Original Article

EFFECT OF BUPRENORPHINE, PENTAZOCINE AND TRAMADOL ON RESPIRATION

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ABSTRACT

Objective: The purpose of this study was to evaluate the effects of Bupernorphine, Pentazocine and Tramadol on Respiration.

Study design: This is a prospective study.

Place and duration of study: This study was conducted at Intensive Care Unit of Nishtar Hospital, Multan from July to December 2001.

Patients and method: Sixty patients belonging to age group ranging between 18-35 years, of ASA-I&II grades undergoing elective cesarean section were selected. All the patients suffering from severe systemic disease, not falling in ASA 1 or 2 and patients allergic to Opioids were excluded from the study. Patients were divided into three groups using the non-probability convenience sampling technique. Each group comprised of 20 patients. All the patients received endotracheal general anesthesia. In postoperative period Group-A received injection Bupernorphine 0.5mg IM. Group-B received injection Pentazocine 30mg IM and Group-C received Tramadol 100mg IM for pain relief. The effects on respiratory rate, tidal volume, minute volume and arterial blood gases were evaluated 30 minute, 1 hour, 2 hour and 4 hour after giving analgesia. Dosages were repeated 8 hourly.

Results: Bupernorphine led to a fall in respiratory rate and minute volume in 30 minute, whereas Pentazocine decreased the respiratory rate after 30 minute but minute volume was decreased in 5 minute, where as Tramadol had no effect on respiratory rate and minute volume. PaO2 was decreased within 30 minute with Bupernorphine and Pentazocine where as PaCO2 raised after 60 minutes with Bupernorphine but within 5 minute with Pentazocine where as with Tramadol there was no significant alteration in arterial blood gas values.

Conclusion: Opioids have a respiratory depressant effect which manifested within 30-60 minute of IM administration, where as Tramadol which is a non opioid, does not cause respiratory depression in equiv. potent doses.

KEY WORDS: Analgesia, Parenteral, Bupernorphine, Pentazocine, Tramadol, Blood Gas Analysis, Respiration, Recovery room.

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INTRODUCTION

Pain is a major concern of patients in the postoperative period & what ever the cause, it demands immediate relief. The international association for the study of pain has defined pain as an unpleasant sensory and emotional expression associated with actual or potential tissue damage or described in the terms of such damage. Pain is a combination of severe discomfort, fear, autonomic changes, reflex activity and suffering.

There are pharmacological and non-pharmacological methods of pain relief. The use of opioids date back to prehistoric times. The Greeks used them in their medicine with

some accuracy (300 BC).

Newer agents have been developed over the last 2-3 decades but opioids analgesics are still considered the gold standard. Traditionally, opioids are given intramuscular or intravenously. Both routes are painful, produce ineffective analgesia in abdomino-thoracic surgery and are not free of side effects. Both these routes do not require a qualified skilled anesthetist and expensive equipment.

This study was carried out in Nishtar Hospital, Multan. Our aim was to compare the respiratory depressant effects of Bupernorphine, Pentazocine, and Tramadol in equiv. analgesic doses.

PATIENTS AND METHODS

Approval for this study was obtained from the Hospital Ethics Committee. After acquiring informed consent, we studied 60 healthy un-pre-medicated parturients, aged 18-35 years, undergoing elective lower segment cesarean section. All the patients suffering from severe systemic disease, not falling in ASA 1 or 2 were excluded from the study. Patients allergic to opioids were also excluded from the study. Rapid sequence induction was performed with injection 2.5% thipentone 4-8 mg/kg, suxamethonium 1.5mg/kg intravenously. When there was evidence of neuromuscular activity, injection atracurium 0.3mg/kg was administered with increments of 0.1-0.2mg/kg intravenously as required. Anaesthesia was maintained with 50% nitrous oxide and 0.2-0.5% halothane in oxygen up to delivery and 60% nitrous oxide in oxygen +0.2-0.5% halothane after the delivery.

Injection nesotigmine 2.5mg and injection atropine 1.2mg intravenously were administered as required on completion of surgery. After the operation suction was done under vision & endotracheal tube was removed and patients were sent to intensive care unit. The patients were allocated randomly to one of the three groups. Each patient received freshly prepared analgesics randomly postoperatively. Group A: patients received Pentazocine 30mg intramuscularly, Group-B patients were given Bupernorphine 0.3mg intramuscularly and Group-C patients were given Tramadol 100mg intramuscularly.

All patients stayed in intensive care unit for 24 hours and were given analgesics intramuscularly at 8 hourly intervals. We kept the patients in ICU because opioids have a strong potential for respiratory depression and continuous monitoring in ICU provides better vigilance and prompt supply of ventilatory assistance if required.

Postoperative follow up included the recording of vital signs (pulse rate, blood pressure, respiratory rate pulmonary function monitoring, evaluation of pain-onset of analgesia and duration of analgesia) recording of the side effect and conscious level (awake, drowsy).

Pulse rate, arterial blood pressure ECG was continuously displayed using bioscope. Endtidal CO2 was noted intermittently with data scope. O2 saturation was monitored with pulse oximeter, minute volume, forced vital capacity with the Wright's Spiro meter and peak expiratory flow rate by wright peak flow meter.

These parameters were recorded at 05 minute, 30 minute & 60 minute after the end of injection and then 4 hourly for 24 hours. Respiratory rate and minute volume was measured by means of a wright's Spiro meter over a period of 3 minute. The time of onset and severity of respiratory depression was recorded in each patient.

Pain was assessed on a vertical scale the bottom of the scale "0" representing no pain (patient could sit up in bed and walk around with out difficulty) and the top scored "5" representing unbearable pain with moderate pain scored "3" (patient had pain on movement but was reluctant to get out of bed). A score of "0" was assigned when patients were found to be asleep. Intensity of pain was assessed immediately before the administration of drug. Time of onset of analgesia was noted after epidural injection and then assessment of pain score was made 4 hourly. The duration of analgesia (the

time between administration of drug and request for additional pain medication) was recorded for each dose.

The presence of adverse side effects were also recorded including, pruritus, nausea, vomiting. An attempt was made to assess the degree of sedation on a 4-point scale.

RESULT

Bupernorphine led to a fall in respiratory rate and minute volume within 30 minute whereas Pentazocine decreased the respiratory rate after 30 minute but minute volume was decreased within 5 minute. Tramadol had no effect on respiratory rate and minute volume. PaO2 was decreased within 30 minute with Bupernorphine and Pentazocine where as PaCO2 raised after 60 minute with Bupernorphine but within 5 minute with Pentazocine, whereas with Tramadol no significant alteration in arterial blood gases values was observed.

Table-I: Demographic Data

Description	*Group A*	*Group B*	*Group C*
Number of patients (Female)	20	20	20
Age (yrs)	25±2	26±1	23±3
Weight (kg)	55±8.5	50±10.7	52±9.5

ASA Categorization

ASA Grade	*I*	*II*
Group A Bupernorphine	17	3
Group B Pentazocine	18	2
Group C Tramadol	16	4

DISCUSSION

The aim of investigation was to determine which of the three analgesics had the least effects on respiration and arterial blood gases.

Respiration:

Bupernorphine causes dose related respiratory depression and as with other narcotic agonist antagonists' drugs, a ceiling or plateau effect has been described[1].

Pentazocine is an analgesic of similar potency to morphine; it is indicated for relief of moderate to severe pain and 30 mg of Pentazocine is said to be equivalent to 10 mg of morphine. This drug produces a similar degree of respiratory depression as other opioids in equiv. analgesic doses[2]. Increasing the dose of Pentazocine beyond 30 mg does not usually produce a further proportionate increase in respiratory depression and the doses response curve is therefore plateau shaped.

Other clinical studies indicate that the respiratory depression induced by Pentazocine

Table-II: Comparison of effects on Respiratory System

Drugs	*Respiratory Rate*	*O2 Saturation with FIO2 21%*
Inj. Pentazocine 30mg IM		
Before	24±2.7	97±1
After	14±5.6	95±2
Inj. Bupernorphine 0.3mg IM		
Before	24±4.1	97±1
After	16±4.5	94.5±3
Inj. Tramadol 100mg IM		
Before	24.3±4.5	97.2±2
After	22.3±2.7	97.0±1

reaches a ceiling at 60 mg in an adult of 70kg[3]. However it is important to monitor the patient for respiratory depression and apnea, which can be reversed by naloxone but not by nalorphine or levallorphan.

In our study Bupernorphine and Pentazocine both significantly reduced respiratory rate and minute volume. Pentazocine depressed respiration rate and minute volume more than Bupernorphine. This observation regarding Pentazocine has been confirmed by other workers[4]. The significant changes in respiration rate after 30mg Pentazocine do not correlate with the results obtained by other investigators[5]. The peak depressant effect of morphine like analgesics is reported to be about five minutes after intravenous injection, but we were only partially able to confirm this. The only exception is Tramadol, which did not significantly alter respiration rate or minute volume after a dose of 100mg; this result was also obtained by other investigators[6]. 100mg Tramadol alters the respiration rate and minute volume. This fact has also been reported in the literature. It is possible that when pain is relieved, respiration deepens.

Arterial Blood Gases -PO2:

The change in arterial oxygen partial pressure cannot be taken as objective criteria. As in most cases the standard deviation is too great and therefore we can only suggest certain tendencies. There was a rise in arterial PO2 with two drugs with the exception of the five and 30 minute values with Pentazocine. After 30mg Pentazocine the arterial PO2 even falls to 95.6% of the control value. The rise in PO2 measured may be interpreted differently.

In the group of patients who underwent surgery and were suffering from multiple traumas there was pain related hypoventilation and subsequent disturbances in pulmonary function comprising of reduced minute volume and raised respiratory rate. This causes distribution disorders due to reduced ventilation of individual alveolar regions, resulting in micro atelectasis and right to left shunt[7]. In many cases adequate analgesia eliminates hypoventilation, thus improving oxygenation of the arterial blood. On the other hand, Morphine like analgesics reduce basal metabolism in humans and the O2 requirements of the tissues. After administration of 30mg Pentazocine and 0.3mg Bupernorphine changes in O2 consumption occurred in eight healthy subjects with Bupernorphine reducing O2 consumption to a significantly greater extent (20-30%) than Pentazocine (approx, 10%). In another comparative study between Pethidine, Piritramide & Pentazocine arterial PO2 decreased after Pentazocine and rose after the others two drugs. A brief fall in O2 pressure and content after administration has also been reported elsewhere. Other workers did not find any significant decrease in O2 consumption after morphine Pethidine or Pentazocine[8]. A significant rise in the O2 content in mixed venous blood after intravenous administration of Piritramide suggests improved tissue perfusion. Other authors even with high doses have described no significant changes in PaO2 after Tramadol.

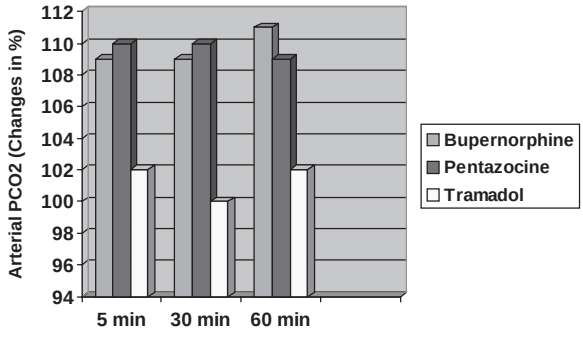

Fig. 1: Changes in Arterial PCO2.

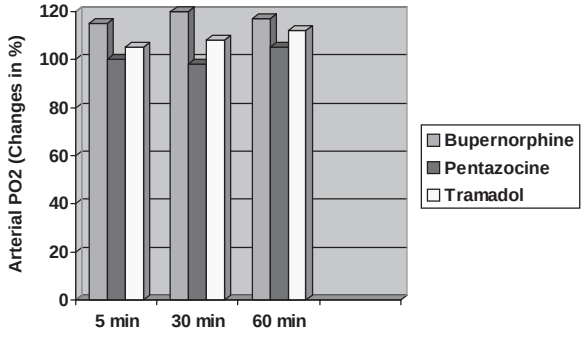

Fig. 2: Changes in Arterial PaO2.

Arterial Blood Gases PCO2:

After Pentazocine and Bupernorphine there was significant rise in arterial carbon dioxide tension, whereas with Tramadol, the 2.5% rise was not significant. Our results with Pentazocine show that the initial rise in CO2 partial pressure after five minutes was much higher than after Bupernorphine. However it fell more rapidly again. Respiratory depression after Pentazocine has also been reported elsewhere. The initial peak appears to be a characteristic of Benzomorphines and has also been found with Pentazocine. Thus, equiv. analgesic doses of Pentazocine have no greater advantages or disadvantages over Bupernorphine. The 30mg of Pentazocine is reported to have the same respiratory depressant effects as 10mg morphine. However with higher doses of Pentazocine the increase in respiratory depression is lower and not proportional (ceiling, effect). This has also been confirmed by other authors. There are extremely divergent reports in the literature on changes in PCO2 after Pentazocine. On one hand, distinct rises in PaCO2 have been observed but on the other hand no significant changes have been found.

Our results as regards the respiratory depressant effect of equiv. analgesic doses of Buprenorphine & Pentazocine correlate with those of the other workers. Of the analgesics we investigated, only Tramadol differed having practically no effect on PCO2. Similar results have been reported elsewhere with higher doses of Tramadol. Thus, Tramadol is analgesia with distinctly few side effects on respiration.

CONCLUSION

From this study it is concluded that:

1. Bupernorphine and Pentazocine both significantly reduce respiratory rate and minute volume but Pentazocine reduces respiratory rate greater than Bupernorphine. With Pentazocine there was greater reduction of PaO2.
2. Arterial partial pressure of CO2 increased with both Bupernorphine and Pentazocine, but with higher doses of Pentazocine the respiratory depressant effect was not proportionate due to ceiling effect. With most opioids the ventilatory depressant effect is dose dependent although the agonist antagonist agents claim to have a ceiling effect.
3. Tramadol is an interesting drug as it has an unusual mechanism of action. Although it does not cause respiratory depression but the problem of nausea in clinically effective analgesic doses and risk of intraoperative awareness are significant disadvantages of Tramadol.
4. The incidence of side effects like nausea, vomiting, sedation, urinary retention and respiratory depression are more common with Bupernorphine and Pentazocine than with Tramadol.

REFERENCES

1. Heel RC, Brogden RN, Spight TM. Bupernorphine: a review of its pharmacological properties and therapeutic efficacy. Drugs 1997; 17:89-104.
2. Lal S,Savidge RS Chabra GP. Cardiovascular and respiratory effects of Morphine and Pentazocine in patients with Myocardial Infarction. Lancet 1989; 379-381.
3. Schmukar P, Vanackern K, Franko N, Noisser H. Hemodynamic and respiratory effects of Pentazocine. Anaesth 1980; 29:475-480.
4. Torda TA, Pybus DA. A comparison of four opiates for analgesia. Br J Anesth 1982; 54:291-9.
5. Green DW, Micheal MS. Bupernorphine versus Pentazocine. A comparison of intraoperative and postoperative pain. Anaesth 1985; 40:371-5.
6. Foldes F, Zeedick L, Kouhal J. The effects of narcotic analgesic and narcotic antagonists on respiration. Am J Med Sci 1995; 89: 211-9.
7. Dickson AH. Mechanism of analgesic action of opiates and non-opioids. Br J Anesth 1999; 44: 525-38.
8. Tsui SL, Chan S. Postoperative analgesia for esophageal surgery: A comparison of three analgesic regimens. Anaesth Intens Care 1996; 19: 329 -37.