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Original Research Paper

Anaesthesiology

A COMPARATIVE EVALUATION OF DEXEMEDETOMIDINE AND HYALURONIDASE USED AS ADJUVANTS TO LOCAL ANAESTHETICS FOR SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK

Uditi parmar — Senior Resident Department of Anaesthesiology, Gandhi Medical College, Bhopal, Madhya Pradesh, India

Rajni Thakur* — Associate Professor(designated) , Department of Anaesthesiology, Gandhi Medical College, Bhopal, Madhya Pradesh, India *Corresponding Author

ABSTRACT

Background: Dexmedetomidine is a new alpha 2 agonist approved by FDA in 1999.Low plasma concentration results in analgesia ,sympatholysis and mild sedation without any respiratory depression. Perineural Dexmedetomidine causes augmentation of Local Anesthetic effect without causing nerve damage. Hyaluronidase has temporary reversible depolymerising action on polysaccharide hyaluronic acid which is a important component of intercellular matri

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1) To Evaluate the effect of addition of Dexmedetomidine and hyaluronidase to local anesthetic mixture on the pattern of sensory and motor block: Onset of Sensory and Motor block, Peak effect , duration of blockade and on duration of perioperative analgesia.

2) To evaluate and compare the hemodynamic parameters and sedation score in the two groups respectively.

SECONDARY OJECTIVES:

1)To study the side effects and complications related to dexmedetomidine and hyaluronidase if any.

Material and Method: It was a randomized, prospective, double blinded, comparative hospital based study at Department of Anaesthesiology, Gandhi Medical College, Bhopal. 40 ASA Grade I-II patients, age ranging from 20-40 years of either sex, scheduled for upper limb orthopaedic surgeries were randomly allocated into two groups of 20 patients each:

- Group D-inj Bupivacaine(0.5%)1mg/kg+inj lignocaine(2%)3mg/kg+inj dexem (50micrograms)diluted upto 20ml.
- Group H-inj Bupivacaine(0.5%)1mg/kg+inj lignocaine(2%)3mg/kg+inj hyaluronic acid 3000IU diluted upto 20ml.

Results: There was significant decrease in time to each the sensory and motor block in group D as compared to group H with prolonged duration of sensory and motor block and reduction in post operative analgesic requirement in group D as compared to group H($P < 0.05$) which shows that dexmedetomidine (50mcg) was effective as adjuvant to local anesthetics in early onset and prolonged duration of sensory and motor block.

The duration of analgesia was significantly higher in the patients belonging to the Group D. Likewise, the average number of rescue analgesic doses received by Group H patients were more compared to patients in Group D.

Conclusion: From our study we conclude that Dexmedetomidine 50 mcg is significantly superior to Hyaluronidase 3000IU as adjuvant to local anesthetics for supraclavicular brachial plexus block.in patients undergoing upper limb orthopaedic surgeries.

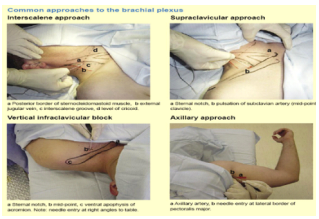
KEYWORDS : Dexmedetomidine, Hyaluronidase , supraclavicular brachial block.

INTRODUCTION

- There are many drugs which have been used as adjuvants to local anesthetic agents to prolong the duration of peripheral nerve blocks. Dexmedetomidine is a new α2 agonist[1] approved by FDA in 1999 .Low Plasma Concentration results in analgesia, sympatholysis and mild sedation[2] without any respiratory depression. Perineural Dexmedetomidine Causes augmentation of local Anesthetic effect without causing nerve damage [3].

- Hyaluronidase has temporary reversible depolymerizing action on polysaccharide Hyaluronic acid [4] which is a important component of intercellular matrix. It Improves the dispersal of solution and is used for retrobulbar block [5][6] to reduce the latency of anesthesia, attenuate an increase in intraocular pressure and to improve the spread of local anesthetic in orbit.

- Considering these facts we carried out this study to evaluate the effect of addition of dexmedetomidine and hyaluronidase to local anesthetic mixture in supraclavicular brachial plexus block on the sensory and motor block characteristics with duration of perioperative analgesia .The study also observes the effects of dexmedetomidine and Hyaluronidase on pulse rate,blood pressure,respiratory rate,SpO2,Ramsay sedation score ,side effects and complications .



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MATERIAL AND METHODS

The present prospective randomized study was conducted in department of Anesthesia; GMC Bhopal and associated Hamidia Hospital in patients posted for upper limb orthopedic surgeries under supraclavicular brachial plexus block. After approval by institutional ethical committee and written informed consent; 40 patients of ASA grade 1 and 2 posted for

upper limb orthopedic surgeries; age ranging from 20-40 years were taken.

Patients were randomnly divided into 2 groups of 20 patients each. The randomization was done on the basis of chit and envelop method.

- ***Group D-inj Bupivacaine(0.5%)1mg/kg+inj lignocaine (2%)3mg/kg+inj dexem (50micrograms) diluted upto 20ml.***
- ***Group H-inj Bupivacaine(0.5%)1mg/kg+inj lignocaine (2%)3mg/kg+inj hyaluronic acid 3000IU diluted upto 20ml.***

- **PATIENT EXCLUSION CRITERIA:**

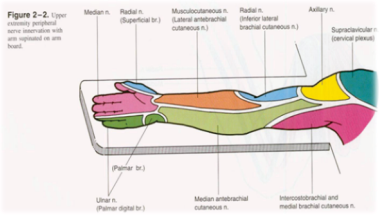
1) Patient refusal
2) Known hypersensitivity to local anaesthetics
3) Known case of major bleeding disorders
4) Patient on anticoagulant therapy.
5) Local infection, pre existing neurological disorders and nerve palsy.

- In the operation theatre, intravenous line, pulse oximeter, electrocardiography and a non invasive blood pressure monitor was attached. Baseline parameters HR, SBP, DBP, MAP, SpO2 and ECG were noted.
- Patients were premedicated with Inj. ondansetron 0.08mg/kg and after thorough explanation of the procedure, maintaining strict asepsis supraclavicular brachial plexus block was performed using nerve stimulator technique.
- After completion of supraclavicular brachial plexus block; HR, SBP, DBP, MAP, Spo2 were again noted and sedation was assessed using Ramsay sedation score at 2min, 5min and 10 minutes thereafter for every 10 minutes for 1 hour and then every 20 minutes thereafter till end of surgery.

The Ramsay Scale

Scale	Description
1	Anxious and agitated or restless, or both
2	Cooperative, oriented, and tranquil
3	Response to commands only
4	Brisk response to light glabellar tap or loud auditory stimulus
5	Sluggish response to light glabellar tap or loud auditory stimulus
6	No response to light glabellar tap or loud auditory stimulus

- Sensory block was assesed along the different nerve territories as:
- **MEDIAN NERVE**:ALONG THENAR EMINENCE
- **RADIAL NERVE**:LATERAL SIDE OF DORSUM OF HAND
- **ULNAR NERVE**:LITTLE FINGER
- **MUSCULOCUTANEOUS NERVE**:LATERAL BORDER OF FOREARM OVER SITE OF RADIAL ARTERY.
- **Sensory block assessment was done using 3 point scale:*0)NORMAL SENSATION 1)LOSS OF SENSATION TO PINPRICK(ANALGESIA) 2)LOSS OF SENSATION TO TOUCH(ANESTHESIA)***

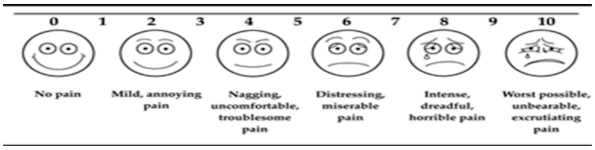


ASSESSMENT OF MOTOR BLOCK WAS DONE AS FOLLOWS:

- RADIAL NERVE:THUMB ABDUCTION,EXTENSION AT ELBOW AND WRIST.
- MEDIAN NERVE:THUMB OPPOSITION
- ULNAR NERVE:THUMB ADDUCTION
- MUSCULOCUTANEOUS NERVE:FLEXION AT ELBOW.

Score	Criteria
0	No block-total arm and forearm flexion
1	Partial block-total forearm and partial arm flexion
2	Almost complete block-inability to flex the arm and decreased ability to flex the forearm
3	Total block-inability to flex both the arm and forearm

Effect of sensory and motor block and post operative analgesia were assessed every 30 minutes for first 2 hours ,every 60 minutes for next 4 hours and then at 9, 12,18 and 24 hours.pain was assessed using 10 point visual analogue score.rescue analgrsia was given in the form of inj diclofenac sodium 1.5mg/kg im when VAS score was noted as >4



- Complication due to procedures like hematoma, pneumothorax, inadverent arterial puncture, post block neuropathy, hypotension, bradycardia, respiratory depression, dry mouth , hypersensitivity or local anesthetic toxicity were looked for.
- HYPOTENSION IS DEFINED AS FALL IN SBP MORE THAN 20% FROM PRE OPERATIVE VALUE.
- BRADYCARDIA IS DEFINED AS FALL IN PULSE RATE OF MORE THAN 20% FROM PRE OPERATIVE VALUE.
- RESPIRATORY DEPRESSION IS DEFINED AS FALL IN SPO2 LESS THAN 90% OR RESPIRATORY RATE LESS THAN 10/min

Statistical Analysis

The data was compiled and subjected to stastical analysis.

Results are tabulated and analyzed using spss software. Student t test is used for continuous variables and Chi square test for discrete variables is applied. Results are expressed as Mean ± SD P value < 0.05 will be considered significant and p value < 0.01 will be considered highly significant.

Observation and Results

DEMOGRAPHIC PARAMETERS

The group under study were comparable with regards to age, gender and ASA status. Sample size was taken on the basis of power of study and data was analyzed using t test and Chie square test.

	NO OF PATIENTS	AGE(YEARS) MEAN+SD	GENDER (M:F)	ASA STATUS 1/2
GROUP D	20	32+11	12:8	12/8
GROUP H	20	32+10.4	14:6	14/6

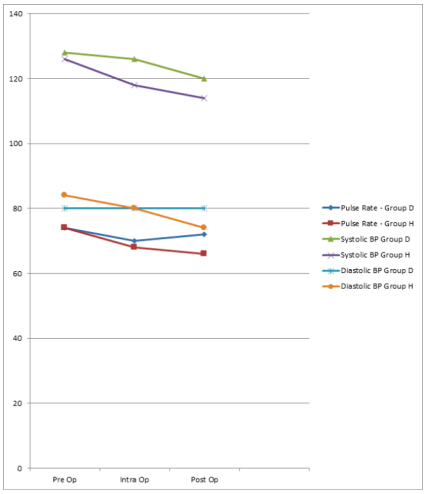
2)COMPARISON OF SENSORY AND MOTOR BLOCK CHARACTERISTICS BETWEEN THE TWO GROUPS.

	Onset of sensory block(minutes)	Peak effect (minutes)	Duration of sensory block(minutes)	Onset of motor block(minutes)	Peak effect(minutes)	Duration of motor block(minutes)
GROUP D	1.9+0.8	4.8+1.8	622+166.4	2.9+0.9	6.2+2.1	432+130.3
GROUP H	4.2+1.2	10+2.8	260.4+60.4	5.6+1.2	9.8+3.2	180+46.4
P Value	0.038	0.046	0.042	0.032	0.045	0.037

3)EVALUATION OF POSTOPERATIVE ANALGESIA

	Duration of Analgesia(minutes)	Time for 1st rescue analgesia(minutes postoperatively)	Number of doses of Analgesia required 24 hours postoperatively			
			0	1	2	3
GROUP D	536+33.46	580	6patients	4	10	0
GROUP H	380+84.60	420	2patients	8	8	2
P Value	0.0001	0.046	0.042	0.0018	0.004	0.0001

PERIOPERATIVE HEMODYNAMIC PARAMETERS IN THE TWO GROUPS RESPECTIVELY:



The hemodynamic parameters including heart rate, systolic blood pressure and diastolic blood pressure were comparable in both the groups in preoperative, intraoperative and in postoperative period and there was no significant difference in hemodynamic parameters in the two groups respectively with P value being insignificant($p>0.05$)

COMPARISON OF SEDATION SCALES BETWEEN TWO GROUPS:

The ramsay sedation score was comparable in both the groups throughout the intraoperative period(p value>0.05) .

Ramsay Sedation Score	Group D	Group H
1	0	0
2	12	11
3	8	9
4	0	0
5	0	0
6	0	0

DISCUSSION

Dexmedetomidine, the pharmacologically active d-isomer of medetomidine is a highly specific and selective 2 adrenoceptor agonist [1][2] with 2: 1 binding selectivity ratio of 1620:1 as compared to 220:1 for clonidine, thus decreasing the unwanted side effects of 1 receptors. Presynaptic activation of 2 adrenoceptor in central nervous system (CNS) inhibits the release of norepinephrine, terminating the propagation of pain signals and their postsynaptic activation inhibits sympathetic activity, thereby decreasing HR and BP.

Because of its effects on spinal α2 receptors, it prolongs analgesia when used with local anesthetics. Yoshitomi *et al*., demonstrated that dexmedetomidine as well as clonidine enhanced the local anesthetic action of lignocaine via peripheral α-2A adrenoceptors. [7]

Masuki *et al*., suggested that dexmedetomidine induces vasoconstriction via α2 adrenoceptors in the human forearm [8] possibly also causing vasoconstriction around the site of injection, delaying the absorption of local anesthetic and hence prolonging its effect. Esmaoglu *et al*., reported prolongation of axillary brachial plexus block when dexmedetomidine was added to levobupivacaine[9].

Hyaluronidase degrades hyaluronic acid, promoting the flow of drugs through tissue [4]. It has been available as an additive to local anesthetic solutions since 1948. Its most common anesthesia application is in ophthalmic cases.

Hyaluronidase depolymerises hyaluronic acid, which is a major component of the extracellular matrix[5]. Through this mechanism of action, hyaluronidase is known to accelerate the onset and improve the quality of anaesthesia for retrobulbar, peribulbar and subcutaneous infiltration blocks by increasing the spread and dispersion of local anaesthetics[10-11].

This point may be particularly relevant for supraclavicular brachial plexus block, since incomplete blocks are generally attributed to limited spread of local anesthetic fluid due to connective tissue barriers within the brachial plexus sheath

In the present study, the addition of Dexmedetomidine (50mcg) to local anesthetic mixture significantly shortened the time to achieve complete sensory block and surgical anaesthesia,as compared to addition of 3000IU of hyaluronidase to local anesthetic mixture for supraclavicular brachial plexus block. therefore reducing the anaesthetic time before the start of the operation.

The duration of perioperative analgesia was more in group D as compared to group H. The use of hyaluronidase reduced the duration of the sensory block. The duration of motor block analgesia were also reduced and it was statistically significant. There was significant difference in the total administered dose of postoperative analgesic medication in the two groups respectively. The patients in group H had more analgesic requirements as compared to group D and the difference was statistically highly significant.

A previous study reported the effect of the addition of hyaluronidase to bupivacaine 0.5% for axillary brachial plexus blocks [12]. In that study, 3000 IU hyaluronidase mixed with bupivacaine significantly reduced the duration of the sensory and motor block, and had no effect on the number of patients experiencing a complete sensory block after 30 min.

These results were similar to those obtained in the present study, as success rates for surgical anaesthesia were similar between the two experimental groups tested, while the duration of sensory anaesthesia was significantly shorter in the hyaluronidase group and the duration of motor block showed a shorter trend. However, the former study performed pinprick tests only twice, at 15 and 30 min after the block placement, so the exact time of complete sensory block was not measured. Furthermore, the block was conducted via the landmark-guided technique without the use of a nerve stimulator or ultrasound guidance.

In the present study we have used dexmedetomidine(50mcg)in dose that causes earlier onset and prolonged duration of sensory and motor block with better postoperative analgesia with out any side effects .

Hemodynamic parameters were comparable in both the groups with p value being insignificant($p>0.05$).None of the patients in the two groups showed hypotension, bradycardia or respiratory depression.

We have also compared the Ramsay sedation scale in the groups and it was also comparable in both the groups with p value being insignificant. None of the patients were deeply sedated in the two groups .

Reports of adverse effects associated with hylauronidase are rare, with most reported adverse effects involving allergic reactions to hyaluronidase [13]. No adverse effects were associated with the use of hyaluronidase in the present study.

CONCLUSION

Dexmedetomidine in comparison to hyaluronidase when added in supraclavicular brachial plexus block leads to :

Early onset and prolonged duration of sensory and motor block, prolonged duration of analgesia and decreased need for post operative analgesics with adequate intraoperative sedation with stable perioperative hemodynamics. Thus Dexmedetomidine can be used as a safe and effective adjuvant to local anesthetics in supraclavicular brachial plexus block to provide excellent peri-operative analgesia with minimal side effects.

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Conflicts of Interest: None

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