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Comparing the Effectiveness of 0.2% Ropivacaine and 0.25% Bupivacaine for Impacted Mandibular Third Molar Surgery at Rural Dental College, Loni

Dr. Srishti Salunke, Dr. Anuj Dadhich, Dr. Seemit Shah, Dr. Harish Saluja, Dr. Pulkit Khandelwal, Dr. Kedar Kawsankar, Dr. Megha Kiran, Dr. BL Himaja Reddy

Abstract:-

Background: Ropivacaine is a long-acting amide local anesthetic agent and firstproduced as a pure enantiomer. It produces effects similar to other local anesthetics via reversible inhibition of sodium ion influx in nerve fibers. Ropivacaine is lesslipophilic than bupivacaine and is less likely to penetrate large myelinated motorfibers, resulting in a relatively reduced motor blockade. Thus, ropivacaine has agreater degree of motor sensory differentiation, which could be useful when motorblockade is undesirable. The reduced lipophilicity is also associated with decreasedpotential for central nervous system toxicity and cardiotoxicity. The drug displayslinear and dose proportional pharmacokinetics (up to 80 mg administeredintravenously). It is metabolized extensively in the liver and excreted in urine. Thepresent article details the clinical applications of ropivacaine and its current place asa local anesthetic in the group.

Materials and methods: The research was undertaken following approval from the institutional ethics committee and spanned a duration of two years, during which a comprehensive evaluation was performed on 52 participants.

Results: A bigger sample size should beconsidered for more specific comparison. Bupivacaine has a very long duration ofaction which is not required for minor surgical procedure whereas Ropivacaine alsois long acting but less than Bupivacaine which is perfect for more time requiredprocedures and post –operative analgesia. Ropivacaine has vasoconstrictive natureand the difference was seen bleeding was more when Bupivacaine was used. In ourstudy no adverse effects were encountered when we used both the drugs butBupivacaine is cardiotoxic in nature and changes in blood pressure and heart ratewere seen when Bupivacaine was used so Ropivacaine can be considered to be usedin Oral and Maxillofacial surgery

Conclusion: So, to conclude, my opinion when 0.2% Ropivacaine and 0.25%Bupivacaine was compared in sample size 52, 0.2% Ropivacaine was better in termsof early onset and duration than 0.25% Bupivacaine.

Keywords:- *Anesthesia, Local anaesthetic, Ropivacaine, Bupivacaine.*

I. INTRODUCTION

Local anesthetics effectively eliminate sensation (and, in higher concentrations, motor function) within a specific region of the body. This is achieved by temporarily obstructing the transmission of impulses along nerve axons and other excitable membranes that primarily rely on sodium channels for generating action potentials. Importantly, this process does not induce unconsciousness. [1,2,3] Besides their role in blocking nerve axon conduction in the peripheral nervous system, local anesthetics also disrupt the functioning of all organs where conduction or transmission of impulses takes place. Consequently, they exert significant impacts on the central nervous system, autonomic ganglia, the neuromuscular junction, and various muscle types. [2]

Local anesthetics share specific foundational characteristics. These include a lipophilic component linked to a carbon chain via an amide or ester linkage, and this carbon chain is further connected to a hydrophilic component. Classification of local anesthetics is based on these amide or ester linkages.

Ropivacaine, also known by its trade name Naropin, is a relatively recent addition to the class of aminoamide local anesthetics. It is derived from the monohydrate of the hydrochloride salt of 1-propyl-2',6'-pipecoloxylidide and is manufactured as the pure S-enantiomer. Ropivacaine belongs to a category of local anesthetic medications known as pipecoloxylidides, which were initially synthesized in the year 1957.[4] Ropivacaine causes reversible inhibition of sodium ion influx, and thereby blocks impulse conduction in nerve fibers.[5] This effect is enhanced through dose-dependent inhibition of potassium channels. Notably, Ropivacaine exhibits lower lipophilicity when compared to bupivacaine, making it less likely to penetrate large myelinated motor fibers. As a result, its action is more selective in affecting pain-transmitting A δ and C nerves, as opposed to Aβ fibers that play a role in motor function.[6] Adverse effects of ropivacaine include hypersensitivity reaction (such as anaphylaxis, angioneurotic edema, urticaria), though rare, can occur. The most common adverse effects include hypotension, nausea, paresthesia, dizziness, headache, bradycardia, tachycardia, hypertension, vomiting, urinary retention, raised body temperature, rigors and back pain. Less common adverse effects include anxiety, symptoms of central nervous system toxicity,

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hypoesthesia, syncope, dyspnea, hypothermia, cardiac arrest, and cardiac arrhythmias. [7]

Bupivacaine (Marcaine, Sensor Caine) is a white crystalline powder freely soluble in 95% ethanol and water and is slightly soluble in chloroform or acetone. The drug is an amide derivative the structure of bupivacaine is 1-butyl-2', 6'-pipecoloxylidine similar to mepivacaine, with a butyl group replacing a methyl group in hydrophilic end. In all respects the toxic effects of bupivacaine on the central nervous, cardiovascular, and respiratory systems are similar to those of other amide- type's local anesthetics. [8]

In humans, ropivacaine also causes less central nervous system (CNS) and cardiovascular system (CVS) toxicity than bupivacaine.[9] Ropivacaine has been reported to have an approximately 70 to 75 percent greater margin of safety than bupivacaine.[10]

Our study is comparative evaluation of efficacy of 0.2% ropivacaine and 0.25% bupivacaine as local anesthetic agents for cases of surgical removal of impacted mandibular third molar. In today's world time for third molar surgery is more as compared to normal extraction so the duration of anesthesia for a longer time is required with minimum systemic toxicity.

II. ROPIVACAINE

Ropivacaine is the first and only pure S enantiomer of a long-acting amide local anesthetic drug. Ropivacaine was first developed in 1988 and authorized for use in North America in 1996[11, 12]. Ropivacaine has a molecular weight of 274, which is somewhat lower than Bupivacaine, and a pKa of 8.1, which is similar to Bupivacaine. S-(-)-1-propyl-2, 6, -pipecolixilidide hydrochloride monohydrate is its chemical name [12] Ropivacaine binds to 94 % proteins. The half-life is between 200 and 300 minutes.

Ropivacaine is metabolized extensively in the liver, primarily via aromatic hydroxylation, and eliminated in the urine as free and conjugated 3- hydroxy Ropivacaine, as well as N-dealkylated metabolites. A single dose of 3mg/kg is the maximum allowed. The average duration of action following epidural Ropivacaine administration is 180-300 minutes. When compared to Bupivacaine and Levobupivacaine, the CC/CNS dosage ratio is greater. For small surgical operations where motor block is not required, lower doses of Ropivacaine are used [12, 13] on the amide portion of pipecoloxylidide, Ropivacaine has a propyl group, whereas Bupivacaine has a butyl group. Compared to Bupivacaine, Ropivacaine is substantially less lipophilic. Large, myelinated motor fibers are less likely to be penetrated by ropivacaine.

Ropivacaine exhibits a greater preference for A and C nerve fibers associated with pain sensation compared to A nerve fibers responsible for motor function. This results in considerably less impairment of motor fibers when compared to Bupivacaine. While Ropivacaine and Bupivacaine produce similar sensory block patterns, Ropivacaine induces a motor block with a delayed onset, lower intensity, and relatively brief duration.

Table 1: Pharmacological properties of Ropivacaine

Molecular weight	-	274.4
pKa	-	8.1
Partition coefficient	-	2.9
Protein Binding	-	94%
Blood Clearance	-	0.72 L/min

III. PHARMACOKINETICS

A. *Absorption and Distribution*

The place of injection, dosages, addition of a vasoconstrictor agent, and the pharmacologic profile of the agent itself all influence systemic absorption of local anesthetics. A two-compartment model can adequately describe the distribution of local anesthetist total dose administered and the method of administration, as well as the patient's hemodynamic and circulatory status and the vascularity of the administration site all influence the plasma concentration of ropivacaine. [14] Ropivacaine binds to plasma proteins 94% of the time, primarily to 1-acid glycoprotein. An increase in the degree of protein binding and consequent decrease in ropivacaine clearance causes the total plasma concentration to rise with continuous epidural infusion of ropivacaine [14,15]

During epidural injection for caesarean delivery, ropivacaine crosses the placenta quickly, resulting in near full balance of the free fraction of ropivacaine in the maternal and fetal circulation. [16]

B. *Metabolism and excretion*

Ropivacaine is extensively metabolized in the liver, with cytochrome P450 (CYP) 1A2 converting it to 3'-hydroxy-ropivacaine and CYP3A4 converting it to 2', 6'-pipecoloxylidide. [17, 18] After a single intravenous injection, the kidney is the primary excretory organ for ropivacaine, accounting for 86 percent of the drug's excretion in urine.

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IV. PHARMACODYNAMICS

- Cardiovascular System Impact Ropivacaine exhibits lower lipophilicity compared to bupivacaine, and this, in conjunction with its stereoselective properties, contributes to a significantly higher threshold for cardiotoxicity. Notable alterations in cardiac function, such as contractility, conduction time, and QRS width, have been observed. It's important to note that ropivacaine induces a considerably smaller increase in QRS width compared to bupivacaine.
- Central Nervous System Influence Subjective central nervous system symptoms associated with ropivacaine administration encompass disorientation and drowsiness, often accompanied by light-headedness, as well as occasional visual and auditory disturbances. It's worth noting that the risk of neurotoxicity is lower with ropivacaine compared to bupivacaine.
- Other Effects Ropivacaine has been demonstrated to inhibit platelet aggregation in plasma at concentrations ranging from 3.75 mg/mL (0.375 percent) to 1.88 mg/mL (0.188 percent). These concentrations are consistent with those encountered in the epidural space during infusion.[19]

V. BUPIVACAINE

Bupivacaine, marketed under the brand name Marcaine among others, is a medication used to decrease feeling in a specific area.[20] In nerve blocks, it is injected around a nerve that supplies the area, or into the spinal canal's epidural space.[20] Bupivacaine was discovered in 1957.[21] It is on the World Health Organization's List of Essential Medicines.[21] Bupivacaine is available as a generic medication.[19][22] An implantable formulation of bupivacaine (Xaracoll) was approved for medical use in the United States in August 2020.[23][24][25]

VI. BUPIVACAINE STRUCTURE

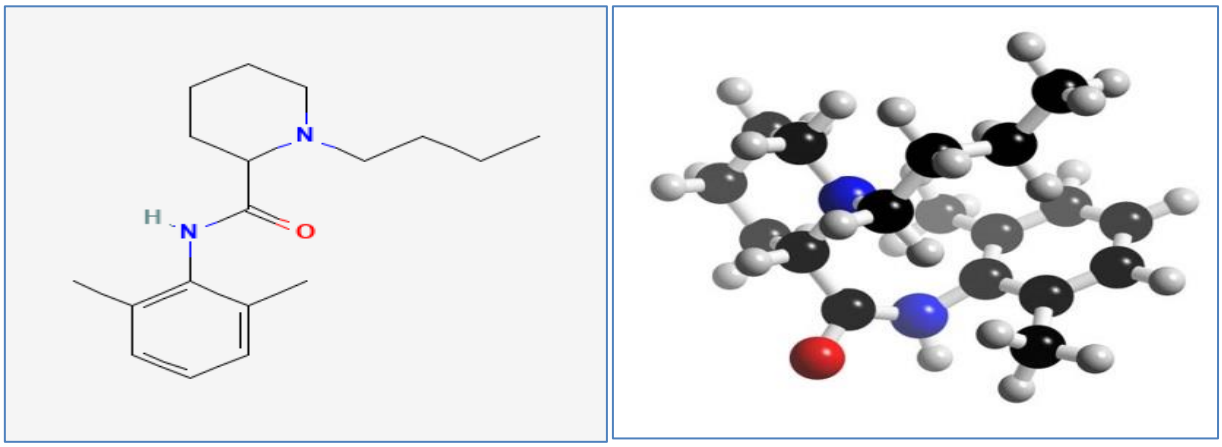

Fig. 2: Structure of Bupivacaine

A. *Mechanism of action*

Local anesthetics like bupivacaine operate by inhibiting the initiation and transmission of nerve signals. This is thought to occur through multiple mechanisms, including the elevation of the nerve's excitation threshold, the deceleration of nerve signal propagation, and the reduction in the rate of action potential increase. Bupivacaine specifically prevents depolarization by attaching to the intracellular region of sodium channels and hindering the flow of sodium ions into nerve cells. It's important to note that the onset and intensity of anesthesia typically correlate with the diameter, myelination, and conduction speed of the nerve fibers affected by the anesthetic.[26]

VII. PHARMACOKINETICS

- Onset of action (route and dose-dependent): 1-17 min
- Duration of action (route and dose-dependent): 2-9 hr.
- Half-life: neonates, 8.1 hr., adults: 2.7 hr.
- Time to peak plasma concentration (for peripheral, epidural, or caudal block): 30-45 min
- Protein binding: about 95%
- Metabolism: hepatic
- Excretion: renal (6% unchanged)[27]

VIII. MATERIALS AND METHODS

- Study Type: Observational
- Study Design: Descriptive cross-sectional study
- Period Of Study: Two years
- Study Start Date: October 2019 (After the IEC RDC approval)
- Setting: Department of oral and maxillofacial surgery, RDC, Loni.
- Sample Size: n= (copy of print out attached)
- Calculated using open epi software for 95% confidence limit and power of study to 80%

IX. STUDY GROUP

Patients aged 18 years and older, who have been recommended for surgical removal of bilaterally impacted third molars, will undergo hypersensitivity testing through a patch test. During this test, a subcutaneous injection of 0.5-1 ml of both 0.2% Ropivacaine and 0.25% Bupivacaine will be administered on the back of the arm. The injection sites will be observed for any reactions over a 10-minute period before proceeding with the subsequent procedures.

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X. METHODOLOGY

The above study will be commenced after obtaining the institutional ethical committee clearance and obtaining written informed consent from the patient. All the patients satisfying the above inclusion and exclusion criteria will be grouped into:

Table 3: Total volume of local anesthetic agent per block

	DRUGS	DOSES
1	0.2% ropivacaine hydrochloride (I.P.)	1.5-1.8 ml per block
2	0.25% bupivacaine	1.5-1.8 ml per block

All the groups will be assessed for the following variables using the Measurement method, scale and statistics as tabulated below:

XI. STUDY CONDUCT

All the patients in all the groups who have received the same concomitant therapy before and after treatment efficacy and safety will be assessed by following ways:

Table 4: How the variables were assessed

Variables Studied	Assessment scales
Onset of Anesthesia (Measured in Seconds).	This will be measured both objectively and subjectively by the patient in seconds. Anesthesia will be confirmed objectively by a pinprick test using a sterile probe which will be applied over third molar area. It will be confirmed subjectively when the patient first describes symptoms of anesthesia for example—numbness or tingling sensation. Measurement of the onset will be done using a stopwatch.
Duration of Anesthesia (Measured in Minutes).	This will be the time interval between the onset of anesthesia and when the patient reported subjective feelings of normal sensation. This will be confirmed objectively by the pinprick test as described above.
Depth of Anesthesia	This will be judged subjectively by the patient using a standardized visual analogue score (VAS). The score ranged from “0” to “10” with “0” being “no pain” and “10” being the most severe intense pain, which the patient could not bear. Each patient will be asked to score the “amount” of pain he/she felt during the third molar extraction Low score (0) meant that the patient felt no pain at all Moderate score (1 and 3) meant that the patient felt mild pain A score of (4 and 7) meant that the patient felt moderate pain A high score (8-10) meant that the patient felt excruciating and unbearable pain.
Vitals: Pulse rate Respiratory rate Blood pressure	The systolic and diastolic blood pressure (BP) will be measured in mm of mercury, and the pulse rate will be measured using beats per minute. The measurements will be done preoperatively (base line), and then at 10-, 30- and 60-minute intervals after the administration of the LA. All patients will be seated and in the resting position when the measurements will be recorded. The same sphygmomanometer will be used for all patients.
bleeding	Bleeding will be recorded on the basis of number of equal sizes of gauze completely soaked with blood. (wet gauze used)
Drug total volume administered (mg/ ml)[10]	Total amount of drug required for infiltration will be summed to be the volume in ml

Adverse effects will be recorded as immediate and delayed reactions

- **Immediate:** Those occurring within 1 hour of drug administration
- **Delayed:** Those occurring between Day-1 to Day 7

Table 5: Scoring of how the VAS score was calculated for depth of anesthesia

SCORES		Definitions
0	Absent	Symptom is not present
1	Mild	Symptom is present but is not annoying or troublesome
2	Moderate	Symptom is frequently troublesome but would not interfere with normal daily activity or sleep
3	Severe	Symptom is sufficiently troublesome to interfere with normal daily activity or sleep

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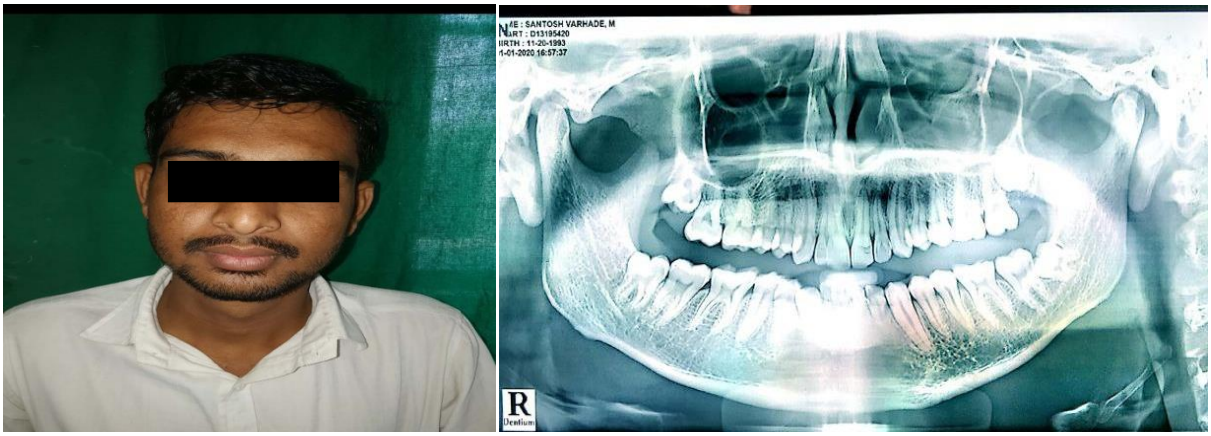

Fig. 3: Clinical profile photo of patient and orthopantogram

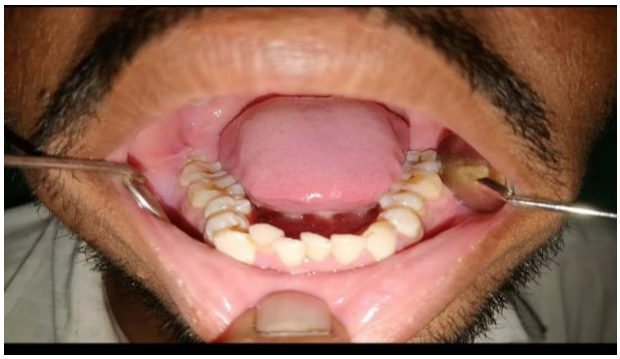

Fig. 4: Intra-oral photo of patient

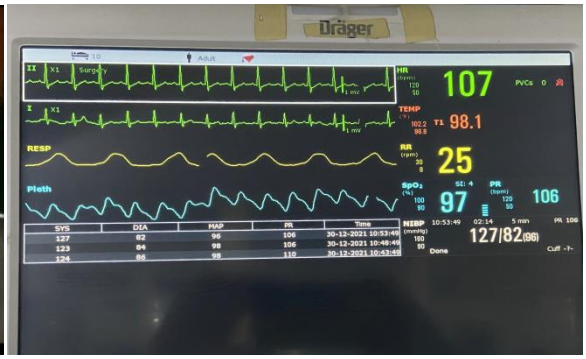

Fig. 5: Vitals recorded

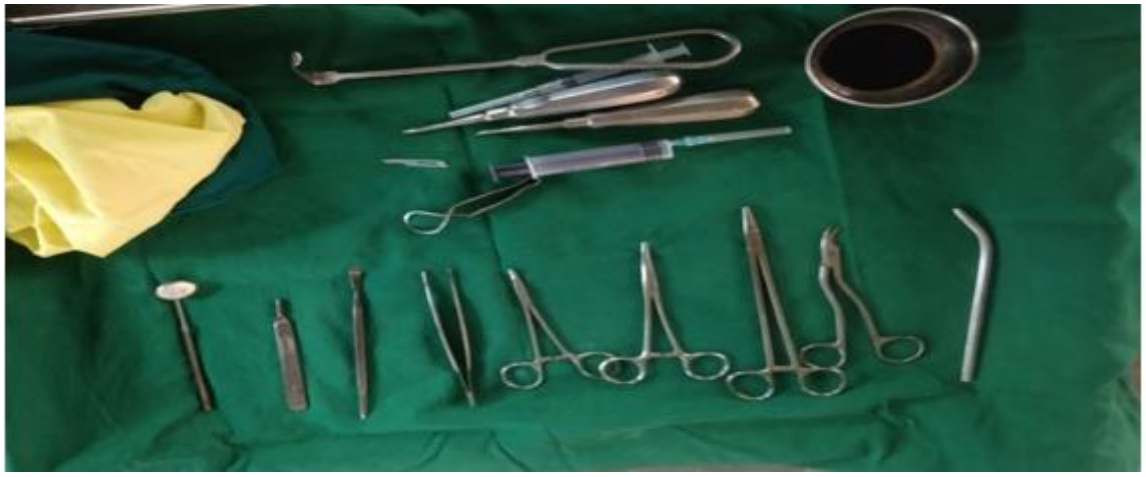

Fig. 6: Instruments used for impaction

Fig. 7: Vial of 0.2% Ropivacaine

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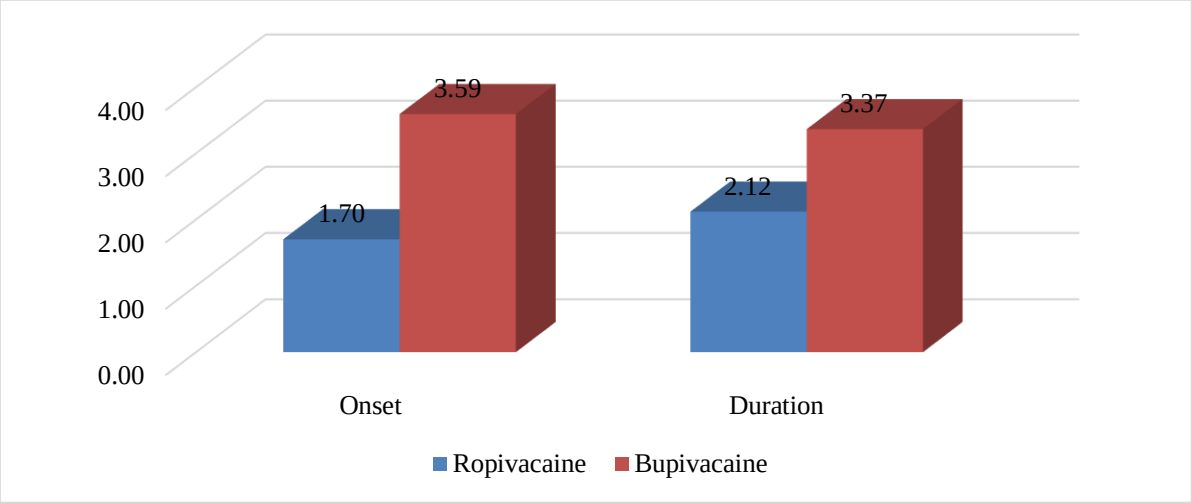
XII. OBSERVATIONS AND RESULTS

Table 6: Distribution of study population according to onset and duration

	Ropivacaine		Bupivacaine				
	Mean	**Std. Deviation**	**Mean**	**Std. Deviation**	**Mean Difference**	**t-test value**	**p-value**
Onset	1.70	0.99	3.59	1.31	-1.89	-8.322	0.001*
Duration	2.12	0.66	3.37	0.61	-1.25	-10.074	0.001*

The mean Onset and Duration was compared between 0.2 % Ropivacaine and 0.25 % Bupivacaine using the unpaired t-test. The mean Onset and Duration was significantly more among 0.25 % Bupivacaine compared to 0.2% Ropivacaine.

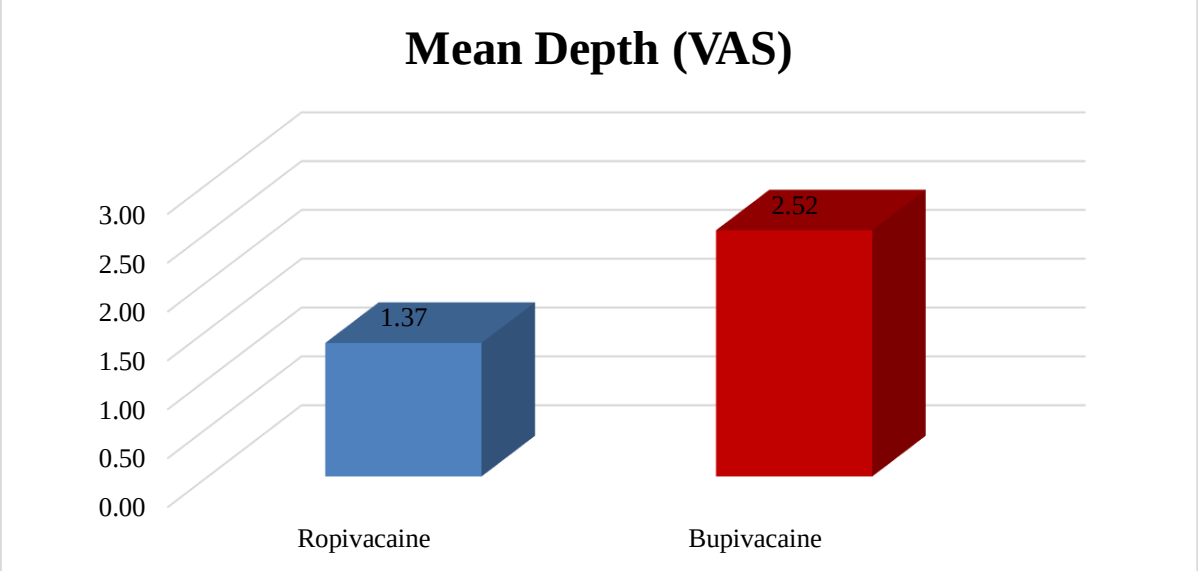


Graph 1: Distribution of study population according to onset and duration

Table 7: Distribution of study population according to depth of anesthesia

	Depth (VAS)				
	Mean	**Std. Deviation**	**Mean Difference**	**t-test value**	**p-value**
Ropivacaine	1.37	1.12	-1.15	-4.212	0.001*
Bupivacaine	2.52	1.63			

The mean Depth (VAS) was compared between 0.2% Ropivacaine and 0.25 % Bupivacaine using the unpaired t-test. The mean Depth (VAS) was significantly more among 0.25 % Bupivacaine as compared to 0.2 % Ropivacaine.



Graph 2: Distribution of study population according to depth of anesthesia

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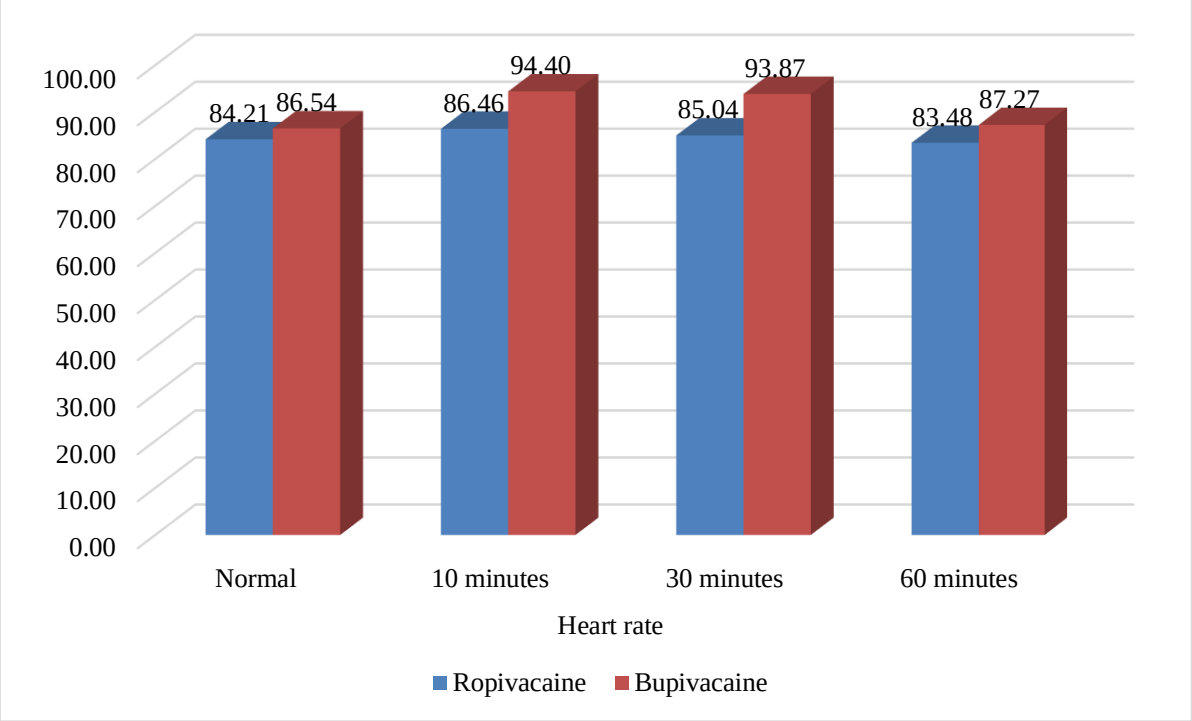
Table 8: Distribution of study population according to heart rate

	Ropivacaine		Bupivacaine				
Heart rate	Mean	Std. Deviation	Mean	Std. Deviation	Mean Difference	t-test value	p-value
Normal	84.21	10.78	86.54	9.64	-2.33	-1.161	0.249
10 minutes	86.46	10.40	94.40	11.85	-7.94	-3.634	0.001*
30 minutes	85.04	9.49	93.87	14.16	-8.83	-3.734	0.001*
60 minutes	83.48	8.06	87.27	9.40	-3.79	-2.206	0.030*

The mean Heart rate at Normal, 10 minutes, 30 minutes and 60 minutes was compared between 0.2 % Ropivacaine and 0.25 % Bupivacaine using the unpaired t-test. The mean Heart rate at Normal, 10 minutes, 30 minutes and 60 minutes was significantly more among 0.25 % Bupivacaine as compared to 02 %Ropivacaine.



Graph 3: Distribution of study population according to heart rate

A. Distribution of study population according to respiratory rate

The mean Respiratory rate at Normal, 10 minutes, 30 minutes and 60 minutes was compared between 0.2% Ropivacaine and 0.25% Bupivacaine using the unpaired t-test. There was no significant difference in mean Respiratory rate at Normal, 10 minutes, 30 minutes and 60 minutes between 0.2% Ropivacaine and 0.25% Bupivacaine.

B. Distribution of study population according to Bleeding

The mean Bleeding was compared between 0.2% Ropivacaine and 0.25% Bupivacaine using the unpaired t-test. The mean Bleeding was significantly more among 0.25% Bupivacaine compared to 0.2% Ropivacaine.

C. Distribution of study population according to systolic blood pressure

The mean Systolic blood pressure at Normal, 10 minutes, 30 minutes and 60 minutes was compared between 0.2% Ropivacaine and 0.25% Bupivacaine using the unpaired t-test. The mean Systolic blood pressure at 10 minutes was significantly more among 0.25% Bupivacaine compared to 0.2% Ropivacaine.

D. Distribution of study population according to diastolic blood pressure

The mean Diastolic blood pressure at Normal, 10 minutes, 30 minutes and 60 minutes was compared between 0.2% Ropivacaine and 0.25% Bupivacaine using the unpaired t-test. The mean Diastolic blood pressure at 10 minutes was significantly more among 0.25% Bupivacaine compared to 0.2%Ropivacaine.

XIII. DISCUSSION

The word 'pain' is derived from the Latin word 'Poena,' which means 'punishment.'

Pain is one of the first sensations known to mankind, since the beginning of life. Pain was the most unmanageable and debilitating form that has ruled people's lives. Pain is described by Merskey as a "painful sensory and emotional experience associated with real or potential tissue injury." A sufficient amount of pain alleviation should be available. It is considered a fundamental human right it is immoral and unethical to fail to relieve pain. [28]

Using the lowest possible concentration of local anesthetics is crucial to minimize motor block and side effects. Newer local anesthetics like Ropivacaine have less systemic toxicity, making minimal doses effective in dentistry.

Our study compares the effectiveness of 0.2% Ropivacaine and 0.25% Bupivacaine for removing impacted mandibular third molars, which require longer anesthesia.

We assessed onset time, duration, efficacy, depth, adverse effects, heart rate, and blood pressure. Ropivacaine has a delayed onset, lower intensity motor block, and is less lipophilic compared to Bupivacaine.

In our study, 0.2% Ropivacaine showed faster onset (45 seconds to 2 minutes) than 0.25% Bupivacaine (2 to 5 minutes), attributed to its reduced binding to fat and tissues, as explained by Akerman et al. [29]

In our study, 0.2% Ropivacaine lasted 2-3 hours, while 0.25% Bupivacaine provided 3-4 hours of analgesia.

When comparing the depth of anesthesia using VAS scores, 0.25% Bupivacaine was more effective than 0.2% Ropivacaine (see TABLE 11). Anesthetic potency is influenced by the lipid-water partition coefficient, and Ropivacaine, while second only to Bupivacaine in lipid solubility among injectable amides, had lower potency.

Our research showed that Ropivacaine can differentiate sensory and motor effects based on concentration. Lower concentrations are more selective in blocking thin A δ and C nerve fibers. However, higher concentrations are required for effective surgical anesthesia. [29,30,31]

In our study, we assessed bleeding by measuring the amount of gauze completely saturated with blood. Our findings indicate that the use of 0.25% Bupivacaine led to a statistically significant increase in mean bleeding compared to the use of 0.2% Ropivacaine.

In terms of hemodynamic changes, when 0.25% Bupivacaine was administered, there was a temporary rise in systolic and diastolic blood pressure as well as heart rate within the first 10 minutes, which was more pronounced than when 0.2% Ropivacaine was used. No significant change in respiratory rate was observed in either case.

Importantly, no adverse effects were observed with either of the anesthetic agents. In conclusion, our study suggests that 0.25% Ropivacaine may be a promising choice for local anesthesia in dentistry, especially in procedures such as third molar extractions and minor surgeries where extended duration of action and post-operative pain management are required.

XIV. CONCLUSION

In conclusion, based on the comparison of 0.2% Ropivacaine and 0.25% Bupivacaine in a sample size of 52, it can be observed that 0.2% Ropivacaine demonstrated superior characteristics in terms of early onset and duration when compared to 0.25% Bupivacaine. It's worth noting that a larger sample size should be considered for a more specific and robust comparison.

Bupivacaine exhibits an extended duration of action, which may not be necessary for minor surgical procedures. On the other hand, Ropivacaine, while also long-acting, has a shorter duration compared to Bupivacaine, making it more suitable for procedures requiring extended analgesia.

Additionally, Ropivacaine's vasoconstrictive properties were advantageous, as there was less bleeding observed when compared to Bupivacaine. In our study, no adverse effects were encountered with either drug. However, it's essential to note that Bupivacaine carries a cardiotoxic nature, with observed changes in blood pressure and heart rate when used. Considering these findings, Ropivacaine appears to be a favourable choice for oral and maxillofacial surgery

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