CORRESPONDENCE

ERYTHROCYTE STABILITY IN ETHANOL–SALINE SOLUTIONS

Sir,—In a clinical evaluation of ethanol as an anaesthetic agent, ISAAC and Dundee (1969) and Dundee and co-workers (1970) established that 8% w/v (10% v/v) ethanol in Hartmann's solution was the most satisfactory concentration for i.v. infusion in man and was associated with a low frequency of thrombophlebitis. Sanderson and co-workers (1970) confirmed that in vitro ethanol solutions in concentrations of 2.0–2.5 mol litre\(^{-1}\) (approximately equivalent to 10% v/v) in Hartmann’s solution are least likely to cause erythrocyte lysis. Studies in our laboratory have shown that in vitro haemolysis of human erythrocytes is prevented (less than 5%) in 0.9% sodium chloride solution containing 0.0–10.0% v/v ethanol (Ku and Cadwallader, 1974). Also, our determination of “haemolytic” isotonic coefficients indicated that ethanol at the 10% v/v concentration provided a stabilizing effect on erythrocytes. Higher concentrations of ethanol, however, caused haemolysis; haemolysis was initiated in 11% v/v ethanol and was complete when the concentration reached 14% v/v. To examine this more closely, we obtained from the forearm veins of several 22–46-yr-old Caucasian and Oriental subjects 10 different blood samples, which were placed in 0.9% (0.154 mol litre\(^{-1}\)) sodium chloride solutions containing various concentrations of ethanol. After 45 min at 37 °C, the maximum ethanol concentration which was not associated with haemolysis was 10.1% v/v + SD 0.52. These data confirm that 10% v/v is an optimum infusion concentration for ethanol in an isotonic vehicle and that higher concentrations cause haemolysis.

DONALD E. CADWALLADER

REFERENCES


ANTAGONISM OF KETAMINE BY PHYSOSTIGMINE

Sir,—The preliminary report of Balmer and Wyte (1977) describing a ketamine/physostigmine combination to provide awake analgesia without psychological upset was noted with interest. However, this combination may produce convulsions in some patients. Ketamine alone produced generalized convulsions in 0.28% of 4205 patients, and tonic and clonic movements, without e.g. seizure activity, have also been reported on induction of anaesthesia with ketamine (Parke–Davis monograph).

Physostigmine salicylate is an anticholinesterase which penetrates the blood–brain barrier and possesses analeptic properties (Goodman and Gilman, 1975). It is used in recovery rooms in North America (Brebner and Hadley, 1976) and for rousing patients who have poisoned themselves with tricyclic antidepressants (Newton, 1975). Although imipramine, in large doses, may provoke grand mal seizures, the addition of physostigmine occasionally precipitates them. Convulsions occurred twice in Newton’s study of 21 patients and other instances have occurred in a pilot study (personal communication).

It appears, therefore, that the combination of ketamine with physostigmine could produce convulsions and caution is advised.

ALBAN HOUGHTON

REFERENCES


Sir,—Thank you for the opportunity to reply to Dr Houghton’s letter. His comments are entirely justified, but in our defence may I plead that the rate of dosage of ketamine which we employed is very low indeed. In addition, the very small doses of diazepam administered i.v. may have afforded the patient a degree of protection from seizure activity.

Barnard’s group have experience of approximately 5000 administrations of physostigmine in the past 10 years with no serious sequelae (DiLiberti and O’Brien, 1975) and although ketamine has been associated with e.g. evidence of seizure activity or even frank convulsions, there is a possibility that it may act occasionally as an anti-convulsant (Rucci and Caroli, 1974).

In presenting the paper, I emphasized that we were not recommending the use of physostigmine for awakening patients who had received normal anaesthetic doses of ketamine, and I regret that this stricture was not included in the abstract.

H. G. R. BALMER

REFERENCES


PENTAZOCINE AND TREMOR FOLLOWING HALOTHANE ANAESTHESIA

Sir,—Muscular spasticity and tremor occurs during recovery from general anaesthesia, especially following halothane (Dawkins, 1961), and may be associated with hypoxaemia (Jones and McLaren, 1965). This condition may be prevented or controlled by methylphenidate (Brichard and Johnstone, 1970). However, this drug is an unreliable analgesic, may provoke adrenergic overactivity (Brichard and Johnstone, 1970), causes amphetamine-like drug dependence (Willis, 1974) and is usually included in the D.D.A. drug schedule.

To test the hypothesis that pentazocine might be an effective substitute for methylphenidate in controlling muscular spasticity and tremor following halothane we studied 100 consecutive patients who developed this condition. Fifty-four patients were given pentazocine 30 mg i.v., and 46 received methylphenidate 20 mg i.v. The patients were allocated randomly to the groups which were comparable in terms of age of the patient and type of operation. The same anaesthetic technique was used although this was not standardized and the duration of anaesthesia was not recorded. The patients were observed in the recovery room for 30 min by a trained nurse who did not know which drug had been given. The nurse was asked to record only the presence of tremor, which was regarded as a more objective assessment to make than spasticity.

In all except one of the patients given methylphenidate tremors stopped within a few minutes of the drug being administered and they did not recur. In the one exception, tremor ceased immediately after administration of methylphenidate but recurred slightly. With pentazocine the tremors stopped quickly and did not recur in 46 of the patients, but recurred slightly in seven and were not affected in three.

Pentazocine does not control tremor following halothane anaesthesia as well as methylphenidate, but, where hypoxia is not a serious problem and pain is present, pentazocine 30 mg i.v. reduces both rigidity and tremor and provides useful analgesia with less book-keeping for the nursing staff.

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REFERENCES


London: Faber and Faber.

TRACHEAL CYLINDROMA: ANAESTHETIC MANAGEMENT

Sir,—After the publication of our article “Tracheal cylindroma: anaesthetic management” (Lippmann and Mok, 1977), a further literature survey revealed an article by Geffin, Bland and Grillo (1969). We would like to inform your readers of this paper and to acknowledge that, in ignorance, we failed in our articles to refer to its existence.

Your readers should be made aware also that in the forthcoming Proceedings of the 14th Scandinavian Society of Anaesthesiologist’s meeting (1977) Dr A. Baraka’s presentation on “Anaesthetic problems during the tragic civil war in Lebanon” deals with a case report of a transsected trachea and its management which is similar to the description in both our article and that of Geffin, Bland and Grillo (1969).

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REFERENCES


TOXICITY OF LOCAL ANAESTHETICS

Sir,—Recent advances in the field of local anaesthesia have stirred lively interest in the tissue distribution and metabolism of these drugs. Unfortunately, although much valuable information has been gained from these studies, often much of this work has been done in a clinically irrelevant setting or conclusions have been reached that are at the moment still speculative, or both.

The recent study by Malagodi, Munson and Embro (1977) on the effect of infusion rates on the acute toxicity of etidocaine and bupivacaine in Rhesus monkeys concluded that etidocaine was less toxic than bupivacaine. Accidental intravascular injection of a local anaesthetic solution is the most obvious possibility for acute systemic toxicity. Therefore, it is desirable that acute toxicity studies duplicate infusion rates used clinically in extradural block or peripheral nerve block. In the clinical studies where extradural infusion rates are indicated (Bromage, O’Beirn and Dunford, 1974; Tucker and Mather, 1975) they are in the range 150–450 mg min⁻¹. The low end of this spectrum would correspond to the fastest infusion rate in Malagodi’s study. Contrary to the overall conclusion of the authors, at these injection rates, etidocaine appeared more toxic than bupivacaine, with the seizure dose for etidocaine being 4.76 mg kg⁻¹ as opposed to 5.33 mg kg⁻¹ for bupivacaine. Clinical studies (Scott, Jebson and Boyes, 1973; Scott, 1975) have shown also that the etidocaine toxicity threshold decreases as the infusion rate increases.

The toxicity from systemic absorption of the local anaesthetic also deserves brief consideration. A number of studies have disregarded the behaviour at fast infusion rates, and assumed that the characteristics of the slow infusion rates simulate the systemic absorption from the injection site and that serum concentrations correlate with the appearance of toxicity.

A comparison of the arterial and venous drug concentrations after giving etidocaine and bupivacaine in equal dose (milligram for milligram) have suggested that the resulting plasma concentrations tend to be greater for bupivacaine. However, these differences seem to be less at the higher doses (Bridenbaugh et al., 1974a, b; Moore et al., 1976). These data are again of questionable clinical relevance since they assume that the two local anaesthetics are equipotent. There are a number of studies indicating that this is not so. The potency of bupivacaine has been estimated to be 1.5 to 2 times that of etidocaine (Bromage,