In humans, the addition of epinephrine has not emerged as a risk factor for neurological injury associated with PNB, and bupivacaine-associated neurological injury has been reported inconsistently. To date, no nerve localization or monitoring technique has been shown to be superior in terms of reducing the frequency of clinical injury.[7] Although the experience with the "perivascular ultrasound-guided technique" is actually less extensive, there is no reason to think that it would be more prone to induce neurological injury than would be a transaxillary artery technique. A tourniquet may cause neurological damage. High inflation pressures (> 400 mmHg) and longer tourniquet times increase the likelihood of a tourniquet-induced neurological injury. There is no convincing evidence that patients with underlying neurological disease have an increased susceptibility to any of these factors. In their recently published recommendations, the American Society of Regional Anesthesia suggests the adoption of a prudent approach for these patients: consider avoiding the more potent local anesthetics, reducing the local anesthetic dose and/or concentration, and avoiding or limiting vasoconstrictive additives (epinephrine 1:400,000 or less).[7] In animal studies, at a concentration of 2.5 $\mu g \cdot mL^{-1}$, epinephrine alone produces a transient increase in peripheral nerve blood flow, while at higher concentrations a decrease is most often reported.

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Gabapentin and post-thoracotomy shoulder pain

To the Editor:

In their editorial, Drs. MacDougall and Slinger[1] comment about the wide range of a single dose of preemptive gabapentin (neurontin) studied in clinical trials, i.e., from 300 mg to 1200 mg.[2-3] This, I believe, underscores a lack of understanding of the pharmacology of gabapentin in the anesthesiology community.

The absorption of gabapentin is dose dependent, secondary to a saturable transport mechanism in the intestine. Hence, the bioavailability of doubling a single dose of gabapentin from 300 to 600 mg decreases from 60 to 40%.[4] In other words, doubling the dose of gabapentin in the clinical range of 300 to 600 mg will not double the amount of drug absorbed. Instead, it will only increase the quantity of drug absorbed by 33%. This has been noted in a recent systematic review of perioperative gabapentin.[5] In their paper, Tiippana and colleagues observed that metaregression analysis suggested that the single dose of preemptive gabapentin induced reduction in the 24-hr opioid consumption was not significantly dependent on the gabapentin dose. The dose studied varied from 300 to 1200 mg.

A word of caution: Pfizer Inc. has launched a new drug with properties very similar to gabapentin, i.e., pregabalin (lyrica). In the near future, this drug will likely be studied extensively in the perioperative setting. Although acting on the same receptors, both drugs differ markedly in their absorption characteristics. Contrary to gabapentin, pregabalin has a bioavailability of 90% that does not vary in the normal range of 25 to 300 mg *po* (equivalent to 150 mg to 1800 mg of gabapentin). So, in contrast to gabapentin, increasing doses of pregabalin should significantly increase the bioavailability of the drug, which, in turn, may increase its effectiveness or improve its side-effect profile.

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Reply:

We wish to thank Dr. de Médicis for his comments on our recent editorial. He has noted an interesting point regarding gabapentin, specifically, the saturable gut transport mechanism. In the world of chronic pain management, this phenomenon is well known.[1] Improved transport has been quoted by the manufacturer as a reason to use pregabalin in the treatment of neuropathic pain. Pregabalin has undergone limited trials in the perioperative period.[1–6] Pain reduction and opioid sparing effects have both been noted after perioperative administration. In a manner reminiscent of the perioperative studies of gabapentin, pregabalin doses have spanned a wide range from 50 mg to 600 mg.[2–6] At least one study has included a postoperative dose.[5] Recently, Agarwal et al.[2] demonstrated that a single dose of 150 mg of pregabalin, given before laparoscopic cholecystectomy, significantly reduced pain and opiate requirements. Pandey et al.[7] conducted a placebo-controlled dose-ranging study of gabapentin for spine surgery and, using visual analogue scale scores and opiate sparing as outcome measures, reported that 600 mg was the optimal dose. Pregabalin 300 mg and 600 mg, given in two divided doses before and after surgery, did not improve pain control after laparoscopic hysterectomy when compared to a diazepam active placebo.[5] However, in a similar trial of 75 mg and 150 mg given prior to laparoscopic gynecologic surgery, the latter dose was noted to be superior to an active placebo.[6] Clearly, more work is necessary to define the role of pregabalin in the perioperative period. Results such as this might suggest that, in addition to a saturable gut receptor, there may be a saturable or modifiable receptor involved in the modulation of pain by this unique class of drugs.

Again, this unique class of drugs provides us with a clinical advantage in management of acute pain as well as a unique opportunity to improve our understanding of the mechanisms responsible for pain.

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