pressure and flow during the forced expiratory manoeuvre. It also breaks a fundamental law of the science of measurement: that units of measurement such as litre per minute should have an absolute definition and meaning.

Finally, Dr Wright states that the resistance of the meter has a marked effect on a rigid mechanical flow generator of the type used by us. This is untrue, for our calibration is independent of the resistance of the meter under test.

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DOES KETAMINE METABOLITE II EXIST IN VIVO?

Sir,—In their review of the pharmacological properties of ketamine, Chang and Glazko (1974) postulated a tentative scheme for the biotransformation of this interesting anaesthetic agent (fig. 1). An N-demethylation, yielding nor-ketamine (M1) followed by a hydroxylation of the cyclohexane ring at two optional positions yields hydroxy-nor-ketamine (M11 and M1V, respectively). These two metabolites are then conjugated and excreted or dehydrated to dehydro-nor-ketamine (M1l).

Following the work of Chang and Glazko, no further basic research on this topic has appeared in the literature. Their postulated scheme of biotransformation has been adopted and reappeared, although enlarged, in a recent update by Zsigmond and Domino (1980). These authors postulated the presence of another dehydrated metabolite, dehydroketamine (MVII).

In our opinion, there are several reasons to question the in vivo existence of M11. Using the bioassay of Chang and Glazko (1972), we were not able to detect the presence of M11 in cerebrospinal fluid, while simultaneously collected plasma samples (man or rat) contained easily determined concentrations of this compound (table 1). These experiments included collections following prolonged anaesthesia times. In contrast, ketamine and M1 were easily determined in c.s.f., with concentrations amounting to approximately 30–60% of those seen in plasma even within 15–20 min after induction of anaesthesia. Since there is no obvious reason to believe that M11 should be less lipophilic or more strongly bound to plasma proteins than ketamine and M1, other explanations for this apparent "inhibited diffusibility" of M11 across the blood–brain barrier have to be considered.

The bioassay utilizes gas–liquid chromatography and includes benzene extraction of a strongly alkalized sample and subsequent derivatization with heptafluorobutyric anhydride in the presence of pyridine. Since alpha and beta-hydroxyketones such as M11 and M1V respectively (and possibly also their conjugates) would be expected to be converted easily to M11 under the conditions described, and since there are reasons to believe that these less lipophilic compounds would diffuse slowly or not at all into the c.s.f., we believe there is a strong argument for considering M11 as an artefact.

If M11 does not exist in vivo, there is no obvious reason to postulate the presence of MVII.

If ketamine administration does not result in M11 or MVII in vivo, man has never been exposed to these compounds unless given them directly. Consequently, during future research in this field, administration of M11 and MVII to man should be carried out with extreme care.

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INHALATION OF GASTRIC CONTENTS

Sir,—We report two cases, one fatal, of aspiration pneumonitis following regurgitation and inhalation of gastric content during general anaesthesia for emergency evacuation of an incomplete abortion.

A 24-yr-old African female of average size was admitted at 09.00 h with a septic incomplete abortion. She received papaveretum 15 mg and atropine 0.6 mg i.m. at 14.00 h. The haemoglobin concentration was 10.5 g dl⁻¹. She had starved overnight. At 14.30 h the patient inhaled pure oxygen for 3 min through a Mapleson A system. Anaesthesia was induced at 14.40 h with Althesin 3 ml and diazepam 10 mg i.v. The patient developed severe laryngospasm. Suxamethonium 100 mg was injected i.v. to facilitate tracheal intubation. On direct laryngoscopy, approximately 15 ml of clear fluid was seen in the pharynx. After suction, a size 8 mm cuffed tracheal tube was inserted and the cuff inflated. Endotracheal suction before ventilation of the lungs revealed no obvious evidence of airway contamination. Anaesthesia was maintained with 50% nitrous oxide in oxygen with manual ventilation of the lungs; supplementary suxamethonium was given as required. Steroids were not administered and neither bronchoscopy nor bronchial toilet was performed.

REFERENCES


TABLE I. Concentrations (μmol litre⁻¹) of ketamine, M1 and M11 in simultaneously collected samples of plasma and c.s.f. in five rats and one man during steady-state ketamine anaesthesia.

<table>
<thead>
<tr>
<th>Duration of anaesthesia (min)</th>
<th>Ketamine</th>
<th>M1</th>
<th>M11</th>
</tr>
</thead>
<tbody>
<tr>
<td>Man</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>2.8</td>
<td>4.5</td>
<td></td>
</tr>
<tr>
<td>60</td>
<td>5.6</td>
<td>9.4</td>
<td></td>
</tr>
<tr>
<td>180</td>
<td>6.5</td>
<td>11.0</td>
<td>1.3</td>
</tr>
<tr>
<td>Rat</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>15</td>
<td>30.3</td>
<td>1.5</td>
</tr>
<tr>
<td>2</td>
<td>20</td>
<td>21.3</td>
<td>1.6</td>
</tr>
<tr>
<td>3</td>
<td>70</td>
<td>32.1</td>
<td>8.4</td>
</tr>
<tr>
<td>4</td>
<td>90</td>
<td>33.8</td>
<td>13.1</td>
</tr>
<tr>
<td>5</td>
<td>120</td>
<td>27.5</td>
<td>12.7</td>
</tr>
<tr>
<td>n.d. = not detectable</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

FIG. 1. Postulated biotransformation of ketamine according to Chang and Glazko (1974).

Table 1.
At the end of anaesthesia, the patient was turned on her side and the tracheal tube removed. She was transferred to the recovery room, where she was observed for 2 h, breathing 40% oxygen through a Mix-o-mask. Auscultation of the lungs was normal and the patient returned to the ward breathing air at 17.20 h. Within 30 min the patient complained of shortness of breath and appeared distressed with sweating, tachycardia and hypotension. The level of consciousness deteriorated gradually despite the administration of supplementary oxygen by mask. Diffuse rales and bronchospasm were audible over the chest. The trachea was intubated with a cuffed Portex 8 mm endotracheal tube and the lungs ventilated mechanically. Chest x-ray showed the classic “snow storm” appearance consistent with a diagnosis of Mendelson’s syndrome. \( P_{aO_2} \) was 5 kPa \((F_{IO_2} 0.6)\). PEEP, 5 cm H\(_2\)O, was given. Blood-gas and acid-base status improved and, together with her heart rate, central venous and arterial pressures, remained stable over the next 48 h. Chest x-rays showed some improvement of the lung condition.

Two days later \( P_{aO_2} \) was 8.75 kPa \((F_{IO_2} 0.6)\) and haemoglobin 9.6 g/dl. Two days later, \( P_{aO_2} \) decreased dramatically to 3 kPa. \( F_{IO_2} \) was increased to 1.0 and PEEP from 5 to 10 cm H\(_2\)O. Despite these measures, the patient’s condition deteriorated and she collapsed and died suddenly at 12.10 h, 5 days after admission to hospital. At postmortem examination, there was straw-coloured fluid present in the bronchi and a 3-cm embolus was discovered in the right ventricle and pulmonary artery. Death was attributed to massive pulmonary embolus complicating Mendelson’s syndrome.

A 22-yr-old obese African woman was admitted to hospital in severe shock. There was a history of induced abortion using a salt and soap solution douche administered with a rubber pump. Following appropriate resuscitation and premedication with metoclopramide 10 mg i.v., the patient was transferred to the operating theatre, where general anaesthesia was induced with i.v. Althesin 5 ml and diazepam 10 mg, the patient having starved for at least 8 h.

On being placed in the lithotomy position, the patient regurgitated approximately 500 ml of green bile-stained fluid. The mouth, larynx and pharynx were suctioned under direct vision and a tracheal tube was passed, with subsequent endotracheal suction. A small Ryle’s stomach tube was passed and suction applied with little result. The lungs were ventilated with pure oxygen. At termination of the operation, the patient was transferred to the critical care unit for observation, with a Ryle’s tube in place. Air entry in the left lung was noted to be diminished. Twenty-four hours later, she was transferred to the ward, breathing air.

Subsequently the patient developed evidence of aspiration pneumonia, septicemia and acute renal failure which responded to conservative treatment. Later she underwent total abdominal hysterectomy under general anaesthesia. A badly lacerated septic uterus was removed. After secondary suture of her abdominal wound 1 month later, again under general anaesthesia, she was discharged from the hospital two-and-a-half months after admission.

Regurgitation and aspiration of acid gastric content is well known in association with emergency obstetric anaesthesia, at or near term (Hodgkinson, 1980; Moir, 1980). The patients described here present a disturbing new facet, in that this complication arose in the early months of gestation. We have since adopted a policy that all women presenting for emergency uterine evacuation under general anaesthesia are managed in a manner similar to those presenting for Caesarean section, with the exception of routine endotracheal intubation (Brock-Utne and Downing, 1978; Buley et al., 1978).

References


Oxygen Failure Protection Device

Sirs,—In their description of a new oxygen failure protection device for use in anaesthetic apparatus (Flower, Naqvi and Woods, 1980) the authors state that it fulfils six of the seven principles advocated by Rosen and Hillard (1971), but that the requirement for operation by a gas supply only is “felt to be outdated in 1980”. Unfortunately, the reasons for this view, for which the reader is referred to the introduction, appear to have been omitted, but I cannot agree that abandonment of this principle represents an advance in the specification or performance of an oxygen failure protection device. Though their design is fail-safe, electronic circuits and solenoids are not infallible and there will be times when an anaesthetic machine in good order is unusable for want of a battery. Rosen and Hillard’s requirements are difficult, perhaps impossible, to achieve with a gas-operated device, but it is not clear how recommendations 2 (c) (i) and (ii) (inspired oxygen concentration not less than that of air; no increase in carbon dioxide concentration during either spontaneous or controlled breathing irrespective of breathing system in use) are met by this new device any more successfully than they are by existing designs. Devices such as those fitted by B. O. C. Medishield and Penlon to their anaesthetic machines work reliably, do not need to be switched on or off and are automatically tested during routine checking of the anaesthetic machine. The device proposed by Flower and his colleagues would not meet the requirements of the recently published Canadian criteria for anaesthetic machines (Canadian Standards Association, 1980) and is unlikely to conform to the proposed British and International standards.

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References

