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Neurotoxicity of Local Anesthetics

To the Editor:—The altered perineural permeability, edema, and nerve fiber injury after local anesthetics as described by Myers *et al.*¹ provide interesting reading. It is unfortunate that the two local anesthetics incriminated in causing some degree of nerve damage were not plain local-anesthetic solutions. The 3% 2-chloroprocaine HCl used contained 0.2% sodium sulfite and the 1% tetracaine HCl contained 0.2% sodium bisulfite. The amide local anesthetics used contained no antioxidants.

As there already exists the question of possible neurotoxicity from the antioxidants rather than the local anesthetic,^{2,3} perhaps it would be more relevant if the control group in the article by Myers *et al.*¹ had been the antioxidant with sodium chloride. If the results were unchanged, then their conclusion, that the two ester local anesthetics are less safe than the two amide local anesthetics, is given more credence.

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In reply:—Our investigations into the neurotoxicity of local anesthetics were stimulated by the clinical reports and debate concerning the neurotoxicity of Nesacaine-CE[®] following inadvertent injection into the subarachnoid space. As noted by Dr. Cartwright, Wang *et al.*¹ have developed a rabbit model to mimic the clinical problem and have shown that sodium bisulfite is neurotoxic when evaluated with clinical measurements of function. Many of the initial investigations by other laboratories appeared to be inconsistent, variably reporting that neurotoxicity might be the result of the Nesacaine-CE[®] vehicle,¹ the local anesthetic 2-chloroprocaine,² or any local anesthetic.³ These results appeared to be resolved by the observations of Gissen *et al.*,* who attributed nerve injury

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to sodium bisulfite at low pH. Unfortunately, their model does not explain cases in which nerve injury was observed with other local anesthetics (*e.g.*, reference 3) or in which neurotoxicity was not differentially produced by the bisulfite-containing 2-chloroprocaine solution when compared with other local anesthetics.⁴

In the discussion we stated that, "On the basis of these findings, we would not agree that local anesthetics of the ester type are relatively more safe than the amide type. Dose-response studies are necessary, however, to further test this hypothesis." We have subsequently found no evidence for distinguishing between the toxicity of ester- and amide-linked local anesthetics in this model.⁵† Commercial preparations of four amide-linked and three ester-

* Gissen AJ, Datta S, Lambert D: The chloroprocaine controversy. II. Is chloroprocaine neurotoxic? *Regional Anesthesia* 9:135-145, 1984.

† Kalichman MW, Powell HC, Myers RR: Pathology of local anesthetic-induced nerve injury. (submitted for publication).

linked local anesthetics were studied in addition to fresh preparations of lidocaine, 2-chloroprocaine, and procaine. Numerous control solutions have also been tested, including: distilled water; bacteriostatic 0.9% saline; 0.2–10% sodium chloride; and 0.1–0.4% sodium bisulfite in 0.2% NaCl and water. Our conclusion is that local anesthetics and not their antioxidants or preservatives are neurotoxic in a dose-dependent manner.⁵

These additional studies do not support the hypothesis originally proposed by Gentilli *et al.*³ that ester-type local anesthetics are more neurotoxic than amide-type local anesthetics. In addition, it is clear in this model that the local anesthetics, including 2-chloroprocaine, and not the Nesacaine-CE® vehicle, are neurotoxic. We thank Dr. Cartwright for this opportunity to elaborate on our report.

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On the Efficacy of the Priming Principle with Vecuronium

To the Editor:—We read with interest the recent report by Taboada *et al.*¹ on priming with vecuronium (VEC). The authors, in evaluating priming doses of 5, 10, 15, and 20 µg/kg VEC administered to sedated patients prior to anesthesia, found a decrement in twitch tension in none of the ten patients receiving 5 µg/kg and only one of the 11 patients receiving 10 µg/kg VEC. This is surprising, since O'Hara *et al.*² found 6% twitch depression in young adults receiving 10 µg/kg, and Engbaek *et al.*³ report significant decrements in train-of-four ratios and numerous subjective signs and symptoms after both 5 and 10 µg/kg.

An additional consideration is the fact that the patients of Taboada *et al.* were heavily sedated. They received morphine sulfate 10 mg im, diazepam 10 mg po, fentanyl 50–100 µg iv, and/or diazepam 5–10 mg iv. A comparison of the side effects and symptoms listed by Taboada *et al.* with those of Engbaek *et al.* for 5, 10, and 15 µg/kg VEC doses shows a much higher incidence in Engbaek's

unmedicated patients. We suggest that the heavy sedation may have resulted in underestimation of these problems.

We share the view of Taboada *et al.* that a priming dose causing the fewest side effects should be the one advocated. They selected the 10 µg/kg VEC dose using this criterion. However, inspection of their table 2 clearly shows that the incidence of "blurred vision" was significantly lower in the 5 µg/kg VEC group than in all other groups. The 5 µg/kg group, therefore, had the fewest overall side effects.

Taboada *et al.* note that the 5 µg/kg VEC priming dose provides no improvement in time to 80% or 100% reduction of twitch tension over their controls (0 µg/kg) when administered 4 min prior to an intubating dose of 0.1 mg/kg VEC. This, along with a previous report,⁴ puts the efficacy of priming with VEC in doubt.

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