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Full Length Research Paper

Treatment of postanesthetic shivering in children: A randomized control study comparing tramadol to pethidine

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Post-anaesthetic shivering (PAS) is a common and distressing complication, with most studies conducted in adults (Kranker et al., 2003). The aim of this study was to compare the effectiveness of tramadol and pethidine in the treatment of PAS in children. A randomized, double blind, comparative study was carried out on 80 children of American Society of Anesthesiologists (ASA) physical status I or II who presented with PAS during recovery from general anaesthesia. The children were randomized to receive 0.4 mg/kg of either drug. The response to treatment was assessed in 5, 15, 30, 45 and 60 min. The mean time [SD] for cessation of shivering following treatment with tramadol was 5.57 min (0.8) while with pethidine cessation occurred after 7.42 min (0.94), which was statistically significant. However, 17 patients in the pethidine group developed significant side effects when compared with the 4 patients in the tramadol group. Finally, there was a 10% recurrence of PAS with tramadol as against 50% with pethidine after 45 min. Both regimens were effective in treating PAS, but tramadol had a quicker onset time, with less side effects and recurrence rates of PAS.

Key words: Shivering, anaesthesia, pethidine, tramadol.

INTRODUCTION

Post-anaesthetic shivering (PAS) is common in the postoperative period and varies according to gender, age, and the duration for the surgery (Buggy et al., 1997; Piper et al., 2004; Macario et al., 1997; Powell and Buggy, 2000). The incidence of PAS following general anaesthesia ranges from 6 to 65% (Mohta et al., 2009). Several pharmacological agents have been studied for the treatment of PAS, including clonidine, ketamine, doxapram, tramadol, and pethidine (Kranker et al., 2002; Piper et al., 2000; Alfonsi, 2001).

Among these agents, pethidine and tramadol have been widely used, in the treatment of PAS (Dhimar et al., 2007; Bhatnagar et al., 2001; Seifi et al., 2008). However, the mechanism of action of both drugs is different. Pethidine acts through the opioid K-receptors, while tramadol acts through serotogenic and/or noradrenergic receptors (Witte and Sessler, 2002; Mathews and Al Mulla, 2002). Previous studies have shown varied results regarding its effectiveness in treating PAS in adults (Zahedi, 2004; Tsai and Chu, 2001). Akin et al. (2005)

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also studied postoperative shivering in children and causative factors. The present study was designed to evaluate the effectiveness, duration, and side effects of tramadol on PAS in children and to compare it with those of pethidine.

METHODOLOGY

This randomized controlled, double-blinded, clinical trial was conducted at the University of Nigerian Teaching Hospital, Enugu, a 700 bedded tertiary health institution serving Enugu and most of the South Eastern and Middle Belt states in Nigeria. The study period spanned 18 months, between March, 2006 and September, 2007. The Research and Ethical Committee approved the study protocol, and a written informed consent was obtained from parents or guardians of the patients.

Eighty children were recruited, aged 5 to 18 years suffering from PAS following general anaesthesia for herniotomy or herniorrhaphy, who were American Society of Anaesthesiologist class I and II. Children were excluded from the study with age less than 5 or greater than 18 years of age, emergencies, and patients with known allergies to tramadol or pethidine.

The study was a randomized, double-blind, placebo-controlled comparative study. Patients were randomly allocated, using a draw of lots technique, into two groups namely, tramadol (Group T) and pethidine (Group P). This randomization was done by sequentially drawing numbered sealed envelopes containing drug codes known only to the pharmacist who subsequently prepared and delivered the study drug to the recovery room refrigerator in similar-sized, equal volume, coded syringes.

In our hospital, PAS is routinely managed with warmed isolation blankets and by administering oxygen with nasal prongs at a rate of 4 L/min. For this study, either tramadol or pethidine was intravenously administered to each patient with Grade II or greater PAS according to the randomization schedule.

Prior to the induction of general anaesthesia, standard hemodynamic monitors for recording vital signs were used for all patients, including non–invasive blood pressure, electrocardiograph, pulse rate, pulse oximetry, and tympanic temperature. The temperature of the operating room was maintained between 22 to 24°C. Intravenous access was gained with 20 or 22G cannulae.

A standardised general anaesthetic technique was used. Intravenous atropine (0.02 mg/kg) provided premedication. Anaesthesia was induced with intravenous propofol (2 mg/kg). Suxamethonium (1.5 mg/kg) was given intravenously to facilitate orotracheal intubation. After securing the endotracheal tube, a temperature probe was inserted into the nasopharynx, to a point equal to the nose-ear distance. The nose-ear distance is the length from the inner brim of the nostril to the tragus. Measurement of nasopharyngeal temperature at this point had a high precision. Nose-ear distance was anatomically the closest to the brain base, and core temperature was recorded (Ko et al., 2001). Anaesthesia was maintained with isoflurane 0.8% volume with oxygen in air, with intermittent positive pressure ventilation in a circle system. Intravenous fentanyl (1 μg/kg) provided analgesia. All fluids and drugs used were at room temperature. During anaesthesia, patients were covered with sheets, but not actively warmed. After surgery, the residual muscle relaxants were reversed, and the patient's trachea extubated. The patients were then covered with a blanket and transported to the recovery room.

The presence of PAS was graded, using the validated scale by Crossley A.W.A. and Mahajan R.P. (Appendix Table 1) (Crossley and Mahajan, 1994). When PAS of grade II or higher occurred, the patients were given intravenous coded-medications containing either pethidine 0.4 mg/kg or tramadol 0.4 mg/kg. Further assessment of the patients' response to treatment was observed at time intervals of 5, 10, 15, 30, 45, and 60 min after PAS therapy. The time to cessation of shivering was recorded after injection of the treatment drug (Table 1). The attending anaesthetist assessed the degree of sedation on a four-point scale (Appendix Table 2). Nausea and vomiting were also recorded as shown in Table 2. Recurrence of shivering was recorded and treated with 0.25 mg/kg of the initial drug for the patient (Table 1). Nausea and vomiting was treated with ondansetron 0.1 mg/kg intravenously, while sedated patients were closely observed until full recovery.

Statistics

Based on the previous studies, the incidence of PAS was estimated to be 60%. A sample size of approximately 40 for each group was needed to determine the effectiveness of either drug in reducing PAS by 50%, with 95% confidence ($\alpha = 0.05$), and the power of the study being 90%.

Demographic data, surgical duration, and side effects were expressed as means standard deviation (SD) (Table 3). The Students T-test was used to compare continuous demographic data and times to respond to treatment, while the incidence of side effect of drugs and recurrence rates were compared using the Chi-square test. A P value of 0.05 or less was considered statistically significant.

RESULTS

Eighty patients were enrolled into the study (40 in each group) comprising 53 males and 27 females. The age ranged between 5 and 18 years. There was no statistical difference in age, weight, sex ratio, American Society of Anesthesiologists (ASA) status and duration of surgery between both groups (Table 3). The mean incidence of PAS in both groups was 10%.

The mean time (SD) for cessation of PAS following treatment with tramadol was 5.57 min (0.88), while with pethidine was 7.42 min (0.94, P = 0.04). This difference was statistically significant. Four (10%) patients in the tramadol group and 17 (42.5%) patients in the pethidine group developed significant side effects (P = 0.03) (Figure 1 and Table 2). There was a 10% recurrence of PAS after 45 min in the tramadol-treated group and a 50% recurrence with the pethidine-treated group. Rescue treatment with 0.25 mg/kg of the original coded-medication was successful in all cases.

DISCUSSION

A low incidence of PAS was observed in children, which is in agreement with other studies (Akin et al., 2005). Higher values have been obtained from adult studies to justify prophylactic treatment of PAS (Vida et al., 2011). The low incidence of PAS in children in this study does not support this view (Akin et al., 2005). Kranke et al. (2003), has advocated a "wait and see" approach in the management of PAS in children since the overall incidence

Table 1. Time of cessation of shivering and recurrence.

Parameter	Group tramadol	Group pethidine	P- value
Cessation	5.57±0.88 min	7.42±0.94 min	0.04
Recurrence (after 45 min)	4 patients (10%)	20 patients (50%)	0.05

Table 2. Complications.

Complication	Group tramadol	Group pethidine
Nausea	1 patient	2 patients
Vomiting	2 patients	1 patient
Sedation	1 patients	14 patients
Total	4 patients	17 patients

P-value= 0.03.

Table 3. Demographic data.

Data	Group tramadol	Group pethidine	P- value
Age (years)	9.92±24.00	8.88±19.15	0.07
Weight(kg)	20.00±10.00	21.65±15.45	0.25
Male:Female	28:12	25:15	0.55
ASA I:II	35:5	34:6	0.85
Nasophapharyngeal temperature (°C)	36.70±0.30	36.65±0.27	0.06
Temperature change (°C)	0.5±0.20	0.5±0.30	0.65
Surgery duration (min)	45±0.9	50±0.88	0.07

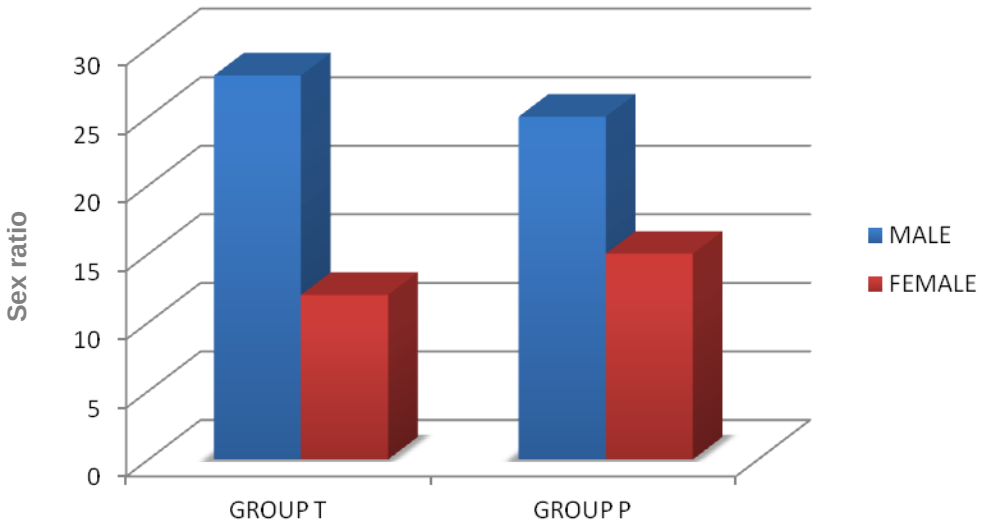

Figure 1. Sex ratio of groups.

incidence is low (Kranke et al., 2003). PAS is influenced by the type of anesthetic agent used (Seifi et al., 2008). Volatile agents like halothane are associated with a high incidence of shivering when compared with opioid and nitrous oxide based anesthesia (Seifi et al., 2008). In a study by Akin et al. (2005) on 1507 children, the use of

intravenous general anesthetic agents was associated with 3% shivering (Akin et al., 2005). In this study, anaesthesia with intravenous propofol were induced and maintained with isoflurane. The use of volatile general anaesthetic agents is associated with a higher incidence of shivering than observed with intravenous agent (Cheong and Low, 1995). This may explain our higher incidence of 10%.

Various dose regimens of tramadol and pethidine have been studied to control PAS; however, the optimal dose regimen in children remains undetermined (Parvin and Gholamreza, 2008; Wrench et al., 1997; Chan et al., 1999). In this study, we used 0.4 mg/kg based on previous works by Parvin and Gholamreza, (2008) and Wrench et al. (2008). The relative efficacy and side effects of the two drugs have also been compared with varying results (Chan et al., 1999; Faisal et al., 2006). In this study, equipotent doses of 0.4 mg/kg pethidine or 0.4 mg/kg tramadol were used (Faisal et al., 2006). Tramadol controlled PAS faster than pethidine with less recurrence. Similar data has been reported in adults (Singh et al., 2012; Dhimar et al., 2007). Recurrence was easily treated with 0.2 mg/kg of the treatment drug. The cumulative effects of this may account for the higher incidence of side effects also noted with pethidine in this study.

Conclusion

Tramadol and pethidine are effective in treating PAS. Tramadol is recommended for the treatment of PAS in children as it has a faster onset, with less rates of recurrence, and with less observed side effects when compared with pethidine at a dose of 0.4 mg/kg.

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APPENDIX

Table 1. Grades of shivering.

Grade	Meaning
0	No shivering
1	Piloerection or peripheral vasoconstriction but no visible shivering
2	Muscular activity (fasciculation) in only one muscle group
3	Muscular activity in more than one muscle group but no generalized shivering
4	Shivering involving the whole body, with generalized shaking

Table 2. Grades of sedation.

Grade	Meaning
1	Awake and alert
2	Drowsy, responsive to verbal stimuli
3	Drowsy, arousable to physical stimuli
4	Unrousable