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COMPARISON OF POSTOPERATIVE ANALGESIC EFFICACY AND SAFETY OF IV BUTORPHANOL TARTRATE AND IV TRAMADOL HYDRO CHLORIDE IN PATIENTS UNDERGOING MAJOR UPPER ABDOMINAL SURGERIES. A PROSPECTIVE RANDOMIZED DOUBLE BLIND STUDY

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ABSTRACT

Background: Butorphanol and Tramadol are synthetic opioid analgesics frequently used for management of post operative pain.

Aim: The purpose of this study was to evaluate and compare the post operative analgesic efficacy and side effects of equipotent moderate doses of Butophanol and Tramadol in patients undergoing major surgical procedures.

Materials and Methods: This prospective randomized double blind study was carried out on 60 patients belonging ASA grade I & II aged between 18-60 years including either gender, scheduled for elective upper abdominal surgical procedures under general anesthesia. Patients were randomly divided into 2 groups of 30 each. Group B received Butorphanol (2 mg IV) and group T received Tramadol (100mg IV). Anasthesia was standardized in both groups. Study drugs were administered when patient reported pain in the immediate post operative period. The patients were monitored for intensity of pain by visual analogue scale, duration of analgesia, the number of doses required in 24 hours, parameters such as pulse rate, blood pressure, SpO2, Respiratory rate and side effects were noted.

Results: Mean duration of analgesia after the first dose of Butorphanaol was 4.24 ± 0.68 hours compared to 5.43 ± 0.52 in Tramadol group. There was significant decrease in pain scores in Butorphanol group compared to tramadol group. This statistically significant decrease in VAS was observed upto 24 hours. The mean number of doses required in 24 hours was 4.1 in group B and 2.6 in tramadol group. Sedation was more in Butorphanaol group, but no patient developed respiratory depression. Side effects such as nausea, and vomiting were more in Tramadol group.

Conclusion: Butorphanaol was found to be an effective analgesic than Tramadol. It provides good quality of post operative analgesia with minimum side effects.

KEYWORDS : Butorphanol, Tramadol, Upper abdominal surgeries, Postoperative Pain, Pain scores.

INTRODUCTION:

Parentral opioids remain the primary pharmacological therapy for moderate to severe post operative pain.[1] The current options for post operative pain management include opioids, NSAIDS, regional anaesthesia with intrathecal or epidural opioids and local blocks. On demand analgesia using patient controlled analgesia is becoming popular and reducing the side effects of parenterally administered drugs.Butorphanol is mixed agonist antagonist opioid analgesic.[2] Butorphanol and its major metabolites are agonists at 'K' opioid receptors and mixed agonist-antagonist at mu opioid receptors. This receptor specificity results in low incidence of respiratory depression, gastro intestinal side effects and reduced risk of dependence. Theoritically it offers an advantage over traditional opiates such as morphine and pethidine in the treatment of moderate pain. Tramadol is centrally acting analgesic with low affinity for opioid receptors and activates the mono- aminergic spinal inhibition of pain.[3,4] It is one fifth to one tenth as potent as morphine. It has low abuse potential. Butorphanol injection was approved in 1978.[5]and the nasal spray was approved in 1991[6]. Extensive search revealed very limited literature regarding IV use of butorphanol.

We have contemplated a study to compare the commonly used opioid tramadol with Butorphanol for post operative analgesia.

MATERIALS AND METHODS:

After obtaining approval from institutional Ethical committee and informed written consent, this randomized double blind study was carried out on 60 patients of either sex aged between 20-60 years of ASA physical status I & II. Patients undergoing elective upper abdominal surgeries under General Anaesthesia (more than 2 hours duration) were enrolled in the study. Pregnant and lactating women, patients with H/O drug abuse, known allergy to trial drugs,Patients with significant renal and hepatic disease, patients prone to respiratory depression (ASA III& IV, patients with H/o Bronchial Asthma, COPD) and patients on psychotropic drugs were excluded from the study. Patients were randomly assigned to two groups of 30 each.

Group B received 2mg Butorphanol IV and Group T received 100mg Tramadol IV.

The following parameters were recorded in a mean observation of 24 hours. Pain intensity was measured by visual analogue scale, Level of consciousness by sedation score, Saturation of O2 (SpO2), Pulse rate, Blood Pressure, Respiratory rate, complications such as nausea and vomiting. The 1st dose of either of study drug was given when patients reported pain, in the immediate postoperative period. Repeated doses were given when patients complained of pain (VAS >4).

Antiemetic injection ondansetran 4mg was given if the patient had one episode of vomiting. Respiratory depression was taken as RR< 10 breaths /min. Excessive sedation with respiratory depression, hypotension, and bradycardia were taken as evidence of central nervous system depression.

Statistical analysis: Statistical analysis was done using SpSS version 19, (SPSS Inc. Chicago).Continuous variables was expressed as mean ± standard deviation with students analysis for comparison. Categorical variables were expressed as percentages and comparison was by chisquare analysis, A p value <0.05 was considered as statistically significant.

Prior to surgery patients were explained about visual analogue scale. Patients were kept fasting overnight after 10.00 PM and received tab. Ranitidine 150mg , and Tab. Alprazolam 0.5 mg orally, night before surgery.

In the operation theatre monitoring devices for ECG, HR, SpO2, ETCO2 were attached. All patients wre premedicated 15 minutes prior to surgery with Inj. Glycopyrolate 0.2 mg IV, Inj. Midazolam 0.03 mg/Kg and Inj. Fentanyl 2mcg/kg. Patients were then preoxygenated with 100% O2 for 3 min. Patients were induced with sleep dose of 2.5%Thiopentone 5mg/kg, and muscle relaxation was facilitated with suxamethonium 1.5mg/kg. After 1 minute when the patient was fully paralysed trachea was intubated with appropriate size endotracheal tube. Anaesthesia was maintained with mixture of N2O and O2 (67% and 33% respectively) and non depolarising muscle relaxant vecuronium with a loading dose of 0.1 mg/kg and maintanance dose of 0.02 mg/kg and isoflurane 1-2%. IPPV was provided with volume control mode ventilation.

At the end of surgery patients were adequately reversed with Inj. Glycopyrollate 0.008ug/kg and Inj. Neostigmine 0.05mg/kg.

All the parameters were recorded at 0,10,20,30,60,120 minutes and 3,6,12 and 24hrs. Sedation score was assessed as 0: patient fully awake, 1 : drowsy but arousable to verbal command, 2:drowsy,

responds to tactile stimulation 3:patient asleep, responds to painful stimulation, 4 : unarousable.

OBSERVATION AND RESULTS:

The groups were comparable in terms of age, sex, weight, duration of surgery and distribution of surgeries.(Table1&Table2)

Demographic data : Table 1

Variable	Group B	Group T	P Value
Age	40.40 ± 9.76	40.48 ± 8.62	>0.05
Sex M/F	15:15	15:15	>0.05
Weight in Kg	50.53 ± 5.36	51.56 ± 4.25	>0.05
Duration of surgery	125.26 ± 24.10	124.20 ± 23.24	

Distribution of Surgeries: Table 2

	Group B	Group T
Cholecystectomy	8	8
Laparotomy	15	15
Incisional hernia repair	7	7

Pain assessment was done by recording the intensity of pain with 100 mm VAS. The results were shown in Table: 3. The onset of analgesia was faster in butorphanol group. There was significant decrease in pain scores from 10 minutes onwards in 2 groups, But this decrease is more in butorphanol group, compared to tramadol group (P<0.05). This statistically significant difference between butorphanol and tramadol group were observed up to 24 hours.

Visual Analogue Pain Score: Table 3

Group	0 min	10 min	20 min	30 min	60 min	120 min	3Hrs	6Hrs	12 Hrs	24 Hrs
Group B	88.89±2.89	14.44±3.75	10.56±3.56	11.67±1.09	16.67±5.09	21.52±3.98	34.44±4.65	26.53±2.56	10.5±1.76	16.86±1.97
Group T	87.50±4.82	21.67±5.89	27.50±1.78	23.33±1.54	26.67±4.64	32.68±5.00	35.83±6.76	38.0±1.15	32.13±2.50	26.48±1.32
p Value	P>0.05	P<0.05	P<0.05	P<0.05	P<0.05	P<0.05	P<0.05	P<0.05	P<0.05	P<0.05

Mean duration of analgesia after the 1st dose of butorphanol was 4.24 ±0.68 compared to 5.43 ±0.52 in Tramadol group. Mean number of doses required in 24 hours was 4.1 in group B and 2.6 in Tramadol group (Table 4)

Duration of Analgesia	Group B	Group T
Duration of analgesia after the 1st dose	4.24 ± 0.68	5.43 ± 0.52
Number of doses required in 24 hours	4.1 ± 1.0	2.6 ± 0.88

There was statistically significant change in sedation scores was observed between two groups (P< 0.05)

Duration of Analgesia: Table 4

Sedation Score: Table :5

Group	0 min	10 min	20 min	30 min	60 min	120 min	3Hrs	6 Hrs	12 Hrs	24 Hrs
Group B	1.00+0.05	2.00+0.46	2.25+0.37	2.67+0.37	2.62+0.58	2.60+0.64	2.52+0.44	2.63+0.52	2.42+0.37	1.86+0.25
Group T	1.00+0.09	1.10+0.08	1.17+0.97	1.66+0.42	1.45+0.57	1.52+0.47	1.63+0.36	1.44+0.58	1.36+0.65	0.92+0.43

All patients were monitored PR, BP, SpO2, and RR. There was no statistically significant difference between two groups (P >0.05). No patient developed respiratory depression. Incidence of nausea and vomiting were more in tramadol group than butorphanol group, which was statistically significant (P<0.05) Table 6.

Incidence of Side Effects: Table 6

Side effects	Tramadol Group	Butorphanol Group	P Value
Nausea and Vomiting	9(30%)	3(10%)	<0.05
Sedation	10(30%)	24(80%)	<0.05

DISCUSSION:

Post operative pain leading to pulmonary complications have always been a hazard following upper abdominal surgeries. Despite the recent advances in the understanding of postoperative pain clinical surveys indicate that routine treatment of post operative pain remain unsatisfactory, nearly 80% of patients reporting moderate to extreme pain following surgery[7]. opioids have been mainstay of postoperative pain control for decades.

The main aim of postoperative pain relief is to provide subjective comfort and also to reduce nociceptive induced responses caused by surgical trauma and to blunt autonomic as well as somatic reflexes to pain , this enables patient to breath , cough , and to be easily ambulent. The goal of post operative pain management is to reduce or eliminate pain with a minimum side effects.

Tramdol a weak opioid which acts on mu receptors has been most commonly used for management of postoperative pain. Butorphanol is agonist at Kappa receptors, but weak antagonist at mu receptors. Several clinical studies with the injectable form of butorphanol have shown that it is effective in relieving moderate to severe post operative pain.[8] Because of its antagonist action on mu receptors which are involved in supraspinal analgesia results in lower incidence of respiratory depression.

In our study we used equipotent, moderate doses of each drug routinely used by most anaesthesiologists. In our study we found that there was statistically significant difference in pain relief obtained between two groups. onset of analgesia was faster in butorphanol group as studied by Andrews.[9] comparing the mean differences in VAS scores in two groups, it was clear that there was a greater reduction in VAS scores of butorphanol group compared to tramdol group. This is consistent with previous reports by Galloway et al., Ahluvalia et al., & Ameer et al., [10,11,12] Mean duration of analgesia after the first dose of butorphanol was 4.24 in group B and 5.58 hr in group T. These findings are in agreement with previous studies done by DA Laffy, stehling and zaudevetal[13,14] However in these studies drugs were given intramuscularly.

Mean number of doses required in group B were 4.1 , where as in group T 2.6 over a period of 24h. Torokoli et al., and vogel sang et al., [15,16] conducted several double blind studies to evaluate the analgesic efficacy of butorphanol tartarate and they reported that 2mg butorphanol ,10mg morphine ,40mg pentazocin and 80mg meperdine were found to have approximately equivalent analgesic effect. Sedation was found to be more in butorphanol group, due its action on kappa receptors, where as incidence of sedation is less in tramadol group , This group of patients were drowsy but easily arousable. This observation was consistent with previous studies done by Lutfal Aziz et al., Ahluvalia et al.,[17] This property of sedation and efficient analgesia provided by butorphanol has been used in some minor outpatient surgical procedures like oral surgeries.[18,19, 20, 21.] In our study there was no incidence of respiratory depression , in either group.[22,23,24, 25] In this study most frequently observed side effects were nausea , vomiting in tramadol group. This finding is in lines with onake and yamamoto et al.,[26,27] The enchancing action of tramadol on seratonin and its action on chemoreceptor trigger zone contributes to occurance of emesis[27].None of the patients in either group showed post operative shivering.

Butarphanol being a non narcotic it has a low propensity for addiction.[28]

CONCLUSION:

From the above study it was concluded that Butorphanol Tartrate has faster onset of action, better analgesic efficacy, with fewer side effects when compared with Tramadol hydro chloride. Though tramadol has a longer duration of analgesia the quality of analgesia is poor with associated adverse effects. Hence Butorphanol appears to be safe and effective analgesic for the relief of moderate to severe post operative pain.

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