

CORRESPONDENCE

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In Reply:—We appreciate the interest in our manuscript and the comments contained in these two letters. Drs. Tanaka and Nishikawa express concern regarding our use of a phenylephrine solution containing sodium bisulfite. The purpose of our study was to determine whether transient neurologic symptoms commonly follow spinal anesthesia with 0.5% tetracaine and whether the presence of phenylephrine affects their occurrence.¹ Phenylephrine was chosen for our study because it is one of two standard vasoconstrictors used for prolongation of spinal anesthesia, and it is the agent most commonly used for this purpose at Shimane Medical University. The solution contained sodium bisulfite because, to our knowledge, all phenylephrine (and epinephrine) commercially available in Japan and in North America contains this antioxidant. Thus, aside from the practical problems of using a solution free of antioxidant, use of a nonstandard formulation would have limited the clinical relevance of our study.

Drs. Tanaka and Nishikawa question whether the sodium bisulfite might be responsible for the high incidence of neurologic symptoms associated with phenylephrine. We agree that such an effect cannot be excluded on the basis of our study. However, their statements regarding the toxicity of this compound are misleading, and their review of relevant literature is incomplete. They comment that the phenylephrine solution "contained 0.1% sodium bisulfite, well known for its neurotoxicity intrathecally" but fail to consider appropriately the significance of the dose and concentration administered. First, concerns regarding the potential toxicity of bisulfite arose from persistent neurologic deficits associated with possible intrathecal administration of intended epidural doses of chloroprocaine.²⁻⁴ In these cases, patients received between 16 and 27 ml of solutions containing 0.2% bisulfite, which corresponds to 40–70 times the maximum dose of sodium bisulfite used in our study. Second, they comment that the amount of sodium bisulfite our patients received was "approximately half the dose that caused permanent hind-limb paralysis in rabbits," but fail to consider the relative size of the experimental animal, e.g., if expressed on a per-kilogram basis, the dose of bisulfite given to these animals was approximately 25 times our maximum.⁵ Finally, Tanaka and Nishikawa note that the concentration of sodium bisulfite we used was "approximately one tenth the concentration causing irreversible loss of a spinal monosynaptic reflex in rats." However, a 10-fold difference in concentration is not insignificant, a point that can be readily appreciated if one attempts to apply a similar standard of safety to intrathecal local anesthetics. Additionally our phenylephrine solution was diluted fourfold before administration; thus, the concentration of bisulfite producing loss of reflex in the rat was actually 24 times greater than that used in our study, whereas concentrations eight times greater than ours had no apparent toxicity.⁶

Drs. Tanaka and Nishikawa fail to adequately review the conflicting evidence concerning bisulfite toxicity.^{7,8} As they note, some investigators found the antioxidant to be neurotoxic,^{5,6} but others observed toxicity with preservative-free 2-chloroprocaine but not with 0.2% sodium bisulfite.⁷ Moreover, other experiments documented bisulfite toxicity only in the presence of a low pH, suggesting that liberation of sulfur dioxide might be the etiology of injury.⁸ The pH of our

solutions ranged from 7.52 to 7.62, well above the range associated with toxicity in these experiments.

Dr. Lambert's comments reiterate our concerns regarding continued use of phenylephrine to extend tetracaine spinal anesthesia. We also question the need to use vasopressors in combination with intrathecal local anesthetics and believe the evolving clinical data¹ and experimental evidence⁹ justify careful reexamination of this practice.

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