Forum

Total intravenous anaesthesia for military surgery.
A technique using ketamine, midazolam and vecuronium

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Summary
Ketamine and midazolam were used for induction of anaesthesia and by continuous intravenous infusion for maintenance to assess their suitability for use in a total intravenous anaesthetic technique in the management of battle casualties. Muscle relaxation was provided by vecuronium in the patients' lungs ventilated with air. Ketamine was infused at a rate of 2 mg/kg/hour. This was achieved by mixing ketamine 200 mg, midazolam 5 mg and vecuronium 12 mg in 50 ml normal saline. The rate of infusion of the mixture (ml/hour) was then equal to 50% of the body weight in kg. The technique proved to be simple, effective and versatile and should be adaptable for use in the management of battle casualties.

Key words
Anaesthetic techniques; infusion.
Hypnotics; midazolam.

The overriding principle of military surgery is the delayed primary suture of wounds. Therefore, by definition, battle casualties will receive more than one anaesthetic for the treatment of their injuries. The use of the Triservice anaesthetic apparatus (TSA) has been well tried and documented. It is a drawer system that uses ambient air as the primary carrier gas, and halothane and trichloroethylene as the volatile anaesthetic agents.

However, in view of current opinions about liver damage due to repeated halothane anaesthetics, it would be preferable if this agent was not used in the first instance. In addition, the manufacture of trichloroethylene has been threatened in the past and the future production of this agent cannot be guaranteed. The use of the newer inhalational agents, enflurane and isoflurane, has been recommended. Unfortunately, enflurane, which does have analgesic properties, has a high MAC and isoflurane, at present, is very expensive.

We felt that a total intravenous technique is an obvious alternative in the treatment of battle casualties. This study was therefore designed to assess the suitability of such a technique using a mixture that contained ketamine, midazolam and vecuronium, accurately delivered intravenously by means of a syringe pump. Ketamine has been used widely as the induction and maintenance drug of choice for trauma cases but the high incidence of unpleasant side effects has limited its acceptance. Vecuronium bromide, one of the more recently introduced non-depolarising muscle relaxants, has been used because it is available as an anhydrous powder and therefore stores well. Vecuronium is free of adverse circulatory effects and the incidence of release of histamine is minimal.

It is our contention that all battle casualties will have a full stomach, irrespective of the interval between time of injury and time of surgery. Therefore, tracheal intubation is mandatory and intermittent positive pressure ventilation can be used for the duration of the surgical procedure. Another essential requirement for war surgery is that patients should recover quickly and be able to maintain a clear airway as soon as possible.

Methods
One hundred patients, 36 male and 64 female, age range 16-50 years, who presented for elective abdominal, thoracic or body surface surgery at this hospital were studied. All patients were in ASA classes 1 and 2. It was estimated that their operations would last at least 45 minutes. Patients with a past medical history of psychiatric illness, with hypertension and those with a history of a previous cerebrovascular accident were not studied.

All patients were seen pre-operatively. The following details were recorded: initials, sex, body weight, relevant medical history and physical findings. All were premedicated with papaveretum and hyoscine one hour pre-operatively. Monitoring of the electrocardiogram and blood pressure (Dinamap) was commenced on arrival in the anaesthetic room and a vein on the dorsum of the hand or forearm was cannulated. Systolic, diastolic and mean arterial pressure and pulse rate were recorded 5 minutes before induction and at 3-5 minute intervals thereafter.

Anaesthesia was induced with midazolam 0.07 mg/kg followed 2 minutes later by ketamine 1.0 mg/kg and vecuronium 0.1 mg/kg, and maintained by constant infusion of a mixture of the same three drugs using an electrically driven syringe pump (IMED 800) at the following rates:

Accepted 2 April 1987.

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midazolam 50 μg/kg/hour, ketamine 2.0 mg/kg/hour and vecuronium 120 μg/kg/hour. This mixture is obtained by mixing midazolam 5 mg, ketamine 200 mg and vecuronium 12 mg and making up to 50 ml with normal saline. A convenient method to the rate of administration of this mixture is:

\[
\text{patient's body weight in kg} \times \frac{2}{\text{ml/hour}}
\]

The patient's lungs were ventilated with oxygen-enriched air, with an \(P_{\text{O}_2}\) of 0.35, tidal volume 10 ml/kg at a respiratory rate of 12 breaths/minute using a Pennin Oxford ventilator. In 10% of cases the end tidal carbon dioxide was monitored by capnography (Datex) and the efficacy of neuromuscular blockade was assessed with a peripheral nerve stimulator (Datex Relaxograph) that delivered train-of-four stimuli to the ulnar nerve.

The infusion was stopped 10–15 minutes prior to the end of surgery and residual neuromuscular blockade reversed with either atropine and neostigmine, or glycopyrrolate and neostigmine. The times of relaxant reversal and tracheal extubation and the time at which the patient regained consciousness in the recovery area were recorded. The latter was when the patient was able to give name, military number (where appropriate) and ward number. The patient's behaviour in the recovery area was recorded as either satisfactory or unsatisfactory. Specific problems were recorded in the case of the latter.

All patients were visited 24 hours postoperatively and questioned with regard to awareness during the operative procedure, the occurrence of dreams or hallucinations, and the occurrence of nausea or vomiting. The time from reversal to the first dose of narcotic was noted from the nursing Kardex.

**Results**

The types of operation performed are shown in Table 1. The details of the patients' age and weight are given in Table 2, and the duration of anaesthesia, total volume of infusion, and extubation to awakening time in Table 3. No patient complained of pain on injection of the drugs and induction of anaesthesia was very smooth; no excitatory phenomena were noted. The mean duration of anaesthesia was 73.6 minutes and the mean volume of infusion administered was 33.7 ml. The mean time from tracheal extubation to awakening was 12.5 minutes.

**Cardiovascular effects.** Some cardiotranslatory action was observed in all patients. Figure 1 shows the mean heart rate and Fig. 2 the mean systolic and diastolic blood pressures. There was an initial increase in heart rate and arterial blood pressure associated with tracheal intubation. The heart rate and blood pressure began to decrease after 5 minutes and had returned to pre-operative levels by 30 minutes. At no time was the arterial blood pressure lower than the level prior to induction of anaesthesia (Table 4).

**Recovery.** None of the patients in this study was aware during the operative period and all but one said that they would be perfectly happy to have the same anaesthetic again. The patient suffered nightmares but had had a similar experience after a previous general anaesthetic when thipentone, nitrous oxide, oxygen and halothane were used. The behaviour of all the patients was rated to be entirely satisfactory by the recovery nursing staff. They were not nursed in silence or darkness. Two patients were given perhexazine 5 mg for nausea and two were given doxapram 50 mg to stimulate respiration.

The incidence of postoperative dreaming was 15%; five patients complained that the dreams were unpleasant. Post-

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**Table 1. Types of operation performed.**

<table>
<thead>
<tr>
<th>Operation</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal hysterectomy</td>
<td>21</td>
<td>19</td>
</tr>
<tr>
<td>Vaginal hysterectomy</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Laparotomy</td>
<td>2</td>
<td>15</td>
</tr>
<tr>
<td>Other gynaecological operations</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Thoracotomy</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Upper abdominal surgery</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>Varicose veins</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Herniorrhaphy</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Orthopaedic procedures</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Others</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>36</td>
<td>64</td>
</tr>
</tbody>
</table>

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**Table 2. Mean (SEM) and range of age and weight of patients.**

<table>
<thead>
<tr>
<th>Age, years</th>
<th>Range</th>
<th>Weight, kg</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>36</td>
<td>29.6 (8.6)</td>
<td>17.49</td>
</tr>
<tr>
<td>Female</td>
<td>64</td>
<td>35.8 (7.5)</td>
<td>19.49</td>
</tr>
</tbody>
</table>

operative vomiting occurred in only one male patient (2.8%) and in 24 female patients (37.5%). Seventy-eight of the patients required postoperative analgesia; the mean time of administration of the first dose was just over 4.5 hours after extubation.

**Discussion**

The concept of a total intravenous anesthetic technique for war surgery is attractive but it suffers a severe setback at Pearl Harbour. Thiopentone was used as the sole agent and lack of knowledge of its cardiovascular and respiratory depressant effects led to disastrous consequences. Halford stated that intravenous anaesthesia is an ideal method of euthanasia.

When we decided to examine again a total intravenous technique for war injuries we had three objectives; firstly, to find a safe and simple method to anaesthetise battle casualties in such a way that they are in the best possible condition for surgery, asleep, relaxed and with reflexes suppressed; secondly, to develop a technique which ensures that patients awaken rapidly postoperatively and are able to maintain a safe airway, and thirdly, to develop a technique that can be supervised safely by paramedical personnel.

We chose three drugs which are all water soluble and can be mixed together without any precipitation. They would appear to be stable in solution and the mixture can be used at least 72 hours after preparation. The individual drugs have a long shelf-life and do not need to be stored in a refrigerator. Pharmacokinetically the combination of ketamine and midazolam is attractive. The distribution half-life of both drugs is 10–15 minutes, the elimination half-life of ketamine is 2.5–3.1 hours and of midazolam 1.5–2.5 hours. The clearance of ketamine is 18.0 ml/kg/minute and of midazolam, 8.1 ml/kg/minute. When midazolam is mixed with ketamine, which has pH 3.5–5.5, the open ring configuration of the former drug outside the body is maintained.

Ketamine is a controversial drug. The slow onset of action, its relatively prolonged duration, together with the high incidence of adverse reactions during recovery, seem to make it unsuitable for continuous intravenous infusion. The emergence phenomena consist of dreams, pleasant and unpleasant, and disturbance of sensory perception. Various methods have been tried to overcome emergence phenomena: patient selection, heavy opioid premedication, benzodiazepine combinations, diazepam, lorazepam, fluni-
Table 3. Mean (SEM) and range of duration of anaesthesia, recovery time and total volume of infusate.

<table>
<thead>
<tr>
<th></th>
<th>Duration of anaesthesia, minutes</th>
<th>Range</th>
<th>Tracheal extubation, awakening, minutes</th>
<th>Range</th>
<th>Total volume of infusate, ml</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>36</td>
<td>94.5 (55.4)</td>
<td>25 - 281</td>
<td>11.8 (12.1)</td>
<td>1 - 60</td>
<td>50.7 (37.7)</td>
</tr>
<tr>
<td>Female</td>
<td>64</td>
<td>61.9 (19.4)</td>
<td>30 - 119</td>
<td>12.8 (15.5)</td>
<td>1 - 92</td>
<td>24.1 (10.4)</td>
</tr>
</tbody>
</table>

Table 4. Mean (SEM) increases or decreases (−) in heart rate and systolic arterial pressure.

<table>
<thead>
<tr>
<th>Time, minutes</th>
<th>Heart rate, beats/minute</th>
<th>Systolic arterial pressure, mmHg</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>22.2 (17.3)</td>
<td>27.4 (19.2)</td>
</tr>
<tr>
<td>10</td>
<td>21.4 (18.1)</td>
<td>20.0 (18.1)</td>
</tr>
<tr>
<td>15</td>
<td>11.6 (18.7)</td>
<td>15.9 (17.5)</td>
</tr>
<tr>
<td>20</td>
<td>6.6 (18.0)</td>
<td>9.0 (19.7)</td>
</tr>
<tr>
<td>30</td>
<td>0.6 (15.3)</td>
<td>3.2 (17.5)</td>
</tr>
<tr>
<td>45</td>
<td>-5.7 (14.6)</td>
<td>5.4 (17.2)</td>
</tr>
<tr>
<td>60</td>
<td>-8.5 (14.0)</td>
<td>4.9 (17.7)</td>
</tr>
</tbody>
</table>

satisfactory postoperatively, patient acceptability was high and there were no cases of awareness. The fact that there is no simple, reliable and objective index that indicates awareness during anaesthesia is probably the single most restricting factor in the use of a total intravenous technique with relaxant drugs.8

Midazolam has proved to be the ideal benzodiazepine for use in this field.15 It is water soluble, mixes with the other drugs and does not cause phlebitis. It provides good anterograde amnesia and, unlike the earlier benzodiazepines, has no second peak effect. It should be noted that the benzodiazepines lose potency when mixed with Hartmann’s solution, and normal saline should be used for the preparation of this mixture.

Vecuronium is the non-depolarising muscle relaxant with the least adverse side effects. Histamine release is minimal, the breakdown products are innocuous, it is cardiotropic and does not produce tachycardia even though it is a derivative of pancuronium. The fact that vecuronium is prepared as an anhydrous powder is most useful to us since it stores well, has a long shelf life and does not require refrigeration.

The changes in heart rate and blood pressure found in this study were similar to those found by Lilburn et al.16 using tubocurarine. The haemodynamic response to intubation is well documented;17 midazolam does give protection but in much larger doses.18 It is doubtful if midazolam has much effect on the cardiostimulatory action of ketamine or the plasma catecholamine level. We feel that the tachycardia and hypertension are acceptable in the management of the previously fit soldier, aged 18-45 years whose cardiovascular system will withstand swings in pulse rate and arterial blood pressure. There were no instances of unusual cardiac dysrythmias.

Recovery, as evidenced by the tracheal extubation to awakening time, was fairly rapid and emergence was smooth. The mean awakening time (12.5 minutes) would have been even shorter had not three cases taken over 60 minutes to recover. Swift recovery is particularly important in the military context. In a combat area there will be a shortage of skilled anaesthetists and nurses; therefore, patients must recover consciousness and reflexes quickly. There is likely to be a limited postoperative holding capability and casualties may have to be evacuated early. Postoperative behaviour was normal in all patients despite the absence of special precautions such as silence and darkness.

The incidence of nausea and vomiting was no higher than
that found using any other technique and compares favourably with a previous report.\textsuperscript{19} The much higher incidence in the females was probably due to the nature of the surgery. Many of the patients who vomited had done so previously after a conventional technique had been used.

Early observations suggested that anaesthesia following ketamine administration outlasted the period of anaesthesia and that this anaesthetic effect occurred at an even shorter anaesthetic doses of ketamine. In this series the mean time from extubation to the administration of the first dose of postoperative analgesia was 272 minutes. We do not feel that any conclusions can be drawn from this observation about the duration of the anaesthetic effect of ketamine. However, only one patient required postoperative analgesia whilst still in the recovery area. This factor must have been significant in the smooth emergence of these patients from anaesthesia.

It is unlikely that battle casualties will be premedicated with papaveretum and hyoscine. Previous experience has shown that casualties will receive doses of analgesic on the battlefield and in transit to the field hospital.\textsuperscript{2} At present, the drug that is likely to be used is papaveretum and that is why this drug was chosen as the premedicant. If necessary, supplements of analgesic can be given at the time of induction or during the procedure. Suxamethonium was not used for intubation but when casualties are treated it can be used for a crash induction followed by a loading dose of vecuronium in the normal way.

We do not recommend that this technique be adopted to the exclusion of all others in military surgery but we believe that it can be used to advantage. When inhalational agents are not available or are not the most suitable agents. This method is simple, effective, versatile and can be used in combination with other techniques. It is cheap and effective, with air as the carriag gas. Once established, minimum monitoring and minimum interference are required. In conclusion, we believe that there is a place for total intravenous anaesthesia in the treatment of battle casualties and that the technique that we have described will prove to be significant and safe.

References

Anaesthesia, 1988, Volume 43, pages 49-51

Temazepam and recovery in day surgery

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Summary

A double-blind trial of temazepam premedication for day cases was undertaken. Effective anxiolysis was recorded in the groups that received temazepam 10 or 20 mg and there was no prolongation of delayed recovery times as measured by memory test cards. All patients were discharged from the day unit 3 hours after the administration of general anaesthesia.

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Accepted 7 April 1987.