Available online at http://www.journalijdr.com

IJDR

International Journal of
DEVELOPMENT RESEARCH

ISSN: 2230-9926

International Journal of Development Research
Vol. 4, Issue, 6, pp. 1249-1252, June, 2014

Full Length Research Article

A COMPARATIVE STUDY OF THE EFFECT OF INTRAVENOUS TRAMADOL HYDROCHLORIDE AND INTRAVENOUS CLONIDINE HYDROCHLORIDE ON POST SPINAL ANAESTHESIA SHIVERING

[1*]Jalpa Balat, [2]Sushil Damor and [3]Jigar Shah

[1](M.D.), Anesthesia, GCRI Hospital, Ahmedabad
[2](M.S., FMAS) General Surgery, Assistant Professor Medical College & SSG Hospital, Vadodara, Gujarat
[3](M.S.) General Surgery, 2nd year Resident, Medical College & SSG Hospital, Vadodara, Gujarat

ARTICLE INFO

Article History:
Received 26th March, 2014
Received in revised form
28th April, 2014
Accepted 19th May, 2014
Published online 25th June, 2014

Key words:
Anaesthesia spinal,
Clonidine, shivering,
Tramadol

ABSTRACT

Background: Control of post spinal shivering is essential for optimal perioperative care, which can be achieved either by oral or parental medications. The present study is designed to evaluate the efficacy and safety of intravenous low-dose clonidine and tramadol in the treatment of post spinal shivering.

Materials and Methods: In this prospective, a double blind, randomized study, 90 ASA grade I or II, patients aged 18 – 35 years, undergoing operations under spinal anaesthesia, who subsequently developed shivering grade 3 or 4, were randomized into two groups, to receive either clonidine or tramadol. The efficacy and response rate of the study drugs were evaluated and recorded. Side effects like, nausea, vomiting, hypotension, bradycardia, dry mouth, sedation, skin rash and headache, if present, were recorded. All data were analyzed by using the Chi square test and the Z-test.

Results: There were significant differences in the response rate between the drugs ($P < 0.05$). Time taken from the starting of treatment to cessation of shivering was significantly less with the tramadol group ($P < 0.05$), however, the frequency of nausea, vomiting, sedation and headache were also significantly more in the tramadol group

Conclusion: In our study we concluded that both clonidine and tramadol control shivering. However, the response rate was higher and time taken to control shivering was lesser with tramadol, but the response rate and the side effects were lesser with clonidine.

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INTRODUCTION

Shivering is one of the most common complications of a central neuraxial blockade, due to impairment of thermoregulatory control.[1] An incidence of 57% of shivering during regional anaesthesia has been reported.[2] Shivering during a neuraxial block could have potentially detrimental effects and it may contribute to increased wound pain.[3] Various pharmacological and non-pharmacological[4] methods have been proposed, of which tramadol[5] and clonidine[6] are the recently used drugs to control shivering. This prospective, double blind, randomized clinical study was designed to compare the anti-shivering effects and side effects of clonidine and tramadol in the treatment of post spinal shivering.

Corresponding author: Jalpa Balat
(M.D.), Anesthesia, GCRI Hospital, Ahmedabad

MATERIALS AND METHODS

After obtaining permission from the Institutional Ethics Committee and written informed consent from all patients, 90 ASA grade I and II patients, between the ages of 18 and 35 years, who subsequently developed shivering intraoperatively during elective or emergency operations, under spinal anaesthesia, were enrolled by random allocation in this study and divided into two groups of 45 each. Patients with known hypersensitivity to tramadol and clonidine, cardiopulmonary, liver, or renal disease, psychological disorders, hypo- or hyperthyroidism, a need for blood transfusion during surgery, an initial body temperature > 38°C or < 36°C, a known history of alcohol or drug abuse, those receiving vasodilators, those who received drugs for labor analgesia, or other medications likely to alter thermoregulation, were excluded from the study. The patients did not receive any premedication. On arrival into the operating room, an 18G venous cannula was inserted and preloading done with Ringer's Lactate

solution at 10 ml kg–1 h–1 before insertion of spinal anaesthesia and reduced to 6 ml kg–1 h–1 after spinal anaesthesia. Volume of preloading intravenous fluids, use of mephenteramine for hypotension and the dose of local anaesthetic were determined by the attending anaesthesiologist and were not affected by enrollment in the study. All preloading fluids and drugs were stored and administered at room temperature. Subarachnoid anaesthesia was instituted at the L3 – L4 spinal interspaces, with 0.5%, hyperbaric bupivacaine 10 mg (2 ml) using a 25G Quincke spinal needle. The patients were randomly (envelope randomization) allocated to receive Clonidine 50 µg (Group-C, n = 45) or Tramadol 50 mg (Group-T, n = 45). Patients who developed grade 3 or 4 shivering for at least three minutes after spinal anaesthesia were included in the study; both the drugs were given as slow i.v. bolus injections. The treatment drugs were diluted to a volume of 5 ml in a 5 ml syringe and presented as coded syringes by an anaesthesiologist who was blinded to the group allocation. Supplemental oxygen (5 liters min–1) was delivered via a facemask during the operation. All patients were covered with one layer of surgical drapes over the chest, thighs and calves during the operation and one cotton blanket over the entire body after operation.

The presence of shivering was observed by an observer anaesthesiologist blinded to the administered study drug. Shivering was graded using a scale similar to that validated by Tsai and Chu[7] grade-0: No shivering; grade-1: Piloerection or peripheral vasoconstriction, but no visible shivering; grade-2: Muscular activity in only one muscle group; grade-3: Muscular activity in more than one muscle group, but not generalized; and grade-4, shivering involving the whole body. The antishivering effect of the study drug was assessed by both the parturient and observing anaesthesiologist. The patients were asked to evaluate the effect of treatment, two minutes after injection as, no response, slight response, or marked response. This was then recorded as per the statement of the patients. The attending anaesthesiologist independently assessed and recorded the time of cessation of shivering after treatment. Fifteen minutes after the administration of the study drug, if the shivering grade continued to be the same, the treatment was regarded as ineffective and i.v dexamethasone 5 mg was administered to control the shivering. Heart rate, respiratory rate and peripheral oxygen saturation were monitored continuously, arterial blood pressure was recorded every two minutes, for first 30 minutes and every five minutes for additional 60 minutes using the standard noninvasive monitors, before and after intrathecal injections, till the development of shivering, as well as after administration of study drug.

During the perioperative period, body temperatures (tympanic and axillary temperature) were recorded with an ear and an axillary thermometer. The ambient temperature was measured by a wall mounted thermometer. The ambient temperature was maintained at 24°C – 26°C, with constant humidity. Side-effects such as nausea, vomiting, hypotension, bradycardia, dry mouth, sedation, skin rash and headache, if present, were recorded. Hypotension was defined as a decrease in arterial pressure of more than 20%, in relation to a baseline pressure or systolic pressure of less than 100 mmHg. If patients developed nausea and vomiting, i.v. metoclopramide 10 mg was administered. The attending anaesthesiologist also assessed the degree of sedation on a five-point scale: 1: Fully awake and oriented; 2: Drowsy; 3: Eyes closed, but rousable to command; 4: Eyes closed, but rousable to mild physical stimulation; and 5: Eyes closed but unarousable to mild physical stimulation.[8] All data were analyzed using the Chi squire test and Z-test

Statistical Analysis

Previous studies have found an incidence of shivering of the order of 40 – 65%. We anticipated an incidence of 50%. Hence, we assumed that < 35 patients were required in each group for a type I error of 0.05 and the power of the study was > 90%, a sample size of 45 was calculated. Statistical comparisons of patient characteristics and time taken to control shivering, between the groups, were performed using the Z-test. Nominal or categorical data, including the overall incidence of shivering, response rate and side effects between the groups were analyzed and compared using the chi square test. The value of $P < 0.05$ was considered as statistically significant.

RESULTS

Ninety patients experienced shivering of grades 3 and 4 after spinal anaesthesia, during the operation. Patients characteristics in respect of age, weight, body temperature and duration of surgery were similar between the groups [Table 1]. Response rate (shivering ceased after treatment within 15 minutes) was found to be 95.56% in the tramadol group and 86.67% in the clonidine group and the time required to cease shivering was shorter in the tramadol group than in the clonidine group [Table 2].

Table 1. Patient characteristics

Variables	Tramadol (50 mg)	Clonidine (50 µg)	*P* value
Number	45	45	
Age (in years)	21.62 ±2.35	22.15 ±2.34	>0.05
Body Weight (kg)	63.62 ±3.41	62.71 ±2.76	>0.05
Temperature (°F)	37 .05±0.2	37.04±0.21	>0.05
Duration of surgery (minutes)	30 ±4.52	32.11 ±3.45	>0.05

Values are mean ± SD

Table 2. Shivering grade and response to treatment

Parameter	Tramadol	Clonidine	P value
Shivering grade	41 / 4	42 / 3	> 0.05
Time taken to control shivering mints	2.2 ± 0.41	3.17 ± 0.03	< 0.05
Response Rate	95.56%	86.67%	< 0.05

Values are number, mean ± SD and percentage

Nausea, vomiting, sedation and headache were more common in the tramadol group. No patient in any group developed hypotension or skin rash before or after treatment [Figure 1]. In addition the heart rate, respiratory rate and oxygen saturation were not significantly different after spinal anaesthesia, before treatment and 15 minutes after treatment, between the groups.

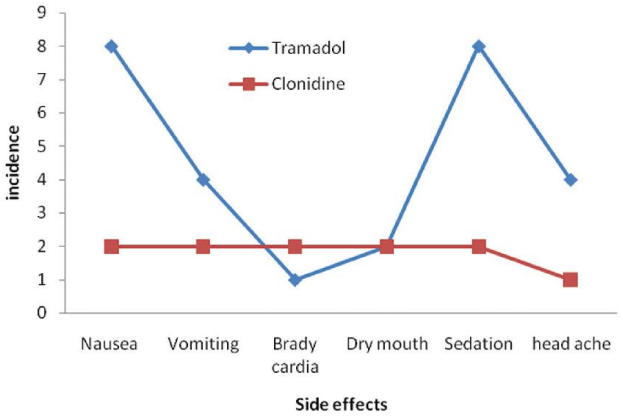

Figure 1. Showing incidence of side effects, nausea, vomiting, sedation and headache, which were more common in the tramadol group and less common in the clonidine group

DISCUSSION

The results of this study indicate that the response rate is less and the time taken to control shivering is longer, but the side effects are fewer in the clonidine group. The response rate is better and time taken to control shivering shorter in the tramadol group, but with more side effects. Shivering occurs as a thermoregulatory response to hypothermia or muscle hyperactivity with clonic or tonic patterns and different frequencies have been reported. However, in the post spinal period shivering has been reported in patients with normothermia, suggesting that other mechanisms, other than heat loss and subsequent decrease in core body temperature may contribute to the development of shivering.[9] These mechanisms include inhibited spinal reflexes, apprehension, decreased sympathetic activity, pyrogen release, adrenal gland suppression and respiratory alkalosis. Hypothermia during central neuraxial blockade is common,[10] and can be nearly as severe as that observed during general anaesthesia.[11] There are three principal reasons for hypothermia under spinal anaesthesia. First, spinal anaesthesia leads to an internal redistribution of heat from the core to the peripheral compartment,[12] secondary to sympathetic block and peripheral vasodilatation.

Second, loss of thermoregulatory vasoconstriction below the level of the spinal block, leads to increased heat loss from the body surfaces. Last, there is altered thermoregulation under the central neuraxial block, characterized by a decrease in shivering thresholds. In addition rapid administration of cold intravenous fluids contributes to the development of shivering. Treatment modalities include covering the patient with blankets, application of radiant heat and warming the operating room.[13] The use of warm local anaesthetic solution or warm intravenous fluids has met with various degrees of success.[14] Various pharmacological treatments like i.v. opioids, alfentanil, pethidine;[15] nalbuphine and meperidine,[16] non-opioid analgesic tramadol,[17] 5-HT3 antagonists;[18] ondansetron,[19] dolasetron; and cholinomimetic agent physostigmine[20] have been used; however, side effects like hypotension, hypertension, sedation, respiratory depression, nausea and vomiting, limit their use. Our study was designed to compare a small dose (50 µg) of clonidine, an α2 adrenoceptor agonist, with that of tramadol a non-opioid analgesic for control of shivering during spinal anaesthesia. Clonidine is an α2 adrenoceptor agonist, with antihypertensive, sedative, analgesic and anti-shivering properties. The antishivering effects of alpha (α) adrenoceptor agonists are mediated by binding to α2 receptors mainly the α2b receptors that mediate vasoconstriction and the anti-shivering effect.[21] In addition clonidine has hypothalamic thermoregulatory effects,[22] as it may exert an inhibitory action on the hypothalamus, by decreasing the nor-adrenaline synaptic release through α2 receptors located at the pre-synaptic nerve terminals, thus contributing to its anti-shivering effect.[23] Tramadol has been used as an analgesic for postoperative pain and labor analgesia without any adverse effects on the mother or baby.[24] It has been shown to be effective in controlling post spinal shivering.[25] Tramadol has got agonist properties on opioid receptors, with the main opioid effect being mediated through µ receptors, with minimal effect on κ (kappa) and σ (Sigma) receptors. It activates the monoaminergic receptors of the descending spinal inhibitory pathway of pain. It also inhibits the synaptosomal nor-adrenaline and serotonin uptake and may also contribute to its analgesic effect.[26] In our study both clonidine and tramadol controlled shivering at doses of 1 µg and 1 mg per kg respectively, although better control was observed with tramadol. However, the incidences of side effects were more with tramadol than with clonidine.

Conclusion

Clonidine 50 µg is less effective than Tramadol 50 mg, in the treatment of post spinal shivering. However, the side effects were fewer with clonidine, but were significantly high with tramadol. Our study has limitations of small sample size, hence, further controlled large sample-sized studies with different doses of clonidine are required to confirm the optimal dose and the results of this study.

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