

12. Harrison RF, Brennan M, North PM, Reed JV, Wickham EA. Is routine episiotomy necessary? *Br Med J* 1984; 288: 1971-1975.
13. Reading AE, Sledmere CM, Cox DN, Campbell S. How women view post-episiotomy pain. *Br Med J* 1982; 284: 243-246.
14. Coats PM, Chan KK, Wilkins M, Beard RJ. A comparison between midline and mediolateral episiotomies. *Br J Obstet Gynaecol* 1980; 87: 408-412.
15. Lieberman BA. Repair to injuries of the genital tract. *Clin Obstet Gynaecol* 1980; 7: 621-638.
16. Roberts ADG, McKay Hart D. Polyglycolic acid and catgut sutures, with and without oral proteolytic enzymes, in the healing of episiotomies. *Br J Obstet Gynaecol* 1983; 90: 650-653.
17. Beukens P, Lagasse R, Dramaix M, Wollast E. Episiotomy and third degree tears. *Br J Obstet Gynaecol* 1985; 92: 820-823.
18. Ekeocha CEV, Jackson P. The 'Birth Plan' experience. *Br J Obstet Gynaecol* 1985; 92: 97-101.
19. Bex PJM, Hofmeyr GJ. Perineal management during childbirth and subsequent dyspareunia. *Clin Exp Obstet Gynecol* 1987; in press.

# Intramuscular buprenorphine compared with morphine for postoperative analgesia

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## Summary

The postoperative analgesic efficacy of buprenorphine (Temgesic; R & C Pharmaceuticals) 0,004 mg/kg and morphine 0,15 mg/kg were compared in 60 patients, both agents given by intramuscular injection. According to patients, buprenorphine gave better analgesia. There was no difference in the number of analgesic injections the two groups received in the 24-hour postoperative period. Cardiovascular and respiratory systems were not depressed by either drug. Side-effects were not marked, nausea being the most common in both groups. Morphine had a greater effect on the mood of patients. Buprenorphine proved a satisfactory analgesic for postoperative use by intramuscular injection.

*S Afr Med J* 1987; 71: 359-361.

Morphine has been a standard postoperative analgesic for many years. However, as a result of its potential for abuse and its tendency to cause respiratory depression, the search has been widened for safer agents. Agonist-antagonist agents have less chance of causing these unwanted side-effects.<sup>1</sup> This new group of drugs has agonistic action at some opiate receptor sites and antagonistic action at others, the so-called dualism effect.<sup>2</sup> This is said to explain the ceiling effect on respiratory depression<sup>3</sup> and may explain the ceiling effect on analgesia.<sup>2</sup>

Buprenorphine (Temgesic; R & C Pharmaceuticals) is an analgesic of this type. It is a highly lipophilic orpivaine derivative of thebaine, similar in efficacy to morphine.<sup>1,3</sup> It can be given by intramuscular or intravenous injection.

In order to ascertain whether this agent has advantages over the time-tested morphine, a clinical trial was conducted to compare these two agents in a busy hospital environment.

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## Patients and methods

Patients over the age of 18 years graded as 1 or 2 on the American Society of Anesthesiologists' scale scheduled for laparotomy or orthopaedic surgery were selected for this study. They were assigned to one of two groups by blind-card draw until there were 30 patients in each group. At a pre-operative visit it was explained that analgesic efficacy was to be investigated in the postoperative period and the methods of assessment were discussed.

As premedication, diazepam 0,15 mg/kg was given orally 2 hours before operation. A pentothal induction was used and suxamethonium 1 mg/kg was used for intubation. Maintenance of anaesthesia was achieved with nitrous oxide, oxygen and halothane, muscle relaxants being used where indicated. Thirty minutes before the end of anaesthesia, a single dose of the test agent was given intravenously. Thereafter, postoperative analgesia was given at the request of the patient — 0,15 mg/kg morphine in one group and 0,004 mg/kg buprenorphine in the other. In both groups the analgesic was administered postoperatively by intramuscular injection into the gluteus maximus.

The ward nursing staff noted blood pressure, pulse and respiration 2-hourly for 24 hours, baseline readings being those taken at 06h00 before surgery. Sedation and nausea were graded 2-hourly on 4-point scales (sedation: awake (1), drowsy (2), asleep (3), unrousable (4); and nausea: nausea (1), vomited 1-2 times (2), vomited 3-10 times (3), vomited > 10 times (4)). Side-effects, especially urticaria and urine retention were looked for. The number of injections given in the first 24 hours was noted.

Twenty-four hours postoperatively all patients were visited by two of the investigators (K.P. and H.B.) who were not aware of which analgesia the patient had received. The maximum and minimum pain experienced during the test period was assessed by the face scale (FS) and by the visual analogue scale (VAS). Mood changes following analgesia were assessed as unchanged, feeling good or feeling bad. Statistical analysis was done by the chi-square test. A *P* value of < 0,05 was taken as significant.

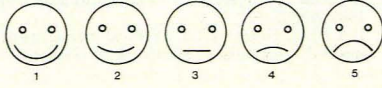
## Results

The two groups were comparable for sex, age, weight, duration of anaesthesia and operations performed. The maximum pain felt in this period assessed by the FS is shown in Table I, with buprenorphine significantly better than morphine (*P* < 0,05).

The VAS also showed a significant difference (*P* < 0,05) between the two groups in the maximum pain experienced (Table II). The number of patients assessed on this scale is low as only those who clearly comprehended this method were used for statistical analysis.

There was no significant difference in minimal pain levels experienced between the groups, or in the number of injections

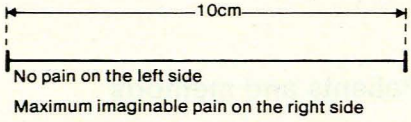
**TABLE I. MAXIMUM PAIN EXPERIENCED ON THE FACE SCALE**



	1	2	3	4	5
<b>Buprenorphine</b>	0	3	13	11	3
<b>Morphine</b>	0	2	4	17	7

**TABLE II. MAXIMUM PAIN EXPERIENCED ON THE VISUAL ANALOGUE SCALE**

	0-2	2-4	4-6	6-8	8-10 cm
<b>Buprenorphine</b>	1	9	2	4	2
<b>Morphine</b>	1	2	3	9	8



required in the 24-hour test period, although 2 patients in the buprenorphine group required no further analgesic after the intra-operative dose and all in the morphine group required further injections.

There was a highly significant difference ( $P < 0,02$ ) between the two groups in terms of mood postoperatively (Table III). Buprenorphine had less of an effect on mood than morphine, which tended to induce a good mood despite pain. Most buprenorphine patients did not experience any change of mood.

**TABLE III. MOOD EXPERIENCED POSTOPERATIVELY**

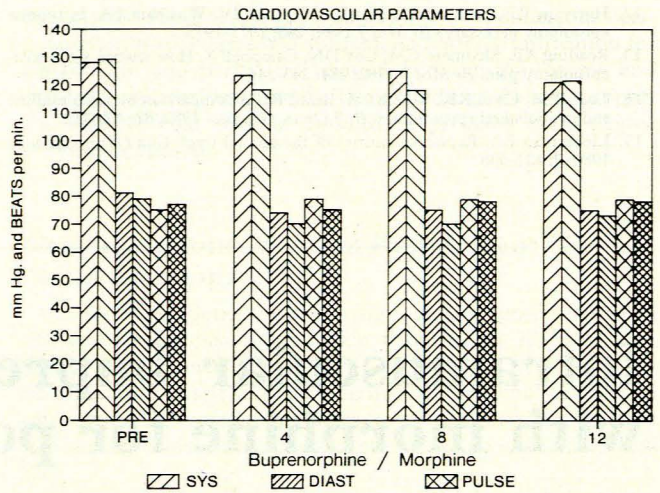
	Good	Unchanged	Bad
<b>Buprenorphine</b>	6	22	2
<b>Morphine</b>	15	12	3

Cardiovascular changes due to either analgesic were minimal (Fig. 1). No clinical respiratory depression was seen. There were no statistically significant differences in the side-effects experienced. No patients had bad dreams or dysphoric reactions and 1 patient in each group had a mild skin itch. Sedation was not noticeable in either group. Urine retention did not occur in any uncatheterised patient. Nausea occurred in 15 of the buprenorphine patients, 9 of whom vomited. Morphine caused nausea in 22 patients, 15 of whom vomited ( $0,05 < P > 0,1$ ).

**Discussion**

Allowing the patient to be his own pain assessor is commonly practised,<sup>4,5</sup> since pain is a very personal experience. The FS was easily interpreted by all patients and is likely to be the most reliable of the assessments. The VAS showed definite differences between the two groups, but it was clearly poorly understood by one-third of the patients and therefore its usefulness is in doubt. Other studies have had similar problems with the VAS.<sup>6</sup>

Buprenorphine is agonistic at  $\mu$ - and  $\delta$ -receptors with some antagonistic action at  $\kappa$ -receptors.<sup>7</sup> It has a slow association/dissociation receptor time,<sup>7</sup> which explains why its analgesic



**Fig. 1. Graphic representation of the mean systolic blood pressures, diastolic blood pressures and pulse rates taken pre-operatively and at 4, 8 and 12 hours postoperatively. The buprenorphine values precede the morphine values.**

activity outlasts its  $\beta$ -plasma half-life of 2-3 hours. Because of this slow receptor association time, it was administered in this study 30 minutes before the end of surgery. Thereafter, the low receptor dissociation time would have allowed postoperative follow-up injections to be given when pain became apparent but before the analgesia had worn off significantly. This would explain the finding that patients in the buprenorphine group experienced a lower maximum level of pain than those in the morphine group and would give patients some leeway if the sister in a busy ward could not respond immediately. This slow dissociation is said to give buprenorphine a more prolonged action than morphine, although this was not confirmed by the number of postoperative injections patients received in this study.

Alterations in mood will affect the interpretation of pain.<sup>8,9</sup> Opiates may cause euphoria via  $\mu$ -receptors or dysphoria via  $\sigma$ -receptors.<sup>1</sup> Mild euphoria would tend to make pain less worrying for the patient. Mood elevation was more marked with morphine, but despite this the analgesic properties of buprenorphine proved better. The lack of mood alteration is probably a beneficial property in the modern world of potential drug abuse.

The cardiovascular stability seen with buprenorphine is in agreement with other studies,<sup>4-6</sup> as is the lack of clinical respiratory depression.<sup>5,6</sup> Nevertheless when respiratory depression does occur it is reported to be difficult to reverse with naloxone.<sup>6,10</sup> Supportive ventilatory therapy is preferable should this unusual complication occur.

Side-effects in this study were minimal and of no consequence. Drowsiness has been reported with buprenorphine<sup>5,10</sup> although other studies,<sup>11</sup> including the present one, have not noted this. A postulate is that this reported drowsiness might indicate a lower level of pain causing less arousal of the patient.

This trial showed buprenorphine to have better postoperative analgesic efficacy than morphine while having no significant cardiovascular or respiratory effects at clinical dosage. Therefore we feel justified in concluding that buprenorphine is an effective postoperative analgesic.

Thanks to Mrs S. Venter for typing the manuscript, the anaesthetists and surgeons who allowed themselves to be bothered with the extra paper work, and the ward nursing staff and the patients for participating.

## REFERENCES

1. Offermeier J, Van Rooyen JM. Opioid drugs and their receptors. *S Afr Med J* 1984; **66**: 299-305.
2. Hull CJ. Receptor binding and its significance. *Br J Anaesth* 1985; **57**: 131-133.
3. Downing JW, Leary WP, White ES. Buprenorphine, a new potent long-acting synthetic analgesic: comparison to morphine. *Br J Anaesth* 1977; **49**: 251-254.
4. Schmidt JF, Chraemmer-Jorgensen B, Pedersen JE, Risbo A. Post-operative pain relief. *Anaesthesia* 1985; **40**: 583-586.
5. Tigerstedt I, Tammisto T. Double-blind multiple-dose comparison of buprenorphine and morphine in post-operative pain. *Acta Anaesthesiol Scand* 1980; **24**: 462-468.
6. Bradley JP. A comparison of morphine and buprenorphine for analgesia after abdominal surgery. *Anaesth Intensive Care* 1984; **12**: 303-310.
7. Boas RA, Villiger JW. Clinical actions of fentanyl and buprenorphine — the significance of receptor binding. *Br J Anaesth* 1985; **57**: 192-196.
8. Angell M. The quality of mercy. *N Engl J Med* 1982; **306**: 98-99.
9. Donovan BD. Patient attitudes to postoperative pain relief. *Anaesth Intensive Care* 1983; **11**: 125-128.
10. Freedman M. A comparison of buprenorphine and pentazocine for the relief of postoperative pain. *S Afr Med J* 1986; **69**: 27-28.
11. Dobkin AB, Esposito B, Philbin C. Double blind evaluation of buprenorphine hydrochloride for postoperative pain. *Can Anaesth Soc J* 1977; **24**: 195-202.

# A sensitive immunoradiometric assay for serum thyroid-stimulating hormone

## A first-line investigation for thyroid function

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### Summary

The value of a highly sensitive immunoradiometric assay for thyroid-stimulating hormone (TSH) in distinguishing between hyperthyroid patients and normal controls is discussed. The assay has a sensitivity of 0,3  $\mu\text{U/ml}$  and correctly categorised all patients in this study as either hyperthyroid or euthyroid. An approach to thyroid function testing using this sensitive TSH assay as a first-line investigation is presented.

*S Afr Med J* 1987; **71**: 361-362.

### Subjects and methods

Fasting TSH concentrations from the sera of 76 normal subjects (51 women aged 19 - 57 years, 25 men aged 22 - 58 years) and 148 untreated thyrotoxic patients (130 women aged 20 - 74 years, 18 men aged 25 - 66 years) were measured. Thyrotoxicosis was diagnosed on the basis of clinical symptoms and signs and elevated serum free thyroxine ( $\text{fT}_4$ ) and free tri-iodothyronine ( $\text{fT}_3$ ) concentrations.

The Serono TSH Maiacalone is a solid phase immunoradiometric assay (IRMA) employing three distinct high affinity monoclonal antibodies, two of these labelled with iodine-125 and the third with fluorescein isothiocyanate (FITC). The three monoclonal antibodies are premixed as a single liquid reagent. The  $\text{fT}_4$  and  $\text{fT}_3$  were measured by Amerlex Kit radio-immunoassays (Amersham International, UK).

### Results

The analytical sensitivity, calculated by analysing the zero standard in replicate (20 times) and determining the two-standard deviation value, was 0,3  $\mu\text{U/ml}$ . The intra- and interassay coefficients of variation of three controls run in 7 assays are shown in Table I.

TSH concentrations were less than 0,5  $\mu\text{U/ml}$  in the sera of all 148 thyrotoxic patients tested, and less than the analytical sensitivity (0,3  $\mu\text{U/ml}$ ) in 130 (88%). All euthyroid patients in the reference group had a TSH concentration  $> 0,6 \mu\text{U/ml}$ . The range of TSH concentrations in the reference group was 0,6 - 4,1  $\mu\text{U/ml}$ , with a mean ( $\pm$  SD) of  $1,82 \pm 0,89 \mu\text{U/ml}$ .

### Discussion

The Serono TSH Maiacalone assay is a solid phase IRMA employing three high affinity monoclonal antibodies and magnetic separation technology. This study demonstrates that this rapid, sensitive TSH IRMA assay, with an analytical sensitivity of 0,3  $\mu\text{U/ml}$ , can distinguish between the low TSH found in hyperthyroid patients and TSH concentrations found in normal controls. Although TSH was not undetectable

In a previous report<sup>1</sup> it was mentioned that a sensitive thyroid-stimulating hormone (TSH) immunoassay could meet the quest for a single thyroid function test which would correctly categorise the majority of patients as hyper-, hypo-, or euthyroid.

Until recently, most commercially available immunoassays for TSH lacked sufficient sensitivity to differentiate between hyperthyroid and euthyroid patients.<sup>2</sup> Evaluation of a recently commercialised assay, the Serono TSH Maiacalone, is described.

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