

Original Research Article**Effect of Centrally Acting Skeletal Muscle Relaxants Nitrazepam and Diazepam in Albino Mice :A Comparative Experimental Study**

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ABSTRACT

Relaxants of muscle are a varied group of drugs.They are structurally and pharmacologically different. Skeletal muscle relaxants(SMR's) are used as adjunct therapy when initial treatment fails. They are commonly used to treat fibromyalgia, low back pain, neck pain, head ache, myofascial pain and muscle spasm. Increased muscle tone is a common feature of anxiety states in humans and may contribute to the aches and pains including head ache that often trouble anxious patients.This study was carried out to evaluate the muscle relaxant property of nitrazepam and diazepam by rota rod test. It was found that both the drugs

demonstrated muscle relaxant action. But diazepam produced more muscle relaxant property as compared to nitrazepam for every concentration and increases relaxant property with increase in dose

Key Words: Muscle relaxant, Central action, Diazepam, Nitrazepam, Rota rod Test

Introduction

SMR's are a varied group of drugs. As a group, they are structurally and pharmacologically diverse⁹. SMR's are usually used as adjunct therapy when initial therapy fails. They are commonly used to treat fibromyalgia, low back pain, neck pain, tension head ache, myofascial pain and muscle spasm. Increased muscle tone is a common feature of anxiety states in humans and may contribute to the aches and pains including head ache that often trouble anxious patients¹. The relaxant effect of benzodiazepines may therefore be clinically useful. Benzodiazepines reduce muscle tone by a central action that is independent of their sedative effect. Cats are particularly sensitive to this action and some benzodiazepines like Diazepam, clonazepam, nitrazepam, flunitrazepam reduce decerebrate rigidity in doses that are much smaller than those needed to produce behavioural effects². In other species the difference is less clear, coordination can be tested by measuring the length of time for which mice can stay on a slowly rotating horizontal plastic rod. Nitrazepam is a benzodiazepine having muscle relaxant property but much studies are not available. Hence the present study was undertaken to evaluate and compare the centrally acting skeletal muscle relaxant property of diazepam and nitrazepam in albino mice.

SMR's effects skeletal muscle function and decreases the muscle tone. It may be used to alleviate symptoms such as muscle spasm, pain and hyperreflexia⁸. Skeletal muscle relaxants act directly at the level of cerebro-spinal axis and cause relaxation of skeletal muscles. They reduce muscle tone, stiffness, exaggerated tendon reflexes, involuntary movements and spasms in a diverse variety of conditions including multiple sclerosis¹⁰, cerebral palsy, spinal cord injuries, traumatic brain injury. SMR's are used to treat two different underlying conditions, spasticity from upper motor neuron, muscular pain or spasm from peripheral musculo skeletal conditions.

Similar comparative studies were conducted and published to compare skeletal muscle relaxant property of various drugs. These include comparative study of centrally acting skeletal muscle relaxants diazepam and thiocolchicoside in albino mice (naveen and syam kumar 2013)⁵. Skeletal muscle relaxant property of diazepam by using rotarod on albino mice (sundara veena and sivaji 2015)⁶. Evaluation of centrally acting skeletal muscle relaxant activity of aqueous extract of *Cinnamomum zeylanicum* bark in albino mice (Jayasree Tirumalasetty and Kavitha Rasamal 2012)⁷. comparative study of centrally acting skeletal muscle relaxants nitrazepam and thiocolchicoside in albino mice (Suresh Babu Sayana 2018)¹¹.

Aims & Objectives

To evaluate SMR's effect (muscle grip strength) of nitrazepam and diazepam in experimental animal model (Rota rod). To compare SMR's effect (muscle grip strength) of nitrazepam and diazepam in experimental animal model (Rota rod)

Material and Methods:**Materials:****Drugs and Solutions**

Nitrazepam (10mg), diazepam(4mg/2ml)

Distilled water, Normal saline

Equipment:

Rota rod, Insulin syringes, Measuring jar, Glass beakers, Animal weighing balance, Animal cages, Cotton, Spirit

Animals: 28 Albino mice of either sex weighing 30 g were used for this study⁵. Animals were maintained under standard husbandry conditions. The experimental protocol was approved by the IAEC of Maharajah's Institute Of Medical Sciences. Study period was from 25 february 2018 to 24 april 2018. This study was conducted in Department of Pharmacology, Maharajah's Institute Of Medical Sciences, Nellimarla, Vizianagaram, Andhra Pradesh.

Experimental design

Rota rod model : The apparatus used for evaluation and comparison of muscle relaxant property is rota rod^{3,4}. The rota rod assembly^{5,6} is immensely useful for screening drugs effecting motor coordination. It consists of four experimental compartments with a rotating rod of about 25 mm diameter and having speeds of approximately 5, 10, 15, 20, 25 revolutions/min. Time intervals are provided in each compartment.

28 mice were randomly divided into seven groups, each group consists of 4 mice

Group 1(Control): Mice were treated with normal saline and placed on rotating rod with a speed of 18 rpm (ideal speed).

Group 2 (Standard-S1): Mice were treated with Nitrazepam at the dose of 2mg/kg body weight and placed on rotating rod.

Group 3 (Standard-S2): Mice were treated with Nitrazepam at the dose of 3mg/kg body weight and placed on rotating rod

Group 4 (Standard-S3): Mice were treated with Nitrazepam at the dose of 4mg/kg body weight and placed on rotating rod

Group 5 (Test-T1): Mice were treated with Diazepam at the dose of 2mg/kg body weight and placed on rotating rod.

Group 6 (Test-T2): Mice were treated with Diazepam at the dose of 3mg/kg body weight and placed on rotating rod

Group 7 (Test-T3): Mice were treated with Diazepam at the dose of 4mg/kg body weight and placed on rotating rod.

Statistical analysis: The result were expressed as mean+ SEM. Statistical analysis was performed by using unpaired student t- test. $P < 0.05$ was considered statistically significant.

Observations and Results:

The study was performed in albino mice having the weight of 30 g. In each group four albino mice were included for the evaluation and comparison of the muscle relaxant property of both nitrazepam and Diazepam in various concentrations such as 2,3 and 4 mg/kg .

Albino mice is one of the best animal for initial screening of any drug as it is easy to hold and can be used repetitively since the mice is not sacrificed by rota rod method. Albino rat is the second choice of animal for this type of experiments. In this present experiment it was found that the percentage of fall of free ride time for Nitrazepam is 7.96, 12.26 and 23.24 with 2mg/kg, 3mg/kg, and 4mg/kg respectively (Table No : 1&2).Where as for Diazepam it is 19.42, 32.24 and 33.74 with 2mg/kg, 3mg/kg and 4mg/kg respectively (Table:2) when assessed by rota rod method.

The percentage of fall of free ride time for nitrazepam is 7.96, at 2mg/kg dose where as for Diazepam it is 19.42(Table No : 1&2)..At this concentration the difference is high for nitrazepam and Diazepam The unpaired student t test result is highly significant for these drugs. This study shows that Diazepam is more potent than nitrazepam at this concentration and it reduces the muscle grip property is more than the nitrazepam.

The percentage of fall of free ride time for nitrazepam is 18.42, at 3mg/kg dose where as for Diazepam it is 34.92(Table No : 1&2).At this concentration the difference is high for nitrazepam and Diazepam.The unpaired student t test result is highly significant for these drugs. This study shows that Diazepam is more potent than nitrazepam at this concentration and it reduces the muscle grip property is more than the nitrazepam.

The percentage of fall of free ride time for nitrazepam is 26.86 at 4mg/kg dose where as for Diazepam it is 42.26 (Table No : 1&2).At this concentration the difference is high for nitrazepam Diazepam The unpaired student t-test result is highly significant for these drugs. This study shows that t Diazepam is more potent than nitrazepam at this concentration and it reduces the muscle grip property is more than the nitrazepam.

Discussion :

The non specific muscle relaxant effect and CNS depression can decrease the response of motor activity . Increased muscle tone is a regular feature of anxiety states in human beings and may contribute to the aches and pains including headache that often trouble anxious patients⁴. Therefore the muscle relaxant effect of benzodiazepines may be useful clinically. A reduction of muscle tone appears to be possible without appreciable loss of coordination. SMR's are used to treat two different types of conditions.1) spasticity from upper motor

neuron syndromes 2) muscular pains or spasms from peripheral musculoskeletal conditions. In this study centrally acting skeletal muscle relaxants nitrazepam and Diazepam were used and muscle relaxant activity of Diazepam is compared with nitrazepam⁸. This study shows at all concentrations Diazepam reduces muscle grip property is more than nitrazepam. So Diazepam is very potent than nitrazepam in exhibiting muscle relaxant property.

Conclusion :

The present experimental study was carried out to evaluate and compare the central muscle relaxant property of nitrazepam and Diazepam in different concentrations in experimental model. The experimental model is rota rod test in albino mice. Both Nitrazepam and Diazepam were given in concentrations of 2mg/kg, 3mg/kg and 4mg/kg body weight in rota rod method for each mice in each group respectively.

It was found that both nitrazepam and Diazepam produced central muscle relaxant effect when assessed by rota rod test. On inter drug comparison of nitrazepam and Diazepam it was found that by increasing concentration of drug, increased the muscle relaxant property, when assessed by rota rod.

Thus it can conclude that nitrazepam and Diazepam demonstrated central muscle relaxant property but with increased doses of Diazepam produced more muscle relaxant property than increase in doses of nitrazepam.

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Table No : 1 Treatment with Nitrazepam at the dose of 2,3,4mg/kg body weight

S. No	Body wt. in gm (Mice)	Fall of Free ride time								% fall of free ride time		
		Normal Saline		Nitrazepam						2mg/kg	3mg/kg	4mg/kg
		0.2ml		2mg/kg		3mg/kg		4mg/kg				
		Before	After	Before	After	Before	After	Before	After	kg	kg	kg
1	30	270	273	275	250	280	244	269	204	7.96	12.26	23.24
2	30	250	268	250	20	240	227	261	195	3.46	4.57	25.27
3	30	282	280	235	226	252	202	245	201	4.36	18.42	18.13
4	30	275	250	290	258	280	252	284	206	11.35	8.75	26.86

Table No : 2 Treatment with Diazepam at the dose of 2,3,4mg/kg body weight

S. No	Body wt. in gm (Mice)	Fall of Free ride time								% fall of free ride time		
		Normal Saline		Diazepam						2mg/kg	3mg/kg	4mg/kg
		0.2ml		2mg/kg		3mg/kg		4mg/kg				
		Before	After	Before	After	Before	After	Before	After	kg	kg	kg
1	30	270	273	265	212	261	170	270	174	19.42	32.24	33.74
2	30	250	268	292	222	285	183	264	162	23.23	32.62	36.10
3	30	282	280	270	214	256	158	264	150	21.24	37.20	42.26
4	30	275	250	242	235	290	194	270	170	24.12	31.64	36.75

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