



A Comparative Study of Intrathecal Dexmedetomidine and Fentanyl as an Adjuvant to Bupivacaine (Research Article)

Authors

Dr Rashmi Bengali¹, Dr Tushar Patil², Dr Priya Buddhadeo³

¹Associate Professor, ²Prof & Head of Department, ³Resident

Dept of Anaesthesiology, Govt Medical College and Hospital, Aurangabad, 431001 Maharashtra (India)

Corresponding Author

Dr Rashmi Bengali

C-19 Town Centre, Behind Cidco Bus Stand, CIDCO, Aurangabad

Email---drrvbengali@gmail.com, Mobile no.9822441318

Abstract

In recent years, the use of intrathecal adjuvants has gained popularity. The quality of spinal anaesthesia is improved with addition of opioids and other drugs but no drug is without side effects. The aim of this study was to compare the addition of either Dexmedetomidine or Fentanyl to intrathecal Bupivacaine as regards the onset and duration of sensory and motor block, hemodynamic effects, postoperative analgesia and adverse effects of either drug.

Sixty patients with ASA grade I and II scheduled for lower limb and lower abdominal surgeries were randomly allocated to two groups (30 patients each): Group D received 2.5 ml 0.5% hyperbaric Bupivacaine and 5 µg of Dexmedetomidine intrathecally. Group F received 2.5 ml 0.5% hyperbaric Bupivacaine and 25 µg of Fentanyl intrathecally.

Patients in group F had faster onset of motor and sensory block than group D (P = 0.000). Patients in group D had significantly longer duration of motor and sensory blockade as compared to those in group F (P = 0.000). Postoperative analgesia was significantly longer in group D than group F (P = 0.000). Incidence of side effects among the two groups was not statistically significant.

Fentanyl has faster onset compared with Dexmedetomidine but prolonged duration of sensory and motor blockade with postoperative analgesia was seen with Dexmedetomidine without significant side effects.

Keywords: *Dexmedetomidine, Fentanyl, Spinal Anaesthesia, Postoperative analgesia.*

Introduction

Regional anaesthesia has emerged as an important technique with simplicity, effectiveness, reliability and safety. It possesses less risk of pulmonary aspiration with excellent muscle relaxation. Additional benefits include reduction in metabolic response to surgery, reduction in blood loss, decreased incidence of thromboembolism,

decreased pulmonary compromise (particularly in patients with advanced pulmonary disease) and ability to monitor patient's mental status. Due to short duration of action of local anaesthetics and need for extending the analgesia in postoperative period necessitated the introduction of adjuvants like Midazolam, Neostigmine, Ketamine, Magnesium sulfate, Opioids, $\alpha 2$ agonists etc⁽¹⁾.

Dexmedetomidine is a selective α_2 -adrenergic receptor agonist. It prolongs analgesia when used intrathecally with local anaesthetics⁽²⁾. Analgesic action of α_2 -adrenergic receptor agonists is a result of depression of the release of presynaptic C-fibre transmitters and by hyperpolarisation of postsynaptic dorsal horn neurons⁽³⁾. It decreases central nervous system (CNS) sympathetic outflow in a dose dependent manner and has analgesic effects best described as opioid-sparing. Its organ protective effect against ischemic and hypoxic injury makes it cardioprotective, neuroprotective and renoprotective⁽⁴⁾. Neuraxial administration of opioids along with local anaesthetics improves the quality of intraoperative analgesia and also provides postoperative pain relief for longer duration. Intrathecally Fentanyl, has rapid onset of action being lipophilic opioid,. It does not tend to migrate to the fourth ventricle in sufficient concentration to cause delayed respiratory depression. It provides better intraoperative analgesia and a safer alternative than morphine for management of early postoperative pain⁽⁵⁾. The capacity of spinal opiates to reduce the release of excitatory neurotransmitter from C fibers and decrease the excitability of dorsal horn neuron accounts them for the powerful and selective on spinal nociceptive processing.

Material and methods

After the approval of the ethical committee, written informed consent was obtained from all patients. Inclusion criterias were -patients between 18 and 50 years of age of either sex, height more than 150 cm, (ASA) physical status I and II and patients scheduled for elective lower abdominal or lower limb surgeries. Exclusion criterias were- pregnancy and lactation, allergy to the study medications, heart block and dysrhythmias, hypertension, therapy with adrenergic receptor antagonist, calcium channel blocker, and/or angiotensin converting enzyme inhibitor, and patients with contraindications for spinal anaesthesia. After detail history, complete

physical examination and laboratory investigations were carried out. Standard monitors with -ECG, noninvasive arterial blood pressure, and oxygen saturation were applied. Patients were preloaded with intravenous lactated Ringer's solution 10 ml/kg. Spinal anaesthesia was induced in the sitting position at the L3–L4 interspace using a 25 G Quincke's spinal needle with all aseptic precautions.

Study Design:

Prospective, Randomized, Double blind study

Group D

Inj Bupivacaine 0.5% (H) 2.5 cc (12.5mg)
+ Inj Dexmedetomidine 5 μ g in 0.5 ml NS
[Total volume 3 cc]

Group F

- Inj Bupivacaine 0.5% (H) 2.5 cc (12.5mg) + Inj Fentanyl 25 μ g [Total volume 3cc]

Injection was given over 10–15sec; immediately patients were made to lie supine. All patients were given 4 lit/ min supplemental oxygen with face mask.

Pulse rate and blood pressure were monitored immediately after injection and then every 2 min till 10 min and every 5 min for 30 min and then every 15 min thereafter till the end of surgery and till the recovery from block. Thereafter every 2 hours till 24 hours. Hypotension was defined as decrease in systolic blood pressure by more than 30% from baseline ,treated with IV fluids and 3 mg Mephenteramine IV. Bradycardia was defined as a heart rate less than 50 beats per minute treated with 0.6 mg of Atropine IV. The incidence of adverse effects such as hypotension, bradycardia, nausea, vomiting, shivering, pruritus, respiratory depression was recorded.

Sedation: was assessed with the Ramsay Sedation Score:

- Score- (1) Anxious, restless or both.
(2) Cooperative, oriented and tranquil.
(3) Responding to commands.
(4) Brisk response to glabellar tap.
(5) Sluggish response to glabellar tap.

(6) No response.

Sensory Block Assessment:

Sensory level was determined by pinprick using 24 G hypodermic needle. Onset of sensory level was defined as time interval from completion of subarachnoid injection i.e. zero time to loss of pinprick sensation at umbilicus (T10). Maximum sensory level was tested in midclavicular line every minute until the level is stabilized for two consecutive tests. Afterwards sensory level was tested every 15 min until two segment regression for duration of anaesthesia. Time taken to achieve maximum sensory level and 2 segment regression was noted.

Postoperatively patients were interrogated every 15 min for pain at surgical site. Analgesics were not given until demanded by patient. Time taken from administration of drug to time patient first demanded analgesic was noted which is considered as duration of effective analgesia.

Motor Block Assessment:

It was assessed by straight leg raising while lying supine and was graded according to modified Bromage scale ⁽⁶⁾.

- Grade 0 - no motor block
- Grade 1 - inability to raise extended leg
- Grade 2 - inability to flex knee but able to flex ankle
- Grade 3 - inability to flex ankle complete motor block

Onset of motor block was defined as time taken from injection of drug till patient was unable to flex ankles.

Recovery of motor block was defined as ability of patient to flex hip and was recorded every 15 min. Duration of motor block was calculated from 0 time up to recovery of motor block.

Postoperative Pain Assessment:

Duration of postoperative analgesia was measured from the time of injection of spinal anaesthesia to the time when pain score becomes more than or

equal to 3 according to VAS. Then patient was given Inj Diclofenac Sodium 75mg IV.

VAS score:

- No pain
- 1, 2, 3- mild pain
- 4, 5, 6- moderate pain
- 7, 8, 9 - severe pain
- worst pain

Data Analysis:

Quantitative data is presented with the help of Mean, Standard deviation; comparison among study group was done with the help of Unpaired T test or Mann-Whitney test as per results of Normality test. Qualitative data is presented with Frequency and Percentage tables; association among study parameters is assessed with the help of Chi-Square test (Fisher Exact test for 2x2 tables). P value less than 0.05 is taken as significant.

Observations and results:

In our observations Group D denotes patients receiving 12.5 mg 0.5% Bupivacaine with 5µg Dexmedetomidine and Group F denotes patients receiving 12.5 mg 0.5% Bupivacaine with 25 µg Fentanyl.

The groups were comparable with respect to age, height, weight and sex (Table 1 and 2)

The onset was significantly faster in group F (369.33±41.27sec) compared with group D (462±61.33sec). In group D, the mean time to reach highest sensory level was 10.65±1.73 min; in group F it was 7.92±0.64min. Group D (138.83±11.5 min) had significantly longer duration of sensory block as compared with groups F (115.5±9.94 min). The onset of motor block in group F (472±49.16 sec) was significantly faster compared with group D (540±66.85 sec). The regression time to modified Bromage score 0 was slower in group D compared with group F; with a total mean duration of motor block in group D was 301.67±19.45 min; in group F was 267.50±11.2 min.

The time to first analgesia request was significantly longer in group D (344.67±25.43 min) compared with group F (240.83±24min) ($P=0.000$). (Table no.3)

There were no significant complications on comparing the two groups (Table no. 4)

Table No.1 Comparison of Demographic Characteristics Including Age, Height and Weight

Study parameter	Group D	Group F	P value
Age (yrs)	33.6±9.74	31.7±9.01	0.436(NS)
Weight (kg)	64.4±6.25	63.77±6.58	0.617(NS)
Height (cm)	161.5±6.42	159.73±6.34	0.288(NS)

(T Test applied, p value is significant if <0.05) Values are represented as mean ± SD

Table No. 2 Comparison of Demographic Characteristics Including Gender

	Group D	Group F	P value
Male	24	21	0.371(NS)
Female	6	9	
Total	30	30	

(T Test applied, p value is significant if <0.05) Values are represented as mean ±SD

Table No. 3 Comparison of Study Group For

Study parameter	Group D	Group F	P Value
Onset of sensory block(sec)	462±61.33	369.33±41.27	0(significant)
Time to cephalic spread(min)	10.65±1.73	7.92±0.64	0(significant)
Two segment regression(min)	138.83±11.5	115.5±9.94	0(significant)
Onset of motor block(sec)	540±66.85	472±49.16	0(significant)
Duration of motor block(min)	301.67±19.45	267.50±11.2	0(significant)
Duration of surgery (min)	101.17±11.72	98.33±13.41	0.387(Not significant)
Post operative analgesia(min)	344.67±25.43	240.83±24	0(significant)

(T Test applied, p value is significant if <0.05) Values are represented as mean ±SD

Table No 4 Comparison of Overall Incidence of Side Effects and Complications

Complication	Group D	Group F	Total
Bradycardia	4(13.3%)	1(3.3%)	5(8.3%)
Hypotension	3(10%)	2(6.7%)	5(8.3%)
Nausea and vomiting	1(3.3%)	2(6.7%)	3(5%)
Pruritus	0(0.0%)	2(6.7%)	2(3.3%)
Shivering	0(0.0%)	2(6.7%)	2(3.3%)
No complication	22(73.3%)	21(70%)	43(71.7%)
Total	30(100%)	30(100%)	60(100%)

($X^2=6.357$, d (f) =5, p value- 0.273 (not significant)

(Chi square test is applied. P value is significant if <0.005)

Discussion

Nature has placed mankind under the government of two sovereign masters – PAIN AND PLEASURE

JEREMY BENTHAM (1748-1832)

The sole essence of anaesthesia is pain relief in perioperative period for which spinal anaesthesia is the most commonly used technique. However, for postoperative pain control, spinal anaesthesia using only local anaesthetics is associated with relatively short duration of action, and thus early analgesic intervention is needed⁽⁷⁾.

The quality of the spinal anaesthesia is improved by the addition of opioids (such as Morphine, Fentanyl and Sufentanil) and other drugs such as Dexmedetomidine, Clonidine, Magnesium sulphate, Neostigmine, Ketamine and Midazolam, but no drug to inhibit nociception is without associated adverse effects.⁽¹⁾

Fentanyl is a lipophilic mu receptor agonist opioid. Intrathecally, Fentanyl exerts its effect by combining with opioid receptors in the dorsal horn of the spinal cord and may have a supraspinal spread and can exhibit various adverse actions⁽⁸⁾.

Sullivan *et al*⁽⁹⁾ have studied the ED₅₀ of 2.5 µg Dexmedetomidine for inhibition of C fibre responses of dorsal horn neurons and Aβ-evoked responses were inhibited to a lesser degree with a maximum inhibition seen above 10 µg dose.

α₂ Adrenoreceptor agonists act by binding to the presynaptic C-fibers and postsynaptic dorsal horn neurons. They produce analgesia by depressing the release of C-fiber transmitters and by hyperpolarization of post synaptic dorsal horn neurons. The complementary action of local anaesthetics and α₂ adrenoreceptor agonists account for their profound analgesic properties. The prolongation of the motor block of spinal anaesthetics may be the result of binding of α₂ adrenoreceptor agonists to the motor neurons in the dorsal horn. Dexmedetomidine is eight times more specific and highly selective α₂ adrenoreceptor agonists compared to Clonidine, thereby making it a useful and safe adjunct in

diverse clinical applications⁽¹⁰⁾. In a few dose finding studies, investigators have used 3, 5, and 10 mcg of intrathecal Dexmedetomidine in human subjects with favorable results,^{(13),(14),(15)} along with preserved hemodynamic stability and lack of sedation.

In our study, the distribution of patients according to age, gender, height and weight was comparable and statistically insignificant ($p > 0.05$). (Table no. 1, 2)

Onset of sensory block was significantly longer ($p < 0.001$) in group D (462 ± 61.33 sec) as compared to group F (369.33 ± 41.27 sec). (Table no.3)

The mean time to achieve maximum sensory block in group D (10.65 ± 1.73 min) and in group F (7.92 ± 0.64 min). (Table no.3)

Similar maximum sensory dermatomal level was achieved by Dexmedetomidine and Fentanyl in equipotent doses.

The mean time to achieve onset of motor block in group D (540 ± 66.85 sec) was significantly higher (P value 0.000) than group F (472 ± 49.16 sec). (Table no.3)

The reason for the observed difference between our results and that seen in the other studies could be attributed to the methodological differences like difference in the drug dosage and baricity or total volume of drug used.

Mean time required for two segment regression was significantly higher (P value –0.000) in group D (139.83 ± 11.5 min) than group F (115.5 ± 9.94 min). (Table no.3)

Mean duration of motor block was significantly higher in group D (301.67 ± 19.45 min) as compared to group F (267.50 ± 11.2 min) (Table no.3)

Duration of postoperative analgesia was significantly longer in group D (344.67 ± 25.43 min) as compared with group F (240.83 ± 24 min). (Table no.3)

Thus Dexmedetomidine prolongs the duration of sensory block, and also the duration of the motor block. Dexmedetomidine acts on α₂ adrenoreceptors in substantia gelatinosa of spinal

cord and blocks C and A delta fibers, it increases the potassium conductance intensifying the conduction block of local anaesthetics. It may have an additive or synergistic effect with local anaesthetic in increasing the time of two segment regression and total duration of complete analgesia. The potentiation of motor block by Dexmedetomidine may be an additive or synergistic effect to the local anaesthetics or related to the interference with neuromuscular activity or binding of α 2-agonists to motor neurons in the dorsal horn⁽¹⁶⁾.

Dexmedetomidine produce sedative effect by acting on α 2-adrenergic receptors in locus ceruleus.

In our study the mean sedation scores were found to be comparable and statistically insignificant ($p > 0.05$) preoperatively and intraoperatively among the two groups.

Preoperatively and intraoperatively the difference between mean PR, SBP, DBP, MAP, RR, SpO₂ were insignificant (p value > 0.005)

Intrathecal narcotics, enhance the sensory blockade and prolong postoperative analgesia. They are associated with increased risk of nausea, vomiting, itching and respiratory depression. Opioids are known to depress all phases of respiration by their action on the opioids receptors in the ventral medulla, irrespective of route of administration. Fentanyl is a μ receptor agonist which can be administered safely intrathecally. It is highly lipophilic which prevents its rostral spread. But, systemic absorption of the drug could contribute to the lower respiratory rates by direct depressant action on μ receptors in brainstem. Although the incidence of intraoperative and postoperative complications were not statistically significant among the two groups. (Table no.4)

Conclusion

It can be concluded from the study that Fentanyl has comparably faster onset of sensory and motor blockade than Dexmedetomidine. Prolonged duration of sensory and motor block with excellent quality of anaesthesia was seen with

Dexmedetomidine as compared to Fentanyl. In addition Dexmedetomidine significantly prolongs the duration of postoperative analgesia as compared to Fentanyl without any statistically significant side effects.

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