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RESEARCH ARTICLE

COMPARISION OF LOCAL ANAESTHETIC POTENTIALS OF DRUGS HAVING MEMBRANE STABILIZING EFFECT ON INFILTRATION ANAESTHESIA IN GUINEA PIGS

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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 Infiltration anaesthesia in guinea pigs

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 guinea pig by pricking on the skin produces a squeak or movement indicating pain is produced.

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.

Keywords: Local Anaesthetics, Membrane Stabilizing, Infiltration 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].

MATERIAL AND METHODS

All the experimental procedures used in this study were reviewed and approved by Institutional Animal Ethical Committee of Kamineni Institute of Medical Sciences, Narketpally, Andhra Pradesh[10]. Guinea pigs (either sex) weighing 250-300 gms were obtained from National Institute of Nutrition, Hyderabad were used. Animals were acclimatized to the laboratory environment for 5 to 7 days before used in the study.

Animals were housed 6 per cage in a temperature and humidity controlled environment under a 12 hour light/dark cycle (lights on at 7 pm). Food and water was available for all animals for their access.

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] Distilledwater (for dissolving lignocaine sodium valproate,carbamazepine and phenytoin sodium).

Methods

The standard procedure for measuring Infiltration anesthesia in guinea pigs was followed were intradermal injection of local anaesthesia on either side of lower back and on the front side inhibits squeak or movement indicating pain has decreased.

Preparation of guinea pig:

Guinea pigs were prepared atleast 24hrs before the experiment by shaving the hair on either side of the lower back and on the front side.

Intra dermal injection of drug:

A sterile sharp 26gx 3/8inch needle was used for each injection**.** Lower back of the guinea pig was stretched taut by holding the animal with the hand placed around the abdomen and by pulling the skin taut with the thumb and forefinger.The drug was injected in the same direction as that in which the skin was being held and the needle is inserted intra dermally. The volume injected (0.1ml) was enough to rise the wheal.Then outlined the wheal with marker pen.Five minutes after the injection the sensitivity of the area was tested by pricking with a needle, six times lightly at the site of injection and control area.Six squeekings were noted on control and test side.Responses at the site of the injection will indicate the degree of anesthesia.

Failure to squeek (out of six)

- 6/6 indicates maximum anesthesia(Peak)
- 0/6 indicates no anesthesia
- 2/6 indicates onset of anaesthesia

Infiltration 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 guinea pigs 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.

Table-1: 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 guinea pigs in each group

RESULTS

In guinea pigs infiltration anaesthesia was tested on either side of lower back and front .Right side was as control and left side was used for test drug. The effect of infiltration anaesthesia was fast on front compared to lower back. Normal saline was used as control for Lignocaine, Phenytoin Sodium, Sodium valproate and Carbamazepine.

Table -2 : Comparison of onset infiltration anaesthesia in guinea pigs 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 onset infiltration anaesthesia in guinea pigs 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 infiltration anaesthesia in guinea pigs 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 infiltration anaesthesia in guinea pigs 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 infiltration anaesthesia in guinea pigs 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 infiltration anaesthesia in guinea pigs 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[11]. 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 – Guinea pigs (infiltration anaesthesia - nerve 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(guinea pig infiltration) 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.

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