CORRESPONDENCE

CORTICOSTEROIDS AND RESISTANCE TO VECURONIUM

Sir,—In the interesting paper [1] on the possible mechanisms for resistance to vecuronium observed in patients receiving chronic treatment with corticosteroids, Parr and colleagues did not mention the steroid-induced proliferation of acetylcholine receptors (AChr) observed by Kaplan and co-workers on cultured human muscle. They reported that dexamethasone seems to act "by inducing de novo AChr synthesis rather than by stimulating insertion of pre-existing AChr into the plasma membrane" [2]. Another important observation is that the response to dexamethasone seems to be species-specific and is not accompanied by alterations in acetylcholinesterase activity.

These observations indicate that the quantity and quality of post-synaptic AChr could be abnormal in skeletal muscles of patients receiving chronic treatment with corticosteroids. Whether the total number of AChr or the relative preponderance of the new population of AChr is the factor to which is ascribed the resistance to vecuronium is unknown.

The second hypothesis should be favoured for the following reasons: the immature form of AChr has a reduced affinity for curare [3]; liability to hyperkalaemic accidents caused by suxamethonium is relatively common in neurosurgical patients (without motor deficit) and seems to be absent in patients with myasthenia gravis [4] in spite of chronic treatment with large doses of corticosteroids.

F. FIACCHINO
A. GIANNINI


Sir,—We acknowledge the useful comments by Drs Fiaccino and Giannini regarding the role of increased numbers of post-junctional acetylcholine receptors (AChr) in the corticosteroid-induced resistance to vecuronium. We agree that increased AChr numbers could explain, in part, the resistance to vecuronium, although we consider enhanced acetylcholine release by betamethasone is potentially the major mechanism, for the following reasons:

1. Enhanced transmitter release reaches a plateau effect within 1 h after steroid administration [1], whereas the induction of steroid increased AChr synthesis and incorporation into the muscle cell membrane in vivo requires up to 24 h to develop [2]. This immediate effect associated with enhanced transmitter release is consistent with our observations in isolated nerve–muscle preparations.

2. Meyers [3] reported a patient receiving long-term steroid treatment who had residual paralysis after pancuronium neuromuscular blockade. The block was antagonized successfully within 4 min of hydrocortisone administration. The rapidity of this response also suggests an effect on neurotransmission rather than AChr numbers.

The mechanisms by which steroids antagonize neuromuscular blockade are likely to be multifactorial, and at present we can only speculate on the cause, based on previous scientific and clinical observations.

B. J. ROBINSON
D. REES
D. C. GALLETTLY


PEAK SERUM BUPIVACAINE CONCENTRATION

Sir,—Dr Pihlajamäki has investigated the relationship between body weight and peak serum concentrations (Cmax) of bupivacaine in a local analgesic agent [1]. Would one expect the relationship to be linear? If so, then the data presented predict a negative Cmax for a patient exceeding 124 kg and a Cmax for a neonate only twice that of an average adult. Clearly, as the title implies, one would expect the data to exhibit a reciprocal relationship:

\[ C_{\text{max}} = \frac{K}{\text{weight}} \]

Would it not have been more appropriate, therefore, to plot 1/Cmax against weight before performing least squares regression? This may have produced a better fit to the data and led to a different conclusion.

A. M. J. ATHERTON

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Sir,—I agree that, from my results, it is not possible to gain any information on blood concentrations in neonates or in overweight adults. However, I would doubt if results from adult patients could be extrapolated to a newborn or even a young child. In contrast, obese adult patients are not a problem, if we take the basic starting point of my study, that the authorities of many countries recommend the dose of bupivacaine to be restricted to 2 mg/kg body weight. Thus both ends of the regression line are not important.

Concerning adult patients weighing 35–100 kg (the range covered in the study), it is possible to assume a linear relation and thus to accept the method and the conclusion [1]. When plotted as 1/Cmax against weight, the least squares regression line is \( y = 0.0073x + 0.2204; r = 0.4483; t = 2.924; \ p = 0.0061. \) Thus only 20% of the total variance could now be explained by regression (\( r^2 = 0.2009 \)).

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IS STEROID THERAPY A CONTRAINDICATION TO EXTRADURAL ANALGESIA?

Sir,—We read with interest the important case report by Dr Sowter and colleagues [1]. They described a patient with rheumatoid arthritis receiving steroids who developed an extradural abscess 23 days after the removal of an extradural catheter and suggested that extradural analgesia should be contraindicated in patients with rheumatoid arthritis taking steroids. In our opinion such a suggestion, based on a single case, is premature.
Another report of iatrogenic extradural abscesses (which makes Dr Sowter's paper the third, and not the second, report of extradural abscesses with delayed presentation), described a woman who developed an abscess 9 days after removal of an extradural catheter. The possibility was suggested of a distant focus of infection from which bacteria could spread to the extradural space, as in the patient reported by McDonough and Cranney [2]. Dr Sowter and colleagues say only that it had not been possible for them to determine how infection developed in their patient, but it is not clear if they looked actively for a distant focus (i.e. dental caries) or if they had negative blood cultures.

Steroids are given frequently by the extradural route for the management of chronic back pain. No cases of delayed extradural abscess have been described in such patients, despite the facts that the steroid is administered directly into the extradural space and that adrenal suppression has been described up to 3 weeks after a single dose of methylprednisolone acetate 80 mg [3]. It is also common to use long-term extradural combination therapy in patients with cancer pain who are taking oral steroids. Again, there are no reports to date of extradural abscesses in this patient group.

We do not see concurrent steroid use as an absolute contraindication, but would suggest that both local steroid injection and systemic steroid therapy may increase the chance of infective complications. The crucial problem with this rare and potentially devastating complication is the delay in presentation which is a common feature of these reports. The only saving grace is the fact that pain appears to be the most consistent presenting symptom. The lesson must be that an extradural abscess should be high on the list of differential diagnoses in patients presenting with pain after extradural analgesia. We agree that, when a patient complains of back pain after the use of extradural analgesia, even some time after discharge from hospital, the diagnosis of extradural abscess must be considered and urgent efforts must be made to exclude it.

H. J. MCQUAY
A. R. JADAD
Oxford


Sir,—We are grateful for the opportunity to respond to the letter from McQuay and Jadad. We agree that, considering the frequent use of extradural analgesia in patients receiving steroid therapy and the use of extradural steroid injections in the management of back pain, the development of an extradural abscess is a surprisingly rare complication of this technique.

Despite a careful search for a distant focus of infection in our patient, we were unable to locate one. Our patient had no evidence of any skin, chest or urinary infection, all his teeth had been removed several years previously, blood cultures were negative and he remained afebrile throughout his postoperative course.

To regard extradural analgesia as contraindicated on the basis of one case report probably is being premature although, following our experience with this patient I think that we should be reluctant to use an extradural block in any similar patient in the future.

However, we do feel that this case has some important lessons. It demonstrates that extradural abscesses may have devastating results: they may evolve rapidly from the first symptoms of pain to irreversible neurological damage; they may present after a symptom-free interval of many days; and they may present after an apparently uneventful postoperative recovery. We agree that, when a patient complains of back pain after the use of extradural analgesia, even some time after discharge from hospital, the diagnosis of extradural abscess must be considered and urgent efforts must be made to exclude it.

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