A COMPARATIVE STUDY OF INTRATHECAL FENTANYL AND DEXMEDETOMIDINE AS ADJUVANTS TO BUPIVACAINE

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ABSTRACT

BACKGROUND
Various adjuvants have been added to bupivacaine to shorten the onset of block and prolong the duration of block. Fentanyl, a lipophilic opioid agonist, is used as an adjuvant, which prolongs the duration of spinal block. Dexmedetomidine, an α2 agonist drug, when given in intrathecal space, significantly prolongs the duration of spinal block.

MATERIALS AND METHODS
A prospective randomised double-blinded comparative study has been conducted in 100 patients belonging to ASA physical status I and II of both sexes were divided into two groups of 50 each. Group F received 3 mL Inj. Bupivacaine heavy with 25 micrograms of fentanyl and Group D received 3 mL Inj. Bupivacaine heavy with 5 micrograms of dexmedetomidine. The time of onset of sensory and motor block, haemodynamic status, duration of analgesia and adverse effects if any were compared in both the groups.

RESULTS
Time from injection to highest sensory level and onset of Bromage 3 was similar in both groups. Time from injection to T10 sensory level was significantly shorter in Group D (p<0.001) and time for regression to Bromage 0 was significantly longer in group D (p<0.001). Intraoperatively, both groups remained haemodynamically stable. Incidence of bradycardia was more in Group D and incidence of pruritus was more in Group F, though it was not statistically significant (p=0.402). Intraoperative sedation was higher in Group D (p<0.001) and postoperatively visual analogue scores were significantly lower with group D (p<0.001).

CONCLUSION
Dexmedetomidine appears to be an attractive adjuvant to intrathecal bupivacaine than fentanyl as there is significantly longer duration of motor block, additional benefits of intraoperative sedation and decreased analgesic requirement in the postoperative period.

KEYWORDS
Intrathecal; Bupivacaine; Fentanyl; Dexmedetomidine; Bromage; Sedation.

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BACKGROUND
Mechanism of action of bupivacaine is similar to that of any other local anaesthetics. The primary action of local anaesthetics is on the cell membrane of the axon, on which it produces electrical stabilisation. The large transient increase in permeability to sodium ion, necessary for propagation of impulse is prevented. Thus, the resting membrane potential is maintained and depolarisation in response to stimulus is inhibited. Initially, the threshold for electrical excitation is raised, the rate of rise of action potential reduced and conduction slowed. Eventually, propagation of the impulse fails.1

Fentanyl citrate is a synthetic phenylpiperidine opioid agonist that is structurally related to meperidine. As an analgesic, fentanyl is 75 to 125 times more potent than Morphine.

After IV administration, onset of action is within 1-2 mins. with duration of action 60 minutes. After epidural route, onset is immediate and duration is 3-4 hrs. In intrathecal route administration, onset is 5 minutes and duration is 3-5 hrs. Therefore, the present study was performed to compare the efficacy of fentanyl and dexmedetomidine as adjuvants to subarachnoid block.

Objectives of Study
The aim of the study is to compare the following factors in two groups, i.e.

a. Hyperbaric bupivacaine 0.5% and 25 μgm fentanyl.
b. Hyperbaric bupivacaine 0.5% and 5 μgm dexametomidine when given intrathecally.

MATERIALS AND METHODS
A prospective randomised double-blinded comparative study has been conducted in 100 patients belonging to ASA physical status I and II of both sexes were divided into two groups of 50 each. Group F received 3 mL Inj. Bupivacaine heavy with 25 micrograms of fentanyl and Group D received 3 mL Inj. Bupivacaine heavy with 5 micrograms of dexametomidine. The time of onset of sensory and motor block, haemodynamic status, duration of analgesia and adverse effects if any were compared in both the groups.

Inclusion Criteria
- ASA physical status, class I and II.
- Age between 18-65 years of either sex.

Exclusion Criteria
- Emergency surgery.
- Deformities of the spine.
- Hypersensitivity to any of the drugs in the study.
- Contraindications to spinal anaesthesia - patient refusal, bleeding diathesis.

Methodology
- After approval from the ethical committee of our college, 100 ASA I and II patients scheduled for major surgeries under spinal anaesthesia were chosen for the study.
- Preanaesthetic checkup was done one day prior to the surgery.
- Patients were evaluated for any systemic diseases and laboratory investigations recorded. The procedure of SAB was explained to the patients and written consent was obtained. The patients were educated about the use of visual analogue scale.
- Preparation of patients included period of overnight fasting.
- Patients were premedicated with Tab. Rantac 150 mg and Tab. Anxit 0.5 mg h.s.

Onset and Duration of Analgesia- Speed of onset and duration of analgesia as determined by lack of appreciation to pinprick.
Motor Blockade- Speed of onset and duration of motor blockade as assessed by Bromage scale.
Intraoperative Sedation- Assessed using modified Ramsay sedation scale.
Postoperative Period- Postoperative pain assessed using visual analogue scale. Analgesic requirements and postoperative complications such as nausea, vomiting, hypotension, shivering, pruritus, seizures and respiratory depression are assessed.

The vertebral column usually consists of 24 separate (presacral) vertebrae, 5 fused vertebrae in the sacrum and variably 4 fused or separate coccygeal vertebrae.

Of the 24 separate vertebrae, 12 support ribs (thoracic), 7 are in the neck (cervical) and 5 are in the lumbar region (lumbar).

Statistical analysis was done by applying Chi-square test, ANOVA test and Student’s t-test to analyse the data, p value was determined.

RESULTS

Graph 1. Shows Age Distribution in Each Group

The patients who took part in this project were in the age group of 18 to 65 years. On statistical comparison, the two groups were comparable.

Gender distribution in both the groups, and on statistical analysis, we found that samples are gender matched with P = 1.000.
Graph 4(A). Time from Injection to Highest Sensory Level

Graph 4(B). Time from Injection to T10 Level

Graph 4(C). Onset of Bromage 3 (in Minutes)

Graph 4(D). Time for Regression to Bromage 0 (in Minutes)

Graph 5. Highest Sensory Level

Graph 6. Comparison of Systolic Blood Pressure Changes in Both Groups

Graph 7. Comparison of Diastolic Blood Pressure Changes in Both Groups

Graph 8. Comparison of Map (mmHg) in Two Groups of Patients Studied

Variables | Group F | Group D | P value
--- | --- | --- | ---
Time from injection to T10 (minutes) | 3.38±0.83 | 2.62±0.56 | <0.001
Time from injection to highest sensory level (minutes) | 11.47±1.23 | 11.72±1.23 | 0.314
Onset of Bromage 3 (minutes) | 10.38±1.08 | 10.59±1.00 | 0.317
Regression to Bromage 0 (minutes) | 152.90±8.31 | 419.70±16.85 | <0.001
Dexmedetomidine is a potent drug at plasma concentrations less than 1.0 ng/mL. It can produce profound physiological alterations. Dexmedetomidine is an isomer and the active component of medetomidine.

Therapeutic role in anaesthesia, haemodynamic stability and prevention of perioperative ischaemia is one of the goals of anaesthesia, especially in those patients at risk of cardiac ischaemia during surgery to maintain myocardial oxygen balance. This can be achieved by attenuating sympathetically mediated hyperdynamic responses to stimulation, while maintaining perioperative circulatory function. The ability of alpha-2 adrenoceptor agonists to modulate sympathetic tone leads to a desirable haemodynamic profile, which may help to maintain the myocardial oxygen supply/demand ratio.

Talke and colleagues reported that a target plasma concentration of dexmedetomidine of 0.45 ng/mL administered to patients with coronary artery disease undergoing vascular surgery resulted in less perioperative ischaemia compared with placebo.

Sedation and anxiolysis sedation along with anxiolysis and an antialagogue effect make alpha-2 adrenoceptor agonists useful premedication drugs. Its disadvantage is that at present it can only be given as an intramuscular or intravenous injection. Dexmedetomidine administered at an intramuscular dose of 2.5 µg/kg as a premedication produced sedation and anxiolysis comparable with a midazolam dose of 80 µg/kg.

anaesthetic Requirements
- Reduction of MAC of 90% by dexmedetomidine.
- Dexmedetomidine has also been reported to be opioid and barbiturate sparing.

Analgesia- Stimulation of the alpha-2 adrenoceptors in the substantia gelatina of the dorsal horn of the spinal cord by intrathecal noradrenaline or specific agonists inhibits the firing of nociceptive neurones stimulated by peripheral Ad and C fibres.

Also, intrathecal noradrenaline inhibits the release of substance P by primary afferents of the dorsal horn and suppresses the activity of wide dynamic range neurones evoked by noxious stimulation.

Recent evidence suggests that the antinociception produced by alpha-2 adrenoceptor agonists maybe due in part to acetylcholine release in the spinal cord. Because, it has been suggested that the spinal cord is the major site of analgesic action of alpha-2 adrenoceptor agonists, the epidural and intrathecal routes have been considered preferable to the intravenous route.

Epidural Administration
Epidural dexmedetomidine is effective and safe in the management of acute postoperative pain, improving analgesia and reducing opioid requirements. It may be beneficial to administer alpha-2 adrenoceptor agonists, opioids and local anaesthetic drugs together. This may make...
it possible to decrease the dose of each agent without loss of efficacy and hence reduce the side effects of each agent. Intrathecal Administration- In a few dose finding studies, investigators have used 3, 5 and 10 mcg of intrathecal dexmedetomidine in human subjects with favourable results along with preserved haemodynamic stability and lack of sedation. A drawback of dexmedetomidone supplemented spinal block characteristics maybe an increase in the duration of motor block, which may not suit ambulatory procedures.

Postoperatively, VAS scores were significantly low for the dexmedetomidine group when compared with fentanyl.

The 4 Classical Side Effects are-

Pruritus-
Incidence - 0-100%.
Maybe generalised, but more likely over face, neck and thorax.
Mechanism - Cephalad migration of the drug in CSF, subsequent interaction with trigeminal nucleus located in medulla.
The “itch-reflex” maybe initiated by opioid interaction in substantia gelatinosa through indirect action on the trigeminal nucleus.

Nausea and Vomiting-
Incidence - 30% more frequent in women than men
mechanism-
- Opioid receptor located at area postrema are activated by cephalad spread of drug.
- Sensitisation of vestibular system to motion.
- Decreased gastric emptying time also play a role in producing nausea and vomiting.

Urinary Retention-
Incidence 0-80%, common in young males related to dose of opioid administered mechanism- interaction with opioid receptor located in sacral cord, which promotes inhibition of sacral parasympathetic nerves, which causes detrusor muscle relaxation and increased bladder capacity leading to retention of urine.

Respiratory Depression-
Early respiratory depression occurs within 2 hrs. of injection, which is very rare following intrathecal fentanyl.
Delayed respiratory depression, which occurs after 2 hrs. of administration has not been described with fentanyl single dose, however, it is dose dependent and higher with concomitant systemic use of sedatives.

Counter Measures for Adverse Effects-
- Pruritus, nausea and urinary retention can be reversed by Inj. Naloxone (antagonist) antihistamine, antiemetic and by catheterisation.
- Respiratory depression - by Naloxone and by mechanical ventilation.
- Bradycardia - Inj. Atropine or glycopyrrolate IV.
- Therefore, the present study was performed to compare fentanyl and dexmedetomidine in their efficacy as adjuvants to spinal anaesthesia.

In our study design, group F received 0.5% of hyperbaric bupivacaine 3 mL with fentanyl 25 µg and group D received 0.5% hyperbaric bupivacaine 3 mL with dexmedetomidine 5 µg injected intrathecally to the patients undergoing infraumbilical surgeries.

The following parameters were observed-
- Time of onset of action.
- Highest level of sensory and motor blockade.
- Time of onset of Bromage 0.
- Intraoperative heart rate, blood pressure, SpO2.
- Intraoperative sedation.
- Regression to Bromage 3.
- Postoperative requirement of analgesia.

Rajni Gupta et al,⁹ they also found that intraoperative ephedrine requirement was more in group D as compared to group R. In our study, intraoperative incidence of hypotension was higher in group F.
Rajni Gupta et al⁠¹⁰ conducted a comparative study of intrathecal dexmedetomidine 5 µgm and fentanyl 25 µgm as adjuvants to bupivacaine and found that intrathecal dexmedetomidine is associated with prolonged motor and sensory block, haemodynamic stability and reduced demand for rescue analgesics in 24 hrs. as compared to fentanyl. In our study also, the postoperative analgesic requirements was significantly less in the dexmedetomidine group than group fentanyl.
They also found that the sedation score was more in group D patients. The mean sedation score was 3.8 ± 0.5 in group D as compared to 2.2 ± 0.53 in group F, which was statistically significant (P<0.05). In our study, the mean sedation score for group F was 2.16 ± 0.37 and group D was 3.40 ± 0.49, which was statistically significant (p <0.001). There was no incidence of respiratory depression.
Pruritus after intrathecal fentanyl is known, but it was not significant in the present study. The α2 adrenergic agents also have anti-shivering property as observed by Talke et al¹¹ and Maroof M et al.¹² We too did not find any incidence of shivering.

CONCLUSION
Dexmedetomidine has higher efficacy with intrathecal bupivacaine with prolonged duration of sensory and motor blockade with decreased incidence of side effects, better haemodynamic stability and intraoperative sedation and also analgesic sparing effect in the postoperative period when compared to fentanyl.

REFERENCES


