methonium), but also a concentration at a higher level than in the control group.

The causes of these contradictory findings are not clear; however, differences existed in respect to age of the patients, and drugs used. Magee and Gallagher apparently studied adults anaesthetized with thiopentone whereas our observations concerned children under halothane–nitrous oxide–oxygen anaesthesia. Possibly the skeletal muscles react differently in respect to potassium release, depending not only on the type of anaesthetic (Dhanaraj et al., 1975) but also on the age of the subject. This certainly occurs in regard to incidence and extent, in adults, for myalgia (Bush and Roth, 1961) and in children, for hyper-CK-emia (Tammisto, Leikkonen and Airaksinen, 1967) and hypermyoglobinemia (Inagaki et al., 1980).

We have carried out further studies exclusively with children under halothane anaesthesia in which self-taming did not prevent the increases in serum CK activity. On the contrary, the activity was greater than in the control (Plötz and Braun, 1982). Dantrolene 2 x 1 mg kg⁻¹ was ineffective in hindering or reducing the increase in serum potassium; here also even increases of the initial concentration of potassium were observed (Plötz, 1984), a noticeable occurrence (Agoston, 1979) in earlier studies also (Collier, 1979). Dantrolene has nevertheless proved itself effective in preventing hyper-CK-emia (Plötz, Braun and Stallenberg, 1981) and hypermyoglobinemia (Plötz, 1984).

Taking bibliographical references into consideration, Magee and Gallagher reach the conclusion (in spite of their findings) that self-taming has only limited clinical application. As shown by the cited papers, this method appears to bring no benefits whatsoever at least in regard to children. In any case, the multitude of proposed preventive measures as well as contradictory evidence in clinical studies indicate that the problem of side effects on the skeletal muscles induced by suxamethonium apparently cannot be solved by a single comprehensive method.

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REFERENCES


Sir,—Thank you for this opportunity to reply to the comments made by Dr Plötz. When Baraka (1977) introduced the concept of "self-taming" he commented on the reduced incidence of suxamethonium-induced fasciculations, a phenomenon also observed by Plötz (1984). In this light it is interesting to note that the results of Dr Plötz are at variance with our own. However, serum potassium is affected by many anaesthetic agents, and there are differences in the agents used in the two studies.

When anaesthesia is induced with thiopentone followed by nitrous oxide–oxygen, there is a decrease in serum potassium concentration, possibly because of its entry into cells as a result of altered cellular metabolism (Bali, Dundee and Assaf, 1975). Where suxamethonium is administered the increase in plasma potassium concentration is less marked following thiopentone induction than following halothane (Henning and Bush, 1982), and halothane also alters the timing of the increase in serum potassium where a delay in peak effect is seen (Bali, Dundee and Assaf, 1975). We agree with Dr Plötz that there may also be differences in the reaction of children as compared with adults. We feel that these differences may explain Dr Plötz's results, and confirm our own conclusions that the technique has limited clinical applicability.

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REFERENCES


NALOXONE—A STRONG ANALGESIC IN COMBINATION WITH HIGH-DOSE BUPRENORPHINE?

Sir,—Buprenorphine is a synthetic opiate, with partial agonist and antagonist properties. The dose–response curve as far as analgesia is concerned is bellshaped when determined in
animals (Rance, Lord and Robinson, 1979; Dum and Herz, 1981). This curve has not been determined in man. Naloxone is an opiate antagonist without intrinsic agonist activity. It has been shown by Rance, Lord and Robinson (1979), in animal studies, that prior treatment with naloxone significantly reduced the analgesic action of low doses of buprenorphine. On the other hand, with the use of high doses of buprenorphine (above the maximum of the biphasic dose–response curve) prior treatment with naloxone potentiates the agonistic properties of buprenorphine; for example, the dose–response curve is shifted to the right. Dum and Herz (1981) injected naltrexone and found a symmetrical shift of the entire buprenorphine dose–response curve to the right. As a result, the agonist potency of the higher doses of buprenorphine was actually increased by the antagonist (naltrexone).

We have used buprenorphine in doses of 30 and 40 μg kg⁻¹ as the sole i.v. analgesic in balanced anaesthesia to patients scheduled for cholecystectomy.

Two otherwise healthy females patients (19 and 28 yr) were premedicated with diazepam 0.3 mg kg⁻¹ orally 2 h before surgery. One patient received buprenorphine 40 μg kg⁻¹ the other 30 μg kg⁻¹. After 15 min anaesthesia was induced with diazepam 0.1 mg kg⁻¹ and thiopentone 2–3 mg kg⁻¹. The patients received pancuronium 1 mg as precurarization, and oral intubation was facilitated with suxamethonium 1.5 mg kg⁻¹. Droperidol 2.5 mg was used as an antiemetic. The lungs were ventilated using a mixture of 70% nitrous oxide in oxygen. Muscle relaxation was maintained with pancuronium. No objective signs of pain were observed during surgery. The durations of surgery were 75 and 105 min. Neur omuscular blockade was antagonized using a mixture of neostigmine 2.5 mg and atropine 1 mg.

Immediately following the termination of anaesthesia both patients complained of severe pain, which was aggravated by deep inspiration. In an attempt to counteract what was assumed to be an antagonistic effect of buprenorphine, naloxone was administered i.v. in repeated small doses to a total of 0.08 and 0.4 mg, respectively, and was followed by total pain relief. The patients could breathe deeply without pain and were only slightly sedated. Respiration was adequate, as judged by respiratory rate and arterial blood-gas analyses. Following the injection of naloxone, the patients were without pain for 17 and 21 h, respectively. They then received buprenorphine 0.3 mg i.m. with good effect.

A possible explanation for these events could be that the high doses of buprenorphine resulted in antagonistic dominance, leading to insufficient pain relief. We counteracted this unintended effect, using a pure opiate antagonist, naloxone, which induced adequate pain relief of long duration. These observations are in agreement with the results found in the earlier studies on animals.

Two immediate questions come to mind: how can such a small dose (0.08 mg) of a short-acting drug such as naloxone have such a prolonged effect (17 h)?, and how is it that a dose of buprenorphine that was unable to obtund the severe pain immediately after the operation was effective as sole analgesic element of anaesthesia during the cholecystectomy? Further speculation based on our limited data would be fruitless, and controlled studies in man are needed to elucidate these matters.

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REFERENCES

RESPIRATORY PROBLEMS AFTER ATROPINE AND NEOSTIGMINE IN DOGS

Sir,—Jones and Clutton (1984) reported that, in their series of 22 canine patients given atracurium besylate, one dog which showed normal reversal of neuromuscular blockade following the injection of atropine and neostigmine, and which was observed 5 min later to have good respiratory function, developed cyanosis with obviously inadequate respiratory movements over the next 5-min period. The problem was resolved by re-intubation, respiratory support with oxygen and the injection of a further dose of neostigmine with atropine.

We have recently experienced what appeared to be a similar problem in two of 66 dogs which were observed to have good respiratory function for several minutes after reversal of atracurium-induced neuromuscular blockade with neostigmine and atropine. One dog stopped breathing 15 min later and the other 25 min later. During these periods both dogs were under constant nurse surveillance and resuscitative measures were instituted promptly.

The incidence of 1 in 22 cases as reported by Jones and Clutton and 2 in 66 of our cases is a cause of some concern to veterinary anaesthetists and we would be interested to learn whether any similar problems have been encountered in the use of atracurium in man.

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REFERENCE