

Surgery in children

The majority of cardiac surgical procedures in children (under the age of 15 years) involved correction or palliation of congenital lesions, operations for valve disease forming only 7-15% of the yearly total (Fig. 7).

A small increase in the total number of operations performed on children, from an annual average of 173 between 1971 and 1975 to 194 between 1976 and 1981, was largely due to an increase in operations for 'simple' congenital conditions such as atrial and ventricular septal defects, patent ductus arteriosus, coarctation, and pulmonary and aortic valve stenosis. The number of operations for Fallot's tetralogy and transposition of the great arteries remained fairly constant, and procedures for the more 'complex' congenital lesions, such as total anomalous pulmonary venous drainage, complete atrioventricular canal, single ventricle, pulmonary atresia and tricuspid atresia have actually diminished (1971 - 1975: 29 a year; 1976 - 1981: 21 a year).

Causes of hospital mortality

Causes of operative and postoperative deaths have not been analysed in detail. There would, however, appear to be no significant change in factors relating to mortality throughout the 11-year period.

Postoperative myocardial failure in patients with advanced valve disease and in children with complex and congenital lesions remains a major cause of death despite improved methods of preoperative myocardial protection and postoperative circula-

tory support. This problem is most commonly related to patients who have presented themselves very late for consideration of surgical treatment; myocardial function is frequently extremely poor as a result of long-standing, unrelieved valve disease. The general state of the patient at the time of operation is also an important factor in postoperative morbidity and mortality; emergency procedures on moribund patients obviously carry a very high risk.

Myocardial infarction in both valve and ischaemic heart disease patients, thrombo-embolism following valve replacement, and respiratory conditions such as adult respiratory distress syndrome and pulmonary infection remain significant causes of mortality. Complications of operative technique or judgement (e.g. failure to relieve pulmonary outflow tract obstruction in Fallot's tetralogy, thrombosis of pulmonary-systemic shunts in infants and children) have become relatively infrequent.

The authors acknowledge and thank the many members of the medical, nursing and laboratory staff who have cared for these cardiac surgical patients. They also thank Sister Elma Steensma and Miss Jenny Bosman, who prepared the figures.

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Epidural and intramuscular pethidine — a pharmacokinetic study

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Summary

Epidural preservative-free pethidine hydrochloride 0,75 mg/kg is rapidly absorbed into the blood. At 1,5 mg/kg the plasma levels reached are similar to those achieved by intramuscular preservative-free pethidine hydrochloride, as is the time course. Plasma levels fall more rapidly after epidural pethidine. Since the plasma levels lag behind the analgesic effects, they are unlikely to be of importance as regards clinical analgesia.

S Afr Med J 1983; **63**: 193-195.

Epidural opiates such as pethidine have been shown to provide effective postoperative analgesia,^{1,2} their site of action being the substantia gelatinosa of the spinal cord.^{3,4}

The epidural space contains many lymphatics and venous plexuses,^{5,6} and systemic absorption can therefore be rapid; as doses of pethidine equal to intramuscular doses have been used epidurally,² blood levels may play a part in their action.

Serial measurements of CSF pethidine levels in patients undergoing routine operations pose ethical problems, but plasma samples are easily and painlessly taken. It was therefore decided to compare plasma levels of pethidine after epidural injection of 0,75 mg/kg and intramuscular injection of 1,5 mg/kg. These were the doses used in a previous study¹ showing that epidural pethidine provided superior quality analgesia but was not associated with an increase in the incidence of side-effects. This study would indicate to what extent absorption and transport via the blood influenced the actions of epidural pethidine.

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Methods

Consent of the hospital ethical committee was obtained, and the patients gave written informed consent. They were all fit, non-

obese, gynaecological or orthopaedic patients in ASA (American Society of Anesthetists) grades 1 or 2, and none was on any medication. Eleven patients received intramuscular and 10 epidural pethidine.

Premedication was with oral diazepam 10 mg 2 hours pre-operatively. Two patients in the epidural group received metoclopramide 10 mg intravenously for nausea during the trial. Bupivacaine 0,5% (plain) was used for all skin infiltration. The intravenous fluid lines were inserted into the feet. Blood sample lines were inserted into the cubital fossae of all patients, Teflon catheters being used. Three-way taps allowed all the samples to be taken from the same vein.

The patients in the intramuscular group were operated on under brachial plexus block with bupivacaine 0,5%, tourniquets being used. Intravenous diazepam was used in 7 cases for mild sedation. Patients received no fluids via their intravenous lines until all blood samples had been taken. Preservative-free pethidine hydrochloride 1,5 mg/kg was given by deep intramuscular injection into the quadratus femoris muscle on the opposite side to the intravenous line. Blood samples were taken during the operation, one before the intramuscular pethidine and thereafter every 5 minutes for 45 minutes.

In the patients in the epidural group the epidural catheters were placed by routine methods, bupivacaine 0,5% being used for all skin infiltration. The intravenous lines were not inserted into the same arm as the blood sample lines. No intravenous fluids were given until all blood samples had been taken. Preservative-free pethidine hydrochloride 0,75 mg/kg in 10 ml normal saline was then introduced down the catheter. Blood samples were taken before and during the operation. Thereafter

bupivacaine 0,5% was given through the catheter and a satisfactory block elicited. If the block proved unacceptable, the patient was taken out of the trial.

The blood samples were taken into heparinized glass test tubes and centrifuged immediately, and the plasma was decanted into glass test tubes and stored in the deep-freeze at 0°C until analysed. The plasma extract was passed through a Philips GCV gas chromatograph using a 1,1 metre glass column of 2% Carbowax 20M + 3% KOH on Chromasorb W-AW 80/100 at an oven temperature of 200°C according to the method of Tucker.⁷ Samples were assayed in duplicate wherever possible.

Results

The two groups were well matched for age and weight (Table I). Males predominated 9 to 2 in the intramuscular group, while there were 5 males and 5 females in the epidural group. Tables II and III show the range in values and standard deviations; these show great variability, which was marked in both groups. The epidural group definitely received their pethidine into the epidural space, as operation was later undertaken with the catheter *in situ*; similarly, the intramuscular group received truly intramuscular injections.

Fig. 1 shows the mean plasma levels in the two groups. The initial values are remarkably close, both rising at similar rates to peak in 25 minutes at 110 ng/ml for the intramuscular group and 98 ng/ml for the epidural group. Up to this time there was no statistical difference between the groups ($P > 0,05$). Thereafter the values in the epidural group rapidly dropped to a mean of 68

TABLE I. THE PATIENTS

| Patient No. | Intramuscular group | | | | Epidural group | | | |
|-------------|---------------------|-------------|-----|------------|----------------|-------------|-----|------------|
| | Age (yrs) | Weight (kg) | Sex | ASA rating | Age (yrs) | Weight (kg) | Sex | ASA rating |
| 1 | 22 | 75 | M | 1 | 33 | 80 | M | 1 |
| 2 | 21 | 75 | M | 1 | 49 | 75 | F | 2 |
| 3 | 48 | 52 | M | 1 | 36 | 44 | F | 1 |
| 4 | 14 | 50 | M | 1 | 20 | 79 | M | 1 |
| 5 | 20 | 50 | M | 1 | 49 | 60 | F | 2 |
| 6 | 22 | 53 | M | 1 | 43 | 59 | M | 2 |
| 7 | 27 | 72 | M | 1 | 28 | 50 | F | 1 |
| 8 | 59 | 88 | M | 1 | 16 | 50 | M | 1 |
| 9 | 29 | 54 | F | 1 | 44 | 64 | M | 1 |
| 10 | 54 | 60 | F | 1 | 28 | 56 | F | 1 |
| 11 | 38 | 80 | M | 1 | | | | |
| Mean | 32,2 | 64,4 | | | 34,6 | 61,7 | | |

TABLE II. PLASMA PETHIDINE LEVELS (ng/ml) IN THE INTRAMUSCULAR GROUP

| Patient No. | 0 | 5 min | 10 min | 15 min | 20 min | 25 min | 30 min | 35 min | 40 min | 45 min |
|-------------|-------|-------|---------|----------|----------|--------|----------|--------|--------|----------|
| 1 | 0 | 25 | 61,5 | 28,5 | 29,5 | 13 | 11,7 | 11 | 7 | 34,5 |
| 2 | <12,5 | 31 | 20 | 36 | 45 | 67,5 | 64,5 | 89 | 92 | 76 |
| 3 | 0 | 8,5 | 40 | 87 | 97 | 73 | 36 | — | 31 | — |
| 4 | 0 | — | 187 | 86 | 52 | 100 | 164 | 64 | 133 | 96 |
| 5 | 0 | 50 | 72 | 104 | 152 | 177 | 146 | 146 | 143 | 137 |
| 6 | 0 | 11,5 | 90 | 158 | 158 | 158 | 190 | 162 | 114 | 197 |
| 7 | 0 | 50 | 62 | 64 | 64 | 124 | 118 | 102 | 66 | 41 |
| 8 | 0 | 0 | 8,5 | 32 | 54 | 104 | 108 | 158 | 60 | 143 |
| 9 | 0 | 35 | 185 | 240 | 90 | 187 | 170 | 147 | 216 | 94 |
| 10 | 0 | 21 | 48 | 56 | 61 | 67 | 63 | 54 | 51 | 50 |
| 11 | 0 | 47 | 82 | 157 | 147 | 147 | 142 | 139 | 136 | 133 |
| Mean | 0 | 27,9 | 77,7 | 95,3 | 86 | 110,6 | 110 | 107 | 95 | 100 |
| Range | | 0-50 | 8,5-187 | 28,5-240 | 29,5-158 | 13-187 | 11,7-190 | 11-162 | 7-216 | 34,5-197 |
| SD | | 17,8 | 58,8 | 65,8 | 46,4 | 53,7 | 58,9 | 51,6 | 60,2 | 52,2 |

TABLE III. PLASMA PETHIDINE LEVELS (ng/ml) IN THE EPIDURAL GROUP

| Patient No. | 0 | 5 min | 10 min | 15 min | 20 min | 25 min | 30 min | 35 min | 40 min | 45 min |
|-------------|------|-------|---------|--------|--------|----------|--------|--------|--------|--------|
| 1 | 0 | 61 | 70 | 88 | 102 | 81 | 84 | 76 | 74 | 82 |
| 2 | 0 | 21,5 | 68 | 120 | 121 | 84 | 82 | 71 | 69 | 46 |
| 3 | 0 | 18 | 30 | 25 | 25 | 22,5 | 23 | 21 | 21 | 18 |
| 4 | 12,5 | 17 | 20,5 | 45 | 73 | 48 | 38 | 37 | 34 | 32 |
| 5 | 0 | 6 | 8,5 | 23 | 58 | 52 | 30 | 43 | 54 | 59 |
| 6 | 0 | 75 | 156 | 165 | 138 | 129 | 119 | 102 | 97 | 96 |
| 7 | 0 | 12 | 12,5 | 30 | 32 | 211 | 92 | 61 | 166 | 92 |
| 8 | 0 | 36 | 153 | 153 | 226 | 203 | 189 | 124 | 156 | 137 |
| 9 | 0 | 16 | 36 | 61 | 66 | 104 | 63 | 61 | 57 | 43 |
| 10 | 0 | 0 | 18 | 27 | 28 | 47 | 53 | 80 | 70 | 42 |
| Mean | 0 | 26,2 | 57,2 | 73,7 | 86,9 | 98,1 | 77,3 | 67,6 | 79,8 | 64,7 |
| Range | | 0-75 | 8,5-156 | 23-165 | 28-226 | 22,5-211 | 23-189 | 21-124 | 21-166 | 18-137 |
| SD | | 24,1 | 55,4 | 54,7 | 62,4 | 60,5 | 49,4 | 30,5 | 47,7 | 36,3 |

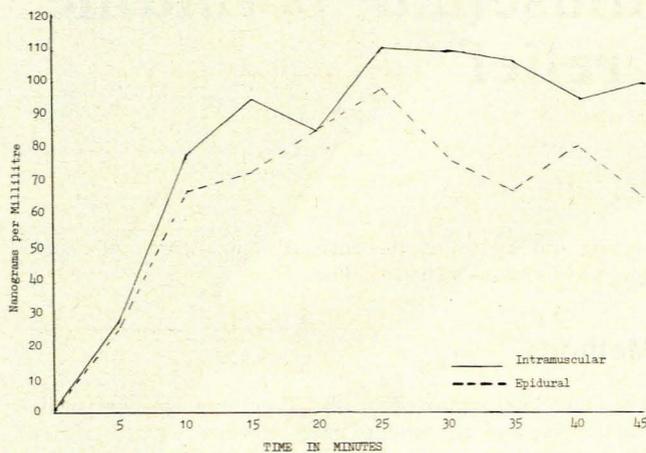


Fig. 1. Mean plasma pethidine levels. At 35 and 45 minutes these levels are significantly different ($P < 0,05$).

ng/ml at 35 minutes, while those in the intramuscular group fell more slowly to 100 ng/ml at 45 minutes. The differences at 35 and 45 minutes were significant at a confidence level of 95% ($P < 0,05$).

Discussion

Intramuscular pethidine has long been used for postoperative pain relief, but like all intramuscular analgesics its efficacy is variable,^{8,9} probably because varying rates of absorption lead to differences in plasma levels.¹⁰⁻¹² This variability is well shown in this study. The range of blood levels reached and the different times for peak levels are marked. Intramuscular pethidine is said to reach peak plasma levels at 60 minutes,¹²⁻¹⁴ but the peak in this study was much earlier (25 minutes) and the levels fell slowly for the remainder of the time. The fact that these were all fit patients whose cardiovascular homeostasis was unaffected by operation or pain is likely to be the reason for the early peak levels.

It is reported that plasma pethidine levels of 200 ng/ml are needed for analgesia.^{2,11,12} The mean peak level in the intramuscular group was only half this and no individual patient surpassed this level. This supports the clinical impression that intramuscular pethidine does not provide powerful analgesia at 1,5 mg/kg.

The vascularity^{5,6} of the epidural space suggests rapid absorption. This has been shown with local anaesthetics.¹⁵ The plasma levels in the epidural group show that the absorption rate was close to that of the intramuscular group, although the patients received only half the dose. However, the more rapid fall in

plasma levels in the patients who received epidural pethidine probably reflects the smaller dose, producing less of a reservoir. The values up to 25 minutes are close to those reported by Cousins *et al.*,² who used double the dose. In that study the peak value was maintained to 45 minutes, probably because the dose of 100 mg provided a reservoir; furthermore, the pethidine levels in Cousins *et al.*'s study were measured postoperatively and those in the present study pre- and intra-operatively, so perfusion and absorption rates may be different. As with intramuscular pethidine, the variation in levels reached is very large. The highest plasma level reached was just on the analgesic level, but the rapid fall-off makes it unlikely that it would be significant in pain relief.

The analgesia produced by epidural pethidine takes effect in 5 - 10 minutes^{1,16} when the plasma levels are low. Analgesia at this stage is therefore probably due to rapid spread in the CSF, resulting in analgesic levels in the CSF at this time.² However, with the plasma concentrations in both groups reaching similar levels at 25 minutes, it is surprising that epidural pethidine does not lead to the central depression associated with intramuscular pethidine. Reports all stress the lack of sensory clouding.^{1,2,11,17} Early drowsiness, with onset at 5 minutes and wearing off again at 30 minutes, has been reported.¹ This is not due to spread in the blood as the patients are recovering at the time the plasma levels peak.

The plasma levels achieved suggest that blood spread may play a part in the clinical effect of epidural pethidine but that this is less significant than spread in the CSF, especially with regard to analgesia.

I wish to thank Mrs W. Visser for typing the manuscript, Dr A. Bunn for statistical help and Dr D. Morrell of Groote Schuur Hospital, Cape Town, for determining the plasma pethidine levels. Roche Laboratories financed the study.

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Epidural versus intramuscular pethidine in postoperative pain relief

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Summary

Twenty-one patients received epidural pethidine 0.75 mg/kg in 10 ml normal saline for postoperative analgesia. A control group of 20 patients received intramuscular pethidine 1.5 mg/kg. Respiratory and cardiovascular parameters in both groups were stable, and in both side-effects were similar and not serious. In the epidural group analgesia was more intense and of longer duration and the level of consciousness was better. Central depression was present in both groups but less so in the epidural group.

S Afr Med J 1983; 63: 196-200.

Epidural opiates are enjoying some vogue at present, their effective duration being reported as varying from several hours¹⁻³ in acute pain to several days in chronic pain.^{4,5} The reported incidence of side-effects varies from low^{2,3,6} to high.⁷⁻⁹ Most reports have been on morphine, but obtaining preservative-free solutions and avoiding respiratory depression^{4,5,10} are problems.

Pethidine hydrochloride was chosen for this trial because it is supplied as a preservative-free drug. Cousins *et al.*¹ and Scott and McClure¹¹ reported good analgesia using epidural pethidine. The site of action is thought to be the substantia gelatinosa of the spinal cord, as with other opiates.^{3,5,6,12}

The aim of the study was to determine the effectiveness and duration of pain relief with epidural pethidine in the postoperative period, and the side-effects, including cardiovascular instability, respiratory instability, change in consciousness, nausea,

itching and sensory disturbance. A control group of patients received intramuscular pethidine.

Methods

The study was approved by the Tygerberg Hospital Ethical Committee, and all patients gave informed written consent. Gynaecological and orthopaedic patients were chosen because their operations were suitable for epidural anaesthesia.

Patients were allocated to the epidural group or the intramuscular group purely on an alternate basis on the pre-operative ward round. At this time the patient's resting blood pressure and pulse rate were noted. The tidal volume, respiratory rate and partial arterial oxygen (Pao₂) and carbon dioxide (Paco₂) pressures were measured. Blood samples were taken into 2 ml heparinized glass syringes by radial artery puncture, and if there was any difficulty in obtaining arterial blood this investigation was abandoned. The blood was packed on ice and immediately taken to the laboratory for analysis. All analyses were made with the same machine, a Radiometer ABL1 blood gas analyser, using a standard technique. The tidal volumes were measured by a Wright's respirometer with patients breathing through a cardboard mouthpiece of standard lung function test size. The same Wright respirometer was used throughout; it consistently read -10% on testing.

Patients were told that postoperative analgesia would be given whenever they felt the need for it. The assessment of their pain would be left entirely up to them and they would receive analgesia whenever they became uncomfortable, i.e. on request. Patients were asked to grade their postoperative pain according to the following scale: 1 — poor; continuous, unacceptable pain; 2 — moderate; continuous, acceptable pain; 3 — good; pain present intermittently but not worrying patient; 4 — total; no pain. All pain assessments were therefore subjective. The day after the operation the patients were asked to comment on and grade the postoperative analgesia.

Standard premedication of pethidine 0.75 mg/kg and promethazine 0.35 mg/kg was given intramuscularly 1 hour pre-operatively. In patients in both groups an epidural catheter was then inserted at L2-3 or L3-4. Lignocaine 1.5% with adrenaline was used because of its short action, and the operation was

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Date received: 18 February 1982.

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