Correspondence

Perioperative glycemic control and postoperative cognitive dysfunction: an expression of caution

To the Editor:

If we are to try to decrease the incidence of postoperative cognitive dysfunction (POCD) by aggressively treating hyperglycemia perioperatively, we first need to be sure we are not harming our patients while we try to attain this laudable goal. In his informative editorial about hyperglycemia and POCD, Dr. Grocott asserts that “the best clinical studies in this field of research to date are observational and thus define only an association of hyperglycemia to POCD”.¹ Assuming that stroke is accepted as a form of POCD, a recent prospective, randomized, controlled trial (not observational data) has demonstrated a higher rate of stroke in patients treated with intensive insulin therapy during cardiac surgery.² In this study, 4% of patients in the intensive insulin arm had a stroke, *vs* 1% in the conventional treatment arm. Rather than highlighting “some potential flaws in these links between hyperglycemia and other adverse outcomes”,¹ this study raises disturbing questions about whether anesthesiologists are too quickly adopting a treatment that we do not yet fully understand. In an editorial concerning this trial, Van den Berghe writes “... we should regard tight glucose control during cardiac surgery as experimental and confine its use to clinical trials”.³

Although it is true that Van den Berghe’s trial in 2001⁴ (in mostly cardiac surgical patients) demonstrated a mortality reduction in the group of patients treated with tight glucose control in the intensive care unit (ICU), four subsequent prospective randomized controlled trials in critically ill patients have not shown any mortality benefit of intensive insulin therapy in the ICU, but *have* demonstrated a fourfold to tenfold higher incidence of hypoglycemic episodes.^{5–8} Two of these trials were stopped early because of safety concerns in the intensive insulin arms,^{6,7} and the use of tight glucose control in the critical care literature is currently being actively debated.⁹ (Hopefully, with

the publication of the NICE-SUGAR trial,^A expected to enroll 6,100 patients in over 35 ICUs throughout Australia, New Zealand, Canada, and the USA, we will have more information – at least in the ICU setting).

Extrapolating data from the critical care domain into the intraoperative domain must be done with due caution. Anesthesiologists should be committed to providing evidence that any novel therapies proposed as part of intraoperative/perioperative management will ensure a measurable benefit to our patients, with an acceptable risk profile. The animal data on glycemic control are promising, and while the pathophysiologic link is compelling, the clinical data is not incontrovertible in this particular case. Further research will clarify the role of commencing tight glycemic control intraoperatively.

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Reply:

I appreciate the interest in my editorial regarding a potential link between perioperative hyperglycemia and postoperative cognitive dysfunction (POCD).¹ As previously alluded to, despite the associative link that was demonstrated in the study by Puskas et al.,² we are far from understanding whether there is any causative link between hyperglycemia and POCD. Although it is convenient to think of POCD and stroke on different ends of the same cerebral ischemic continuum, this may be an erroneous assumption, particularly as the pathophysiology of POCD is not well understood. As a result, putting the Puskas et al. POCD findings in the same context with the Gandhi et al.,³ where patients receiving intensive insulin therapy had a higher stroke rate, may be misleading.

I wholeheartedly agree with you that anesthesiologists are at risk of “too quickly adopting a treatment that we do not yet fully understand”. Although the adoption of this therapy is clearly well-intentioned, changing practice patterns based on a single positive trial (van den Berghe et al.)⁴ or a negative trial (Gandhi et al.)³ should be cautioned against. Rather, it should be the overall weight of the evidence that determines what therapy is best adopted. To that end, we should await future trials of glycemic control in cardiac surgery⁵ to determine how best to deal with these patients; until then, it is prudent to be cautious in how aggressively we manage perioperative hyperglycemia.

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Safeguarding against errors with free flow protection devices of patient controlled analgesia systems

To the Editor:

Patient controlled analgesia (PCA) devices can provide improved treatment of postoperative pain. Despite their apparent safety, adverse drug events (ADE) continue to be associated with their use. Etiologies of ADE include errors in programming, errors in preparation of the narcotic solution, and unintentional free flow of narcotics into the patient's intravenous tubing. Free flow protection devices (FFPD) have been incorporated in these pumps in order to prevent the latter problem, in an effort to improve safety.

I read with interest the recently published letter by Dr. Doyle et al.,¹ entitled: “Another failure mechanism leading to patient-controlled analgesia overdoses”. In this case, failure of a Baxter PCA pump was attributed to failure of the FFPD, as a result of unrecognized damage to the device. There was a similar case in our hospital, which involved a different manufacturer of PCA. The patient was initially stable in the postanesthesia care unit, following laparoscopic abdominal surgery. Immediately after starting postoperative analgesia with a Curlin Medical PCA (Huntington Beach, CA, USA), the patient became obtunded, and was nearly apneic. The entire content of the PCA medication bag, containing 100 mg morphine, had been administered to the patient. As in the case reported by Dr. Doyle et al., the patient responded to treat-

B *ClinicalTrials.gov*. A service of the US National Institutes of Health. Available from URL: www.clinicaltrials.gov/ct2/show/NCT00524472?term=hyperinsulinemic&rank=1 (accessed May 2008).