SUBLINGUAL BUPRENORPHINE FOR POST-OPERATIVE PAIN

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SYNOPSIS

This study was made in the University departments of Surgery at the Singapore General Hospital and National University Hospital on the effects of buprenorphine for control of post-operative pain.

2 groups of 30 patients who underwent surgery were involved. One group received sublingual buprenorphine and the other intramuscular pethidine over 48 hours post-operatively.

The results of both anagelsic groups were compared in terms of number of doses required, pain control and side effects.

The study showed that buprenorphine was comparable to pethidine in terms of potency and was useful in controlling post-operative pain in the majority of cases although the incidences of some side effects like nausea, vomiting and giddiness was slightly higher in the buprenorphine group.

INTRODUCTION

The usual practice at Government and University Surgical Departments in Singapore hospitals for the management of moderate to severe post-operative pain is to give the patients intramuscular pethidine injections of 50 or 75 mg doses depending on their body weight at 4 to 6 hourly intervals over the first 48 hours.

Recently, buprenorphine has also been shown to be an effective means of treating post operative pain in Western studies (1,2,3,4,5,6,7,8,910). With the recent introduction of this strong analgesic into the Far East a study was carried out on local Asian patients to determine the efficacy of this drug for control of post-operative pain and to compare this drug with pethidine in terms of efficacy, dosage, number of doses required, and side-effects.

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PHARMACOLOGY OF BUPRENORPHINE

Buprenorphine, a new partial agonist-antagonist synthetic analgesic agent was synthesized in 1966. Its clinical history started 11 years ago in Britain and 9 years ago in Belgium, with the pioneer work of Orwin, Masson, Hovell, Gibbs and others (10). Buprenorphine is known to be of high potency and has prolonged actions. Administration of buprenorphine can either be sublingually or parentally.

Buprenorphine acts via the opiate receptor mechanism and unlike nalorphine and pentazocine, it possesses agonist activity at the morphine receptor but its intrinsic activity is relatively low, thus a partial agonist. Like morphine, it shows no evidence of receptor activity, in keeping with the lack of hallucinogenic effects in man. It was also shown that buprenorphine/u receptor interaction is a very stable one and that the rate at which the drug associates and dissociates with the receptor is slow. Studies carried out at the Addiction Research Centre, Lexington Ky., U.S.A. showed that buprenorphine has a low dependence profile. In determining dependence liability, the rate at which a compound binds with and dissociates from its receptor is of greater importance. The receptor kinetics of buprenorphine are such that abrupt withdrawal of the compound from the receptor does not occur, either by challenge with a pure antagonist or following cessation of buprenorphine dosing. The result is that buprenorphine is removed from the system in a controlled manner defined by the rate of dissociation of the agonist/receptor complex.

Buprenorphine is metabolised chiefly in the liver and excreted predominantly in the bile. When administered sublingually, it is easily absorbed through the buccal mucosa. It is less likely to induce respiratory depression when given epidurally and has very little effect on the Cardiovascular System. However, side effects such as giddiness, nausea, vomiting and sweating have been reported but the incidences were very low (6-8%).

Self administration of narcotic analgesics 'on demand' has recently been explored in the UK as a method of improving post-operative patient care. Ogg (1980) (10) gave buprenorphine by injection in the recovery room followed by 6 hourly sublingual buprenorphine and found this to be an efficient and well tolerated regime following major surgery.

MATERIALS

The study involves 60 patients undergoing surgery with resultant moderate to severe post-operative pain. 30 cases were given buprenorphine over the first 48 hours post-operatively if they complained of pain and 30 cases pethidine.

Patients were selected to participate in the study according to the following criteria:

A) Patients undergoing surgical procedures that would be expected to require analgesia over at least 2 day period.
B) Both male and female patients
C) Between 18 and 70 years old
D) Standard Anaesthetic Technique

Patients with the following conditions were excluded from the study:

A) Severe hepatic or renal dysfunction.
B) Marked ventilatory impairment due to underlying respiratory disease.
C) Raised intracranial pressure
D) Patients who have been receiving regular maintenance doses of narcotic analgesics or who are receiving monoamine oxidase inhibitors.
E) Pregnancy
F) Immediate surgical or anaesthetic complications which may require emergency treatment during the post-operative period.
G) Persistent mental confusion, severe enough to interfere with the patients' ability to maintain reliable communication with the investigators.

Cases were selected randomly and consisted of 2 groups of patients of broadly similar age groups and type of surgical procedure. All the surgery was carried out by one of the authors.

Table 1 and Table 2 shows the age group and types of major surgery by operation site, respectively.

TABLE 1: AGE GROUPS OF PATIENTS

Age Group	Buprenorphine group	Pethidine group
20 yrs	2	1
21-40 yrs	19	19
40 yrs	9	10
Total	30	30

TABLE 2: TYPE OF SURGERY BY REGIONS

Type of surgery	Buprenorphine group	Pethidine group
Head & Neck	14	13
Abdominal	11	11
Chest/Breast	2	4
Miscellaneous	3	2
Total	30	30

METHODS

Patients chosen for this study were divided into 2 groups according to the treatment they received for post-operative pain i.e.

A) Buprenorphine sublingual 0.2 mg 6 hourly p.r.n.
or B) I/M pethidine 4-6 hourly p.r.n.
(dosage 50 mg for those under 50 kg and 75 mg for those over 50 kg)

Post-operatively patients were closely monitored hourly for the first 6 hours, 3-hourly for the next 12 hours and 6-hourly thereafter with regards to respiratory rate, blood pressure, pulse rate, pain severity, conscious level and specific symptoms like nausea and vomiting.

Pain severity was classified into 4 groups i.e. none, mild, moderate and severe.

The conscious level was also classified into 4 groups i.e. alert, drowsy, asleep and non-arousable.

RESULTS

Number of doses required

The average dose required for the buprenorphine group of patients was 2 to 3 tablets of 0.2 mg dose sublingually over the first 48 hours.

The average dose required for the pethidine group of patients was 1 to 2 injections (50 or 75 mg dose, intramuscular) over the first 48 hours.

Pain control

The patients in both groups had satisfactory pain relief in that in the majority of cases, the pain was reduced to none or mild after the initial treatment with the respective post-operative anagelsic. In no case in either group was there still severe pain after the administration of the respective analgesic.

TABLE 3: AVERAGE NO. OF DOSES REQUIRED

	Buprenorphine group	Pethidine grup
Total doses for 30 cases	68	40
Average dose per cases	2.26	1.33

TABLE 4: POST OPERATIVE PAIN EXPERIENCED DURING FIRST 48 hours

	none	mild	moderate	severe
Buprenorphine group	10	15	5	0
Pethidine group	9	15	6	0

TABLE 5: NAUSEA AND VOMITING

	Buprenorphine group	Pethidine group
comfortable	25 (83%)	28 (93%)
Nausea & vomiting	5 (17%)	2 (7%)

Side effects

The majority of patients in both groups were comfortable after the administration of the analgesic (83.3% for buprenorphine group and 93.3% for pethidine group.)

16.7% of the patients on buprenorphine and 6.7% of the patients on pethidine experienced discomfort in the form of nausea and/or vomiting following administration of the analgesic.

3 patients (or 10%) of the buprenorphine group also mentioned a state of 'giddiness' while on the drug althoug this was not asked for in the protocol.

DISCUSSION

This study shows that sublingual buprenorphine is comparable to intramuscular injection of pethidine in the control of post-operative pain in adult surgical patients of our local Asian population.

An average of 2-3 doses of buprenorphine are required in comparison to 1-2 doses of pethidine.

Buprenorphine however causes a slightly higher incidence of nausea and or vomiting (17%) than pethidine (7%). We are however unable to ascertain that this was entirely due to the analgesic used or related to the anaesthesia given.

Three patients in the buprenorphine group experienced a state of "giddiness" following administration of the analgesic.

However the administration of buprenorphine is much simpler as it is taken sublingually and can even be left at the bedside for the patient to take when he feels the pain. Pethidine on the other hand requires an intramuscular injection by a staff nurse. From the hospital administration point of view it is more expensive to administer and from the patient point of view there may be delays in administration if ward staff are busy, not to mention the initial pain from the injection before pain relief comes.

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