Correspondence

Neuromuscular blockade and ventilatory failure after cyclosporine

To the Editor,

In the retrospective study by Sidi *et al.*[1] we feel that the authors fail to support their conclusions adequately. They reported incidents of prolonged neuromuscular blockade and ventilatory failure after renal transplantation – eight patients out of 65 over a one-year period. They conclude that the administration of 5 $mg \cdot kg^{-1}$ cyclosporine *iv* contributed to this complication. As support for their argument they state that three of the eight patients with respiratory failure received cyclosporine ($P < 0.05$ by Fisher's exact test). They quote the publications by Gramstad *et al.* and Fragen *et al.* – work performed in an animal model (cats) and *in vitro*, but not yet confirmed in humans. In the other five they were unable to offer an explanation, disregarding the drugs used for premedication.

Their routine premedication included ranitidine 150 mg and 20 patients received diazepam 5–10 mg. Was there any correlation between the patients with prolonged neuromuscular blockade and respiratory failure and premedication with diazepam?

Diazepam has muscle relaxant properties[2] and an elimination half-life of 20–40 hr with active metabolites which have an even longer half-life.[2] It is also highly protein bound and patients with chronic renal failure have an increased unbound fraction.[2,3] Further, histamine H_2 receptor antagonists inhibit the oxidative metabolism of diazepam.[2]

Despite the routine infusion of 5 $mg \cdot kg^{-1}$ of cyclosporine commenced one hour prior to surgery and given over four hours, prolonged neuromuscular blockade and respiratory failure is an extremely uncommon complication in our renal transplant patients. We reviewed all our renal transplants performed in 1989 (104 patients) and 1990 (107 patients). In the 211 transplants, all but six patients received cyclosporine. Our routine does not include premedicant drugs; induction is with thiopentone and succinylcholine and maintenance with oxygen, nitrous oxide, halothane and fentanyl 1–2 $\mu g \cdot kg^{-1}$. A peripheral nerve stimulator is used intraoperatively. Reversal is with neostigmine and atropine. When the patient is breathing spontaneously, is fully awake, and neuromusuclar function is adequate as shown by peripheral nerve stimulation, the trachea is extubated and he is returned to the renal unit.

Three of our 211 cases needed postoperative pulmonary ventilation. Two because of acute pulmonary oedema and only one because of muscular weakness and depressed respiration. This was the only patient to receive diazepam, 10 mg as premedication, contrary to our protocol. He required four hours of postoperative ventilation before he could be safely extubated.

In conclusion we feel that cyclosporine has been unjustifiably implicated in the cases of prolonged neuromuscular blockade and ventilatory failure. In the three patients in the study by Sidi *et al.* other causes for respiratory failure such as the use of diazepam and ranitidine for premedication could well have played a role.

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2 *Wood M.* Intravenous anesthetic agents. *In*: Wood M, Wood AJJ (Eds.). Drugs and Anesthesia. Baltimore: Williams and Wilkins 1990: 198–9.

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REPLY

In response to the comments, we report additional information on the premedications used for the patients in our retrospective study,[1] who had undergone kidney transplantation: According to Fisher's exact probability test, the incidence of respiratory failure did not differ among those patients who did and did not receive tranquillizers. In fact, none of the patients who presented with respiratory failure received diazepam or midazolam (Table).

Of 211 patients reported by Kadieva et al., two needed postoperative ventilation because of pulmonary oedema. Although we are not given information on the causes of pulmonary oedema in these particular patients, it may have been caused by respiratory failure resulting from aspiration or