



Use of Intrathecal dexmedetomidine and fentanyl as adjuvants to low dose spinal anesthesia with levobupivacaine in patients undergoing transurethral resection of prostate -A Comparative study

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Abstract

Purpose of the study: Patients undergoing transurethral resection of prostate are usually elderly patients with unstable hemodynamics. As far as transurethral resection of prostate cases are concerned, anesthesia level up to T10 dermatome is sufficient. This will minimize the hemodynamic alterations in geriatric age group. So the aim is to use low dose spinal anesthesia but this low dose spinal anesthesia alone using single drug levobupivacaine does not provide sufficient surgical anesthesia. So addition of adjuvants was considered. The aim of the study was to compare the adjuvant effects of intrathecal dexmedetomidine and intrathecal fentanyl with low dose levobupivacaine spinal anesthesia.

Methods: Comparative study was double blinded randomized trial which included 60 patients of ASA grade I,II,III posted for transurethral resection of prostate. They were divided into two groups. Group D receiving Dexmedetomidine and Group F receiving Fentanyl with low dose levobupivacaine intrathecally. Outcomes which were compared between two groups were characteristics of block; hemodynamical changes intra-operatively and post-operative analgesic requirements.

Results: Baseline demographic attributes were comparable. peak sensory levels were similar in both groups D and F around T8. Group D has quicker onset of sensory block than group F.

[Group D 10.7 ± 2.24 min][Group F 11.8 ± 1.75 min]

Duration of block was more in group D (197.033 ± 12.71 min) compared to Group F with (187.8 ± 8.23 min). The requirement of first analgesic dose was based on VAS score. It was delayed in Group D where the mean time of analgesic requirement was (212.033 ± 15.07 min) where as in fentanyl it was (200.27 ± 7.45 min).

Conclusion: Intrathecal dexmedetomidine with low dose levobupivacaine provided faster onset of anesthesia with increased duration of sensory and motor block. The duration for rescue analgesic requirement was more in group D with lower post-operative VAS scores. However, the haemodynamics in both groups were similar.

Keywords: Adjuvants, levobupivacaine, dexmedetomidine, fentanyl, spinal anesthesia, TURP.

Introduction

The most common problem encountered in geriatric population is benign prostatic hypertrophy. Unstable hemodynamics during anesthesia is common in this age group. Spinal anesthesia is the most commonly used technique for transurethral resection of prostate.

A block up to T10 is considered sufficient in patients undergoing TURP as this will abolish the discomfort of bladder distension and gross hemodynamic changes.

Any block beyond T10 will mask the early diagnosis of capsular signs due to bladder perforation. So in our study we used smaller doses of local anesthetic with adjuvants which provides adequate motor and sensory block.

Dexmedetomidine is the s-enantiomer of medetomidine which has not been widely used in urological procedures while fentanyl is the synthetic opioid whose use has been rise in recent days.

Levobupivacaine is the s-enantiomer of bupivacaine belonging to amino-amide group. It is comparatively less cardiotoxic. Hence, the use of levobupivacaine for spinal anesthesia is increasing these days.

In this study we tried to compare the characteristics of spinal block, hemodynamic changes and analgesic requirements.

In Group-D, 5µg of Dexmedetomidine was used as adjuvant to 10mg (2ml) isobaric levobupivacaine and in Group F 25 µg of Fentanyl was used as adjuvant to 10mg (2ml) of levobupivacaine.

Methods

Study was double blinded, prospective randomized was conducted in King George Hospital, Visakhapatnam between February 2018 to May 2018. Informed Consent was taken from all patients

Sixty elderly male between age group 50 to 80 years and ASA grade I, II, III who were posted for TURP were included in the study. Patients were randomly allocated into two groups, Group D and Group F. Patients with history of spine surgery,

bleeding disorders and coagulopathy, allergic reactions to local anaesthetics were excluded from the study.

In Group D consisting of thirty patients 2ml (10mg) of 0.5% isobaric levobupivacaine with 0.5ml (5µg) of dexmedetomidine hydrochloride as adjuvant was used in spinal anesthesia.

In Group F (thirty patients) 2ml (10mg) 0.5% isobaric levobupivacaine with 0.5ml (25µg) Fentanyl as adjuvant was used. The anesthesiologists involved in the study were not aware of the adjuvant being used until the entire sixty patients were completed according to the randomized numbers allotted to the patients.

All the patients were kept nil oral from mid night. They were administered T. Alprazolam 0.25mg in the night before surgery.

Inj. Ondansetron 4mg and Inj Metoclopramide 10mg, Inj. Ranitidine 50mg were given 30min. before surgery.

The patients were then brought to operation theatre. Intravenous lines were secured. Preloading was started with normal saline. Non-invasive Blood pressure monitoring, peripheral oxygen saturation monitor and ECG were attached. All the baseline vitals were noted. Study drug solution used in both groups D and F was identical with same 2.5ml volume. Drug solution was prepared by anesthetist who was not involved in the study.

Dexmedetomidine 1ml diluted to 10ml with normal saline so that each ml contains 10 µg, out of each 0.5 ml i.e., 5 µ of Dexmedetomidine was taken and added to 2ml of isobaric Levobupivacaine. Total 2.5 ml solution was prepared. Similarly 0.5 ml of undiluted fentanyl amounting to 25 µg was added to 2ml isobaric levobupivacaine thus making it to 2.5 ml

Preparation of both solutions was done in strict aseptic precautions. Help was taken from colleague anesthetists and post graduate students who were unaware of the study to monitor all aspects of the study like.

- a) Characteristics of spinal block
- b) Incidence of adverse events

c) Analgesic requirements in two groups

Assessment of Characteristics of Spinal Block

After giving spinal anesthesia following strict aseptic precautions, level of anaesthesia was checked and after attaining T10 level surgeon was asked to proceed. Then assessment was done every 30 minutes to assess for the regression of spinal anaesthesia. Regression by two segments was taken as criteria. Motor block was assessed by using modified Bromage scale before the start of surgery and at the end of surgery followed by every 30 minutes until complete motor recovery. If patient complains of pain or discomfort, 100 μ fentanyl was given and attempted to continue the procedure failing which general anesthesia was given and the patient was eliminated from our study.

Post Operative Pain Assessment and Analgesic Requirement

VAS \rightarrow 11 Point visual analogue scale

0 -No pain

10 -worst pain was used for pain assessment.

Inj. Butarphanol. 1mg I.V. was used as rescue analgesic when the patient needed. Assessment of pain was done every 2nd hourly until 24 hours post operatively.

Time for first analgesic dose was noted.

Adverse Events

Heart Rate below 45 was considered as bradycardia and Mean arterial pressure < 60 was considered as Hypotension. Bradycardia and Hypotension were noted and treated accordingly with Inj. Atropine and Inj. Mephenteramine. For patients complaining of nausea and vomiting, Inj. Ondansetron 4 mg I.V. given. Intra operative Respiratory Depression if any was treated with mask ventilation and case was excluded from study.

Statistical Methods

The main derivative of the study was duration of sensory block assessed by time of regression of

two dermatomes levels from initial level. This was taken from a previous study(s).

In group D the mean time \pm SD to the sensory regression of two dermatomes from highest level was 125.833 \pm 9.88 min. while in Group F was 120 \pm 5.20 min in previous study. Sample size was calculated using $\alpha = 0.05$ and power of 80% which come up to 24 patients required for group to detect or 25% difference in time for 2 segment dermatome regression of sensory Block. So in our study we involved thirty patients per group to allow for possible drop out.

Student t-test was used to analyse age; weight, duration of surgery, duration of Sensory and Motor Block; VAS scores every hourly upto 4 hours, total duration of Analgesia and requirement of rescue analgesic first dose. The differences between two groups in various derivatives were tested with many Man-whitney U test. Z test i.e., test of proportion was used to test the significant differences between two groups. Values were expressed as mean \pm SD. $p < 0.05$ was considered statistically significant.

Results

The Demographic variables like age; weight, ASA physical status in both groups were comparable and there is no significant statistical difference between the two groups.

Table 1:

CHARACTERISTICS	GROUP D (n=30)	GROUP F (n=30)	P VALUE
AGE(YEARS)	57.8 \pm 4.31	58.2 \pm 4.78	0.7348
WEIGHT(IN KGS)	65.567 \pm 11.18	66.06 \pm 11.76	0.8684
DURATION OF SURGERY(MINS)	82.93 \pm 7.07	83.43 \pm 7.31	0.7887
ASA PHYSICAL STATUS	11(36.7)	20(66.7)	1.0000
GRADE I			
GRADE II	17(56.7)	9(30)	
GRADE III	2(6.6)	1(3.3)	

The mean time taken to reach T10 sensory Block was (10.70 \pm 2.24min) was lower in Group D than with Group F which was (11.8 \pm 1.75min) which is comparable and statistically significant. Peak sensory Block levels were similar in both groups D & F while the maximum level of sensory block achieved in both groups was T8.

Duration of two segment regression of sensory block was higher in Group D (125.833±9.88) and in Group F (120.7±5.20mins) was Significant (P =0.0146).

Motor Block lasted for a longer duration in Group D (197.033±12.71min) than in Group F (187.8±8.23 min) and it was statistically significant (p=0.0015).

Duration of first analgesic requirements with Group D (212.033±15.07min) while in Group F it in (200.667±7.44min) which is comparable and statistically significant (p=0.0005)

Table 2

CHARACTERISTICS	GROUP D (n=30)	GROUP F (n=30)	P VALUE
Time to reach T ₁₀ sensory block	10.7±2.24	11.8±1.75	0.0383
Peak sensory level T ₈ T ₁₀ >T ₁₀	14(46.67) 10(33.33) 6(20)	15(50) 14(46.7) 1(3.3)	1.000
Modified Bromage Scale At The End Of Surgery			
0	0	0	
1	3(10)	0	
2	12(40)	16(53.3)	0.896
3	15(50)	14(46.7)	
TIME TO TWO- SEGMENT REGRESSION (MIN)	125.833±9.88	120.7±5.207	0.0146
TIME TO MOTOR RECOVERY (MIN)	197.033±12.71	187.8±8.23	0.0015
TIME TO FIRST POSTOPERATIVE ANALGESIC REQUIREMENT	212.033±15.07	200.667±7.44	0.0005

Data represented as mean ± SD or number of patients n (%) SD- Standard Deviation

Comparison of Visual Analogue Scale

VAS SCORE	GROUP D	GROUP F	P
1 HOUR POST SURGERY	1.60±0.62	2.36±0.67	<0.0001
2 HOUR POST SURGERY	2.03±0.49	2.8±0.89	0.0001
3 HOUR POST SURGERY	2.53±0.57	3.1±0.92	0.0101
4 HOUR POST SURGERY	3.13±0.73	3.63±0.76	0.0118

Group D patients had low postoperative VAS score and reduced analgesic requirements.

Intra operative Side Effects

None of the patients developed severe Complications like severe hypotension (MAP < 60). While very few patients reported nausea and shivering which were treated with Inj. Ondansteron 4mg. None developed respiratory depression.

SIDE EFFECTS	GROUP D (n=30)	GROUP F (n=30)	P VALUE
NAUSEA	3(10%)	2(6.67%)	0.643
HYPOTENSION	3(10%)	2(6.67%)	0.643
BRADYCARDIA	2(6.67%)	1(3.33%)	0.556
VOMITING	1(3.33%)	1(3.33%)	1.000
PRURITIUS	0	0	
SHIVERING	1(3.33%)	2(6.67%)	0.556

Discussion

Transurethral Resection of prostate for benign prostatic hypertrophy is frequently performed in elder patients with cardiovascular comorbidities and systemic diseases. Considering this, it is desirable to limit the spinal block level to as low as possible to avoid hypotension owing to high sympathetic block and also maintain required level of anesthesia.

For these reasons, local anesthetics combined with other drugs i.e., an opioid (Fentanyl) or α - agonist (dexmedetomidine) have been used as adjuvants to provide synergistic analgesia and to reduce the dose of local anaesthetic used. Opioid like Fentanyl has been used as adjuvant most commonly nowadays to reduce the dose of intrathecal local anaesthetics and improve the block quality.

However some adverse effects are associated with the use of opioids such as urinary retention, pruritus, nausea, vomiting and respiratory depression. It has been found that dexmedetomidine prolong the post operative analgesia of local anesthetics with less side effects and is a very promising adjuvant to improve the quality of spinal anesthesia.

The comparative study was designed to evaluate the efficacy and characteristics of dexmedetomidine and fentanyl as adjuvants to local anesthetics during spinal anesthesia.

In this comparative study dexmedetomidine significantly prolonged the duration of sensory and motor block compared with fentanyl. Also the time to achieve maximum sensory level was less though not significant in dexmedetomidine group. There was a longer pain free period and post operative analgesic requirement was late in Group D than Group F. In spite of certain biased hypothetication regarding pruritis there was no

incidence of any pruritis or respiratory depression in any group.

Coombs et al first introduced the analgesic properties of α_2 adrenergic receptor agonist during intrathecal injection. Subsequent studies have shown that the injection of intrathecal α_2 adrenoceptoragonist is mainly achieved by inhibiting the release of C peptide transmitters and substance P and hyper polarizing post synaptic dorsal horn neurons and the analgesic effect has a good correlation with their binding affinity to the spinal α_2 adrenergic receptors. Therefore dexmedetomidine as a highly selective α_2 adrenoceptor agonist (α_2/α_1 1600:1) has greater advantage in intrathecal injection. However there are some dose related side effects of α_2 agonist (dexmedetomidine) i.e sedation and neurotoxicity. The dose of dexmedetomidine used in our study was at the end of dosing spectrum and didn't produce any sedative effects. The greatest concern of dexmedetomidine is neurotoxicity. It can cause moderate to severe demyelination of white matter when it was administered by epidural route at a dose of upto 10 μ g/kg in rabbits However in an experiment with sheep dexmedetomidine (2.5-100 μ g) intrathecal injection did not cause neurological deficits

In the systematic review by Abdallah and Brull¹ doses of dexmedetomidine upto 0.2 μ g/kg for intrathecal and 1 μ g/kg for peripheral administration didn't produce any neurotoxic manifestations

Limitations of our Study

We could not perform a follow up for our patients to asses any signs of neurotoxicity or neurological deficits due to the use of dexmedetomidine in the study group

Conclusion

In conclusion when compared to fentanyl (25 μ g) we found that Dexmedetomidine (5 μ g) as adjuvant to 2cc of 0.5% isobaric levobupivacaine for intrathecal injection in TURP surgeries can statistically significantly prolong the duration of

sensory and motor block as well as prolonged post-operative analgesia without significant hemodynam changes

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