Mintage Journal of Pharmaceutical & Medical Sciences
RESEARCH ARTICLE

# COMPARISION OF LOCAL ANAESTHETIC POTENTIALS OF DRUGS HAVING MEMBRANE STABILIZING EFFECT ON CENTAL NEURONS IN FROGS PLEXUS ANAESTHESIA

**Amar Kumar Y[1]*, Naveen Kumar T [2], L Nagakrishna[3]**

[1]Lecturer , Department of Pharmacology, Kamineni Institute of Medical Sciences, Narketpally, A.P. India . [2]Associate Professor, Department of Pharmacology , Apollo Institute of Medical Sciences and Research ,Jubilee hills, Hyderabad , A.P, India.[3]Lecturer, Department of Pharmacology , Malla Reddy Institute of Medical Sciences , Hyderabad , A.P, India.**Email ID:** doctornaveen1@rediffmail.com

Received -23-08-13; Reviewed and accepted -29-08-13

**ABSTRACT**

**Objective:** To compare the local anaesthetic action of central neuron sodium channel blockers Phenytoin Sodium, Sodium Valproate and Carbamazepine with peripheral neuron sodium channel blockers Lignocaine using Plexus anaesthesia in frogs. **Material and Methods:** In the present study,the local anaesthetic effect of Lignocaine with concentration of 0.2%, 0.1% ,0.05% was compared with Phenytoin Sodium, Sodium Valproate and Carbamazepine in concentrations of 0.2%, 0.1% ,0.05% using different dilutions of 0.05N,0.1N,0.2N HCL in frog plexus anaesthesia by testing foot-withdrawl reflex of the frog. **Results :** The results of our present study suggest onset of local anaesthesia with lignocaine 0.2% is significantly fast when compared with concentration of 0.1%, and 0.05% indicating it has better efficacy when using for various local anaesthetic procedures. In addition onset of local anaesthesia with Phenytoin sodium concentrations of 0.2%, 0.1% ,0.05% is fast when compared with Sodium valproate concentrations of 0.2%, 0.1% ,0.05% and Carbamazepine concentrations 0.2%, 0.1% ,0.05%. **Conclusion:** Among antiepileptic drugs with local anaesthesia and membrane stabilizing activity Phenytoin sodium showed fast on set of action when compared with sodium valproate and carbamazepine indicating it has better efficacy.

**Keyword:** Local Anaesthetics, Membrane Stabilizing, Plexus anaesthesia.

## INTRODUCTION

Local anaesthetic agents are drugs which upon topical application or local injection cause reversible loss of sensory perception especially of pain, in a restricted area of the body [1]. Local anaesthetics bind reversibly to a specific receptor site within the pore of the sodium channels in the nerves and block ion movement through this pore. When applied locally to the nerve tissue in appropriate concentrations, local anesthetics can act on any part of nervous system and on every type of nerve fibre, reversibly blocking the action potentials responsible for nerve conduction[2]. Drugs like Antiepileptics and class I Antiarrhythmic drugs at high concentration can block voltage sensitive sodium channels and inhibit generation of action potential[3]. Blocking of specific sodium channels subtypes is seen as a promising therapeutic strategy of various clinical conditions including neuropathic pain[3]. Antiepileptic drugs like Phenytoin, Sodium Valproate, Carbamazepine effect membrane excitability by action on voltage dependent sodium channels which carry inward membrane current necessary for generation of action potential. They block preferentially the excitation of the cells that are firing repetitively[3]. Antiepileptic drugs are widely used in pain clinics to treat neuropathic pain. They have a long track record in this regard, Phenytoin having first been used in the early 1940s for the treatment of trigeminal neuralgia . Subsequently, Carbamazepine and Sodium valpraote were studied and found to be successful in this alleviating this condition[4]. Antiepileptic drugs work in a number of different ways, all of which have relevance to their effect on pain [5,7,8]. Phenytoin is now used infrequently although given i.v. may have some utility in the management of acute flare-ups of neuropathic pain[6]. Sakaue etal demonstrated Phenytoin Sodium, Sodium Valproate and Carbamazepine generated more frequency dependent local anaesthetic action with their obvious effect on higher frequency action potential in acute pain induced models in mice [9].

## MATERIALS AND METHODS

The study was conducted in the Amphibian Laboratory in the department of Pharmacology, Kamineni Institute of Medical Sciences, Narketpally during the period 1/8/2012 to 10/3/2013.Frog (Rana tigrina) 30 in number ,weighing 150-250-g, reared in central animal house of the Kamineni Institute of Medical Sciences (KIMS) were used.The present study was approved by Institutional Animal Ethics Committee.

### Drugs used in the experiment

(1) Normal Saline( 0.9 % sodium chloride) (2) 0.05N,0.1N,0.2N Hydrochloric acid, (3)Lignocaine (0.2%, 0.1% ,0.05%) (4) Carbamazepine(0.2%, 0.1% ,0.05%) , (5) Phenytoin sodium (0.2%, 0.1% ,0.05%) (6)Sodium valproate (0.2%, 0.1% ,0.05%), (7) Acetone 0.1% (for dissolving carbamazepine) (8) Distilled water (for dissolving lignocaine sodium valproate,carbamazepine and phenytoin sodium)

## METHODS

The standard procedure for measuring Plexus anaesthesia ( nerve block anaesthesia) in frogs where the drug is added close to nerve trunk as described by sollma method was followed . Double pithed frog was fastened over the frog board cut open the abdomen and remove all the abdominal organ,so that a pouch (sac)is made of abdominal wall .Expose the spinal nerves in the cavity and the abdominal pouch was filled with local anesthetic solution. With drawl reflex of frog was tested by immersing both feet of the frog every two minutes for not longer than 60 seconds into 0.05N,0.1N,0.2N Hydrochloric acid. Later the legs are immersed in saline to wash off the Hydrochloric acid each time.

The results of Frog plexus anaesthesia onset for different dilutions of HCL to elicit leg withdrawal reflex was graded as brisk (+++), sluggish (+) and absent (0) for recording the observations. Onset time in minutes for sluggish response and peak time in minutes when leg withdrawal reflex was completely absent.

Plexus anesthesia is used to indicate relative speed of onset of anesthesia, rather than duration, since such a preparation presumably undergoes constant deterioration.So duration of action was not compared.

Plexus Anaesthesia Model : 30 frogs of either sex has been selected for the study which were categorized in to 5 groups as shown in the table -1 ,with six animals in each group.

**Table1: Grouping of animals, Concentration and Route of Administration of Drug**

| Group (n= 6) | Drug | Concentration of the drug | Route |
|---|---|---|---|
| 1 | Normal Saline | 0.9% Sodium chloride | Infiltration |
| 2 | Lignocaine | 0.2%, 0.1% ,0.05% | Infiltration |
| 3 | Phenytoin sodium | 0.2%, 0.1% ,0.05% | Infiltration |
| 4 | Sodium valproate | 0.2%, 0.1% ,0.05% | Infiltration |
| 5 | Carbamazepine | 0.2%, 0.1% ,0.05% | Infiltration |

**n = number of frogs in each group**

## RESULTS

**Table 2 : Comparison of onset frog Plexus Anaesthesia with Lignocaine 0.2%, 0.1% ,0.05% with other drugs Phenytoin sodium, Sodium valproate and Cabamazepine in different concentration 0.2%, 0.1% ,0.05% using different dilutions of HCL 0.05N,0.1N,0.2N**

| | NS | L0.2% | L 0.1% | L 0.05% | P 0.2% | P 0.1% | P 0.05% | S.V 0.2% | S.V 0.1% | S.V 0.05% | C 0.2% | C 0.1% | C 0.05% |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Mean± S.E(min)** | 20.00± 0.00 | 2.83± 0.31 | 3.17± 0.40 | 3.50± 0.34 | 3.50± 0.22 | 3.67± 0.82 | 4.17± 0.31 | 3.83± 0.31 | 4.00± 0.26 | 4.33± 0.42 | 4.67± 0.33 | 4.83± 0.31 | 5.50± 0.22 |
| **P value** | <0.0001 | 0.25 | 0.566 | _ | 1.000 | 0.774 | 0.252 | 0.566 | 0.389 | 0.153 | 0.389 | 0.489 | 0.669 |

**L: Lignocaine, P-phenytoin sodium, S.V – sodium valproate, C- carbamazepine, NS – normal saline**

The onset of frog plexus anaesthesia with Lignocaine is fast with concentration of 0.2% (2.83± 0.31 ) ,0.1% (3.17± 0.40), 0.05% (3.50± 0.34 ) when compared with Phenytoin three concentrations 0.2% (3.50± 0.22 ), 0.1% (3.67± 0.82 ), 0.05% (4.17± 0.31 ), Sodium valproate three concentrations 0.2% (3.83± 0.31 ), 0.1% (4.00± 0.26), 0.05% (4.33± 0.42 ) and Carbamazepine three concentrations 0.2% (4.67± 0.33),0.1% (4.83± 0.31), 0.05% (5.50± 0.22).

**Table : 3 Comparison of onset frog Plexus anaesthesia with Phenytoin sodium, Sodium valproate and Cabamazepine in different concentration of 0.2%, 0.1% ,0.05% using different dilutions of HCL 0.05N,0.1N,0.2N**

| | NS | P O.2% | P 0.1% | P 0.05% | S.V 0.2% | S.V 0.1% | S.V 0.05% | C 0.2% | C 0.1% | C 0.05% |
|---|---|---|---|---|---|---|---|---|---|---|
| Mean± S.E (min) | 20.00± 0.00 | 3.50± 0.22 | 3.67± 0.82 | 4.17± 0.31 | 3.83± 0.31 | 4.00± 0.26 | 4.33± 0.42 | 4.67± 0.33 | 4.83± 0.31 | 4.33± 0.42 |
| P value | <0.0001 | 1.000 | 0.774 | 0.252 | 0.566 | 0.389 | 0.153 | 0.389 | 0.489 | 0.669 |

**P-phenytoin sodium , S.V – sodium valproate, C- carbamazepine, NS – normal saline**

The onset of frog plexus anaesthesia with Phenytoin Sodium three concentrations 0.2% (3.50± 0.22 ) , 0.1% (3.67± 0.82 ), 0.05%( 4.17± 0.31 ) is faster when compared with Sodium valproate three concentrations 0.2% (3.83± 0.31 ) , 0.1% (4.00± 0.26), 0.05% (4.33± 0.42 ) and Carbamazepine three concentrations 0.2% (4.67± 0.33). 0.1% (4.83± 0.31), 0.05% (5.50± 0.22).

**Table : 4 Comparison of onset frog Plexus anaesthesia between Sodium valproate and Cabamazepine in different concentration 0.2%,0.1% and 0.05% using different dilutions of HCL 0.05N,0.1N,0.2N**

| | NS | S.V 0.2% | S.V 0.1% | S.V 0.05% | C 0.2% | C 0.1% | C O.05% |
|---|---|---|---|---|---|---|---|
| Mean± S.E(min) | 20.00± 0.00 | 3.83± 0.31 | 4.00± 0.26 | 4.33± 0.42 | 4.67± 0.33 | 4.83± 0.31 | 5.50±0.22 |
| P value | <0.0001 | 0.566 | 0.389 | 0.153 | 0.389 | 0.489 | 0.669 |

**S.V – sodium valproate, C- carbamazepine, NS – normal saline**

The onset of frog plexus anaesthesia with Sodium valproate three concentrations 0.2% (3.83± 0.31),0.1% (4.00± 0.26), 0.05% (4.33± 0.42), is faster than Carbamazepine three concentrations 0.05% (5.50± 0.22), 0.1% (4.83± 0.31), 0.2% (4.67± 0.33).

## DISCUSSION

Lignocaine is an amide type local anaesthetic agent used therapeutically for surface, infiltration, nerve block and spinal anaesthesia. Local anaesthetics (Lignocaine) and antiepileptic drugs like Phenytoin Sodium ,Sodium Valproate and Carbamazepine share a common mechanism of action i.e sodium channel blockade (leading to decreased nerve conduction) and these drugs have role in acute as well as chronic pain conditions[10]. As these (antiepileptic drugs) drugs have the property to prolong the inactivated sodium channels like lignocaine,the present study was chosen to evaluate local anaesthetic action of Phenytoin sodium, Sodium valproate and Carbamazepine in experimental animals – frogs(lumbar plexus anaesthesia –conduction block) . The studies evaluating the local anaesthetic action of antiepileptic drugs are limited and scarcely found in literature.

Local anaesthesia produced by Lignocaine(0.2%, 0.1% ,0.05% ) and local anaesthetic effects observed with Phenytoin Sodium, Sodium valproate & Carbamazepine of similar concentrations(0.2%, 0.1% ,0.05% ) is compared with control group in the animal models of local anaesthesia( frog lumbar plexus) and the following observations are made.

The results of our present study suggest onset and peak of local anaesthesia with Lignocaine 0.2% is significantly fast when compared with concentration of 0.1%, and 0.05% indicating it has better efficacy when using for various local anaesthetic procedures. In addition onset of local anaesthesia with Phenytoin sodium in concentration 0.2%, 0.1% ,0.05% is fast when compared with Sodium valproate concentrations of 0.2%, 0.1% ,0.05% and Carbamazepine concentrations of 0.2%, 0.1% ,0.05% .Comparision of onset of action between Phenytoin Sodium ,Sodium valproate and Carbamazepine showed no statistical significance (p> 0.05) by applying student unpaired "t" test.

## CONCLUSION

Phenytoin Sodium all the three concentrations has better efficacy as local anaesthetic and memebrane stabilizing when compared with Sodium Valproate three concentrations and Carbamazepine three concentrations.Further studies are required to evaluate the local anaesthetic actions of Lignocaine, Phenytoin ,Sodium Valproate and Carbamazepine in various experimental models.

## REFERENCES

1. William A, Catterall A, Kenneth M. Local Anesthetics. In: Laurence Bruton L,Goodman and Gilmans The Pharmacological Basis of Therapeutics, 12 th ed.New Delhi :Mc Graw Hill Medical ; 2011.p.564.
2. Tripathi KD. Local Anaesthetics. In:Tripathi KD.Essentials of Medical Pharmacology, 7th ed .New Delhi :Jaypee Brothers Medical Publishers (p) Ltd; p.361.

3. Rang HP,Dale MM,Ritter JM, Flower RJ,Henderson G.Antiepileptic drugs.In: Rang HP,Dale MM.Rang And Dales Pharmacology, 7th ed .London:Elsevier Churchill Livingstone ;2007.p.543-44.
4. Ryder SA, Stannard FC. Treatment of chronic pain:antidepressant,antiepileptic and antiantiarrythmic drugs. Continuing Education in Anaesthesia, Critical Care and pain. 2005; 5(1):18-21.
5. Rogawski MA, Loscher W. The neurobiology of antiepileptic drugs for the treatment of non epileptic conditions .Nat Rev Neurosci. 2004; 5:553-64.
6. McCleane GJ. Intravenous infusion of phenytoin relieves neuropathic pain: a randomized, double-blinded, placebo-controlled, crossover study.Anesth Analg .1999;89:985-8
7. Kyle DJ, Ilyin VI: Sodium channel blockers. J Med Chem .2007, 50(11): 2583-88.
8. P Priest BT, Kaczorowski GJ: Blocking sodium channels to treat neuropathic pain.Expert Opin Ther Targets. 2007 March; 11(3):291-06.
9. Akkio S, Motoko H, Mitsuo T. Antinociceptive effect of Sodium channel –blocking agents on Acute Pain in Mice.Journal of Pharmacological sciences .2004; 1-8.
10. Krafte DS, Bannon AW. Sodium channels and nociception: recent concepts and therapeutic opportunities. Current Opinion in Pharmacology. 2007; 7:1–7.