Changes in S100B levels rather than absolute values may be a better marker of severity of septic encephalopathy

Editor—We read with interest the article by Piazza and colleagues,1 where they report that elevated S100B levels did not correlate with the severity of encephalopathy during sepsis. We would like to ask the authors that even though the S100B levels did not correlate with the severity of encephalopathy on ICU admission, whether the rate of increase in serum S100B levels could be indicative of severity of encephalopathy. The time of ICU admission is a variable in itself, in terms of when the duration of sepsis began. In fact, a third of the patients, three with GCS scores ≤8, had normal range S100B levels at the time of admission. We assume that these values did not remain at normal levels but proceeded to increase. Investigating the rate of change of serum S100B levels at an individual level would allow the removal of inherent individual variation due to sex or to age—which in this study spans 47–84 yr.

S100B expression is not restricted to neuronal tissues2 and serum S100B levels have been shown to be increased after bone fractures3 or after ischaemia of the liver, gut, or kidney.4 Therefore, S100B may be elevated during sepsis alone, and it may be that the rate of release of serum S100B is higher if there is an underlying encephalopathy, in addition to sepsis. This rate of increase in serum S100B levels may be a more sensitive readout of ongoing pathology, with high rate of increase indicating an underlying brain encephalopathy. In the present study, the average S100B levels seem to be increased at day 7 compared with levels at ICU admission, with a larger spread indicating some patients have lower levels whereas other patients have much higher levels than the average. It would be interesting if this rate of release of S100B was an indicator of prognosis, where if S100B levels are still increasing by day 7, prognosis may be poor and a slight increase or decrease would indicate a better prognosis.

J. K. Panni*
M. K. Panni
TX, USA
*E-mail: joana.k.panni@uth.tmc.edu

Drs Panni suggest that S100B changes rather than absolute values may be a better marker of severity of sepsis-associated encephalopathy. They assume that comatose patients who have normal S100B values on ICU admission may proceed to higher values later. As previously described,1 our sepsis patients showed alteration of consciousness at admission; they did not develop it during their ICU stay. In our experience, S100B was measured at ICU admission and after 3 and 7 days: there was not any correlation with neurological outcome at any time point. Any prognostic marker should be precocious and specific: we respectfully disagree with Drs Panni when they suggest that the rate of S100B increase after 7 days of coma may add useful information in prognosis formulation but we support the hypothesis that S100B serum levels measured by commercial ELISA kit do not allow the observers to distinguish brain S100B release from peripheral tissues production.5

O. Piazza*
E. Russo
S. Cotena
G. Esposito
R. Tufano
Naples, Italy
*E-mail: orpiazza@unina.it
Effects of acetylcholinesterase inhibitor therapy for Alzheimer’s disease on neuromuscular block

Editor—Acetylcholinesterase inhibitors (donepezil, rivastigmine, and galantamine) are now currently recommended in the management of moderately severe Alzheimer’s disease.1 Therefore, it is likely that over time, an increasing number of anaesthetists will encounter patients taking this type of medication yet there is sparse literature on interactions with anaesthetic drugs nor is there guidance regarding perioperative management. We would like to draw the readers’ attention to a case which illustrates the difficulties which can be experienced with this group of patients when undergoing anaesthesia requiring muscle relaxation.

A 70-yr-old gentleman was being anaesthetized before a hemiarthroplasty for a fractured left neck of femur. His regular medications consisted of donepezil 10 mg, alfuzosin 10 mg, beclometasone 200 μg, Combivent 2 puffs, ferrous sulphate 200 mg, and Co-careldopa 12.5/50 mg. After induction with propofol, he was given atracurium 30 mg. A train-of-four (TOF) stimulus with a peripheral nerve stimulator produced four twitches with no evidence of fade. Intubation was achieved, but the patient coughed due to the lack of neuromuscular block. The patient breathed throughout the 45 min operation; a further 10 mg of atracurium was given during surgery, but there remained a full response to further TOF stimulation. He was extubated successfully 45 min post-induction without the use of reversal agents.

Reference to the British National Formulary supports the suspicion that donepezil was the agent most likely to be responsible for the lack of neuromuscular block as it ‘possibly antagonizes the effects of non-depolarizing muscle relaxants’. The patient’s other medications do not share this property. Rivastigmine is also known to antagonize the effect of non-depolarizing neuromuscular blocking agents.2

As previously mentioned, there is currently little literature on the subject. A study in rats found that tacrine (a centrally acting anticholinesterase) administered chronically caused resistance to neuromuscular block with d-tubocurarine. This would add weight to the hypothesis that donepezil antagonized the atracurium in our patient’s case. In this animal study, resistance decreased with time, possibly due to Ach-receptor down-regulation.3

Depolarizing neuromuscular blocking agents can also be affected by anticholinesterases. Donepezil may, and galantamine and rivastigmine are, known to enhance the effect of suxemethonium.2 Prolonged relaxation in a patient taking donepezil who was paralysed with suxemethonium has been described in the literature.4

An abstract from a Spanish article describes prolonged relaxation with succinylcholine and inadequate response to high doses of atracurium in a patient taking donepezil, demonstrating both of the aforementioned phenomena in one patient.5

We think it important and timely that these significant interactions are brought to the attention of other anaesthetists as we expect that patients on anticholinesterases requiring anaesthesia with neuromuscular blocking agents will present with increasing frequency in the future. We would also recommend the cessation of anticholinesterases 3–4 weeks before anaesthesia wherever possible. This should not have a detrimental effect on the patient’s overall cognitive function, as anticholinesterases may have no disease modifying action.6

J. Baruah
J. Easby
G. Kessell*
Dundee and Middlesbrough, UK
*E-mail: gareth.kessell@stees.nhs.uk

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