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Research Article

COMPARISON OF INTRAOPERATIVE ANALGESIC EFFECT OF I.V TRAMADOL AND I.V BUTORPHANOL – A RANDOMISED PROSPECTIVE STUDY

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A B S T R A C T

Introduction: Butorphanol and tramadol are both synthetic opioids with potent analgesic properties which are used for intra operative and post operative analgesia. This study tried to evaluate & compare the analgesic efficacy and side effects of intravenous butorphanol and tramadol in patients undergoing surgery. **Patients and methods:** The study was conducted by Department of Anesthesiology, MKCG Medical College, Berhampur, Odisha. It was a prospective, randomized, double blind controlled trial with 100 patients. Patients were allocated randomly into one of two groups of 50 patients each to receive tramadol hydrochloride (100mg IV) Group 1 or butorphanol tartarate (1mg IV) Group 2 before induction of general anaesthesia as per their randomization. The patients were monitored for cardiovascular changes (pulse rate, systolic blood pressure and diastolic blood pressure), duration of analgesia, intraoperative analgesic supplementation and adverse effects with respect to the 2 groups. Result: The cardiovascular pressor response was attenuated more in the patients who received butorphanol in comparison to the tramadol group after intubation. The post-operative analgesia was also significantly longer with butorphanol. Incidence of nausea and vomiting was higher in tramadol group than in butorphanol which was statistically significant. Sedation was seen more in butorphanol group than tramadol group but no patient developed respiratory depression. **Conclusion:** Butorphanol tartarate is a better analgesic during general anaesthesia than tramadol hydrochloride, having less CVS effect, better operative and prolonged post- operative analgesia without the supplementation of other analgesics during the intraoperative period.

INTRODUCTION

Background

The discovery of opiate receptors in the central nervous system(1,2) and in particular their existence in the spinal cord(3), changed the face of management of post-operative pain. Analgesia without the loss of other sensations, motor functions and with minimal effect on the central nervous system and autonomic nervous system have been well documented with the use of opioids (4). Opioids continue to occupy an important place in the anesthesiologist's armamentarium of anaesthetic and therapeutic agents with the discovery of newer opioids.Till date morphine has been more commonly used than the other opioids. It provides long lasting analgesia of good quality, but at the expense of high incidence of side effects. Fentanyl is highly effective with significantly less adverse effects but it is not readily available in remote resource limited settings.

Tramadol is a synthetic phenylpiperdine analogue of codeine with a dual mechanism of action. It is one fifth to one tenth as potent as morphine. It has low abuse potential. It is a centrally acting analgesic with a low affinity for opioid receptors and activates the mono-aminergic spinal inhibition of pain(5,6). Butorphanol, a synthetic morphonian derivative, is a mixed agonist-antagonist; a partial agonist at κ-receptors. Butorphanol and its major metabolites are agonists at κ-opioid receptors and mixed agonist-antagonist at μ opioid receptors. Its activity at μ -receptor is either antagonistic or partially agnostic. It is five to eight times as potent as morphine(7). It is subject to the abuse and has been addictive potential.Although Butorphanol (10 mg IM) produce as much respiratory depression as the same dose of morphine, higher doses reach a ceiling effect(8).

The use of the potent analgesic properties of Tramadol and Butorphanol along with the lack of significant side effects in comparison to morphine and pethidine led us to evaluate whether either of the two can be an ideal drug for intraoperative analgesia in balanced anaesthesia in resource limited setting.So, the present study was carried out in M.K.C.G. Medical College and Hospital, Orissa in the month of January, 2011.

MATERIAL AND METHODS

This study was carried out under the aegis of Department of Anaesthesia, M.K.C.G. Medical College Hospital, Berhampur, Ganjam (Orissa) - a tertiary care teaching hospital in Odisha in the month of January, 2011 with prior approval of Institutional Ethics Committee and written informed consent from the patients.

100 patients with ASA grade I& ASA grade II of either sex within the age group 40-60 years undergoing routine surgical procedures in different operating units of the Hospital were selected randomly for this study.A detailed pre-anaesthetic evaluation of each case was done after noting the medical history, a thorough systemic examination was carried out to detect the presence of any systemic disorder. Routine and special investigations were done accordingly.

Exclusion criteria

1. Patient's refusal.
2. Known allergy to the trial drugs.
3. ASAIII or more.
4. Emergency Surgeries.
5. Patients with bronchospastic disease
6. Patients on psychotropic drugs like MAO inhibitors, barbiturates, tricyclic antidepressants, lithium, major tranquilizers
7. Addiction of alcohol or any narcotics

After detail preanaesthetic assessment these 100 patients were prepared by overnight fasting & Diazepam 10mg prescribed orally at bed time, the day before operation & the patients were advised to remain on fasting on the day of operation. The patients were divided randomly into two identical groups of fifty each. On the day of operation patients were brought to the preanaesthetic room at least one hour earlier to starting of the operation & a slow intravenous infusion was established. The patients were randomly divided into two groups.

Group 1 Tramadol Hydrochloride (100mg IV)
Group 2 ButorphanolTartarate (1mg IV)

These patients received the study drugs intravenously just before induction of general anaesthesia as per their randomization.

All the patients were premedicated with atropine 0.02mg/kg I.V & midazolam 0.03mg/kg. The patients were induced with a sleep dose of 2.5% Thiopentone sodium slowly I.V. (5mg/kg). The patients were intubated with cuffed oral endotracheal tube of appropriate size after relaxation of larynx by suxamethonium 1.5mg/kg & mask ventilation with 100% oxygen. The cuff of the endotracheal tube was inflated to obliterate audible air leakage, after connecting the tube to the Boyle's anaesthetic machine through the catheter mount & confirming the position of the tube in its proper place. An oropharyngeal airway of appropriate size was introduced inside the mouth cavity & the tube was fixed firmly.All the patients were maintained with isoflurane & oxygen-nitrous oxide mixture in the ratio of 1:2 in a closed control anaesthetic technique with a circle absorber & intermittent positive pressure ventilation. The neuromuscular block was done by non-depolarising muscle relaxant vecuronium bromide 0.08 mg/kg I.V. as loading dose & 0.02 mg/kg I.V. as maintenance dose as required after recovery from succinylcholine. The patients were reversed at the end of operation with 0.05 mg/kg Neostigmine methyl sulphate I.V. & 0.02 mg/kg atropine sulphate I.V. Extubation was done after adequate respiratory effort returned.The patients were constantly observed to know the signs of incomplete analgesia. Rescue analgesia was given with injection diclofenac sodium 75 mg IV.

The parameters recorded were cardiovascular changes (pulse rate, systolic blood pressure and diastolic blood pressure), duration of analgesia, intraoperative analgesic supplementation and adverse effects with respect to the 2 groups.

Statistical considerations

Demographic data were obtained from patients' record file. Each patient gave an informed consent. SPSS 17.0 for windows software (SPSS, Inc. Chicago, Illinois) was used for data analysis. Continuous variables were expressed as mean ± standard deviation with student T-test analysis for comparison. Categorical variables were expressed as percentages and comparison was by chi square analysis. Two tailed p-value < 0.05 was considered significant.

RESULTS

The two groups were comparable with respect to age, weight and sex of the patients (Table-1). There was no difference in cardiovascular parameters in the preoperative period in both groups but the pressor response was attenuated more in the patients who received butorphanol in comparison to the tramadol group after intubation (Table-2).

Table 1 Baseline Characteristics

	Tramadol group	Butorphanol group
Median Age (in yrs)	49	50
Mean Weight (in Kg)	49.36	50.74
Male:Female	1.5:1	1.9:1

Table 2 Haemodynamic Changes

Pressor parameters		Tramadol Group	Butorphanol Group	P value
Pulse rate	Preoperative	81 ± 5	79 ± 5	
	After intubation	105 ± 5	99 ± 4	< 0.05
SBP	Preoperative	117 ± 7	116 ± 7	
	After intubation	144 ± 12	130 ± 7	< 0.05
DBP	Preoperative	78 ± 5	79 ± 5	
	After intubation	94 ± 8	86 ± 6	< 0.05

There was no difference between the duration of surgery in both groups but the mean duration of analgesia in patients receiving butorphanol [4.05(± 0.68) hours] was significantly longer than those who received tramadol [1.93 (± 0.77) hours]. The post-operative analgesia was also significantly longer with butorphanol thereby the time to first rescue analgesic was significantly higher in butorphanol group than tramadol group (Table 3).

Table 3 Duration of analgesia (in hrs)

	Tramadol Group	Butorphanol Group	P value
Duration of Surgery	1.63 ± 0.8	1.81 ± 0.5	
Duration of Analgesia	1.93 ± 0.77	4.03 ± 0.68	< 0.05
Duration of Post-operative analgesia	0.1 ± 0.2	1.25 ± 0.9	< 0.05

There was more number of patients who complained of moderate to severe pain intramadol group (18%) than butorphanol group (6%). Post-operative side effects were elicited by direct questioning of the patients (Table-4).

Incidence of nausea and vomiting was higher in tramadol group than in butorphanol which was statistically significant. Sedation was seen more in butorphanol group than tramadol group but no patient developed respiratory depression.

Table 4 Incidence of Post-Operative Side Sffects

Undesirable side effects	Tramadol Group	Butorphanol Group	P value
Nausea & Vomiting	9 (18%)	2 (4%)	<0.05
Pruritus	2	0	
Sedation	0 (0%)	7 (14%)	<0.05
Respiratory Depression	0	0	

DISCUSSION

Opioid drugs differ in their actions due to their character to bind different opioid receptors or to activate the same opioid receptor in a different way. Butorphanol is a mixed agonist antagonist(9,10). Butorphanol is a kappa receptor agonist as well as weak mu-receptor antagonist (7,8,10). Because of its antagonist action on mu receptors which are involved in supraspinal analgesia; it results in a low incidence of respiratory depression. Butorphanol has a ceiling effect on respiratory depression, again mediated by mu receptors. It is also a Kappa receptor agonist whereas tramadol has a weak affinity on mu receptors as an agonist. It also enhances spinal pain inhibiting pathways by inhibiting neuronal uptake of serotonin(7).

In our study, we used equipotent moderate doses of each drug routinely used by most anaesthesiologists. Patients in butorphanol group demonstrated better protection against autonomic stimulation to tracheal intubation as these patients were haemodynamically more stable throughout the operation. This is consistent with previous reports by Pandit et al and Philip et al(9–11).

Gupta &Anand et al. demonstrated the time to first rescue analgesic was significantly higher in butorphanol group (180 ± 40 min) than tramadol group (150 ± 30 min) in their study(11) which is similar to the findings of study. Our findings are consistent with reports by Sung et al & Gupta et al that the rescue analgesia required in butorphanol group was far less than tramadol group because of longer duration of action (11,12).

Butorphanol leads to more sedation due to its action on kappa receptors whereas incidence of sedation is less in Tramadol group. This property of sedation & efficient analgesia provided by Butorphanol has been used in some minor outpatient surgical procedure like oral surgery(8,9,11).

In this study most frequently observed side effect was nausea and vomiting in the tramadol group whereas it was sedation in the butorphanol group. The incidence of nausea and vomiting varied with route and setting of administrations(9,12,13). The enhancing action of tramadol on serotinin and its action on the Chemoreceptor Trigger Zone (CTZ) often contribute to occurrence of emesis (14).

Sedation was observed in 14 % of patients in Butorphanol group whereas there was no sedation in Tramadol group which was similar to the findings reported byPandit and colleagues and various other groups(8,9,11).

Sung and colleagues did not report any incidence of respiratory depression with butorphanol which is in lines with our study (11,12).

Our study suggests that Butorphanol is a better choice than Tramadol for use in balanced anaesthesic technique because of its ability to produce prolonged analgesia and amnesia, stable haemodynamic parameters and no post-operative respiratory depression. Also Butorphanol is effective for relieving post-anesthesia shivering without producing any significant respiratory depression, nausea, vomiting or recurrence of shivering.

CONCLUSION

From the above study it may be concluded that But orphanoltartarate is a better analgesic during general anaesthesia than Tramadol hydrochloride, with better hemodynamic stability, superior operative and prolonged post- operative analgesia without the supplementation of other analgesics during the intraoperative period. So it is an ideal analgesic to be used in a resouce limited setting where availability of fentanyl is a big issue.

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