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A Comparative study on efficacy of intrathecal tramadol and dexmedetomidine on post spinal shivering

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Abstract

Background: Shivering is a frequent complication after spinal anesthesia with multiple etiologies. At present tramadol is a widely used drug for the control of shivering. However, tramadol may cause a lot of nausea and vomiting. Dexmedetomidine (α2 adrenergic agonist) has been used for prevention of post anaesthesia shivering. Its use for the treatment of post-spinal anaesthesia shivering has not been evaluated. Hence, the need to find a better drug with less of side effects. **Aim**: The aim of this study was to evaluate and compare the efficacy, haemodynamic and adverse effects of dexmedetomidine with those of tramadol, when used for control of post-spinal anaesthesia shivering for lower abdominal surgeries. **Methods:** Present study was hospital based, prospective observational study, conducted in patients of age 18-70 years of either gender, ASA grade I and II, undergoing elective lower abdominal surgeries, willing to participate. 100 patients were randomly assigned into Group D (n=50) and Group T (n=50). Group D patients received dexmedetomidine and Group T patients received tramadol. The response rate, time to cessation of shivering and side effects (if any) was noted. All the results were analyzed using Student's *t*-test and Chi-square test. **Results:** Time taken for cessation of shivering was significantly less with dexmedetomidine when compared to tramadol. The time to cessation of shivering was (168.12 ± 12.366 s with

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dexmedetomidine) than with tramadol (274.06 ± 21.374 s) ($P < 0.001$). Nausea and vomiting was found to be higher in the case of tramadol. On the other hand, dexmedetomidine caused moderate sedation (modified Ramsay sedation score = 3–4), there was not much difference in the sedation profile of both the drugs. **Conclusion:** Dexmedetomidine offers better results than tramadol with fewer side effects. The time taken for cessation of shivering is less with dexmedetomidine when compared to tramadol. Moreover, dexmedetomidine has negligible adverse effects, whereas tramadol is associated with significant nausea and vomiting.

Keywords: Dexmedetomidine, postoperative nausea and vomiting, shivering, tramadol, spinal anaesthesia.

Introduction:

Regional anaesthesia (spinal anaesthesia) is widely used as a safe anaesthetic technique for both elective and emergency operations. Shivering is known to be a frequent complication, reported in 40 to 70% of patients undergoing surgery under regional anaesthesia[1,2]

Shivering is a potentially serious complication, resulting in increased metabolic rate; increased oxygen consumption (up to 100-600%) along with raised carbon dioxide (CO2) production; ventilation and cardiac output; adverse postoperative outcomes, such as wound infection; increased surgical bleeding; and morbid cardiac events. It causes arterial hypoxemia, lactic acidosis, increased intraocular pressure (IOP), increased intracranial pressure (ICP); and interferes with pulse rate, blood pressure (BP) And electrocardiographic (ECG) monitoring.[3-5]

The treatment of shivering includes both pharmacological and non-pharmacological methods. The non-pharmacological management is by external heating like the use of forced air warming, warming blankets, warmed fluids etc., According to the results of a meta-analysis, the most frequently reported pharmacological interventions include clonidine, pethidine, tramadol, nefopam and ketamine.[6]

Unfortunately, no gold standard treatment is known for shivering as the administration of all the available drugs is associated with various adverse effects. During the last decade, Tramadol has become a favoured and commonly used drug for post-spinal anaesthesia shivering. However, it has many adverse effects like nausea, vomiting, dizziness etc., which cause further discomfort to the patient.[7,8] Clonidine is another agent which has gained popularity during the last few years. Various studies, which have been conducted to compare them have concluded that

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clonidine has better efficacy and less adverse effects as compared to tramadol.[7,8] But there was 5-10% incidence of hypotension and bradycardia with clonidine.[7] Dexmedetomidine, a congener of clonidine, is a highly selective α2-adrenoceptor agonist. It has been used as a sedative agent and is known to reduce the shivering threshold.[9] Few studies which have explored its anti-shivering potential have inferred that dexmedetomidine is an effective drug without any major adverse effect and provides good haemodynamic stability.[9-11] Hence, we planned to do a comparative study of the efficacy, haemodynamic, and adverse effects of tramadol and dexmedetomidine when used for the control of post-spinal anaesthesia shivering.

Methods:

The present study was conducted in the department of anesthesiology in Government medical collage Srinagar over a period of eighteen months for one hundred patients of (ASA) physical status I-II of both sexes, aged between 18 and 70 years, equally divided in to two groups, Group T (n=50), Group D (n=50), scheduled for elective lower abdominal surgeries.

After getting approval from Institutional Ethical Committee, written informed consent was obtained from all the patients before surgery. Patients with any moderate to severe systemic disorders, patients unwilling to accept regional anesthesia, patients with any contraindication for spinal anesthesia, were excluded from the study.

A detailed history was noted and a complete general and systemic examination was done. Procedure was explained to patients and a written informed consent was taken. In surgical theatre monitor attached to record ECG, NIBP, SpO2, HR and RR. The baseline readings were noted.

Group D: Received 2.5ml of 0.5% hyperbaric bupivacaine with 0.5 ml of 5 mcg dexmedetomidine, total of 3ml.

Group T: Received 2.5 ml 0.5% hyperbaric bupivacaine and 0.5 ml (20 mg) tramadol, total of 3ml.

The procedure began by identifying anatomic landmarks. The patient was placed in the sitting position and the line joining the superior aspect of the iliac crests posteriorly (Tuffier's line) was palpated. When the Tuffier's line crossed an interspinous space, the spinal level was identified as L3–L4 interspace. According to this land-mark, the L2–L3 interspace was identified as one inter-space above. Spinal anaesthesia was performed in sitting position after proper preparation of the area with antiseptic solution, using a 26G Quincke needle at the L3-4 interspace and a midline approach. The direction of the needle was kept cranial during the injection. After free flow of CSF verified, anaesthetic solution along with study drugs was given in 15 seconds.

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All patients were then placed supine and administered oxygen mixture via facemask. During the procedure an electrocardiogram, the heart rate and pulse oximetry were monitored continuously. Non-invasive blood pressure was taken before the conduct of spinal anesthesia and every 5 minutes after the intrathecal injection until the end of surgery. Hypotension was defined as a decrease in the mean arterial blood pressure, more than 20% from baseline within a 5 min interval. Hypotension was treated with either fluid boluses or aliquots of intravenous mephentermine 6 mg since the efficacy of mephentermine was recognized in earlier studies. Bradycardia was defined as heart rate less than 50 beats min^{-1} and was treated with i.v. injection of atropine 0.5–1 mg. The quality of anesthesia was assessed by testing severity of intra operative pain using a 10 cm VAS, where VAS 0 meant no pain and VAS 10 worst pain imaginable.[12] VAS was evaluated every 5 min from the time of skin incision until the end of surgery. The use of VAS had previously been explained to each patient before surgery. VAS 1–3 was considered as mild pain, VAS 4–6 as moderate, VAS 7, 8 as severe and VAS 9, 10 as unbearable pain. Five minutes thereafter, the VAS was assessed. The height of sensory block was also noted. The level of sensory block was determined by the loss of pinprick sensation and was performed using a 22 G hypodermic needle. Sensory block level was tested every 5 minutes during the first 30 minutes after the intrathecal injection. The surgeon started all operations 30 minutes after intrathecal injection in every patient. No sensory testing was performed during surgery.

Grading of shivering was done as per Wrench,[6] which is as follows:

Grade 0: No shivering

Grade 1: One or more of the following: Piloerection, Peripheral vasoconstriction, peripheral cyanosis with, 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

The attending anaesthetist recorded the time in minutes at which shivering started after spinal anaesthesia (onset of shivering), severity of the shivering, time to disappearance of shivering (in minutes) and response rate (shivering ceased after treatment in 15 minutes). Duration of surgery was noted, and duration of spinal anaesthesia 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 minutes, the treatment was considered to be not effective. Recurrence of shivering was also noticed until the patient left the operation theatre.

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Data was analysed using Statistical Package for Social Science SPSS 22.0 software. Independent t test and Chi-square test was used to compare proportion between the groups. P-value < 0.05 was considered for statistical significance.

Conflict of Interest: Nil

Funding: Nil

Results: A total of 100 patients were enrolled in the present study and were randomized into two groups of 50 each (n=50). Both the groups were comparable with respect to age, sex, weight, duration of surgery and ASA class of distribution [Table 1].

Table 1: Demographic profile of the study population

VARIBLES	GROUP D (MEAN±SD)	GROUP T (MEAN±SD)	P-VALUE
AGE (years)	41.048 ± 14.65	39.81 ± 13.95	0.82
WEIGHT (kgs)	62.492 ± 5.46	62.60 ± 4.64	0.91
GENDER (M: F)	31:19	27:23	0.566
ASA (I /II)	37/13	32/18	0.466
Duration of surgery (Min)	58.60±7.20	59.91±11.15	0.765

(p-value less than 0.05 considered statistically significant) *(p-value less than 0.001 highly significant)

All the patients had Grade 3 shivering. There was no statistically significant difference in time for the onset of shivering between the two groups. However, the difference in the time interval between administration of drug after the onset of shivering and cessation of shivering was significantly shorter in the dexmedetomidine group when compared to tramadol group. There was recurrence of shivering in 2 patients in dexmedetomidine group and 3 patients in tramadol group. The patients were given rescue doses of dexmedetomidine or tramadol, respectively [Table 2].

Table 2: Parameters for post-spinal anaesthesia

Variables	Group D	Group T	P value
Onset of shivering (min)	22.45±13.85	21.12±12.45	0.810
Time for cessation of shivering after	2.67±0.54	5.87±0.91	<0.001

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medication (min)			
Response rate (%)	**99**	**98**	**0.976**
Recurrence	**2**	**3**	**0.861**

Nausea and vomiting was observed only in tramadol group, and there was no incidence in the dexmedetomidine group. Almost similar number of patients were sedated in both groups and the sedation score in all the patients was 2. There was no evidence of respiratory depression, hypotension or bradycardia in any of the patients. HR, mean blood pressure, body temperature, and SPO2 remained within normal limits throughout the procedure in both groups [Table 3].

Table 3: Post operative complications among the study groups

Variables	Group D	Group T	P value
Nausea	**0**	**9**	**<0.001**
Vomiting	**0**	**7**	**<0.001**
Sedation	**5**	**6**	**0.543**
Hypotension	**0**	**0**	**0.861**
Bradycardia	**0**	**0**	**0.988**
Respiratory depression	**0**	**0**	**0.988**

The quality of intraoperative anesthesia remained excellent among the study groups and statistical difference between the Groups was not significant (p=0.851) [Fig 1].

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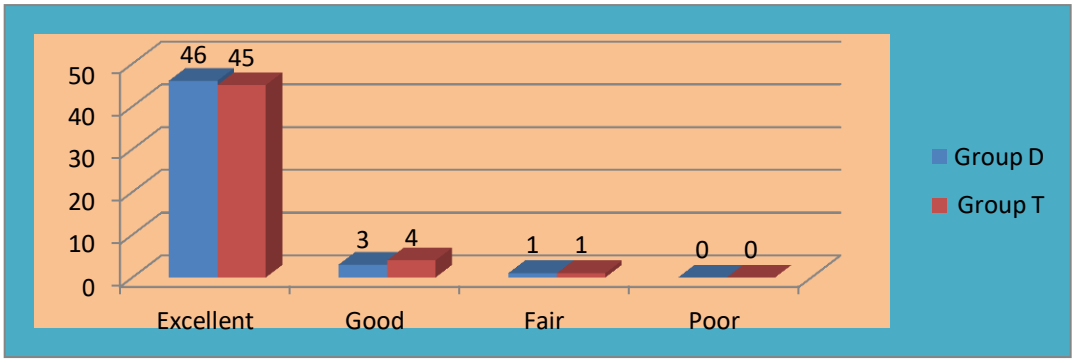

Fig 1

The requirement of rescue analgesic was significantly insignificant among the study groups p>0.05.

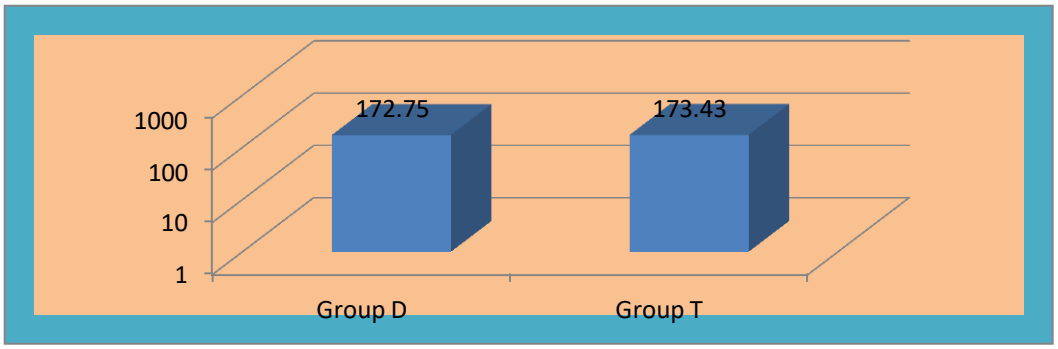

Fig 2

Discussion:

Regional anaesthesia, either central neuraxial block or peripheral nerve block is a safe and very popular technique used for various surgeries. However, 40% to 70% of patients undergoing regional anaesthesia develop shivering, though it is also found to occur after general anaesthesia.[13]

The neurotransmitter pathways involved in shivering are multiple and involve opioids, α2 adrenergic, serotenergic, and anticholinergic receptors. Hence, drugs acting on these systems which include opioids (pethidine, nalbuphine, or tramadol), ketanserin, propofol, doxapram, clonidine, ketamine and nefopam are utilized in the treatment of shivering. However, adverse effects such as hypotension, hypertension, sedation, respiratory depression, nausea and vomiting limit their use. Hence, the hunt for an ideal anti-shivering agent is continuing. [7]

The mechanism which leads to shivering after regional anaesthesia is not very clear, but the probable mechanisms could be decrease in core body temperature secondary to sympathetic block; peripheral vasodilatation; increased cutaneous blood

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flow, which leads to increased heat loss through skin; cold temperature of operation theatre; rapid infusion of cold IV fluids; and effect of cold anaesthetic drugs upon the thermo sensitive receptors in the spinal cord.[14,15]

Tramadol is an opioid analgesic with opioid effect mainly mediated via mu receptor with minimal effect on kappa and delta receptors. It also activates the monoaminergic receptors of the descending spinal inhibitory pain pathway. The anti-shivering action of tramadol is probably mediated via its opioid or serotonergic and noradrenergic activity or both.[16-18] It is a well-established agent in the treatment of post-anaesthetic shivering.

Alpha-2 adrenergic agonists are widely used nowadays in anaesthesia and intensive care settings. Dexmedetomidine is an α2 adrenoceptor agonist, with antihypertensive, sedative, analgesic, and anti-shivering properties.[19] The anti-shivering effects of alpha adrenoceptor agonists are mediated by binding to α2 receptors that mediate vasoconstriction and the anti-shivering effect. In addition, it has hypothalamic thermoregulatory effects.[20] Dexmedetomidine comparably reduces the vasoconstriction and shivering thresholds, thus suggesting that it acts on the central thermoregulatory system rather than preventing shivering peripherally.[21] It has been successfully used as an adjunct to local anaesthetics in spinal anaesthesia and peripheral nerve blockade, for the sedation of mechanically ventilated patients in the Intensive Care Unit, as well as supplementation of post-operative analgesia.[22] The role of dexmedetomidine in the treatment of shivering has been evaluated in a few studies.[9-11] It may be a good choice because of its dual effects related 'anti-shivering' and sedation.

With same dose, that is, 0.5 mg/kg of tramadol, the response rate reported by Shukla *et al*. was 92.5%, by Reddy and Chiruvella as 95.56% and by Tsai and Chu, 87%.[7] We found 98% response rate in our study. Maheshwari *et al*. reported similar recurrence rate with tramadol as in our study (8%) but the dose used in their study was 1 mg/kg.[8] The recurrence rate in the study by Shukla *et al*. was 5%, which is similar to our results. The incidence of nausea and vomiting with tramadol in our study was 18% and 14%, respectively. The results correspond with that of other studies by Reddy and Chiruvella, Tsai and Chu; Bansal and Jain[23,24] However, in the study by Shukla *et al*.,[7] the incidence of nausea was quite high (77.5%), whereas Wason *et al*. have reported the incidence of nausea as only 4%.[25] These variations could be explained by the peculiar patient characteristics in different studies. Maheshwari *et al*. have reported a very high incidence of sedation

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to the extent of 84%, which as mentioned earlier could be due to the higher dose as opposed to 22% sedation in our study.[24]

In a study by Easley, all children who had post-anaesthesia shivering were treated with a single IV bolus dose of dexmedetomidine 0.5 µg/kg over 3-5 min.[26] All children had cessation of shivering behavior within 5 min following the completion of dexmedetomidine administration. There was no recurrence of shivering and no adverse effects occurred.

We found a response rate of 98% and apart from sedation, there was no other adverse effect observed. But there was recurrence in 5 patients who had to be given a rescue dose. All other studies have used higher dose of dexmedetomidine (1 µg/kg), so comparison of results would not be appropriate.

In our study, the incidence of sedation was 22%, which is similar to other studies. One contradictory report was by Karaman *et al*. according to whom intra-operative dexmedetomidine infusion caused negligible sedation in spite of using a loading dose of 1 µg/kg followed by a maintenance infusion of 0.5 µg/kg/h.[11] The results of this study indicate that dexmedetomidine takes lesser time to control shivering. The incidence of adverse effects like nausea and vomiting was found to be higher in case of tramadol compared to dexmedetomidine. More studies need to be undertaken with varying dose ranges to extrapolate the results of this study.

There was not much difference in the number of patients who were sedated in either group. The sedation seen with dexmedetomidine, in the absence of nausea and vomiting, is beneficial for the surgeon, anaesthetist as well as the patient. It provided more comfort to the patient, maintained more cardio-respiratory stability, improved surgical conditions and also provided amnesia during surgery.

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