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Effect of Alkalinization of Plain Lignocaine on Brachial Plexus Block

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Abstract

Background: The sensation of pain is a mechanism to protect an organism from injury. However pain is also an unpleasant experience. The conquest of pain has been considered as a path-breaking achievement in the history of medicine. Lignocaine has been considered as one of the time-tested drug used in regional anesthesia, which helped in the alleviation of pain. The duration and quality of sensory and motor blockade with lignocaine are variable. Several innovations are being tried to overcome this drawback. Therefore, there is a need to evaluate the effect of alkalinizing lignocaine in terms of, time for onset of action, degree and duration of blockade. *Methods:* This double blind, randomized controlled trial was carried out among 60 patients, aged between 18 and 60 years, of ASA Grade I and II, who underwent surgery of the upper limb over a period of six months. The participants were randomly allocated into control group who received 25 ml of 1% plain lignocaine and study group who received 25 ml of 1% alkalinized lignocaine. Onset time of analgesia and paralysis (complete motor block) were recorded. Duration and quality of sensory and motor blockade were also recorded. *Results:* The onset of sensory and motor blockade was earlier in study group than the control group ($p = 0.001$). Similarly the duration of sensory and motor block was significantly increased in the study group when compared to the control group ($p = 0.001$). The number of participants who had complete analgesia and complete paralysis was significantly higher in study group in comparison to the control group. *Conclusion:* In this modern era of anesthesia which demands higher degree of comfort, stress-free anesthetic and surgical techniques, alkalinized lignocaine solution goes a long way in advancement of anesthetic care.

Keywords: Alkalinized lignocaine; Brachial plexus; Regional anesthesia.

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Introduction

Pain is considered as a response to an inflicted stimulus. It is an alert system designed to make the body aware of a dangerous situation. The conquest of pain has been considered as a path breaking achievement in the history of medicine. Truly the central axis of anesthesia is predicated on interruption of pain. In olden times, fruit drugs like alcohol, opium, hashish and mandragora were used to reduce the pain. Trephination was practised by Incas and their tradition holds that the 'Shaman' who performed surgical procedures used to chew cocoa leaves and spat in to the wound, thereby producing the local anesthesia effect.[1]

Regional anesthesia traces its origin to Dr. Carl Koller, who in 1884, employed a solution of cocaine for topical corneal anesthesia in patients undergoing

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eye surgery. This marked the start of a new era in medicine, namely the use of regional anesthetics for prevention of pain associated with surgery. In the following year (1885), the famous surgeon Halstead demonstrated that the injection of cocaine solution around nerve tracts would completely wipe away pain and other sensation from the periphery of the region. In 1904, Einhorn synthesized procaine, an ester formed by the combination of para-amino benzoicacid and diethyl amine ethanol.

Most of the local anesthetics developed between 1900 and 1940 were basically amino ester compounds. They lost their importance due to shorter duration of action, associated allergic reaction and systemic toxicity. The next major advance was in 1930s when Erdtman, while working in Stockholm on the structure of the alkaloid gramine, tasted one of the substances that had been produced as a precursor of gramine. The significance of the numbness was appreciated immediately and the search for a clinically useful derivative was started by Erdtman. This was contributed by Nils Lofgren, who synthesized lignocaine in 1943.[2]

Perhaps almost as important as the synthesis of lignocaine was Lofgren's systematic study of a whole range of compounds (Lofgren 1948), so laying the foundation for all subsequent studies of local anesthetic drugs. From these studies have come derivatives of lignocaine such as mepivacaine, prilocaine, bupivacaine and etidocaine.

The main drawback of the long-acting drugs were, delayed onset of action, varying quality of blockade and unpredictable duration of action. To overcome these drawbacks various methods like addition of enzymes, oils, buffered carbonated solutions, alkalization, glycols and vasoconstricting agents and potentian of blockade by pain and muscular exercise were tried. Of these, only addition of carbonates, potassium and alkalinization of local anesthetics have stood the test of time. Therefore, we evaluated the effect of alkalinizing lignocaine with respect to onset time, degree and duration of blockade.

Objectives

The present study was carried out:

1. To evaluate the scope of alkalinizing plain lignocaine with sodium bicarbonate in supraclavicular brachial plexus block.
2. To compare the results with that of plain lignocaine of same concentration.

Materials and Methods

Study setting and participants

This double blind, randomized controlled trial was carried out in the Department of Anesthesia of a tertiary teaching institution for a period of six months. All the patients aged between 18 and 60 years of ASA Grade I and II, who underwent elective and emergency surgery of the upper limb, were selected for the study. Patients with progressive neurological disorders, severe kidney or liver dysfunction, history of adverse reactions to local anesthetic drugs and history of bleeding disorders were excluded. A total of 60 patients participated in the study.

Ethical approval and informed consent

Approval was obtained from Institutional Ethics Committee prior to the commencement of the study. Each participant was explained in detail about the study and informed consent was obtained prior to the data collection.

Randomization and blinding

This study comprised of two groups –

Group I: The patients in Group I (control group) received 25 ml of 1% plain lignocaine prepared by adding 12.5 ml of distilled water to 12.5 ml of 2% plain lignocaine.

Group II: The patients in Group II (study group) received 25 ml of 1% alkalinized lignocaine (prepared by adding 3 ml of 7.5% sodium bicarbonate and 9.5 ml of distilled water to 12.5 ml of 2% plain lignocaine).

Each participant was allocated into one of the groups randomly, using computer generated random numbers. The study participants and the anesthetist performing the procedure were blinded to this allocation schedule. Each group consisted of 30 participants.

Procedure

Each patient was made to lie supine without a pillow, arms at the side, head turned slightly to the opposite side with the shoulders depressed posteriorly and downward by molding the shoulders over a roll placed between the scapulae. The supraclavicular area was aseptically prepared and draped. The anesthesiologist stood at the side of the patients to be blocked, facing the head of the patient.

An intradermal wheal was raised approximately 1 cm superior to the clavicle above the midclavicular point. The subclavian artery palpable in the supraclavicular fossa was used as landmark.[3,4] A filled 10 ml syringe with a 23 gauge, 32 mm needle was held in the right hand. The needle was inserted through the skin wheal and advanced slowly downward (caudal), rolled slightly inward (medially) and slightly backward (posteriorly), so that the shaft of the needle was almost parallel to patient's head. With the index finger and thumb of the left hand, the hub of the needle was firmly held and the movement of the needle was controlled all the time. As soon as paresthesia was elicited, the needle was fixed in position and 25 ml of respective drug was injected depending on whether the patient was allotted to Group I or Group II.

Data collection

Preliminary investigations were carried out to evaluate the general fitness of the participants. The participants were not given any premedication. The pH of plain lignocaine was 6.45 and the pH of the alkalinized lignocaine was 7.55 as tested in Biochemical Laboratory. The sensory block was recorded using pin prick in skin dermatomes C4–T2, once every 3 minutes for the first 30 minutes after injection and then once every 15 minutes till the patient regained normal sensations.

Onset time of analgesia was from time of injection of drug, to the time of loss of pain on pin prick. Onset time of paralysis (complete motor block), was from time of injection of drug to time of complete loss of movement.

Sensory block was considered complete if there was complete analgesia (Grade I), partial analgesia (Grade II) when there was dermatomal sparing and (Grade III) when there was no analgesia. The motor block was also assessed by the same observer at the same time intervals. The motor block was graded according to the movement of the upper limb by the patient.

Table 1: Grading of Motor Block Among the Study Participants

Grade	Type of movement	Interpretation
5	Normal movement of the upper limb	Total absence of block
4	Movement against resistance but less than normal power	
3	Movement present against resistance	Partial motor block
2	Movement along with gravity but not against resistance	
1	Slight flickering of movements	
0	No movement	Complete motor paralysis

Duration of sensory blockade was the time in minutes from the onset of analgesia to the recurrence of pain to pinprick. Duration of motor blockade was the time in minutes from the onset of paralysis (Grade 1) to the recurrence of motor movements. The quality of sensory and motor block was studied and graded as per whether the blocks were complete, incomplete or totally absent (Table 1).

The usage of adjuvant after block was graded according to whether the surgery was done under general anesthesia (Grade III) due to complete failure of block, whether opioids were used during intraoperative period (Grade II) or if adujvants of any kind were not used throughout the end of the surgery (Grade I). The participants were also watched for bradycardia, convulsions, drowsiness and other complications.

Data analysis

The patient data and characteristics, the onset time, duration, quality of blockade were categrorized and analyzed with students unpaired t-test, Gaussian test and chi-square test using SPSS ver.20 software. The association was considered statistically significant when the p value was <0.05.

Results

Majority of the participants in both the groups belonged to the 38–47 age group and weighed between 50 and 59 kilograms. Orthopedic surgeries were the most common surgeries performed in both the groups (70% in control group and 76.6% in the cases group) (Table 2). The detailed description of the types of surgeries performed showed that majority of the cases and controls underwent closed reduction (Figure 1).

The onset of sensory blockade was achieved in between 9 and 10 minutes in 63.3% of the controls, while the same was achieved in 3–4 minutes in the study cases. Moreover, the duration of sensory blockade was for 65–74 minutes in 50% of the controls while the same lasted for 85–94 minutes in 36.7% of the study cases (Table 3).

The onset of motor blockade was achieved in 8 and 9 minutes in 63.3% of the participants in the control group while the same was achieved in 2–3 minutes among 60% of the study group participants. Similarly, the duration of motor blockade lasted for 80–89 minutes in 46.7% of the participants in the control group, while in 40% of the participants in the study group, the duration of motor blockade lasted between 100 and 109 minutes (Table 3).

Complete analgesia was achieved in 83.3% of the cases in comparison to 30% of the controls. The association was statistically significant ($p < 0.001$) (Table 4). Majority of the participants in the study group achieved complete absence of movement (76.7%) while only 3.3% of the controls achieved complete absence of movement. The association was statistically significant ($p < 0.001$). Moreover, adjuvants were not used in 73.3% of the cases while it was not used only in 43.3% of the controls. The association was statistically significant ($p < 0.05$) (Table 5).

Table 2: Background Characteristics of the Study Participants

S. No.	Characteristics	Group	
		Control N = (30) (%)	Experiment N = (30) (%)
1	*Age (in years)*		
	18–27	5 (16.7)	6 (20.0)
	28–37	5 (16.7)	7 (23.4)
	38–47	8 (26.7)	9 (30.0)
	48–57	7 (23.2)	4 (13.3)
	≥58	5 (16.7)	4 (13.3)
2	*Weight (in kilograms)*		
	30–39	1 (3.3)	1 (3.3)
	40–49	10 (33.3)	6 (20.0)
	50–59	15 (50.0)	17 (56.7)
	≥60	4 (13.3)	6 (20.0)
3	*Surgical procedures*		
	Orthopedic procedures	21 (70)	23 (76.6)
	General surgical procedures	5 (16.7)	3 (10)
	Plastic surgery procedures	4 (13.3)	2 (6.7)
	Neurosurgical procedures	0	2 (6.7)

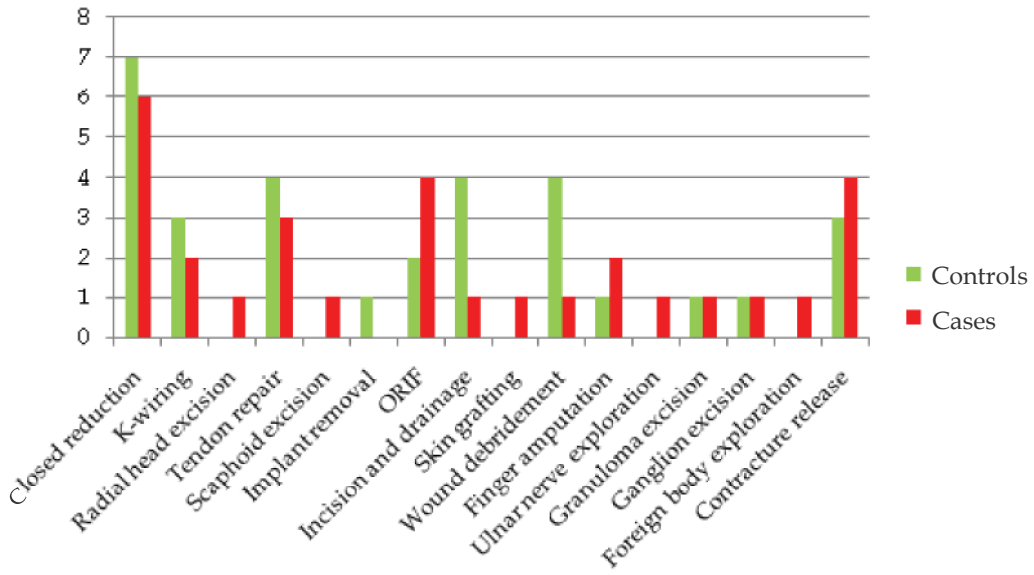

Fig. 1: Type of surgeries among the study participants

Table 3: Onset and Duration of Motor and Sensory Blockade Among the Study Participants

S. No	Characteristics	Group	
		Control N = 30 (%)	Experiment N = 30 (%)
1	Onset of sensory blockade in minutes		
	3–4	0 (0.0)	23 (76.7)
	5–6	1 (3.3)	7 (23.3)
	7–8	4 (13.3)	0
	9–10	19 (63.3)	0
	11–12	5 (16.8)	0
	13–14	0 (0.0)	0
	15–16	1 (3.3)	0
2	Onset time of motor blockade in minutes		
	2–3	0	18 (60)
	4–5	0	12 (40)
	6–7	5 (16.7)	0
	8–9	19 (63.3)	0
	10–11	5 (16.7)	0
	12–13	1 (3.3)	0
3	Duration of sensory blockade in minutes		
	65–74	15 (50.0)	0 (0.0)
	75–84	9 (30.0)	1 (3.3)
	85–94	6 (20.0)	11 (36.7)
	95–104	0	8 (26.7)
	105–114	0	6 (20.0)
	115–124	0	4 (13.3)
4	Duration of motor blockade in (min)		
	70–79	1 (3.3)	0
	80–89	14 (46.7)	0
	90–99	6 (20)	0
	100–109	9 (30)	12 (40)
	110–119	0	11 (36.7)
	120–129	0	7 (23.3)

Table 4: Comparison of Complete Analgesia Between the Groups

S. No	Characteristics	Group		Z value	*p* value
		Experiment N (30)	Control N (30)		
1	Complete analgesia	25 (83.3)	9 (30.0)	5.456	0.001

Table 5: Comparison of Effect of Analgesia Between the Groups

S. No	Characteristics	Group		Chi Sq	*p* value
		Experiment N (30)	Control N (30)		
1	Quality of motor blockade				
	No movement	23 (76.7)	1 (3.3)	34.789	0.001
	Flickering movement	5 (16.7)	13 (43.3)		
	Movement along gravity	2 (6.6)	13 (43.3)		
	Movement against gravity	0	1 (3.3)		
	Movement against resistance	0	2 (6.7)		
2	Use of Adjuvants				
	No use	22 (73.3)	13 (43.3)	6.678	0.035
	Sedation	7 (23.3)	13 (43.3)		
	Converted to GA	1 (3.4)	4 (13.4)		

Discussion

Lignocaine is a weak base with a pKa of 7.61 at 36°C.[5] As such it exists at physiological pH in two forms: a charged, protonated molecule, and an uncharged base. Lignocaine is marketed at a pH between 5.0 and 7.0 since aqueous solubility is higher at this range of pH than at more physiological pH. The lignocaine molecule is most effective at blocking the sodium channel when it is protonated but it primarily gains access to the channel by diffusion through lipid membranes.[6] The preponderance of charged lignocaine in the aqueous solution results in slow transfer of the lignocaine across lipid membranes and slows the onset of the block. Methods of improving clinical efficacy of lignocaine in nerve blockade have been studied for several decades and it was proposed that permeability of local anesthesia solutions was primarily dependent on the free base, while neural blockade was dependent on the cationic form.[7] It is known that as the pH of local anesthetic solution increases, conversion to the free base accelerates, thereby increasing neural permeability. This results in both an increased rate of penetration and a greater total mass of local anesthestic agent in the nerve fiber.[8,9]

The present study was conducted on 60 patients between 18–60 age group. The age distribution was similar in both control and study groups. This was identical to the study by Gormley W.P.[10] The mean weight of the patients in the control group was 50.63 kg and in the study group it was 53.1 kg in our study, similar to the study done by Capogna *et al.* The mean time of onset of sensory blockade was faster in the experimental group (4.13 min) compared to 9.73 minutes in control group. Gormley W.P had similar findings. Similarly Gormley, Quinlan, Bedder[10-12] showed a faster onset of sensory and motor blockade.

There have been several reasons postulated for the alkalinization controversy. Firstly the choice of local anesthetic will influence the degree to which the pH can be altered without the occurrence of precipitation. Precipitation and pH adjustment study by Peter Freund *et al.*[9] suggests that lignocaine is particularly suited for alkalinization. This is because it can be alkalinized to a pH close to the pKa value without the occurrence of precipitation. In our study the change of pH was from 6.45 in the control group to 7.55 in the study group. This change in pH after addition of sodium bicarbonate was large enough to achieve the benefits of alkalinization. Similar results were seen in studies done by Gormley, Quinlan[10,11] and Difagio, Capogna, Chow[13-15] Mary Chow had a change of pH from 6.24 to 7.15.

In our study the depth of sensory and motor blockade was significantly better in the pH adjusted group. Complete analgesia was seen in 83.3% of the patients in alkalinized group and only in 30% of the patients in control group. Similarly complete motor blockade was seen in nearly 93% of the patients in study group and in 44% of the patients in control group. Earlier studies by Nelson L. Cunningham *et al.*[16] also had similar findings. In the study by Gormley W.P. *et al.* adjuvant were used in 81.8% of patients in control group and for 50% of patients in alkalinized group.[10] The decreased requirement of adjuvant suggests greater quality of anesthesia.

The duration of sensory and motor block was significantly increased in our study group when compared with the control group (p = 0.001). Our findings corresponded with the findings of Higlier[8]. Our findings also corresponded with the findings of Gormley, and Capogna[10,14] who that showed that the quality was better in pH adjusted group and there was a significant reduction in the onset time to useful anesthesia. There was no effect on the duration of anesthesia in their studies. The difference in the duration of anesthesia could probably be due to the differences in the concentration of lignocaine.

Anatomic variations, individual patients' responses and the discrepancies in the number of patients studied should also be taken in account to explain such differences among studies. Another possible explanation for the differences among the various studies is that the lignocaine solution used may not have had a similar pH. The pH of lignocaine used in our study was 6.55. Therefore, our results suggest that alkalinization of plain lignocaine has a definitive role in improving the quality of blockade, shortening the onset time and in prolonging the duration of anesthesia.

Conclusion

The present study has demonstrated that the onset time of sensory and motor blockade is lesser with alkalinized lignocaine when compared to plain lignocaine in supraclavicular brachial plexus block. Moreover, the quality of sensory and motor blockade is better with alkalinized lignocaine. The duration of motor and blockade significantly prolonged when alkalinized lignocaine was used in supraclavicular brachial plexus block. In this modern era of anesthesia which demands greater need of comfort, stress free anesthetic and surgical

techniques, introduction of alkalinized lignocaine solution might go a long way in advancement of anesthetic care.

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