Comparative study of efficacy of intrathecal tramadol added to bupivacaine in prevention of intraoperative shivering

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Abstract:

Introduction: *Very few studies regarding the effect of intrathecal tramadol on prevention of perioperative shivering prompted us to design present study aiming to find out efficacy and safety of intrathecal tramadol for prevention of shivering .*

Methods: *A prospective randomized double blind controlled study was conducted on 100 patients of either sex, ASA grade I and II, between ages of 18 and 65years, undergoing various lower abdominal, lower limb, and orthopedic surgeries under subarachnoid block. All subjects were randomly allocated into two groups of 50 patients each (n=50). In group T 0.5% hyperbaric bupivacaine (3ml) + 0.2 ml of (20 mg) tramadol and in group C 0.5% hyperbaric bupivacaine (3ml) + 0.2 ml of normal saline was given intrathecally.*

Results: *Nineteen patients (38%) developed shivering in control group while no patient in group T had shivering. Mean time in minutes at which shivering started was 6.77 minute and in majority of them (14 out 19,73.68 %) severity of the shivering was grade 3 & 4. Incidence of nausea and vomiting was significantly high in tramadol group. Other side effects like itching, sedation and respiratory depression was not observed in any patient from both the groups.*

Conclusion: *Intrathecal administration of tramadol as an adjuvant to 0.5% hyperbaric bupivacaine is a safe and effective route of administration and has a distinct advantage for prevention of shivering. Therefore, Intrathecal tramadol can be an alternative for various kinds of modalities in prevention of shivering.*

Key Words: *Intrathecal tramadol, postspinal anaesthesia shivering, spinal anesthesia, Tramadol*

Introduction

Various attempts are made to prevent and treat peri-operative shivering. Pharmacological therapy has been found to offer a simple, cost effective solution. Many drugs including doxapram, ketanserin, clonidine, propofol, physostigmine, pethidine, nefopam, butorphanol, ondansetron and Tramadol have been tried to prevent and treat peri-operative shivering. [1, 2,]

The opioid are proved to be the most effective [1]. Tramadol is a synthetic opioid introduced initially in mid -1970s. It has central opiate agonist activity at all types of opioid receptors with selectivity for mu receptors. It also inhibits re-uptake of norepinephrine and serotonin in the central nervous system which may contribute to its antishivering action [1, 3]. Though many studies about use of intravenous tramadol for prevention and management of shivering [2, 4 - 6] are found in the literature very few studies regarding the effect of intrathecal tramadol on prevention of perioperative shivering prompted us to design present study aiming to find out efficacy and safety of intrathecal tramadol for prevention of shivering .

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Methods:

This was prospective randomized double blind controlled study, conducted on 100 patients of either sex, ASA grade I and II, between ages of 18 and 65years, undergoing various lower abdominal, lower limb, and orthopedic surgeries under subarachnoid block. After approval from the hospital ethics committee and after obtaining informed consent eligible patients were included in the study. Patients having fever and chills, severe systemic disorder including diabetes mellitus, hypertension, heart disease changing ASA grading to more than II; allergy to bupivacaine or tramadol and all known

contraindications for spinal anaesthesia, such as infection at the puncture site, spine deformity, increased intracranial pressure, neurological disorders, coagulation disorders, on anticoagulant therapy were excluded from the study. Surgeries likely to last longer than 2 hours or requiring blood or blood products were also excluded. All included patients were randomly assigned to one of the two groups. Randomization was done by sequentially numbered opaque sealed envelope method and subjects were allocated into two groups of 50 patients each (n=50):

Group T: 0.5% hyperbaric bupivacaine (3ml) + 0.2 ml of (20 mg) tramadol intrathecally

Group C: 0.5% hyperbaric bupivacaine (3ml) + 0.2 ml of normal saline intrathecally.

Sample size was estimated to be 98 (49 in each group) to get effective reduction of 50 % in incidence of Shivering after spinal anesthesia (55 % according to previous studies [2]) with intrathecal tramadol, assuming type I error of 5% (á=0.05) and power at 80 (â=0.20)

Preoperative preparation:

Patients were kept nil by mouth for six hours preoperatively. They received no sedatives premedication. Using a 20 G cannula, a peripheral venous line was secured and drip of ringer lactate solution was started and pre loaded with 10 ml / kg of solution prior to sub arachnoid block.

Intraoperative anaesthesia management :

Patients were taken into operation room; monitors were attached including electrocardiography, pulse oximetry and non –invasive blood pressure monitoring. Subarachnoid block was given in sitting position under all aseptic precautions. Midline approach was used along with 25 G spinal needle in L3-4 interspace. Once free and clear flow of cerebrospinal fluid was obtained, drug was injected over a period of 10 seconds as per group. Anesthetist injecting the drugs was blinded by coding the syringes. Operating room temperature was kept constant for both groups at 23^0C throughout the procedure. Required intravenous fluids, drugs and other irrigation fluids (like Betadine) were used from the stock which was kept at operating room temperature. All exposed parts of the body were covered by plastic and cotton drapes. On occurrence of shivering; the onset time after administering spinal was noted and also the grade of shivering was noted.

Grading of shivering was done 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

Patients who developed either grade 3 or grade 4 of shivering were treated with iv tramadol 0.25mg/kg. The attending anaesthetist, blinded with the drugs given intrathecally recorded the time in minutes at which shivering started after spinal anaesthesia (onset of shivering) and severity of the shivering.

Peri operative monitoring:

1) Pulse rate and rhythm. Atropine was kept ready to treat bradycardia(<45/min)
2) Blood pressure, systolic and diastolic. Ephedrine was kept ready to treat hypotension (defined as 20% decrease in systolic blood pressure from baseline value.)
3) Oxygen saturation by pulse oximetry.
4) Highest level of sensory block using pin prick method tested in cephalad direction every one minute.
5) Total duration of surgery was noted
6) Time of starting of shivering
7) Grades of shivering
8) Side effects of tramadol like nausea, vomiting and sedation were noted. The data thus obtained was statistically analysed. If any of the patients developed vomiting, then he/she was administered injection metoclopramide 10 mg intravenously.
9) Level of consciousness at the end of surgery was recorded and classified as:

   1: Fully awake

   2: Arousable on calling

   3: Not responsive

   Postoperatively patients shifted to recovery room and monitored till regression of sensory block by two segments.

Results:

Both the groups were comparable in respect of demographic data. (Table I). They were also comparable regarding type of surgeries and duration of surgeries (TableII). Highest level of spinal blockade was also comparable among two groups.(TableIII) All patients from both groups were hemodynamically stable all the times. (Table IV). Table V shows incidence of side effects among both the groups. Nineteen patients (38 %) developed shivering in control group while no patient in group T had shivering. This difference is highly significant. Mean time in minutes at which shivering started was 6.77 minute and in majority of them (14 out 19,73.68 %) severity of the shivering was grade 3 & 4. They responded well to the treatment with iv tramadol. Incidence of nausea and vomiting was significantly high in tramadol group. Ten patients had nausea and 12 patients had vomiting in tramadol group as against 2 and 3 patients had nausea and vomiting respectively in control group. Other side effects like itching, sedation and respiratory depression was not observed in any patient from both the groups.

Discussion

Hypothermia is responsible for shivering in most patients. It occurs due to combination of competitive inhibition of thermoregulatory responses by the anaesthetic drugs, due to decreased metabolism and exposure to cold environment. Immediately after anaesthesia induction there is an internal transfer of core heat to periphery, known as internal redistribution. Second step is drop in core temperature as result of heat losses (via the cutaneous route, by exposure of viscera or by perfusion of cold solutions). Decrease in body temperature varies depending on the anaesthetic products and concentrations used. In our study operating room temperature was kept constant at 23^0C for both the groups. Intravenous fluids, irrigation fluids & disinfectants (like Betadine) were kept at operating room temperature. All exposed parts of the body were covered by plastic and cotton drapes. Volume and temperature of drug used for spinal anaesthesia was similar in both the groups, thus nullifying the effects of above factors on shivering in both the groups. Daniel I et al [7] showed that impairment of thermoregulation under neuraxial anaesthesia depend upon number of spinal segments blocked. In our study the highest level of spinal blockade and haemodynamic parameters during intraoperative period which can have compounding effect were comparable between the tramadol and control group. Tramadol is moderately potent analgesic [8,9]. It is an analogue of codeine. Its analgesic effect is mediated through norepinephrine reuptake inhibition, increased release & decreased reuptake of serotonin in spinal cord & weak u opioid receptor effect [9,10] Our findings are consistent regarding hemodynamic stability with the study of Chakraborty et al [11] who also found no differences in hemodynamics. But J.A. Alhashemi et al [12] found trend of increased pulse rate in tramadol group. Many researchers [2,4,13,14,15] have established efficacy of intravenous tramadol in treating shivering. De Witte J et al in 1997 [13] published that shivering stops 100% after 1-2mg/kg iv tramadol injection. Alfonsi P et al [14] also studied various drugs for treatment of shivering and he found tramadol to be effective in treatment of postanesthetic shivering. Joshi SS et al [2] compared ondansetron, butorphanol and tramadol and found butorphanol and tramadol equally effective in controlling shivering under regional anesthesia. Bhatnagar et al [15] showed that the number of patients who stopped shivering within 10 minutes of receiving iv tramadol was significantly higher than after pethidine. Velayudha S.Reddy et al [4] showed 50mg tramadol is more effective than 50mcg of clonidine in treatment shivering. Our findings are consistent with above studies. All our patients from controlled group who developed shivering responded well to intravenous tramadol. It is also evident from our study that highly significant difference observed in incidence of shivering between two groups proves efficacy of intrathecal tramadol in prevention of shivering. Thus not only iv tramadol used for treatment of shivering but intrathecal tramadol also is very effective in prevention of intraoperative shivering. In both groups, patients were alert at the end of surgery. We can conclude that intrathecal tramadol in dose of 20mg does not have any effect on cerebral function. Our study findings are consistent with studies of Reda S. Abdelrahman, et al [16] who used 0.5mg/kg and 0.25 mg/kg tramadol intravenously, J.A. Alhashemi et al [12] who used 25 mg intrathecal tramadol added to bupivacaine (15 mg) and Chakraborty et al [11] who used 20mg intrathecal tramadol added to bupivacaine (15 mg). All of them found no disturbance in sensorium at the end of surgery. In tramadol group 10 patients had nausea and 12 patients had vomiting. In control group 2 patients had nausea and 3 patients had vomiting . Velayudha S.Reddy et al [4] found higher incidence of nausea and vomiting after iv tramadol. Prosser DP et al [17] found higher incidence of emesis after caudal tramadol. So our study findings are consistent with their studies regarding incidence of nausea and vomiting due to tramadol . We did not find respiratory depression in any patient due to tramadol like J.A. Alhashemi et al [12], Vickers MD et al [18], Tarkkila P et al [8] and O.Kyokong et al [19] who found no respiratory depression after tramadol. None of the patients in our study group developed itching, sedation, urinary retention like Prosser DP et al [17] and Yasser Majid et al [20] who used 1mg/kg tramadol caudally.

Thus we can conclude that intrathecal administration of tramadol as an adjuvant to 0.5% hyperbaric bupivacaine is a safe and effective route of administration and has a distinct advantage for prevention of shivering. Therefore, Intrathecal tramadol can be an alternative for various kinds of modalities in prevention of shivering.

Table I: Demographic characteristics

PARAMETER	GROUP T (N = 50) MEAN± SD	GROUP C (N = 50) MEAN ± SD
AGE (YEARS)	42.48 ± 10.39	45.56 ± 9.56 *
WEIGHT (KG)	63.48 ± 5.02	62.06 ± 5.05 *
ASA grade (I / II)	30/20	31/19 *
SEX (M/F)	29/21	31/19 *
DURATION OF SURGERY (MINUTES)	55.60 ± 13.73	57.14 ± 14.01 *

*** p-value > 0.05 ** p-value significant at 0.05; *** p-value significant at 0.01**

Table II : Comparison of type of surgery

Type of surgery	GROUP T (N = 50) MEAN± SD	GROUP C (N = 50) MEAN ± SD
General surgery	16	15 *
Gynecological surgery	9	11 *
Orthopedics surgery	12	12 *
Urological surgery	13	12 *
Total	50	50

*** p-value > 0.05 ** p-value significant at 0.05; *** p-value significant at 0.01**

Table III : Comparison of highest level of spinal blockade in group T & C

Level of spinal	GROUP T (N = 50) MEAN± SD	GROUP C (N = 50) MEAN ± SD	Total
4	10	11 *	21
6	28	23 *	51
8	12	16 *	28
Total	50	50	100

*** p-value > 0.05 ** p-value significant at 0.05; *** p-value significant at 0.01**

Table IV : Comparison of hemodynamic parameters

Time interval	Pulse rate		Systolic Blood Pressure		Diastolic Blood Pressure	
	GROUP T (N = 50) MEAN± SD	GROUP C (N = 50) MEAN ± SD	GROUP T (N = 50) MEAN± SD	GROUP C (N = 50) MEAN ± SD	GROUP T (N = 50) MEAN± SD	GROUP C (N = 50) MEAN ± SD
Baseline	83.56±14.43	83.90±14.51 *	125.48± 14.44	125.36±13.85 *	71.46±10.35	73.62±10.50 *
5th min	83.48±14.96	83.90±15.20*	122.74±13.24	120.58±12.00*	70.70±10.13	72.68±9.95*
10th min	83.08±14.66	82.69±14.00*	121.20± 13.25	116.96±11.66*	69.26±9.80	71.52±9.34*
15th min	81.72±13.79	82.36±13.10*	114.00±11.03	113.40±11.27*	69.12±9.52	70.68±9.79*
20th min	81.74±13.18	81.06±12.48*	112.06±9.75	111.50±10.38*	68.30±8.74	69.96±9.87*
25th min	80.96±12.78	80.74±12.96*	110.94±8.75	111.26±9.58*	68.20±8.43	69.40±9.62*
30th min	81.16±12.40	80.28±13.19*	110.06±9.12	110.14±10.62*	68.14±8.34	69.58±9.91*
35th min	81.38±12.67	80.04±13.16*	108.52±8.00	109.14±9.62*	68.20±7.93	69.12±9.50*
40th min	80.84±12.68	79.96±12.57*	107.42±7.20	109.16±9.01*	68.10±7.95	69.16±9.29*
45th min	79.80±12.69	78.82±12.36*	106.38±8.05	108.72±10.19*	68.00±8.33	68.92±9.87*
50th min	79.34±12.68	78.56±11.97*	106.92±7.03	108.78±9.06*	68.78±8.12	68.98±9.05*
55th min	79.24±12.98	78.56±11.67*	106.16±6.82	108.52±9.18*	68.40±7.74	68.88±8.84*
60th min	79.76±13.59	78.82±12.09*	105.46±7.07	108.06±10.05*	67.18±7.78	68.24±9.58*

*** p-value > 0.05 ** p-value significant at 0.05; *** p-value significant at 0.01**

Table V : Distribution of patients with respect to side effects

Side effects		GROUP T (N = 50) Number and percentage	GROUP C (N = 50) Number and percentage
Nausea		10 (20%)	2 (4%) **
Vomiting		12 (24 %)	3 (6%) **
Itching		0	0
Sedation		0	0
Respiratory depression		0	0
Shivering	Grade 1	0	3 (6 %)
	Grade 2	0	2 (4 %)
	Grade 3	0	7 (14 %)
	Grade 4	0	7 (14 %)
	Total	0	19 (38%) ***

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