

# Intrathecal Dexmedetomidine 5µg and Fentanyl 25µg as Adjuvants to 12.5mg Of 0.5% Hyperbaric Bupivacaine for Spinal Anaesthesia: A Study on Adverse Effects

Malashree<sup>1</sup>, Vinod M<sup>2</sup>

<sup>1</sup>Assistant Professor, Department of Anesthesiology, SanjayGandhi Institute of Trauma and Orthopedics, Bangalore, Karnataka, <sup>2</sup>Post Graduate, Department of Anesthesiology and Critical care, VIMS, Ballari, Karnataka.

## Abstract

**Background:** Bupivacaine hydrochloride is a white, odourless, crystalline powder with a bitter, numbing taste. It is prepared by chemical synthesis. The hydrochloride salt is available in solution with and without epinephrine. A preparation marketed specifically for intrathecal use contains dextrose. **Subjects and Methods:** Data was collected from 90 patients in the age group of 30-60 years of ASA class I & II, posted for elective TAH without any co-morbid diseases were grouped randomly by using closed sealed opaque envelope technique. The study drug was prepared by an anesthesiologist, who was not involved with the study. All spinal blocks were given by the same anesthesiologist who also was the observer. **Results:** 4 patients in Dexmedetomidine group, 2 patients each in Fentanyl group and control group developed bradycardia which was managed by Inj. Atropine 0.6 mg IV. 11 patients in Dexmedetomidine group, 7 patients in Fentanyl group and 4 patients in control group developed hypotension which was managed by Inj. Mephenteramine 6mg IV incremental doses. 1 patient in Group-F developed vomiting which was managed by Inj. Ondansetron 4mg IV. **Conclusion:** In our study there was no statistically significant difference in the adverse effects throughout the procedure when Group-D and Group-F were compared with group-B and also there was no statistically significant difference when Group-D was compared with Group-F.

**Keywords:** Hyperbaric Bupivacaine, Spinal anesthesia, Adverse effects.

**Corresponding Author:** Dr. Malashree, Assistant Professor, Department of Anesthesiology, SanjayGandhi Institute of Trauma and Orthopedics, Bangalore, Karnataka.

Received: October 2019

Accepted: October 2019

## Introduction

Local anaesthetics consist of a lipophilic and a hydrophilic portion separated by a connecting hydrocarbon chain. The hydrophilic group is usually a tertiary amine such as diethylamine, whereas the lipophilic portion is usually an unsaturated aromatic ring, such as paraaminobenzoic acid. The lipophilic portion is essential for anaesthetic activity and therapeutically useful local anaesthetics require a delicate balance between lipid solubility and water solubility. In almost all instances, esters (-CO-) or an amide (-NHC-) bond links the hydrocarbon chain to the lipophilic aromatic ring. Bupivacaine, the piperidoxylidide local anaesthetics is a chiral drug because its molecule possesses an asymmetric carbon atom and it is available for clinical use as racemic mixture of the enantiomers.

Bupivacaine hydrochloride is a white, odourless, crystalline powder with a bitter, numbing taste. It is prepared by chemical synthesis. The hydrochloride salt is available in solution with and without epinephrine. A preparation marketed specifically for intrathecal use contains dextrose.<sup>[1]</sup>

Bupivacaine, like other local anaesthetics prevents

the generation and the conduction of the nerve impulse. Their primary site of action is the cell membrane. Conduction block can be demonstrated in squid giant axons from which the axoplasm has been removed.

Local anaesthetics block conduction by decreasing or preventing the large transient increase in the permeability of excitable membranes to Na<sup>+</sup> that normally is produced by a slight depolarization of the membrane. This action of local anaesthetics is due to their direct interaction with voltage-gated Na<sup>+</sup> channels. As the anaesthetic action progressively develops in a nerve, the threshold for electrical excitability gradually increase, the rate of rise of the action potential declines, impulse conduction slows, and the safety factor for conduction decreases. These factors decrease the probability of propagation of the action potential and nerve conduction eventually fails.<sup>[2]</sup>

Bupivacaine is rapidly absorbed from the site of injection, the rate of rise in plasma concentration and the peak plasma concentration depending on the particular local anaesthetic technique being used. There is also some inter individual variation, and peak systemic concentrations may occur between 5 and 30min after administration.

The mechanism of action of Dexmedetomidine is unique and differs from currently used sedative drugs. Alpha-2 adrenoceptors are found in CNS in highest densities in the locus ceruleus, the predominant noradrenergic nuclei of the brainstem and an important modulator of vigilance. Presynaptic activation of alpha-2A adrenoceptor in the locus ceruleus inhibits the release of nor-epinephrine and results in the sedative and hypnotic effects.<sup>[3]</sup> In addition, the locus ceruleus is the site of origin for the descending medullospinal noradrenergic pathway, known to be an important modulator of nociceptive neurotransmission. Stimulation of alpha-2 adrenoceptors in this area terminates the propagation of pain signals leading to analgesia. Postsynaptic activation of alpha-2 receptors in the CNS results in decrease in sympathetic activity leading to hypotension and bradycardia.

At the spinal cord, stimulation of alpha-2 receptors at the substantiagelatinosa of the dorsal horn leads to inhibition of the firing of nociceptive neurons and inhibition of release of substance P. The spinal mechanism is the principal mechanism for the analgesic action of Dexmedetomidine even though there is a clear evidence for both a supraspinal and peripheral sites of action.<sup>[4]</sup>

Alpha-2 receptors are located on blood vessels where they mediate vasoconstriction and on sympathetic terminals, where they inhibit norepinephrine release. The responses of activation of alpha-2 receptors in other areas include contraction of vascular and other smooth muscles; decreased salivation and decreased bowel motility in the gastrointestinal tract, inhibition of renin release, increased glomerular filtration and increased secretion of sodium and water in the kidney, decreased release of insulin from the pancreas, decreased intraocular pressure, decreased platelet aggregation and decreased shivering threshold by 2°C.<sup>[5,6]</sup>

Dexmedetomidine is considered as the full agonist at alpha-2 receptors compared to clonidine which is considered as a partial agonist at alpha-2 adrenoceptors. The selectivity of Dexmedetomidine to alpha-2 receptors compared to alpha-1 receptors is 1620:1, whereas with clonidine it is 220:1. The selectivity is dose dependent, at low to medium doses and on slow infusion, high levels of alpha-2 selectivity is observed, while high doses or rapid infusions of low doses are associated with both alpha-1 and alpha-2 activities.

## Subjects and Methods

The study population was randomly selected based on the closed sealed opaque envelope technique.

**Group-B-** received 12.5mg (2.5ml) of 0.5% hyperbaric Bupivacaine with 0.5ml normal saline.

**Group-D-** received 12.5mg (2.5ml) of 0.5% hyperbaric Bupivacaine with 5µg of Dexmedetomidine in (0.5ml normal saline).

**Group-F** – received 12.5mg (2.5ml) of 0.5% hyperbaric Bupivacaine with 25µg Fentanyl in (0.5ml normal saline).

### Inclusion Criteria

Patients aged between 30 – 60 years belonging to ASA class I & II without any co-morbid disease admitted for elective TAH were included in the study.

### Exclusion Criteria

1. Patients with co-morbid conditions like diabetes mellitus, asthma, hypertension, cardiac disease, haematological disease etc.
2. Allergy to local anaesthetics.
3. Patients belonging to ASA class III, IV and V.
4. Patients posted for emergency surgeries.
5. Patients with body mass index more than 28kg/m<sup>2</sup>.
6. Patients having absolute contraindication for spinal anaesthesia like raised intracranial pressure, severe hypovolaemia, bleeding diathesis and local infection.
7. Patient's refusal.

### Methods of Collection of Data

Data was collected from 90 patients in the age group of 30-60 years of ASA class I & II, posted for elective TAH without any co-morbid diseases were grouped randomly by using closed sealed opaque envelope technique. The study drug was prepared by an anaesthesiologist, who was not involved with the study. All spinal blocks were given by the same anaesthesiologist who also was the observer. Hence the patient and the observer were blinded for the study drug.

## Results

**Table 1: Age distribution**

| Age in years | Groups         |      |                |       |                |       |
|--------------|----------------|------|----------------|-------|----------------|-------|
|              | Group-B        |      | Group-D        |       | Group-F        |       |
|              | No of patients | %    | No of patients | %     | No of patients | %     |
| 30-40        | 3              | 10%  | 1              | 3.3%  | 1              | 3.3%  |
| 41-50        | 15             | 50%  | 16             | 53.3% | 16             | 53.3% |
| 51-60        | 12             | 40%  | 13             | 43.3% | 13             | 43.3% |
| Total        | 30             | 100% | 30             | 100%  | 30             | 100%  |
| Mean±SD      | 49.10±6.365    |      | 50.50±5.710    |       | 50.20±5.851    |       |
| Minimum      | 37             |      | 39             |       | 38             |       |
| Maximum      | 60             |      | 60             |       | 60             |       |

P=0.79

The minimum age in Group-B, Group-D and Group-F were 37 years, 39 years and 38 years respectively. The maximum age in all the groups was 60 years. All three groups were similar with respect to age distribution and there was no statistically significant difference between the groups (P= 0.792).

**Table 2: Height distribution in cm**

| Height in cms | Groups      |             |             |
|---------------|-------------|-------------|-------------|
|               | Group-B     | Group-D     | Group-F     |
| No            | 30          | 30          | 30          |
| Mean±SD       | 159.46±4.07 | 160.83±5.42 | 158.26±4.63 |
| Minimum       | 152         | 150         | 151         |
| Maximum       | 166         | 168         | 165         |

P=0.117

The minimum height in Group-B, Group-D and Group-F were 152cm, 150cm and 151cm respectively. The maximum height in Group-B, Group-D and Group-F were 166cm, 168cm and 165cm respectively. There was no statistically significant difference in the height of the patients among three groups (p= 0.117).

**Table 3: Body weight distribution in kg**

| Weight in kg | Groups    |            |            |
|--------------|-----------|------------|------------|
|              | Group-B   | Group-D    | Group-F    |
| No           | 30        | 30         | 30         |
| Mean±SD      | 57.5±3.55 | 56.10±5.13 | 57.16±4.12 |
| Minimum      | 50        | 48         | 50         |
| Maximum      | 66        | 66         | 63         |

P = 0.393

The minimum body weight in Group-B, Group-D and Group-F were 50kg, 48kg and 50kg respectively. The maximum body weight in group-B, Group-D and Group-F were 66 kg, 66kg and 63kg respectively. There was no statistically significant difference between the three groups (P=0.393).

**Table 4: Adverse effects**

| Adverse effect  | Group-B   |       | Group-D   |       | Group-F   |       | P value |
|-----------------|-----------|-------|-----------|-------|-----------|-------|---------|
|                 | No of pts | %     | No of pts | %     | No of pts | %     |         |
| Bradycardia     | 2         | 6.6%  | 4         | 13.3% | 2         | 6.6%  | 0.578   |
| Hypotension     | 4         | 13.3% | 11        | 36.7% | 7         | 23.3% | 0.108   |
| Vomiting        | 0         | 0%    | 0         | 0%    | 1         | 3.3%  | 0.129   |
| Pruritus        | 0         | 0%    | 0         | 0%    | 0         | 0%    |         |
| Hypoventilation | 0         | 0%    | 0         | 0%    | 0         | 0%    |         |
| Desaturation    | 0         | 0%    | 0         | 0%    | 0         | 0%    |         |

In our study there was no statistically significant difference in the adverse effects throughout the procedure when Group-D and Group-F were compared with group-B and also there was no statistically significant difference when Group-D was compared with Group-F.

4 patients in Dexmedetomidine group, 2 patients each in Fentanyl group and control group developed bradycardia which was managed by Inj. Atropine 0.6 mg IV. 11 patients in Dexmedetomidine group, 7 patients in Fentanyl group and 4 patients in control group developed hypotension which was managed by Inj. Mephenteramine 6mg IV incremental doses. 1 patient in Group-F developed vomiting which was managed by Inj. Ondansetron 4mg IV.

## Discussion

CNS is more susceptible to Bupivacaine. The initial symptoms involve feeling of light headedness and dizziness followed by visual and auditory disturbances. Disorientation and occasional feeling of drowsiness may occur. Objective signs are usually excitatory in nature which includes shivering, muscular twitching and tremors; initially involving muscles of the face (perioral numbness) and part of extremities. At still higher doses cardiovascular or respiratory arrest may occur. Acidosis increases the risk of CNS toxicity from Bupivacaine, since an elevation of PaCO<sub>2</sub> enhance cerebral blood flow, so that more anaesthetic is delivered rapidly to the brain.<sup>[7]</sup>

Bupivacaine depresses rapid phases of depolarization (V<sub>max</sub>) in Purkinje fibres and ventricular musculature to a greater extent than Lignocaine. It also decreases the rate of recovery from a dependent block than that of Lignocaine. This leads to incomplete restoration of V<sub>max</sub> between action potential at high rates, in contrast to complete recovery by

Lignocaine. This explains why Lignocaine has antiarrhythmic property while Bupivacaine has arrhythmogenic potential. High level of Bupivacaine prolongs conduction time through various parts of heart and extremely high concentration will depress spontaneous pacemaker activity, resulting in bradycardia and arrest. Cardiac resuscitation is more difficult following Bupivacaine induced cardiovascular collapse and hypoxia along with acidosis which markedly potentiates cardiac toxicity. Bretylium but not Lignocaine could raise the ventricular tachycardia threshold that was lowered by Bupivacaine.

Respiratory depression may be caused if excessive plasma level is reached which in turn results in depression of medullary respiratory centre. Respiratory depression may also be caused by paralysis of respiratory muscles as may occur in high spinal or total spinal anaesthesia.

Continuous or intermittent epidural administration of Bupivacaine has been associated with increased plasma concentration of liver transaminase enzymes that normalized when Bupivacaine infusion was discontinued.

Myelinated preganglionic beta fibres have a faster conduction time and are more sensitive to the action of local anaesthetic including Bupivacaine. Involvement of preganglionic sympathetic fibres is the cause of widespread vasodilation and consequent hypotension that occurs in epidural and paravertebral block. When used for conduction blockade all local anaesthetic particularly Bupivacaine produces higher incidence of sensory blockade than motor fibres.<sup>[8]</sup>

In our study there was no statistically significant difference in the adverse effects throughout the procedure when Group-D and Group-F compared with group-B and also there was no statistical significant difference when Group-D was compared with Group-F. Our study compares with the study conducted by Al Ghanem S M et al<sup>[9]</sup>, Kanazi et al,<sup>[10]</sup> Mahendru V et al<sup>[11]</sup> and Makwana J<sup>[12]</sup> who also did not find statistical significant difference. In our study one patient in Group-F had vomiting which was statistically not significant.

## Conclusion

Both Fentanyl and Dexmedetomidine as adjuvants do not produce significant haemodynamic changes, with minimal effects on ventilation and oxygenation. They produce lesser incidence of pruritus and postoperative nausea and vomiting. Hence it is concluded that Dexmedetomidine is better than Fentanyl as an adjuvant to 0.5% hyperbaric bupivacaine for spinal anaesthesia.

## References

- Cousins MJ. Neural blockade in clinical anaesthesia and pain medicine. 4<sup>th</sup> ed. Philadelphia: Lippincott Williams and Wilkins; 2009.
- Corby MP, Bach AB. Transient radicular irritation (TRI) after spinal anaesthesia in day-care surgery. Acta Anaesthesiol Scand 1998;42:425-9.
- Henderson DJ, Faccenda KA, Morrison LM. Transient radicular irritation with intrathecal plain lignocaine. Acta Anaesthesiol Scand 1998;42:376-8.
- Casati A, Putzu M. Bupivacaine, Levobupivacaine and Ropivacaine: are they clinically different? Best Practice and Research Clinical Anaesthesiology 2005; 19:247-68.

5. Gupta R, Verma R, Bogra J, Kohli M, Raman R, Kushwaha J. A Comparative Study of Intrathecal Dexmedetomidine and Fentanyl as Adjuvant. *Journal of Anesthesiology Clinical Pharmacology* 2011;27930:339-43.
6. Elia N, Culebras X, Mazza C, Schiffer E, Tramèr MR. Clonidine as an adjuvant to intrathecal local anesthetics for surgery: Systematic review of randomized trials. *RegAnesth Pain Med* 2008;33:159-67.
7. Boussofara M, Carlès M, Raucoules-Aimé M, Sellam MR, Horn JL. Effects of intrathecal midazolam on postoperative analgesia when added to a bupivacaine-clonidine mixture. *RegAnesth Pain Med* 2006;31:501-5.
8. Seewal R, Shende D, Kashyap L, Mohan V. Effect of addition of various doses of Fentanyl intrathecally to 0.5% hyperbaric bupivacaine on perioperative analgesia and subarachnoid-block characteristics in lower abdominal surgery: a dose response study. *RegAnesth Pain Med*. 2007;32(1):20-6.
9. Al-Ghanem SM, Massad IM, Al-Mustafa MM, Al-Zaben K, Qudaisat IY, Qatawneh AM, et al. Effect of Adding Dexmedetomidine versus Fentanyl to Intrathecal Bupivacaine on Spinal Block Characteristics in Gynecological Procedure: A Double Blind Controlled Study. *American Journal of Applied Science* 2009;6(5):882-7.
10. Kanazi GE, Aouad MT, Jabbour-Khoury SI, Al Jazzar MD, Alameddine MM, Al-Yaman R, et al. Effect of low-dose Dexmedetomidine or clonidine on the characteristics of bupivacaine spinal block. *ActaAnesthesiolScand* 2006;50:222-7.
11. Mahendru V, Tewari M, Katyal S, Grewal A, Singh MR, Katyal R. A Comparison of Intrathecal Dexmedetomidine, Clonidine, and Fentanyl as Adjuvants to Hyperbaric Bupivacaine for Lower Limb Surgery: A Double Blind Controlled Study. *Journal of Anesthesiology Clinical Pharmacology*. 2013; 29(4):496-502
12. Makwana J, Shivraj TN, Khade A, Bansal S, Mandal N, Goswami S, et al. Comparison between hyperbaric bupivacaine and hyperbaric bupivacaine plus Fentanyl intrathecally in major gynecological surgeries. *International Journal of Medical Science and Public Health* 2014;3(3):319-323.

**Copyright:** © the author(s), publisher. Academia Anesthesiologica Internationalis an Official Publication of "Society for Health Care & Research Development". It is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

**How to cite this article:** Malashree, Vinod M. Intrathecal Dexmedetomidine 5µg and Fentanyl 25µg as Adjuvants to 12.5mg Of 0.5% Hyperbaric Bupivacaine for Spinal Anaesthesia: A Study on Adverse Effects. *Acad. Anesthesiol. Int.* 2019;4(2):222-225.

DOI: [dx.doi.org/10.21276/aan.2019.4.2.51](https://doi.org/10.21276/aan.2019.4.2.51)

**Source of Support:** Nil, **Conflict of Interest:** None declared.