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Comparison between Tramadol and Pethidine in Patient Controlled Intravenous Analgesia

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Abstract

Objective: To compare the efficacy and side effects related to Tramadol with Pethidine in patient controlled intravenous analgesia (PCIA) after total abdominal hysterectomies.

Methods: A total of 60 patients were randomized to receive either Tramadol or Pethidine by PCIA (30 in each group) after total abdominal hysterectomy. Pain assessments were recorded one hour after starting the PCIA and then at 6, 12, and 24 hours by using visual analogue scale (VAS). Nausea vomiting score and sedation score were also recorded. Good attempts, total attempts and total drug consumption was noted from PCIA pump at the end of the study period.

Results: The analgesia achieved in Tramadol group was comparable to Pethidine. The incidence of nausea and vomiting was similar in both groups. Tramadol causes significantly less sedation than Pethidine ($p < 0.05$). Mean drug consumption, total attempts and good attempts were also significantly less in Tramadol group than Pethidine group ($p < 0.05$).

Conclusion: Tramadol produces equivalent analgesia and less sedation and can be used as an alternative to Pethidine in Patient Controlled Intravenous Analgesia for postoperative pain relief after Total Abdominal Hysterectomy (TAH) (JPMA 56:433;2006).

Introduction

Despite constantly increasing understanding of pain mechanisms and improved technology in pain therapy, the provision of adequate postoperative pain relief is still a challenge. Adequate pain control improves recovery from surgery by reducing stress and by avoiding pulmonary complications.¹

Patient Controlled Intravenous Analgesia (PCIA) has become an established technique for the treatment of postoperative pain.² It has been shown to offer a number of advantages including good analgesia, avoidance of fluctuations in analgesia level, lower total analgesic dosage, and improved patient satisfaction.³ The typical side-effects of opioids, such as nausea and vomiting, sedation, respiratory depression, and pruritus may sometimes hamper the successful application of PCIA.⁴

Tramadol is a centrally acting analgesic with a low affinity for μ -opioid receptors. In addition, it also inhibits the neuronal reuptake of noradrenaline and 5-hydroxytryptamine (5-HT) and it facilitates 5-HT release. The advantages of Tramadol over traditional opioids are minimal potential for tolerance, addiction and respiratory depression.⁵ Tramadol has lack of gastrointestinal side-effects and its reduced incidence of constipation (compared with other opioids) gives it great value for prolonged use.⁶

Morphine and Pethidine are the most commonly used drugs in PCIA. Unfortunately, both these drugs are not freely available in Pakistan. This double blind, randomized controlled trial was designed to compare efficacy and side effects between Tramadol and Pethidine in PCIA after total abdominal hysterectomies.

Patients and Methods

The study was performed at a University Hospital after approval from Ethics Review Committee and after informed consent from the patients. The study included 60 ASA I-II patients (30 in each group) with ages of 40 to 60 years undergoing total abdominal hysterectomy who were randomly assigned to one of the group: group A (Tramadol) and group B (Pethidine). The exclusion criteria were contraindications to opioid drugs, inability to understand the instructions because of language barrier, history of substance abuse, severe respiratory disease and patients on Monoamine Oxidase Inhibitors (MAO).

All patients were premedicated with midazolam 7.5 mg orally 45-60 minutes prior to induction of anaesthesia with Pethidine 1mg/kg. Thiopental 5 mg/kg and atracurium 0.5 mg/kg was administered to facilitate tracheal intubation. Anaesthesia was maintained with isoflurane 1-1.5% in a mixture of 60% nitrous oxide and 40% oxygen. Routine monitoring done with electrocardiogram, NIBP (Non Invasive Blood Pressure), Pulse oximetry, Capnography

(ETCO₂), FIO₂ and inhalational anaesthetic concentration were used in every patient. At the end of surgery, residual neuromuscular blockade was antagonized by 2.5 mg neostigmine and 1 mg atropine. All patients were given metoclopramide 10mg intravenous 20 minutes before the end of surgery.

In the recovery room, PCIA pump (Graseby 3300) was connected to the patient through a separate intravenous line. The PCIA drug solution contained either Tramadol (group A) 10 mg/ml or Pethidine (group B) 10 mg/ml (labeled as PCIA drug). The PCIA pump was programmed to deliver a continuous (basal) infusion of study drug 10mg/hr, bolus dose 5 mg (0.5 ml) with a lockout period of 10 minutes in each group. A second intravenous line was used for maintaining fluids.

Pain assessment was done and recorded by primary investigator 1 hour after the start of PCIA and then at 6, 12, and 24 hours by using visual analogue scale (0-10). Nausea vomiting score⁷ assessed and recorded by using a scale of 0-3: (0=no nausea vomiting; 1=mild, no treatment needed; 2=moderate, treatment needed and 3=severe; unresponsive to simple antiemetics). Sedation score⁷ was assessed by using a scale of 0-3: (0=patient awake; 1=mild, occasionally drowsy but easy to rouse; 2=moderate, frequently drowsy and easy to rouse and 3=severe, difficult to rouse, unrousable. Numbers of attempts which include total attempts and good attempts and total drug consumption at the end of study period (at 24 hrs) were also noted from PCIA pump. Total attempts are number of clicks on PCIA remote made by the patient. Good attempts are those clicks in which patient gets the bolus dose.

Data was entered and analyzed, using SPSS (Statistical Package for Social Sciences version 13.0).⁸ Pain score of the two groups were analyzed by using repeated measures ANOVA. The P values at specific time points in nausea vomiting score and sedation score were analyzed by Mann-Whitney U-test. The overall P value for nausea vomiting score and sedation score were analyzed by proportional odds model for repeated ordinal data. Number of attempts and total drug consumption were analyzed by student's t-test. P value < 0.05 was considered as significant.

Results

There were no significant differences with respect to age (45.86 ± 3.94 years vs. 46.50 ± 4.42 years) but there was a significant difference with respect to weight (70.76 ± 5.75 kg vs. 66.49 ± 8.21 kg) in Tramadol group and Pethidine group respectively.

The VAS pain scores between Tramadol and Pethidine groups were found to be insignificant at different time. It indicates that both drugs are equivalent in terms of

Table 1. Distribution of Median (Interquartile Range) of VAS pain scores at different time points.

VAS	Tramadol (n=30)	Pethidine (n=30)	P-Value
At 1 Hour	6 (4,6)	6 (5,7)	> 0.05
At 6 Hour	5 (4,5)	5 (4,6)	> 0.05
At 12 Hour	4 (4,4)	4 (4,4)	> 0.05
At 24 Hour	2 (1,3)	3 (2,3)	. 0.05

n = Number of patients
VAS = Visual Analogue Scale

Table 2. Percentage of patients with nausea vomiting score and sedation score at different time points.

Nausea Vomiting Score	At 1 Hour (%)		At 6 Hour (%)		At 12 Hour (%)		At 24 Hour (%)	
	T	P	T	P	T	P	T	P
0	73.3	66.7	76.7	73.3	80.0	90.0	96.7	93.3
1	20.0	26.7	20.0	62.7	16.7	6.7	3.3	6.7
2	6.7	6.7	3.3	2.3	3.3	3.3	--	--
3	--	--	--	--	--	--	--	--
P - Value	0.606		0.829		0.300		0.557	
Sedation score	At 1 Hour (%)		At 6 Hour (%)		At 12 Hour (%)		At 24 Hour (%)	
	T	P	T	P	T	P	T	P
0	83.3	66.7	93.3	76.7	100.0	86.7	100.0	96.7
1	16.7	33.3	6.7	23.3	--	10.0	--	3.3
2	--	--	--	--	--	3.3	--	--
3	--	--	--	--	--	--	--	--
P - Value	0.139		0.073		0.040*		0.317	

*P < 0.05
T - Tramadol group
P - Pethidine group

Table 3. Comparison of good attempts, total attempts and total drug consumption at 24 hours.

	Tramadol (n = 30)	Pethidine (n = 30)	P-Value
Good attempt	20.70 ± 5.76	26.80 ± 7.09	< 0.05
Total attempts	49.06 ± 15.23	64.13 ± 16.08	< 0.05
Total drug consumption (mg)	341.66 ± 29.19	373.83 ± 41.24	< 0.05

*P < 0.05
n = Number of patients

pain relief at all time points and decrease pain scores progressively (Table 1).

There was no significant difference in nausea vomiting scores at all time points (Table 2) between the two groups. It was found that at 12 hours

time point, Tramadol causes significantly less sedation than Pethidine ($P < 0.05$) (Table 2).

There was a significant difference ($P < 0.05$) in the mean of total number of attempts (20.70 ± 5.76 Vs 26.80 ± 7.19), mean number of good attempts (49.06 ± 15.23 Vs 64.13 ± 16.08) and mean of total drug consumption (341.66 ± 29.19 mg Vs 373.83 ± 41.24 mg) in Tramadol group compared to Pethidine group respectively (Table 3).

Discussion

Post-operative pain control is one of the most important aspects of management of surgical patients. Various studies have been done which show the efficacy of Morphine and Pethidine in Patient Controlled Intravenous Analgesia but these drugs are not freely available in our country. We did this study to identify a drug which is freely available and comparable to other potent opioids like Pethidine.

Tramadol is a central-acting analgesic which has been shown to have dose-related efficacy and is well tolerated.⁹ It appears to be a valuable addition to the analgesic armamentarium as a safe and effective agent across a wide spectrum of acute and chronic painful conditions.⁹

Most studies indicated the efficacy of Tramadol in PCIA. Vickers et al¹⁰ in their study showed that mean pain scores for Pethidine was higher than for Tramadol (2.7 vs. 2.6 at rest and 5.2 vs. 4.0 at movement). Silvasti and colleagues¹¹ have found the similar efficacy of Tramadol and morphine in patient controlled analgesia after microvascular breast reconstruction. Our study has similar results which show that Tramadol and Pethidine are equivalent in terms of pain relief in PCIA.

There was a higher incidence of nausea and vomiting after Tramadol in PCIA. Pang et al¹² have shown a higher percentage of nausea and vomiting after Tramadol than morphine in patient controlled intravenous analgesia. The observed high incidence of nausea and vomiting might be dose and rate related with the highest incidence occurring during the loading phase when a large amount of Tramadol was given in a short period of time. To mitigate this adverse effect, a number of preventive measures could be adopted. Pang and colleagues¹³ have shown decreased incidence and severity of nausea and vomiting if metoclopramide was added to Tramadol PCIA but with an increased incidence of sedation was noticed with this drug combination. We found a similar incidence of nausea and vomiting in our study with no difference between Tramadol and Pethidine in Nausea and Vomiting Scores.

The dose related incidence of drowsiness and sedation with Pethidine has been reported as between 13 -

20% compared to Tramadol which is associated with less sedative effect (10 - 15 %).¹⁰ These findings are comparable to our study in which Tramadol caused less sedation than Pethidine.

The side effects from most analgesic drugs have a direct relationship with the dose and the total drug consumption. Various studies have shown less total drug consumption in PCIA Tramadol. Lehman et al¹⁴ found that in patients recovering from general surgery, the mean consumption of Tramadol was 203 mg compared to 175 mg Pethidine in 18 hours.

The ratio of equipotent doses of two drugs under the conditions of assessment are termed potency ratio. Vickers et al¹⁰ found the mean consumption of Tramadol and Pethidine was 642 mg and 606 mg respectively, giving a potency ratio of Tramadol relative to Pethidine of 0.94. In our study, the mean drug consumption of Tramadol and Pethidine was 341 mg and 373 mg respectively. The estimated potency ratio of Tramadol relative to Pethidine in our study is 1.09 which is slightly higher than proposed by Vickers.

Since Tramadol has virtually no dependence potential¹⁵ and is not a controlled drug in most of the countries in which it is currently marketed, it is encouraging that Tramadol is well tolerated and equipotent to Pethidine in PCIA for management of postoperative pain.

On the basis of the results of our study, we conclude that the analgesic efficacy of Tramadol and Pethidine in PCIA after total abdominal hysterectomy is similar. The incidence of nausea and vomiting is same with both the drugs but Tramadol causes less sedation than Pethidine. Tramadol can be used as a suitable alternative to Pethidine in our setup when the classical opioids are not freely available. The unique composition of Tramadol, with its triple action accompanied by minimal side-effects, will promote further research in this area.¹⁶

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