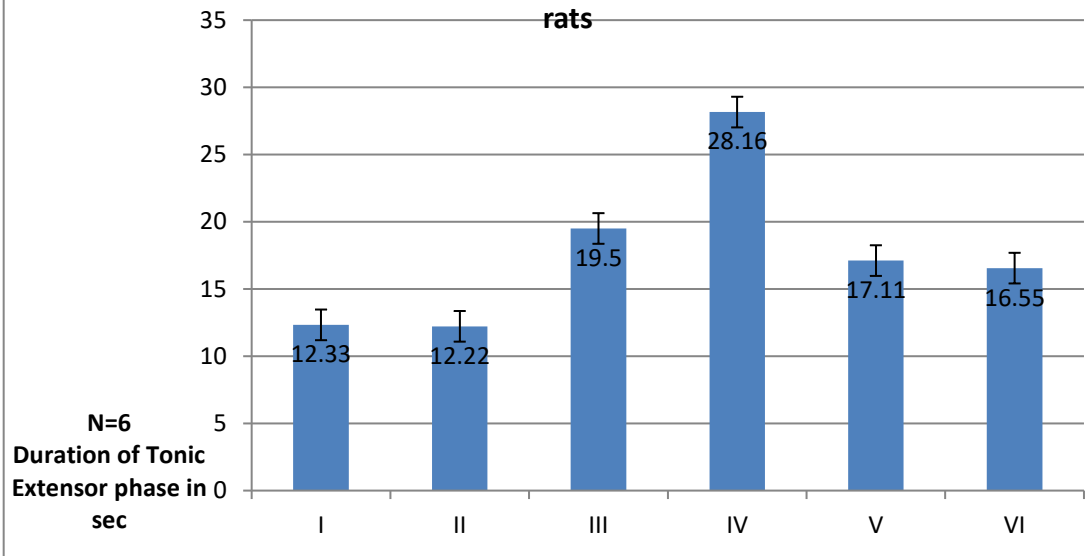
The results of this study show that the proconvulsant activity is not shared by all members of the fluoroquinolone class and that there are differences in the neurotoxicity profile of each agent. Because of the shown potential to increase seizure susceptibility, fluoroquinolones, especially ciprofloxacin and pefloxacin, should be used with care in patients with epilepsy, pre-existing seizure disorders and other risk factors for central nervous system (CNS) toxicity. Additional research is needed to better understand the exact molecular mechanisms involved in fluoroquinolone-induced seizures, and to discover alternative therapeutic agents that are less likely to cause seizures.

REFERENCE:

[1] Majalekar PP, Shirote PJ. Fluoroquinolones: blessings or curses. Current Drug Targets. 2020 Oct 1;21(13):1354-70.
[2] Fornari V, Accardo G, Lupia T, De Rosa FG, Corcione S. Suppressive antibiotic treatment (SAT) in the era of MDRO infections: a narrative review. Expert Review of Anti-infective Therapy. 2025 May 4;23(5):291-303.
[3] Wierzbiński P, Hubska J, Henzler M, Kucharski B, Bieś R, Krzystanek M. Depressive and other adverse CNS effects of fluoroquinolones. Pharmaceuticals. 2023 Aug 4;16(8):1105.
[4] Winter SF, Jo J, Schiff D, Dietrich J. Central nervous system complications among oncology patients. Hematology/Oncology Clinics. 2022 Feb 1;36(1):217-36.
[5] Wanleenuwat P, Suntharampillai N, Iwanowski P. Antibiotic-induced epileptic seizures: mechanisms of action and clinical considerations. Seizure. 2020 Oct 1;81:167-74.
[6] Egunlusi AO, Joubert J. NMDA receptor antagonists: emerging insights into molecular mechanisms and clinical applications in neurological disorders. Pharmaceuticals. 2024 May 15;17(5):639.
[7] Rusu A, Lungu IA, Moldovan OL, Tanase C, Hancu G. Structural characterization of the millennial antibacterial (fluoro) quinolones—Shaping the fifth generation. Pharmaceutics. 2021 Aug 18;13(8):1289.
[8] Bove C, Baldock RA, Champigneulle O, Martin L, Bennett CL. Fluoroquinolones: old drugs, putative new toxicities. Expert Opinion on Drug Safety. 2022 Nov 2;21(11):1365-78.
[9] Swaminathan A. Discontinued Fluoroquinolones. InKucers' The Use of Antibiotics 2017 Oct 2 (pp. 2309-2318). CRC Press.
[10] Rusu A, Munteanu AC, Arbănaşi EM, Uivarosi V. Overview of side-effects of antibacterial fluoroquinolones: new drugs versus old drugs, a step forward in the safety profile?. Pharmaceutics. 2023 Mar 1;15(3):804.
[11] Sankar A, Swanson KM, Zhou J, Jena AB, Ross JS, Shah ND, Karaca-Mandic P. Association of fluoroquinolone prescribing rates with black box warnings from the US Food and Drug Administration. JAMA network open. 2021 Dec 1;4(12):e2136662.
[12] Anwar AI, Lu L, Plaisance CJ, Daniel CP, Flanagan CJ, Wenger DM, McGregor D, Varrassi G, Kaye AM, Ahmadzadeh S, Cornett EM. Fluoroquinolones: neurological complications and side effects in clinical practice. Cureus. 2024 Feb 20;16(2).

[13] Löscher W. Animal models of seizures and epilepsy: past, present, and future role for the discovery of antiseizure drugs. Neurochemical research. 2017 Jul;42(7):1873-88.
[14] Aravind AI, Gopalakrishna HN, Kateel RA, Rai MO, Shridhar DE, D'souza RA. Comparative study on the effect of fluoroquinolones in experimental seizures on wistar rats: An acute study. Int J Pharm Sci. 2015;7(8):305-8.
[15] Donmez F, Dogan A. Investigation of the effects of three different generations of fluoroquinolone derivatives on antioxidant and immunotoxic enzyme levels in different rat tissues. Drug and Chemical Toxicology. 2022 Nov 2;45(6):2686-98.
[16] Gupta T, Gupta T, Mulkalwar S, Kulkarni V, Jadhav S, Tilak A, Rane B. A comparative study of effect of fluoroquinolones on blood glucose levels in rats. Int. J. Basic Clin. Pharmacol. 2020 Aug;9(1217):2319-003.

Table No I Effect of Test Drugs on Maximal electroshock seizures in rats



GroupI =Distilled Water
GroupII=Distilled water+Drop of Naoh
GroupIII=Ciprofloxacin
GroupIV=Pefloxacin
GroupV=sparfloxacin
Group VI=Lomefloxacin
Significance of group III and IV calculated in comparison with group I
Significance of group V and VI calculated in comparison with group II
Statistical analysis by unpaired t test
*P <0.05

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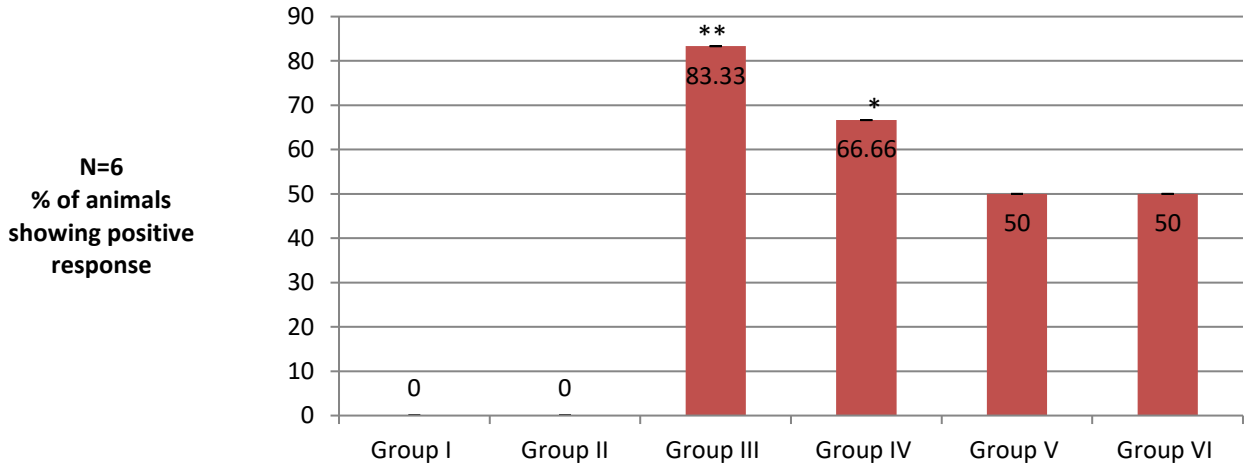
Bar Diagram No II
Showing Percentage of Animals showing Positive Responseon Minimal electroshock threshold in rats sbujected to a current of 24 mA



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