



ORIGINAL RESEARCH PAPER

Anaesthesiology

EFFICACY OF DEXMEDETOMEDINE AND BUTARPHANOL ON POST SPINAL ANESTHESIA SHIVERING---A COMPARATIVE STUDY

KEY WORDS: Post spinal shivering, dexmedetomidine, butarphanol, sedation, nausea vomiting

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ABSTRACT

Purpose of the study: The most common adverse event after spinal anesthesia is shivering. Multiple etiologies have been made responsible for this. Opioids have been used extensively for control of shivering, but opioids are associated with increased incidence of nausea and vomiting. So there is a need to find a drug to control shivering with fewer side effects. In the present study we are comparing the efficacy of dexmedetomidine and butarphanol in the treatment of post spinal anesthesia shivering along with the side effects of both the drugs

Materials and Methods: A prospective double blind randomized controlled trial was conducted in tertiary care hospital in Visakhapatnam over a period of six months. Total 60 patients who developed shivering after spinal anesthesia were taken into consideration for study and were randomly allotted into two groups; Group D, where dexmedetomidine was given and Group B where Butarphanol was given. Time for cessation of shivering with response rate was noted. Any incidence of side effects were noted. All the results were analyzed using students T test and chi-square test

RESULTS: In both groups D and B there was cessation of shivering. Group Dexmedetomidine had faster onset with cessation of shivering in lesser time i.e. (170.12+12.3sec) than with butarphanol (275.06+21.725). The recurrence rate of shivering was less with dexmedetomidine (6.66%) as compared to butarphanol (16.60%). Incidence of nausea and vomiting was high in butarphanol, while moderate sedation of Ramsay sedation score 3-4 was noted in dexmedetomidine group.

CONCLUSION: Dexmedetomidine is more efficacious than butarphanol in control of post spinal anesthesia shivering with lesser side effects.

INTRODUCTION:

Perioperative shivering is a common experience for the patients undergoing regional anaesthesia. Shivering is an involuntary, repetitive activity of skeletal muscles. It is a common post spinal anesthesia adverse event with an incidence of around 40–70% and most commonly associated with cesarean sections and geriatric population. Various mechanisms have been suggested for this shivering. Hypothermia is considered the foremost cause for shivering in 26–90% of all patients who underwent elective surgery. The impairment of autonomic thermoregulatory control while the patient is under anesthesia, cold environment of the theater, and cold intravenous fluids may contribute to fall in body temperature and hence shivering. It is not only unpleasant to the patient but also physiologically results in increased oxygen consumption by up to 300%, an increase in intraocular pressure and other sympathetic over activity, which might pose difficulties in patients with existing intrapulmonary shunts, fixed cardiac output or limited respiratory reserve.

Various drugs have been used for the prevention and treatment of post spinal shivering. Dexmedetomidine, a centrally acting alpha -2- adrenergic agonist, has been known to reduce the shivering threshold. Various studies postulated dexmedetomidine in the prophylaxis of post spinal shivering. But the studies using dexmedetomidine in the treatment of shivering is limited.

Butarphanol, an easily available opioid acts through kappa and mu receptor modulation which have been implicated in reduction of shivering. Vogelsang and Hayes concluded in their study that butarphanol attenuates post anesthesia shivering and is more effective than Pethidine.

The aim of this study was to compare the efficacy of dexmedetomidine and butarphanol in the treatment of post-spinal anesthesia shivering as well as their side-effect profile.

MATERIALS AND METHODS

The present study was a prospective, double-blind, randomized controlled trial conducted on 60 American Society of Anesthesiologists (ASA) Grade I/II adult patients (>18 years) who had spinal anesthesia and developed shivering during surgeries, out of which thirty received dexmedetomidine (Group D) and 30 received butarphanol (Group B).

Exclusion criteria – patients with comorbid conditions, high-grade fever, and patients who developed extreme hypotension and extreme bradycardia after giving spinal anesthesia were excluded from the study.

Patients were randomly allocated to Group D or Group B. Group D included thirty patients who received dexmedetomidine 0.5 mcg/kg at the onset of shivering. Group B included thirty patients who received butorphanol 20 mcg/kg at the onset of shivering. All the study drugs were prepared in identical syringes and in the equal volume (5 ml) and given slowly.

Initiation of subarachnoid block was done by injection bupivacaine (0.5%) at L2-3 or L3-4 interspace. There was no active warming of patients and the fluids were used at room temperature. The room temperature in the entire operation theater was kept constant between 22 and 24°C. Vitals including NIBP, pulse rate, SpO₂ and core body temperature by using naso pharyngeal probe were recorded in the beginning of the surgery and at the onset of shivering, after cessation of shivering and then every 10 min till the end point of study.

- In Group D: Dexmedetomidine (0.5 mcg/kg) was diluted to 5 ml and administered, if there was shivering in patient after initiation of subarachnoid block
- In Group B: Butarphanol (20mcg/kg) was diluted to 5 ml and administered, if there was shivering in patient after initiation of subarachnoid block.

Grading of shivering was done as follows:

- Grade 0: No shivering
- Grade 1: One or more of the following: Piloerection, peripheral vasoconstriction, peripheral cyanosis without other cause, but without visible muscle activity
- Grade 2: Visible muscle activity confined to one muscle group
- Grade 3: Visible muscle activity in more than one muscle group
- Grade 4: Gross muscle activity involving the whole body.

Patients who developed either Grade 3 or Grade 4 of shivering were included in the study. Same criteria were used for grading shivering during recurrence and patients with Grade 3 or 4 shivering were included.

The attending anesthesiologist would record:

1. The time at which shivering started after SA (onset of shivering) and the time of recurrence, if present (defined as the time between cessation of shivering after the first dose of the drug and recurrence of shivering)
2. Severity of the shivering
3. Response rate (number of patients in which shivering ceased after treatment in 15 min)
4. Time to disappearance of shivering (in seconds).

The total duration of surgery was noted and the duration of SA was recorded by assessing spontaneous recovery of sensory block using pin-prick method and observing spontaneous movements of limbs in the postoperative period. If the shivering did not subside by 15 min, the treatment was considered to be not effective. Recurrence of shivering was also noticed. Patients who did not respond or in whom recurrence of shivering occurred were treated with additional dose of dexmedetomidine (0.25 µg/kg IV) or butarphanol (10 mcg/kg IV) in the respective groups. If some patients did not respond to the additional dose, they would be regarded as treatment failure. This would be used to calculate the response rate. Side effects like nausea, vomiting, itching, bradycardia (<60/ min), hypotension (decrease >20% of baseline of systolic blood pressure/diastolic blood pressure [SBP/DBP]) and sedation score were recorded.

Sedation score was assessed as per modified Ramsay score:

Grade	Patient response
1	Anxious, agitated, restless
2	Cooperative, oriented, tranquil
3	Responds to commands only
4	Brisk response to light glabellar tap or loud noise
5	Sluggish response to light glabellar tap or loud noise
6	No response

- Bradycardia treated with Inj atropine 0.6 mg i/v, Inj ephedrine in 6 mg boluses i/v titrated was given for hypotension until blood pressure (BP) reached within 20% of baseline BP and Inj metaclopramide 10 mg i/, for vomiting, when required also has anti shivering mechanism and will interfere in our study.

Postoperatively, after shifting patients to postanesthesia care unit (PACU), patients were not actively warmed and were given fluids at room temperature. The end point for the study was either sensory (using pin-prick method) and motor recovery from subarachnoid block or the patient was given either of the two drugs twice for the treatment of shivering.

For motor recovery from subarachnoid block, the Bromage scale was used as per institutional practice which is as under:

- Bromage 4: Unable to move feet or knees
- Bromage 3: Able to move feet only
- Bromage 2: Just able to move knees

- Bromage 1: Full flexion of knees and feet.

All the results were analyzed using Student's *t*-test and Chi-square test. Data were expressed as mean ± SD or percentage. A *p* < 0.05 was considered statistically significant. A *p* < 0.001 was considered highly significant.

OBSERVATIONS AND RESULTS:

The incidence of shivering in our study came out to be 41%. Written informed consent was taken from 144 patients undergoing various surgeries under Spinal anesthesia, until the time 60 patients developed shivering and were enrolled in the study.

The mean age of our study in group D (dexmedetomidine) was 39.74 and group B (butorphanol) was 37.2 years. The distribution of age, sex in the two groups was almost similar as depicted in table 1.

Table 1: Demographic profile

	Group D (Dexmed)	Group B (butorphanol)
Mean	39.74	37.2
age (years)		
Male %	21 (70)	18 (58)
Female %	9 (30)	12 (42)

There was a significant change of core body temperature at the time of shivering in both groups [*P* < 0.05, Table 2].

Table 2: Core body temperature changes

	Group D	Group B	
Core temperature (baseline)	35.44±0.68	35.578±0.62	
Core temperature (°C) at the onset of shivering	34.95±0.84 (P<0.05)	35.244±0.67	<0.05

*Value: Mean±SD. There was a significant change of core body temperature at the time of shivering in both groups (*P* < 0.05). SD=Standard deviation

There was no difference in duration of surgeries and spinal anesthesia between the two groups

Table 3

Duration of surgery (min)	Duration of spinal anesthesia (min)
Group D 78.72±30.080	121.90±29.964
Group B 86.70±35.020	132.30±31.360
0.225	0.093

Shivering disappeared in 100% patients who received dexmedetomidine and butarphanol. Both the drugs were found to be effective in reducing shivering.

Two patients in Group D (6.66%) and five patients (16.60%) in Group B had recurrence of shivering and were given second doses of dexmedetomidine or Butarphanol, respectively (*P* = 0.110). Shivering disappeared in 100% patients who received the second dose of dexmedetomidine and butarphanol.

Time for onset of shivering and severity of shivering were not statistically significantly different between the two groups. Similarly, the time of recurrence of shivering, whenever it occurred was comparable in the two groups. The mean interval between the injection of drug (dexmedetomidine and butarphanol) and the complete cessation of shivering was significantly lesser in the dexmedetomidine group

Table 4: Comparison of the time of onset of shivering, severity of shivering, time to disappearance of shivering, and time of recurrence in the two study groups

	Dexmedetomidine	Butorphanol	P
Time of onset of shivering (min)	72.30±41.357	72.66±41.640	0.965
Severity of shivering	3.92±0.274	3.96±0.198	0.405
Time to disappearance of shivering (s)	170.12±12.3	275.06±21.77	<0.001
Time of recurrence (min)	70.00±17.321	73.75±21.171	0.792

The Pulse Rate in dexmedetomidine group increased at the onset of shivering to 102.3 ± 13 from the basal PR of 86.8 ± 9.7. The PR gradually decreased at 15 min to 85.0 ± 11.3. The Pulse Rate in butorphanol group increased at the onset of shivering to 101.2 ± 16.6 from the basal PR of 85.0 ± 8.5. The PR gradually

decreased at 15 min to 94.1 ± 8.4.

The Mean arterial blood pressure in dexmedetomidine group increased at the onset of shivering to 9.6 ± 9.1 from the basal MAP of 90.7 ± 11.5. The MAP gradually decreased at 15 min to 87.7.7 ± 7.7. The MAP in butorphanol group increased at the onset of shivering to 101.1 ± 9.3 from the basal MAP of 90.7 ± 11.8. The MAP gradually decreased at 15 min to 90.3 ± 9.2.

The Respiratory Rate in fentanyl group increased at the onset of shivering to 18.1 ± 3.5 from the basal RR of 15.0 ± 2.5. The RR decreased at 15 min to 14.7 ± 2.7. The RR in the butorphanol group increased at the onset of shivering to 17.0 ± 3.6 from the basal RR of 14.2 ± 2.5. The RR decreased at 15 min to 14.0 ± 2.4. The SPO₂ in the fentanyl group decreased significantly at the onset of shivering to 97.2 ± 1.2 from the basal SPO₂ of 98.7 ± 0.8, and it remained low at 15 min of 97.6 ± 1.3 compared to basal SPO₂. The SPO₂ in the butorphanol group decreased significantly from the basal SPO₂ of 99.0 ± 0.8–96.9 ± 1.4 at the onset of shivering. The SPO₂ decreased at 15 min to 96.7 ± 1.5

Table 5: Change of vital parameters before and after treatment of shivering

Time (min)	Dexmedetomidine				Butorphanol			
	PR bpm	MAP mmHg	RR breaths per min	SPO ₂ %	PR bpm	MAP mmHg	RR breaths per min	SPO ₂ %
Baseline	86.8±9.7	90.7±11.5	15.0±2.5	98.7±0.8	85.0±8.5	90.7±11.8	14.2±2.5	99.0±0.8
0	102.3±13	93.0±9.1	18.1±3.5	97.2±1.2	101.2±16.6	101.1±9.3	17.0±3.6	96.9±1.4
5	100.2±11.9	92.3±8.8	17.1±2.8	97.2±1.1	105.1±13.3	95.2±9.5	17.1±2.9	96.4±1.3
10	88.1±12.0	90.9±8.3	15.8±2.6	97.4±1.1	97.2±10.2	92.8±9.3	5.6±2.5	96.5±1.2
15	85.0±11.3	87.7±7.7	14.7±2.7	97.6±1.3	94.1±8.4	90.3±9.2	14.0±2.4	96.7±1.5

RR=Respiratory rate, PR=Pulse rate, MAP=Mean arterial pressure,

Complication rates were significantly higher in Group B than in Group D. Nausea and vomiting were higher in Group B than in Group D. 28.00% patients in Group B had nausea compared to none in Group D with a highly significant $P < 0.001$. Furthermore, 8.00% patients in Group B had vomiting compared to none in Group D with a significant $P = 0.041$. None of the patients in either group had itching and hypotension while one patient in Group D had bradycardia. No patient in Group B had bradycardia ($P = 0.315$). Patients of Group D were more sedated than of Group B. While 8 (28.00%) patients in Group A had Grade 3 sedation score, 21 (72.00%) patients had sedation of Grade 4. On the other hand, all the patients in Group B had a sedation of Grade 2 ($P < 0.001$).

DISCUSSION.

Shivering is a frequent complication in patients undergoing surgery under neuraxial anesthesia. Shukla *et al.* have reported the incidence of shivering in patients undergoing surgery under regional anesthesia as 40–70% based on previous studies. The incidence of shivering in our study was 41%.

Body temperature is controlled by a negative feedback system in the hypothalamus which integrates information from the whole body. Approximately, 80% of this thermal input is derived from core body temperature. The hypothalamus coordinates increase in heat production as well as increase or decrease in heat loss as needed to maintain normothermia. Hypothermia during spinal anesthesia is the most common perioperative thermal disturbance.

Perioperative hypothermia is due to anesthetic impaired thermoregulation and exposure to a cold operating theater environment. After an initial rapid fall in core temperature, there occurs a slow and linear reduction in temperature. Finally, core temperature stabilizes and virtually remains unchanged. On emergency from anesthesia, normal thresholds are restored. Hence, hypothermic patients may shiver which causes considerable metabolic changes. Shivering during a regional anesthetic may be averted by maintaining high ambient temperature, warming skin surface with radiant heat, or using drugs.

sufentanil, alfentanil, butorphanol buprenorphine, doxapram, methylphenidate, clonidine, and ketanserin are known to be effective in suppressing shivering. In this study, we studied the efficacy of dexmedetomidine in the treatment of post-SA shivering in adults and compared its efficacy with butorphanol for the treatment of shivering after SA in patients undergoing various elective surgeries. We found that dexmedetomidine is effective as butorphanol in treating post-SA shivering.

The efficacy of dexmedetomidine is similar to that of a previous study by Blaine Easley *et al.* who studied the role of dexmedetomidine in the treatment of postoperative shivering in children. All children had a cessation of shivering behavior within 3.5 ± 0.9 min, while in our study cessation of shivering occurred in (170.12±12.3sec). This difference could be due to different methodology used to see the time for cessation of shivering. While Blaine Easley *et al.* recorded their results as the number of patients who had stopped shivering after 1 min, after 2 min and so on, and then extrapolated the time taken for cessation of shivering from these data. However, in our study, we directly observed the time taken for shivering to stop (in seconds). In this study, the cessation of shivering with butorphanol occurred in 275.06±21.725 seconds. There is a paucity of literature comparing the efficacy of dexmedetomidine with butorphanol. However, from our study, we found that the time interval from the administration of treatment to cessation of shivering is significantly less with dexmedetomidine (170.12±12.3sec). than with butorphanol (275.06 ± 21.725 s) ($P < 0.001$).

Around six percent patients in dexmedetomidine group in the present study had recurrence of shivering. However, none of the patients had recurrence of shivering after receiving dexmedetomidine in earlier study conducted by Blaine Easley *et al.* This could be due to the fact that in the study conducted by Blaine Easley *et al.* the surgeries were conducted under general anesthesia, while in our study the surgeries were performed under SA. While in general anesthesia patients, shivering occurs only on awakening, in SA patients it can occur at any time post-SA. This may lead to a higher incidence of shivering and recurrence of shivering in

Many drugs such as pethidine, other opioids fentanyl,

patients undergoing SA as compared to patients undergoing surgeries under general anesthesia. The difference could also be due to the fact that the patients studied in Easley's study were children in the age group of 7–16 years. The incidence of shivering has been reported to be less in children as compared to adults. To date, there have been very few studies regarding the treatment of shivering in children. Hence, it is quite difficult to interpret data regarding recurrence of shivering after administration of pharmacological treatment from the limited number of available studies.

About 16% patients who received butarphanol in our study had recurrence of shivering. This incidence was similar to available literature. In this study, the incidence of recurrence of shivering with dexmedetomidine was less (6%) as compared to tramadol (16%), but the difference was not statistically significant ($P=0.110$).

Postoperative nausea and vomiting (PONV) is a very unpleasant experience for the patient. Postoperative vomiting/retching can lead to rare but serious medical complications, such as aspiration of gastric contents, suture dehiscence, esophageal rupture, subcutaneous emphysema, or pneumothorax. PONV may delay discharge from PACUs and can be the leading cause of unexpected hospital admission after ambulatory anesthesia.

The side effects were found to be higher in the case of butarphanol as compared to dexmedetomidine. In this study, the incidence of nausea was highly significant in butarphanol group compared to the dexmedetomidine group ($P<0.001$). Similarly, the incidence of vomiting was significantly higher in the butarphanol group compared to dexmedetomidine group ($P=0.041$).

One patient in the dexmedetomidine group of our study had bradycardia while none in the butarphanol group had bradycardia. However, the incidence was not statistically significant ($P=0.315$). Although dexmedetomidine decreases the HR significantly immediately after cessation of shivering, the incidence of bradycardia (HR <60 /min) is not significant. The fall in HR immediately after cessation of shivering in Group D is due to the inherent property of dexmedetomidine to decrease HR due to postsynaptic activation of α_2 adrenoceptors in the central nervous system. Gradually, the HR picked up in Group d and was comparable in the two groups at all other time intervals.

In our study, 28% patients of dexmedetomidine group exhibited a Ramsay Sedation Score of 3, while 72% patients had a Ramsay sedation score of 4. However, the level of sedation in these patients never went above Grade 4, and these patients were able to maintain their airway and SpO_2 on room air. There was no incidence of hypoxia in our study consequent to the loss of airway due to deeper planes of sedation. This sedation was found to be beneficial in the post-SA patients who were more comfortable in the recovery room with some amount of sedation from which they could be easily awoken.

There was no incidence of hypotension in either group, which is similar to previous studies. Similarly, none of the patients in either group had itching. On overall analysis, more side effects were noted in butarphanol group patients compared to dexmedetomidine group patients.

CONCLUSION

On the basis of the study we conclude that dexmedetomidine is a useful alternative to opioids like butarphanol for cessation of post spinal anesthesia shivering. Incidence of nausea and vomiting are lesser in dexmedetomidine group and it provides faster relief from shivering.

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