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Comparative Study of Butorphanol and Morphine for Postoperative Pain Relief Using Patient Controlled Analgesia (PCA)

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Abstract
Background
Pain Is 'an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage'. Obligation to manage pain and to relieve the patient's suffering is an important part of a health professional's commitment. This study was undertaken to evaluate and compare the analgesic efficacy, respiratory depressant effects, and incidence of hypoxemia following administration of butorphanol and morphine intravenously in postoperative patients using a patient controlled analgesia (PCA) device and to study the convenience of use and acceptability of PCA pump amongst our patient groups.
Methodology
Sixty patients undergoing lower abdominal, pelvic and lower limb surgeries were selected for the study. They were divided randomly into two groups of thirty each. Patients were allowed use of PCA device as they awakened from anaesthesia. Analgesic efficacy of the regimen was assessed by using a visual analogue scale. Four-hourly-assessment was done. Patients were monitored for respiratory depression by regular assessment of homodynamic status, respiratory rate and oxygen saturation.
Results
The demographic profile of the patient in the study is as shown in Table 2. Both groups were well matched for age, sex and weight. Mean VAS scores in both the groups at different times were plotted against time. They are also represented graphically. Mean total pain score in 24 hours mean total drug demanded and mean average pain scores for both the groups and the drug demanded by them are as shown in Table 4 and Table 5. During PCA use the patients were watched for side effects like respiratory depression, nausea, vomiting, pruritus, urinary retention, and sedation scores. Table 6 shows the incidence of various side effects.
Conclusion
Butorphanol is a definite advancement over the conventional opioids with regard to efficacy in pain relief as well as safety and acceptability. Butorphanol is seven times more potent than morphine; however, at equipotent doses the level of analgesia is comparable with lesser incidence of side effects and complications. The status of PCA as an accepted method of pain relief was confirmed.

Key Words *Postoperative pain; Patient Controlled Analgesia (PCA); Butorphanol; Morphine*

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I. Introduction

The International Association for the Study of Pain defines pain as 'an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage' [1]. It is a complex subjective experience comprising of physical and emotional components and serves a biological function. It signals the presence of damage or disease within the body. Obligation to manage pain and to relieve the patient's suffering is an important part of a health professional's commitment. Recognition of the inadequacy of traditional pain management has prompted recent corrective efforts from a variety of health care disciplines including surgery, anaesthesiology, nursing, and pain management groups. Postoperative pain is the result of the trauma of surgery. The goal for postoperative pain management is to reduce or eliminate pain and discomfort with minimum side effects. It should be cheap and must reflect the need of each patient.

For the past 30 years, patient controlled analgesia (PCA) is being used as an effective method to administer postoperative analgesia. PCA allows patients to self-administer small bolus of medication, providing a good dose titration and regulation. The quantity of analgesic available to the patient is controlled by the prescribed PCA variables i.e. demand dose size, lockout period, and hourly or four hourly limits. Over the last century, humans have been administered opioids systemically in an effort to produce analgesia. In the late 1960s, research showed that the analgesic effects of opioids are mediated through specific receptors located in the brainstem. It was also demonstrated that the dose limiting side effects of systemically administered opioids (sedation, respiratory depression, nausea and vomiting) are also mediated through the same areas of the brain. This "co-localization" in the brainstem of receptors mediating both, the analgesic and side effects, is responsible for the inability to separate the analgesic effects from the dose limiting side effects.

The following study aims to compare the analgesic efficacy and side effects of butorphanol and morphine when administered intravenously via a PCA pump. The efforts will also be made to study convenience of use and acceptability of PCA pump amongst our patient groups.

II. Material and Methods

The study was carried out in the Department of Anaesthesiolgy, Colaba, Mumbai from 01 May 2013 to 31 Jan 2015. Sixty patients of either sex were included in present study, and were divided randomly into two groups of thirty each. Patients of either sex aged between 18-60 years in ASA grade I or II, undergoing lower abdominal, pelvic and lower limb surgeries were selected for the study. Those with obesity, lung disease, ischemic heart disease, patients with impaired hepatic or renal functions, patients with history of psychiatric illness or seizures and pregnant patients were excluded from the study. **A** written informed consent was taken from all patients. The use of PCA pump and the visual analogue scale (VAS) were explained to the patient during the preoperative visit.

Patients were randomly allocated to receive butorphanol or morphine intravenously for postoperative analgesia using a PCA device over a period of twenty-four hours. Assessment of pain relief was done at four hourly intervals by a VAS over a period of twenty-four hours by observers blinded to the study. Total dose requirement of relief analgesia and sedation scores were noted. All patients were monitored for any fall in oxygen saturation using a pulse oximeter. A standard anaesthetic regimen was followed for all patients. Postoperatively patients were randomly allocated to receive butorphanol/morphine intravenously, through a PCA device.

An intravenous infusion with ringer's lactate was started in the operating room. Monitoring included ECG with automated ST segment analysis, pulse oximetry, end tidal carbon dioxide and non invasive blood pressure. All patients were premedicated with glycopyrrolate 0.2 mg i.v. and butorphanol 0.06 mg/kg i.v. or morphine 0.1mg/kg i.v. as per their allotted group just before induction. They were induced with thiopentone, intubated with succinylcholine and maintained with halothane, nitrous oxide, oxygen, vecuronium and controlled ventilation. Additional doses of butorphanol/morphine were administered as and when required. No non-narcotic analgesics were permitted during anaesthesia. Patients were extubated and shifted to recovery room.

In the recovery room pain score by VAS and total dose of butorphanol/morphine received intraoperatively were noted. The patients were shifted to a low dependency unit after meeting conventional discharge criteria. Patients were allowed use of PCA device as they awakened from anaesthesia [2]. They were instructed on procedure for using the device again when fully awake. The settings of the PCA pump are shown in Table 1.

Four-hourly-assessed analgesic efficacy of the regimen was accessed using the visual analogue scale [3]. Monitoring of patients for respiratory depression was done by regular assessment of homodynamic status, respiratory rate and pulse oximeter readings [4][5][6]. Monitoring of patients for respiratory depression was done by regular assessment of respiratory rate, pattern and homodynamic status. Any fall in saturation less than 90% was noted and treatment protocol followed as summarized in Table 2

III. Results

A total of sixty patients were studied, thirty in each group. The demographic profile of the patient in the study is as shown in Table 2. Both groups were well matched for age, sex and weight. Mean VAS scores in both the groups at different times were plotted against time. They are also represented graphically. Mean total pain score in 24 hours mean total drug demanded and mean average pain scores for both the groups and the drug demanded by them are as shown in Table 4 and Table 5. During PCA use the patients were watched for side effects like respiratory depression, nausea, vomiting, pruritus, urinary retention, and sedation scores. Table 6 shows the incidence of various side effects.

IV. Discussion

Management of pain continues to pose a practical challenge to the health care provider. Many new strategies continue to evolve in an effort to alleviate pain. Opioid drugs have now been used to treat pain for centuries. The common side effects of opioid therapy are well known. Efforts have been made to develop novel means of drug administration, in order to minimize the side effects, whilst maintaining their ability to combat pain.

Patient controlled analgesia (PCA) involves self-administration of small doses of opioids by patients when they experience pain. PCA was originally conceived and developed to minimize the effects of pharmacokinetic and pharmacodynamic variability among individual patients. It is based on the premise that a negative feedback loop exists when pain is experienced, analgesic medication will be demanded and when pain is reduced, there will be no further demands.

Quality of analgesia with PCA has been considered optimum and satisfaction of patients and nurses is high. The principle advantage of PCA to patients is high quality analgesia autonomy, elimination of delay in decision to medicate for pain and freedom from painful intramuscular injections. Changing the opioid in the pump or using drugs to provide symptomatic relief. The side effects (nausea, vomiting, itching) resulting from PCA can be treated. There is also reduction in the work to be done by the nurse on duty all these advantages help improve efficiency.

Butorphanol is a definite advancement over the conventional opioids with regard to efficacy in pain management as well as safety and tolerability. The drug demonstrates a ceiling effect for respiratory depression, such that use of higher doses will not put the patient at greater risk of respiratory embarrassment. Butorphanol is less apt to produce physical dependence and unlike the currently used opioids, does not cause pruritus, or urinary retention.

The present study was undertaken to compare the analgesic efficacy, side effect profile and safety of use of butorphanol as compared to morphine intravenously via PCA pump. Patients undergoing gynaecologic, lower limb orthopaedic, lower abdominal and pelvic surgeries were enrolled for the study after informed consent. The patients in both the groups did not differ significantly in age or weight and were of either sex. The type of surgery carried out for the patients in each group was representative.

Pain was first assessed in the recovery room and four hourly thereafter. The mean total pain score and the average pain score were noted. In the morphine group the mean total pain score was 14.17 (±2.45) with an average four hourly assessed pain score of 2.02 and in the butorphanol group the mean total pain score was 14.19 with an average four hourly assessed pain score 2.04. The total average for morphine, including the loading dose, was 21(±4.24) and that for butorphanol was 7.12(±1.18). The mean total pain score for the patients in morphine group was 2.02 and for the patients in butorphanol group was 2.04. The difference lacked statistical significance. Neither patient in either group required any nurse administered analgesia for breakthrough pain.

Patients were watched for the same side effects of opioid group. Respiratory depression produced by butorphanol increased in a dose dependent manner like morphine. Unlike morphine butorphanol exhibits a ceiling effect on respiratory depression beyond a dose of 12.5mg. The incidence of nausea and vomiting caused by butorphanol was one-third that caused by morphine. Statistical analysis using standard error of proportions showed this difference to be statistically significant. Butorphanol is also less likely to produce physical dependence as compared to morphine. . These findings are similar to that of other workers [7][8][9][10][11][12].

V. Conclusion

From the study we can conclude that butorphanol is a definite advancement over the conventional opioids with regard to efficacy in pain management as well as safety and tolerability. It is seven times more potent than morphine; however, at equipotent doses the level of analgesia is comparable.

The main advantage of butorphanol over morphine is in the lesser incidence of side effects and complications. Incidence of respiratory depression, pruritus, nausea and vomiting with butorphanol were significantly less as compared to morphine

The status of PCA as an accepted method of pain relief was confirmed. It is an effective, convenient, flexible and user-friendly method. It has an inbuilt safety against overdose and is cost effective as it takes on part of the load from the nursing staff.

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TABLES

Table 1: PCA settings

Nomenclature	Morphine	Butorphanol
Drug concentration (mg/ml)	1	0.1
Bolus dose (mg)	1	0.1
Lockout interval (min)	6	6
Background infusion	-	-
Maximum dose (mg/4hrs)	4	1

Table 2: Demographic profile

	Age (SD)	Sex		Weight
		Male	Female	
Morphine Group	41.5 (±10.45)	12 (40%)	18(60%)	55.93(±7.70)
Butorphanol Group	43 (±9.08)	9(30%)	21(70%)	54.33(±8.18)
Statistical Significance	$p \leq 0.01$	$p \leq 0.05$		$p \leq 0.05$

Table 3: Standard monitoring and treatment for respiratory depression in patients treated with systemic opioids

1.	Respiration and sedation assessment every hour for 8 hrs, every 2 hrs for 8 hrs, and then every 4 hrs till 8 hrs after opioids are discontinued.
2.	Sedation score 0= none (alert) 1= mild (occasionally drowsy, easy to arouse) 2 = moderate (frequently drowsy, easy to arouse) 3 = severe (somnolent, difficult to arouse)
3.	Blood pressure, heart rate, pain scale assessment every 4 hrs
4.	Saturation by pulse oximeter
5.	No narcotics or sedatives unless approved by pain services
6.	At bedside: - Naloxone Suction Self inflating bag and mask
7.	For sedation score 3 and respiratory rate < 8 / min Notify anesthesiologist stat Naloxone 5 mcg/kg i.v. stat, repeated thrice every minute.

Table 4: Analgesic efficacy

Variable	**Group1: Morphine**	**Group2: Butorphanol**
Mean total pain score in 24 hrs	14.17 (±2.54)	14.19 (±1.07)
Mean average pain score (VAS=10cm)	2.02 (1.25)	2.04 (1.72)

$Z = 0.05$ $p \leq 0.01$

Table 5: Total drug demanded

Variable	**Group1: Morphine**	**Group2: Butorphanol**
Mean total drug demanded in 24 hrs	21.00 (±4.24)	7.12 (±1.18)

$Z = 7.12 \quad p \geq 0.05$

Table 6: Side effects and complications

Variable	**Group1:Morphine (N / %)**	**Group2:Butorphanol (N / %)**
Respiratory depression	2 / 6.66	NIL
Nausea	9 / 29.97	2 / 6.66
Vomiting	2 / 6.66	1 / 3.33
Urinary retention	4 / 13.32	1 / 3.33
Pruritus	2 / 6.66	NIL
Sedation score>2	NIL	NIL

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