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Shivering Following Pediatric Day Case Surgery, Evaluation and New Preventive Strategies

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Abstract

Background

Control of shivering after anesthesia is essential for optimal perioperative care which can be achieved by various parental medications. The present study tried to compare the efficacy of intravenous pethidine, ondansetrone and magnesium sulphate in prevention of post anesthetic shivering.

Methodology

150 patients (aged 3-10 years), who were scheduled for day case surgery under general anesthesia, were enrolled in this study. Children were randomly allocated into three groups (50 patients in each) to receive either intravenous pethidine, ondansetrone and magnisum sulphate after induction of anesthesia. The onset, incidence and severity of shivering after recovery of anesthesia were assessed and recorded by a blinded observer in PACU. Also, side effects related to tested drugs were recorded.

Results

Postoperative shivering incidence and severity were comparable between the three studied groups. Shivering onset was delayed in group P when compared to group O and M respectively. The time needed to discharge children from PACU was longer in group P in comparison with both group O and M with no differences between group O and M. Only one child needed overnight stay in group P. Incidence of vomiting and respiratory depression were higher in group P when compared to group O. In group P, the number of over sedated patients were higher when compared to group M.

Conclusion

The prophylactic administration of Ondansetrone and Magnesium sulphate were equally effective as Pethidine in reducing the incidence of post-operative shivering after anaethesia in pediatric day case surgery. Ondansetrone is considered to be superior to pethidine and magnesium sulphate due to its potent anti-emetic property.

Keywords

Post-operative shivering, recovery, pruritus, nausea and vomiting, sedation.

Introduction

Children are considered as proper candidates for day case surgery as they are usually healthy and mostly require minor or intermediate surgical interference of short duration. The psychological effects of being in hospital can be distressing with behavior disturbance on home return [1].

Shivering is a very unpleasant experience following day case surgery under general anesthesia in pediatric patients. It is considered as an important thermoregulatory response that aims at increasing body heat production in response to hypothermia [2]. However, it may lead to patient discomfort, interference with monitoring, increase oxygen consumption and result in delaying hospital discharge [3].

Considering these undesirable consequences of shivering, various drugs have been investigated for prevention and or treatment of postoperative shivering. Pethidine is the most effective treatment for postoperative shivering however it is associated with undesirable sedative effect which may prolong hospital stay and delay home discharge from day care unit [4,5]. Ondansetrone magnesium sulphate, doxpram and dexamethasone are considered as potential alternative anti shivering drugs with less sedative effect.

The principle aim of this study was to compare the efficacy of intravenous ondansetrone and magnisum sulphate to pethidine, in preventing the postoperative shivering after pediatric day case surgery.

Patients and Methods

After obtaining the approval of institutional board review of Mansoura Faculty of Medicine and inf o rmed consent from all patients' guardians or parents. This prospective randomized double blind ed comparative study was conducted as a joint activity between paediatric anaethetic and surgical department in Mansoura university children hospital

Patients aged between 3 and 10 years who were scheduled for elective day case surgery under general anesthesia whom their guardians gave an informed consent were included in the study. Exclusion criteria included parent's refusal, fever, neurological disorders, hemodynamic instability, prolonged use of opioids, ASA status III or IV, and hypersensitivity to the studied drugs.

Patients were randomly allocated into three groups (50 patients in each), using closed envelope method and computer randomization program. Pethidine group: patient received intravenous pethidine 1 mg/kg, group P, ondansetrone group: patient received intravenous ondansetrone 150µg/kg, group O and magnesium sulphate group: patient received intravenous magnisum sulphate 30 mg/kg, group M [6-8]. The anesthesiologist/anesthetic nurse responsible for control and registration of the clinical symptoms were blinded to the study drugs.

On arrival to the operative room intravenous cannula was inserted under effect of EMLA cream applied to the site of insertion 1 hour before. An infusion of 10 mg/kg/hour of balanced Hartman's solution was initiated and warmed to 38 degree Celsius. All patients were monitored by non-invasive arterial pressure measurement every 5 min, continues ECG and peripheral arterial oxygen saturation SpO_2.

Patients were pre-oxygenated with 5 liter/min 100% O_2 and fentanyl 1 µg/kg was administered. Svoflurane was used for induction and maintenance of anesthesia. Tracheal intubation was facilitated by rocuronium 1 mg/kg. Pressure controlled ventilation was used aiming at SpO_2 more than 94% and end tidal Co_2 between 35-45 mmHg. All patients received intravenous paracetamol 15 mg/kg. For hypothermia protection, patients were covered with 3 layers of surgical drapes and the operative room temperature was maintained between 22-24°C during the surgery. Each drug was administered after induction of anesthesia.

Tracheal extubation was done in the operative theatre after surgery completion and the patient fulfilled all criteria for extubation and neuromuscular block was reversed by (Neostigmin 0.04 mg/kg + Atropin 0.02 mg/kg). Anesthetic time (defined from the start of induction of anesthesia up to time of extubation) was recorded.

In PACU, all patients were covered by a single sheet and were not actively warmed. Patients were monitored by a trained anesthesia nurse responsible for the recovery and he/she recorded shivering as soon as it happens. Severity of shivering was staged according to Tsai and Chu. 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 (5). Grade = >2 for more than one minute were covered with a warming blanket, with additional dose of intravenous pethidine 1mg/kg.

The anesthetic time, incidence of shivering, time between recovery and starting of shivering (onset) and the severity of shivering. Duration till time of discharge from PACU to home and need of overnight stay in hospital were recorded. All side effects of the study drugs were recorded as vomiting, respiratory depression and sedation incidence among patients (patient was considered as over sedated if sedation score >2) were also recorded. Sedation was graded as: [0] Awake / Alert, [1] Minimally sedated: Tired / sleepy, appropriate response to verbal conversation and / or sounds, [2] Moderately sedated: Somnolent / sleeping, easily roused with light tactile stimulation, [3] Deeply sedated: deep sleep, rousable only with significant physical stimulation, [4] Unrousable (9). Children were discharged from hospital after being fully awake, with stable vital signs at least for 1 hour free of nausea or vomiting, no pain and can tolerate clear oral fluids [10].

Sample Size Calculation

The sample size was calculated on basis of shivering incidence. 30% difference was expected between the three studied groups. t-test was used for comparison and setting a-value to 0.05, minimum of 41 cases were needed in each group for detecting a similar difference with 80% power. The sample was increased to 50 cases in each group to compensate any possible dropouts. Calculations were made using PS software for Windows version 10 [11].

Statistical Analysis

Klomogorov-Smirnov test was used first for data normality. ANOVA test was used to analyze normally distributed continuous data. Repeated measures ANOVA was used for non-normally distributed continuous and ordinal data analysis. Categorical data were analyzed by Chi-square test. Results were presented as number and % of patients or mean ±SD. P value < 0.05 is considered significant. Statistical analyses were performed using the IPM SPSS for Windows (Chicago, USA), version 18.

Results

A total number of 150 children were recruited in this study. 50 patients were assigned in group P, O, M respectively. Nine patients out of the total one hundred and fifty (6%) experienced postoperative shivering. There were no significant differences between the three groups regarding patients characteristics (age, gender, body weight), and anesthetic time Table 1.

Table 2: Shivering incidence, onset, severity, number of over sedated patients, discharge time and overnight stay in hospital. Data are expressed as mean ±SD, number and %, median ± IQR.

Incidence of vomiting and respiratory depression were higher in group P when compared to group O. No significant differences were observed when group M compared to group P and group O individually. In group P, the number of over sedated patients were higher when compared to group M with no difference when compared to group O, Table 3.

Table (1): Patients characteristics, and anesthetic time of the studied groups. Data are expressed as mean ± SD, number and %.

	Group P NO (50)	Group O No (50)	Group M No (50)	P value
Age (months)	52.16 ± 8.18	50.38 ± 6.24	55.14 ± 6.18	0.47
Gender M/F (No, %)	26/24 (52%, 48%)	27/23 (54%, 46%)	24/26 (48%, 52%)	0.83
Body weight (kg)	26.64± 4.69	29.06 ± 4.64	29.14 ± 4.73	0.81
Anesthetic time (min)	77.22±9.88	80.40±9.90	76.98±6.83	0.19

Table 2. Visual analogue scale (VAS) score in the studied groups. Data are expressed as mean ±SD, number and %, median ± IQR.

	Group P NO (50)	Group O NO (50)	Group M NO (50)	P value
Shivering incidence (No, %)	2 (4%)	4 (8%)	3 (6%)	0.701
Onset of shivering after recovery (min)	12.18 ± 2.23	8.42±2.01*	8.22±2.10†	0.002
Severity of shivering (grade)	2.84 ± 0.79	2.88 ± 0.84	3.01 ± 0.73	0.569
Time to discharge from recovery (hours)	7.16 ± 1.34	6.82± 1.44*	6.08 ± 1.38†	0.012
Need for overnight stay (No, %)	1 (2%)	0 (0%)	0 (0%)	0.356

*P <0.05 significant when Group O compared with Group P.

†P <0.05 significant when Group M compared with Group P.

‡P <0.05 significant when Group M compared with Group O.

Table (3): Drugs related side effects. Data are expressed as number and %.

	Group P NO (50)	Group O No (50)	Group M No (50)	P value
Vomiting (No, %)	6 (12%)	0 (0%)*	2 (4%)	0.025
Respiratory depression (No, %)	5 (10%)	0 (0%)*	1 (2%)	0.0261
Sedation (No, %)	6 (12%)	3 (6%)	1 (2%)†	0.031

*P <0.05 significant when Group O compared with Group P.

†P <0.05 significant when Group M compared with Group P.

‡P <0.05 significant when Group M compared with Group P.

Discussion

Home discharge after pediatric day case surgery may be delayed due to shivering incidence. Although the exact mechanism of shivering has not been sufficiently explained, hypothermia is well known to be the fundamental triggering factor. Other factors include post-operative pain, diminished sympathetic activity and release of pyrogens [12]. Shivering may cause unwanted physiological effects, which result in increased CO2 production, O2 consumption, COP, ICP and IOP [13].

In this study 150 children were recruited in whom the prophylactic effect of Pethidine, Ondansetrone and Magnisum sulphate in preventing postoperative shivering was evaluated. In our study, 9 patients (6%) out of total 150 experienced postoperative shivering which is acceptable when compared to the average shivering incidence between 5% to 65% after general anesthesia reported in previous study [13].

The main finding of the current study was that Ondansetrone and Magnesium sulfate have the same preventive effect as Pethidine on incidence of post-operative shivering in children receiving general anesthesia with less associated side effects.

Pethidine exerts its anti-shivering effect by activation of both κ and μ-opioid receptors. Both κ and μ-opioid receptors are involved in the inhibitory cascade of shivering process [14]. The anti-shivering effect of pethidine is well documented in previous studies by Wrench IJ et al., who compared the effects of pethidine, alfentanil and placebo in the treatment of post-operative shivering and they concluded that alfentanil 250 micrograms was not effective in the treatment of post-anaesthetic shivering as pethidine [15], and also Terasako K et al., found that pentazocine 7.5 mg was not effective in the treatment of post-anesthetic shivering as pethidine [16].

Ondansetrone (5-HT3 receptor antagonists) is another medication which is used frequently to decrease postoperative shivering nowadays. The mechanism of action of 5-HT3 receptor antagonists in decreasing postoperative shivering may be attributed to inhibition of serotonin reuptake on the preoptic anterior hypothalamic region [17]. Meta-analysis which was done by Li M et al., concluded that ondansetron can prevent or attenuate the severity of postoperative shivering [18].

Our results are supported by a study done by Lin H et al, in which fifty-nine children were given intravenous injections of 4 mg ondansetron. They concluded that the pretreatment with ondansetron was associated with decreased post-anesthesia shivering symptoms compared to the control group [19].

Also another studies by Iqbal et al., and Kabade et al., reported that granisetron was as effective as intra venous pethidine in preventing postoperative shivering [20,21].

Magnesium sulfate is a calcium antagonist and a non-competitive antagonist of Nmethyl- D-aspartate (NMDA) receptors. Magnesium sulfate has both central anti shivering effect and mild muscle relaxant effect thus may reduce the gain of shivering [22].

In accordance to our study, S. Kizilirmak et al, reported that patients who received pethidine or magnesium sulphate had significantly shorter duration of shivering than those received saline, although pethidine acted faster than magnesium sulphate, but both were effective 10 minutes after the bolus injection [23].

Sedation and respiratory depression were higher in group P when compared to group M and group O. Pethidine being a synthetic opioid, causes respiratory depression and sedation [24].

Opioids produce their respiratory depressant effects by activating opioid receptors within the respiratory networks of the brainstem as well as other sites outside the central nervous system that might be involved in opioid induced respiratory depression [25,26]. Similar to our study, the respiratory depressant effect of pethidine has been demonstrated in previous studies by Loeschcke et al and Kallos et al. [27,28].

In contrast to our study, Paech MJ, in his study of more than 7000 patients who had received epidural pethidine, did not find any case of respiratory depression following epidural pethidine. However, one patient suffered respiratory arrest requiring treatment with intra venous naloxone [29].

Opioids produce their sedative actions at a cellular level by activating opioid receptors in the nuclei of tractus solitarius, peri-aqueductal grey area, cerebral cortex, thalamus and the substantia gelatinosa of the spinal cord. Opioid receptors are coupled with inhibitory G-proteins and their activation causes hyperpolarization. Overall, the effect is a reduction in neuronal cell excitability and sedation [30].

Similar to the current study, postoperative sedation with pethidine has been described previously. In a study conducted on 245 postoperative patients, pethidine was associated with remarkable postoperative sedation [31].

In our study, ondansetrone caused sedation in (3 children) which is considered less than pethicine induced sedation (6 children). Ondansetron exhibits its sedative effect by detectable binding affinity to 5αHT1C, α1- adrenergic, and μ- opioid receptor sites [32].

Davis and his colleague in their study reported a central sedative effect with a prolonged recovery with ondansetron 150 μg/kg, which is the same dose was used in the current study [33].

In this study pethidine was associated with higher incidence of vomiting in comparison to ondansetrone and magnisum sulphate. Opioid-induced emesis appears to occur either by direct stimulation of vestibular apparatus and chemoreceptor trigger zone or via an alternative pathways from brainstem to chemoreceptor trigger zone [34,35].

Higher incidence of pethidine induced nausea and vomiting were reported in previous studies which matches our finding but with different doses and routs of administration [36-38].

All children who received ondasterone were protected from post-operative vomiting in our study. Ondansetron produces its anti-emetic effect by being a selective 5-HT3 receptor antagonist. However, its mechanism of action has not been fully explained. The serotonin receptors of 5-HT3 type are present in vagal nerve terminals peripherally and in the chemoreceptor trigger zone (CTZ) within the medulla oblongata centrally. It is not confirmed whether antiemetic action of ondansetron is mediated centrally, peripherally or both routs [39].

In a study by Sadhasivam S et al., who evaluated the prophylactic antiemetic effectiveness of ondansetron in children who subjected to strabismus repair which is associated with the highest incidence of PONV concluded that the routine prophylactic use of ondansetron preventing PONV after strabismus repair in children [40].

In this study, we used a high dose of ondansetrone for prevention of postoperative shivering. Further studies may be needed for evaluating the efficacy of different doses of ondansetrone in prevention of postoperative shivering.

In conclusion, the prophylactic administration of Ondansetrone and Magnesium sulphate were equally effective as Pethidine in reducing the incidence of post-operative shivering after anaethesia in pediatric day case surgery. Ondansetrone is considered to be superior to pethidine and magnesium sulphate due to its potent anti-emetic property.

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