A COMPARISON OF EQUIPOTENT DOSES OF TRAMADOL AND NALBUPHINE IN GYNECOLOGICAL LAPAROTOMIES POSTOPERATIVELY

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ABSTRACT

Objective: To compare the mean consumption of equipotent doses of tramadol and nalbuphine for first 12 hours of post-operative analgesia, in patients undergoing gynaecological laparotomies.

Study Design: Randomized clinical trial.

Place and Durration of Study: Hameed Latif Hospital Lahore from 6 months.

Materials and Methods: One hundred American society of anaesthesiologists (ASA) I & II, consenting females, ages between 20 and 50 years were divided randomly into two equal groups. All patients were given a loading dose of either tramadol (1.5mg/kg) or nalbuphine (0.15mg/kg) after the induction of anesthesia. Same drug was continued as baseline infusion; tramadol 0.5mg/kg or nalbuphine 0.05mg/kg respectively was given as a bolus whenever the visual analogue scale (VAS) score was ≥3. Total dose given in bolus was calculated and compared. Time at the instant of first demand of analgesia in postop was also noted in both groups.

Results: Mean SD dose of rescue boluses in Tramadol group was 89.26 ± 40.00 mg, while mean of equipotent dose of Nalbuphine group was 134.72 ± 61.81 mg (p<0.001). The difference between groups was statistically significant.

Conclusion: Requirement for equipotent doses of analgesic were less in case of tramadol as compared to nalbuphin for treatment of breakthrough pain when both drugs were given as bolus at the commencement of surgery and continued as a continuous infusion postoperatively.

Keywords: Postoperative analgesia, nalbuphine, tramadol, VAS score.

INTRODUCTION

Non availability of μ-receptor opioids forces the anesthetists working in some parts of the world to use substitutes like nalbuphine; which is a k-receptor agonist and antagonist at μ-opioid[1]; or tramadol, which acts as a weak μ agonist with additional alpha-2 agonist activity and weak inhibitor of norepinephrine and serotonin reuptake[2]. Tramadol has demonstrated rapid recovery and low incidence of side effects in early postoperative period when given intravenously[3]. It has been advocated as an alternative to intravenous morphine for postoperative pain relief[4]. Analgesia with tramadol has been compared with morphine when given through the epidural and intra-articular route with less adverse effects[5,6]. ED_{50} values (95% confidence interval) of tramadol was 627 ± 69 mg[7]. In another study, the cumulative dose of nalbuphine was compared with morphine and found to be 32 ± 10 mg for nalbuphine and 30 ± 9 mg for morphine[8].

Our literature search did yield a direct comparison of tramadol and nalbuphine for acute postoperative pain. Considering nalbuphine to be ten times more potent than tramadol[9], we undertook this study to compare the amount of tramadol or nalbuphine required to maintain a visual analogue scale (VAS) score at a level less than 3 during first 12 hours after surgery.

MATERIAL AND METHODS

This randomized controlled was carried out in Hameed Latif Hospital within six months and included all ASA 1 and 2 patients scheduled for gynecological laparotomies between age of 20-50 years. Morbidly obese and patients who were unable to interpret American Society of Anaesthesiologists (ASA) were excluded. Sample size of 100 cases; 50 cases in each group was

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calculated with 95% confidence level, 80% power of study and taking magnitude of mean consumption i.e. 62.7 ± 6.9 mg in tramadol group and 32 ± 10mg in nalbuphine group in patients undergoing gynaecological laparotomies. Non probability purposive sampling technique was used.

After approval from hospital ethical commit, 100 patients recruited for the study were divided in two equal groups by lottery method. VAS on a scale of zero to ten was explained to them in the language that they could clearly understand at the time of recruitment. VAS is a measure of pain on a scale of zero to ten; zero being no pain and ten being the most severe pain imagined. Patients in group T received initial intravenous loading dose of 1.5mg/ kilogram tramadol; infusion was started at the rate of 0.2 mg/kilogram/hour and continued for 12 hours of study period; 0.5 mg/ kilogram boluses were given to treat breakthrough pain (defined as VAS score >3). The patients in group N received 0.15mg/ kilogram intravenous nalbuphine, infusion at the rate of 0.02 mg/kilogram/hour for 12 hours; 0.05mg/kilogram nalbuphin was given for break through pain.

All patients received a loading dose of study drug at the time of induction of anesthesia; continuous infusion of the drug at a constant rate was then commenced and continued in post anaesthesia care unit. Additional boluses of the same drug were given in post-anesthesia care

Table-I:Group statistics for ASA.

		Group		Total
		A	B	
ASA Status	1	30	28	58
	2	20	22	42
Total		50	50	100
Chi^2=0.164, *p*=0.685				

Table-II: Group comparison regarding type of surgery.

		Group		Total
		A	B	
Surgery Type	BTL	0	3	3
	Laparotomy	30	20	50
	Myomectomy	11	18	29
	TAH	9	9	18
Total		50	50	100
Chi^2=6.690, *p*=0.082				

Table-III: Comparison of baseline postop infusions of tramadol and equated doses of nalbuphine.

Group	N	Mean ± SD	SD	Q1	Q3
Tramadol	50	162.7 ± 17.7	164	144	180
Nalbuphine	50	160.8 ± 19.2	156	144	180
Mann Whitney U=1179, *p* = 0.62					

Table-IV: Comparison of Equated postop boluses between the groups.

Group	N	Mean ± SD	SD	Q1	Q3
Tramadol	50	89.26 ± 40.04	74	60	111
Nalbuphine	50	134.7 ± 61.8	140	90	180
Mann Whitney U= 700, *p*<0.001					

Table-V: Comparison of time to first requirement of analgesia.

Group	N	Mean ± SD	Median	Q1	Q3
Tramadol	50	1.06 ± 1.46	1	0	1
Nalbuphine	50	0.57 ± 0.48	1	0	1
Mann Whitney U= 1096, *p*=0.026					

unit (PACU) to treat breakthrough pain; they were repeated till VAS score returned to <3. These dosages were calculated assuming nalbuphine to be ten times more potent than tramadol. Additional doses were repeated until a VAS score <3 was achieved or effects of study drugs like excessive sedation (Ramsay 3 or more) or respiratory depression (Respiratory rate <8 or SpO2 <90%) appeared. Those who developed side effects were excluded from the study and managed according to the departmental protocol. Doses in the post-operative area were given by a staff nurse in response to patient's complaint of pain at VAS score >3.

All data were entered in SPSS version 17 and analyzed. Normality was tested by Shapiro Wilks test and the data for quantitative variables like amount of doses were computed as mean ± SD along median (IQR). Amount of doses (mean consumption) and mean time for first requirement were compared by using Mann Whitney U-test. Chi-square test wast used to compare ASA status and surgery type between groups. *P*-value ≤0.05 was considered to be significant.

RESULTS

Out of 100 patients in both the groups no patient was excluded from the study. Both the groups were statistically comparable regarding the distribution of age sub-categorized into 20-29, 30-39, 40-49 and 50-59 (Chi^2=6.075; *p*=0.108; mean ± SD 36.20 ± 8.555 vs 32.72 ± 8.112), weight (t=-0.356; *p*=0.722; Mean ± SD 68.18 ± 7.33 vs 68.72 ± 7.80), ASA status (Chi^2=0.164; *p*=0.685) table-I, and types of surgical procedures (Chi^2=6.690; *p*=0.082) table-II.

The difference between the amount of drugs consumed by continuous infusion after the procedure was not significant (Mann Whitney U=1179, *p*=0.622) table-III. Amount of nalbuphine consumed as on demand boluses was significantly greater than equipotent amount of tramadol (Mann Whitney U=700, *p*<0.001) table-IV. There was no significant difference in interval between on demand boluses (time to first requirement of demand bolus) in Group T as compared to Group N (Mann Whitney U=1096, Z.app= -1.15, *p* = 0.248) table-V.

DISCUSSION

The study was designed to compare mean equipotent dose of the drugs required in bolus form in addition to the baseline infusion of study drugs. Considering nalbuphine to be ten times more potent than tramadol, we multiplied the amount of nalbuphine consumed by a factor of ten to calculate equipotent dose for comparison with taramadol. Our study revealed that total amount of nalbuphine consumed to maintain VAS >3 over a first 12 hours was significantly higher than tramadol. According to our knowledge this is the first direct comparison of these drugs for postoperative analgesia in gynaecological laparotomies.

Hernandez-Palacios et al conducted a similar study in children while comparing postoperative pain relief in children. Their study showed that a bolus dose of tramadol (1,000 µg/kg) followed by an infusion rate of 2.0 µg/kg/min resulted in better control of postoperative pain than a bolus dose of nalbuphine (100 µg/kg) followed by an infusion of nalbuphine (0.2 µg/kg/min)[10].

Mean VAS scores at first demand of analgesia in both groups remained > 4.0 (4.94 ± 0.91 vs 5.66 ±1.239; *p*=0.001) both patients in both groups required additional boluses of study drugs. The groups also showed a significant difference in time to first demand of analgesia (0.057 ± 0.48 vs 1.06 ± 1.46 hours; *p*=0.027).

CONCLUSION

Our study has shown that in comparison with nalbuphine, intravenous tramadol required fewer number of rescue boluses and consumed less amount of drug to achieve satisfactory analgesia during first 12 hours postoperatively. This has logistic implications as every rescue bolus is a demand on nursing care. Whether this also has an impact on side effects like nausea, vomiting, sedation and respiratory depression

was not observed in this study. Hopefully, our study will pave way for more studies to follow.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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