ORIGINAL ARTICLE

THE EFFICACY OF TRAMADOL IN THE PREVENTION OF POST SPINAL ANAESTHESIA SHIVERING IN CAESAREAN DELIVERIES

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ABSTRACT

Background: Shivering associated with subarachnoid block in obstetric patients is a cause of discomfort in this group of patients. Tramadol, a synthetic weak opioid that acts centrally at the mu receptors has been found to be effective in the treatment of shivering after general anaesthesia, but will it be effective in prevention of post spinal shivering also? Objective: The study is aimed at investigating the efficacy of intravenous 1mg/kg tramadol in the prevention of post spinal shivering for Caesarean delivery. **Methodology:** In a double blinded clinical trial, one hundred (100) healthy obstetric patients who were scheduled for elective or emergency Caesarean section under spinal anaesthesia were randomised into two groups. Immediately after the delivery of the foetus, fifty (50) patients received 1mg/kg tramadol diluted to 2ml with sterile water and fifty (50) patients received 2ml of sterile water. The incidence and intensity of shivering, level of sedation and other complications were recorded. The Statistical Package for Social Sciences (SPSS) version 16 was used for analysis of statistical data. The data was presented as frequencies, proportions and means. The demographic numeric data was compared using students't' test. The incidence of shivering and side effects was tested by Chi square test. $P < 0.05$ was considered as statistically significant. **Results:** The incidence of shivering was significantly lower in patients who received tramadol than those who received placebo, 18% versus 72% ($P < 0.001$). In the placebo group 17 (34%) and 19 (38%) patients had grade one and grade two shivering respectively as compared to 7 patients (14%) with grade one shivering and 2 patients (4%) with grade two shivering in the study group. The severity of shivering was significantly higher in the placebo group ($P < 0.001$). There were no significant differences in the sedation scores and other complications, but nausea and vomiting was significantly higher in the study group ($P = 0.004$ and 0.005respectively). **Conclusion**: Intravenous tramadol 1mg/kg is effective in the prevention of shivering following spinal anaesthesia for Caesarean section; however it is associated with nausea and vomiting.

Keywords: Spinal anaesthesia, Caesarean section, Tramadol, Shivering.

INTRODUCTION

Spinal anaesthesia is the anaesthetic technique of choice for Caesarean sections because it is associated with fewer complications when properly conducted. The global rate of Caesarean delivery has risen dramatically in developing countries and in recent years the rate of Caesarean deliveries has reached 46% in China; and more than 25% in most African, Asian and Latin American countries. [1]

The Advantages of spinal anaesthesia for caesarean section include reduced cost to patients, early maternal-baby bonding, reduction of blood loss and blood transfusion rates, reduction of intubation complications, and the risk of aspiration of gastric contents; and the reduction of the use of multiple drugs when general anaesthesia is used. This technique also rules out theatre pollution with anaesthetic gases. [2]

The side effects associated with spinal anaesthetic technique include post spinal shivering among others. Shivering is very unpleasant and occurs in up to 40-50% of cases following spinal anaesthesia

for caesarean sections. [2] It can cause increase in the metabolic demand of oxygen and increased oxygen consumption by the patient. Invariably muscle pains may also be associated with the post spinal shivering. [2]Shivering is of unknown aetiology but some authorities have attributed it to the suppression of the spinal inhibitory reflexes in the central nervous system, and drop in core temperature thereby making the patients vulnerable. [2] Many modalities have been advocated to prevent post spinal shivering; which includes keeping the theatre environment warm and use of warm intravenous fluids, but then shivering still occurs in majority of cases; hence pharmacological interventions have been studied and proposed.[2,3,4] Tramadol is effective in the treatment of post spinal shivering, with it being aborted within a few minutes after intravenous injection of 1mg/kg of tramadol.[2]

This study is aimed at investigating the efficacy of intravenous 1mg/kg of tramadol in the prevention of post spinal shivering for caesarean sections.

MATERIALS AND METHOD

This was a prospective, double blind, randomised clinical trial. The study was performed at the Jos University Teaching Hospital, Jos, Plateau State. An ethical clearance was obtained from the institution ethical committee. All consenting ASA physical status I-II pregnant women scheduled for elective or emergency Caesarean section were allocated to one of two study groups to receive either 1mg/kg tramadol diluted into 2ml (tramadol group) or 2ml of sterile water(control group) via the intravenous route. However, all known epileptic patients and the patients below 50 kg and above 90 kg were excluded from the study.

A pre-operative anaesthetic assessment was done in all eligible patients and informed consent was obtained. Patients for elective Caesarean section were instructed to fast overnight. Acid aspiration prophylaxis was ensured with 10mg metochlorpramide and ranitidine 50mg given intravenously two hours before elective Caesarean surgeries and as early as possible during the time of preoperative evaluation before an emergency Caesarean delivery. Routine anaesthetic –machine check was done, and all necessary resuscitation drugs and airway equipment were made available. In the pre-anaesthetic room, consenting patients were allocated into appropriate group by picking from a sealed envelope. The demographic data as well as baseline vital signs were documented. After IV access with 16G cannula, preloading of the circulation was done with 10ml/kg normal saline or Ringers lactate, and then 10mls/kg/hr intra operatively as a continuous infusion at room temperature.

With the patients in the sitting position and under strict aseptic technique, 3mls of 1% plain lidocaine was employed to infiltrate L3/L4 or L4/L5 interspace; and spinal anaesthesia instituted with 2.5ml of 0.5% heavy Bupivacaine using a 25 G Quincke spinal needle. The patients were then positioned supine with the head and shoulders supported on a pillow and a 15 degree left lateral hip tilt to prevent supine hypotension syndrome. Assessment of sensory (pin prick) and motor block (Bromage scale) was done, and surgery allowed to commence when T6- sensory level was achieved. Oxygen at 5L/min was administered through a facemask throughout the duration of anaesthesia.

The study solutions (either 2ml sterile water or 1mg/kg tramadol diluted to 2ml) were presented in coded 2ml syringes by a skilled assistant; and were administered through the intravenous route slowly immediately after delivery of the foetus. Monitoring of systolic, diastolic and mean arterial pressures, axillary temperature and oxygen saturation were documented every minute for 5 minutes after spinal anaesthesia, 5 minutes after injection of study solutions, every 10 minutes throughout surgery and every fifteen minutes the following 2 hours in the post anaesthesia care unit before the patients were discharged to the ward.

Intra-operative hypotension, (BP of </= 100mmHg systolic or fall in BP >/= 20% from baseline. [5]) was treated with 5mg bolus of ephedrine and further increased intravenous infusion rate of crystalloids. Incidence and Intensity of shivering were recorded. Itching, dizziness, nausea and vomiting were graded as none (0), mild (1), moderate (2) and severe (3), as follows:

Grading for Nausea and vomiting [6]

0: None
1: 1 – 2 episodes separated by 5 mins in 24 hrs
2: 3 – 5 episodes separated by 5 mins in 24 hrs
3: 6 or more episodes separated by 5 mins in 24hrs

Respiratory depression; (respiratory rate < 8/min) was also observed and recorded.

Sedation was graded using a 5 point sedation score as used in a similar study, [4] recorded just before the injection of study solution and every fifteen minutes for two hours as follows :-

0= alert, 1= arouse to voice, 2= arouse with gentle tactile stimulation 3= arouse with vigorous tactile stimulation and 4= no awareness

Shivering was graded as follows [7]*:*

0 – No shivering
1 – Mild fasciculation of face or neck and ECG disturbances in the absence of voluntary activity of the arms
2 – Visible tremor involving > 1 muscle group
3 – Gross muscular activity involving the entire body

When shivering was graded 2 or higher, intravenous pethidine 25mg was administered. Active warming of the patients was instituted if the patient's temperature dropped below 36.2^{0}C, by administration of warmed intravenous fluids, warm body packs and radiant room heaters.

The operating room temperature and the recovery room temperature were taken for statistical comparison in both groups using a wall thermometer.

Nausea and vomiting of grade 2 or higher was treated with intravenous 5mg metochlorpramide. Patients were discontinued from the study in the event of massive blood loss requiring blood transfusion. Also patients were discontinued from the study in the event of failure of spinal anaesthesia requiring conversion to general anaesthesia, shivering before delivery of baby and before injection of study solutions.

Post-operative analgesia was with 1mg/kg pethidine 6 hourly for 48 hours in the ward, after which the patients were converted to oral analgesics.

The data was presented as frequencies, proportions and means. The Statistical Package for Social Sciences (SPSS) version 16 programme was used for analysis of statistical data. Patients' age, weight, height, gestational age and duration of surgery were compared using students't' test. The incidence of shivering and side effects were tested by Chi square test. $P < 0.05$ was considered as statistically significant.

RESULTS

The two groups (study and placebo) were statistically similar in respect to age, weight, height, parity , gestational age, indications for caesarean section and time of surgery ($p>0.05$,Table I). The average duration of surgery in the study and placebo groups were 59.30 $^+$/- 14.52 and 58.50 $^+$/- 12.53 respectively ($P = 0.769$). More of the surgeries were done during the day (75%) as compared to the night (25%).

The operating room and the recovery room temperatures were similar in the two groups and ranged between 26 – 28 ^{0}C (Table II; $P = 0.145$ and $p= 0.125$ respectively). The range of mean axillary temperatures for the placebo group was 36.25^{0}C – 36.38 ^{0}C while the range for the study group was 36.50 ^{0}C – 36.55 ^{0}C. Patients in the placebo group had significantly lower temperature ($P < 0.05$).

Oxygen saturation of patients in the two groups was comparable throughout the study and the difference in the two groups was not statistically significant ($P > 0.05$). Table III shows the incidence and severity of shivering in the two groups.

The incidence of shivering was significantly lower in patients who received tramadol than those who received placebo 18% versus 72% respectively ($P < 0.001$). In the placebo group 17 (34%) patients and 19 (38%) patients had grade one and grade two shivering respectively as compared to 7 patients(14%) with grade one shivering and 2 patients (4%) with grade two shivering in the study group. The severity of shivering was significantly higher in the placebo group ($P< 0.001$). Most of the

shivering in both groups occurred post-operatively in the recovery room. Grade three (3) shivering was not seen in any patient in the two groups. Two (4%) patients in the study group and 19 (38%) in the placebo group who had grade 2 (two) shivering ($p<0.001$) received 25mg intravenous pethidine for control of shivering in addition to other measures such as warming intravenous fluid , warm body packs, and activating radiant room heaters.

Other peri-operative complications and sedation levels in the two groups are shown in Table IV. Nausea and vomiting was more in the study group than in the placebo group and this was statistically significant (P = 0.004 for nausea and 0.005 for vomiting). Nausea was observed in 5(10%) patients in the placebo group as against 14 (28%) patients in the study group. The incidence of vomiting was lower in the placebo group with 2 (4%) patients having vomiting compared with 12 (24%) patients in the study group. Nausea and vomiting was more severe in the study group than in the placebo group. Sedation levels were not statistically different between the two groups (P = 0.526). No patient had sedation level greater than 1 (arousals to voice).

Respiratory depression and pruritus did not occur in any patient. Dizziness occurred in only one patient in the study group during the post-operative period in the recovery room. It lasted for about 3 minutes after which the patient felt spontaneous relief.

Table I: Demographic and clinical data in the two groups

PARAMETER	STUDY(Group 1) (n = 50)	PLACEBO(Group 2) (n = 50)	P- VALUE
Mean Age(+/- SD) (Years)	30.14 (+/- 5.04)	30.84(+/-5.29)	**0.499 ***
Mean Weight(+/-SD) (Kg)	71.71(+/- 9.98)	70.93 (+/- 7.89)	**0.360 ***
Mean Height(+/-SD) (Metres)	1.67 (+/- 0.08)	1.65 (+/- 0.09)	**0.354 ***
Mean Gestational age (+/-SD) (Weeks)	39.04(+/-1.89)	38.80(+/-2.53)	**0.392 ***
Time of surgery			**0.644 ***
- Day	39(78%)	36(73%)	
- Night	11(22%)	14(27%)	
Indication			**0.695 ****
- 2 previous C/S	10(20%)	6 (12%)	
- CPD/FTP	11(22%)	10 (20%)	
- Foetal distress	6 (12%)	7 (14%)	
- Others	23(46%)	27 (54%)	
Mean Duration of surgery(+/-SD) (min)	59.30(+/-14.52)	58.50(+/-12.53)	**0.769 ***
Parity			0.543 **
Primigravida	17(34%)	15(30%)	
Para 1	23(46%)	27(54%)	
Multigravida	10(20%)	8(16%)	

CPD: Cephalo-pelvic disproportion FTP: Failure to progress * (Student t – test) ** (chi-square test)

Table II: Operating and Recovery room temperatures in the two groups

GROUP	Study(Group1) Mean +/- S.D	Placebo (Group2) Mean +/- S.D	P Value
Operating room temperature (^{0}C)	26.51 (+/- 0.63)	26.40 (+/- 0.52)	**0.145 ***
Recovery room temperature (^{0}C)	26.94 (+/- 0.55)	27.03 (+/- 0.49)	**0.125 ***

* (Student t – test)

Table III: Incidence /Grade of shivering in the two groups

PARAMETER	STUDY (Group 1) n = 50 Number (%)	PLACEBO(Group 2) n = 50 Number (%)	P-VALUE
Incidence of	9(18%)	36(72%)	**0.00014 ****
Grade 0 (No shivering)	41(82%)	14(28%)	**0.00010 ****
Grade 1	7(14%)	17(34%)	
Grade 2	2(4%)	19(38%)	
Grade 3	0	0	

** (chi-square test)

Table IV: Other Peri-operative complications in the two groups

Peri-operative Complications	STUDY(Group 1) n = 50 Number (%)	PLACEBO (Group 2) n = 50 Number (%)	P-VALUE
Nausea None	36(72%)	45(90%)	**0.004 ****
Mild	10(20%)	5(10%)	
Moderate	4 (8%)	nil	
Severe	nil	nil	
Vomiting None	38(76%)	48(96%)	**0.005 ****
Mild	12(24%)	2(4%)	
Moderate	0	0	
Severe	nil	Nil	
Pruritus	0	0	1.00 **
Dizziness	1 (2%)	0	**0.09 ****
Respiratory depression	0	0	**1.00 ****
Sedation level			**0.526 ****
Level 0	44(88%)	46(92%)	
Level 1	6(12%)	4(8%)	

** (chi-square test)

DISCUSSION

The study showed an increased incidence and severity of shivering in the placebo group compared to the Tramadol group and the difference was statistically significant for both incidence and severity of shivering ($p< 0.001$). This is similar to reports from previous studies.[2,7,8,9]

Atashkoyi et al, [9] in their randomized double blind clinical trial on the effect of tramadol for prevention of shivering after spinal anaesthesia for Caesarean section, 70 healthy obstetric patients either received 1mg/kg tramadol or normal saline immediately after spinal anaesthesia. The incidence of shivering was significantly lower in patients who received tramadol (28.57%) than those who received normal saline (65.71%) with a P value < 0.001.[9]

Fatemeh et al [2] in a similar study on ninety patients who had spinal anaesthesia for caesarean section, reported a shivering incidence of 86.6% in the placebo group and 8.8% in the study group (1 mg/kg Tramadol), the difference being statistically significant.($P < 0.001$).

A possible reason for the differences observed in the incidence of shivering in the tramadol groups of the two studies mentioned above and our study could be due to timing of the tramadol dose, since the same dose of 1mg/kg was used in the three studies. Atashkoyi[9] who got the highest incidence of shivering in the tramadol group gave the drug at the beginning of surgery just after establishing the spinal block.

In our study, tramadol was given after the delivery of the fetus while, Fatemeh et al,[2] in their study gave tramadol much later, towards the end of surgery. It is possible that giving the tramadol early reduces the effective quantity of the drug available to prevent shivering, since most of the shivering occurred in the post-operative period.

The severity of shivering was significantly higher in the placebo group in our study. This is also similar to what Atashkoyi et al[9] and Fatemeh et al[2] reported. The increased severity of shivering observed in the placebo groups also buttresses the point that tramadol is not only effective in preventing post spinal shivering, but it also reduces the severity of shivering when it occurs.

Some possible causes of shivering in anaesthesia include hypothermia and post-operative pain with the release of cytokines. Shivering associated with spinal anaesthesia may however be due to inhibition of descending spinal reflexes caused by spinal anaesthesia, internal redistribution of core temperature, loss of thermo regulatory vasoconstriction below the level of the blockade and decrease of vasoconstriction threshold. [10,11]

While most shivering occurs in response to hypothermia, non-thermoregulatory shivering also occurs in normothermic patients in response to pain. [12]Adequate pain relief provides improved post operative patient outcome and helps mothers to be more alert.

Reduction in post operative shivering and pain also helps mothers to be more comfortable to take care of their babies [13]. Mothers can breast feed babies early and this will increase bonding between mothers and babies in the first few hours of babies' extrauterine life. [14] This shows that the benefit of preventing post-operative shivering goes beyond reducing discomfort to mothers, it will also improve the quality of care given to the babies by their mothers after Caesarean deliveries.

Modalities that have been traditionally used to reduce postoperative shivering include keeping the theater environment warm and using warm intravenous fluids but these methods have been grossly inadequate. [2] Besides Tramadol, some other pharmacological intervention that have been advocated to control shivering include the use of ketamine, fentanyl, pentazocine , and pethidine each with its attending side effects. [15] In our study, there was no significant difference in the sedation levels and incidence of respiratory depression in the two groups. This is also similar to what was reported in studies done by Fatemeh et al and Atashkoyi et al. This shows that tramadol is safe and will not cause significant respiratory and central nervous system complications when given at the dose of 1mg/kg as was used in our study; and in the studies done by Fatemeh and Atashkoyi.

In this study, nausea and vomiting was noticed to be significantly more in the study group than in the control group. This was not so in a previous study conducted by Atashkhoyi et al, [9] in which only one patient (2.85%) and 4 patients (11.42 %) had nausea in the placebo and study group respectively, the difference not being statistically significant (P = 0.35). No patient in either group was observed to vomit. In their study, although the dose of 1mg/kg tramadol given to patients in the study group is similar to the dose used in this study, the drug solution was diluted to 5ml unlike this study in which the dilution was to 2ml, meaning the concentration was more in the latter. Furthermore in their study, the study solution was given slowly over 2-3mins unlike this study that the solution was given over shorter time duration (1-1.5mins). Probably, tramadol when given slowly intravenously and well diluted is not likely to cause severe nausea and vomiting.

CONCLUSION: Administration of 1mg/kg tramadol is effective in the prevention of shivering after spinal Anaesthesia for caesarean section; however it is associated with nausea and vomiting.

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