Toxic Effects of Amantadine in Patients With Renal Failure

To the Editor:

Amantadine has been used extensively in the treatment of influenza A virus respiratory illness, particularly in nursing homes. The drug is readily absorbed from the gastrointestinal tract, is not metabolized, and is excreted unchanged through the kidneys. Warning has been made repeatedly that patients with renal disease should not be given the drug or that the quantity administered should be reduced in amount.

A wide variety of toxic symptoms may be manifested by patients with renal dysfunction who have been given amantadine. They may become confused, depressed, aggressive, or tense. Ataxia, dizziness, tremulousness, slurred speech, blurred vision, and convulsions have been described. Digestive disturbances, urinary retention, congestive heart failure, and orthostatic hypotension have been noted. Striated muscle weakness of the type manifested by the following patient has not, to our knowledge, been described previously. It is another of the adverse reactions that may be encountered in the presence of renal failure.

A 50-year-old white woman was referred for emergent treatment because of progressive muscular weakness over a period of 48 h. She was unable to walk, and swallowing and breathing became difficult. The presence of a flulike syndrome had led to the administration of 100 mg of amantadine twice a day for the prior 3 days. She had a history of essential hypertension and right pyelonephritis with a renal calculus.

The blood pressure was 190/100 mm Hg, and the respiratory rate was 30 breaths per minute with accessory muscle use. A forced vital capacity of only 500 ml prompted endotracheal intubation with subsequent mechanical ventilation. Pertinent serum values were as follows: potassium, 5.4 mEq/L; phosphate, 9.8 mEq/L; and bicarbonate, 9.0 mEq/L. The blood urea nitrogen level was 111 mg/dl, and the creatinine concentration was 8.0 mg/dl. The creatine phosphokinase concentration was 55 U/L. Initial arterial blood gas values after mechanical ventilation was initiated on an FIO2 of 50 percent were as follows: PO2, 273 mm Hg; PCO2, 22 mm Hg; and pH, 7.16.

The therapeutic response to halting the administration of amantadine and temporary ventilatory support was dramatic. Full muscle strength returned, and the patient was extubated within 36 h.

Amantadine may release dopamine and other catecholamines from neuronal storage sites, and this activity may account for its effect in Parkinson's disease. The drug also enhances the effects of anticholinergic drugs, such as atropine and scopolamine. These modes of behavior, however, would not account for the symptoms seen in this patient. Amantadine has another action, which has been exquisitely demonstrated by Tsai et al. The activity was centered on acetylcholine receptor-mediated postsynaptic conductance. They stressed that amantadine did not react with the recognition site of acetylcholine, but rather with the ionic channel of the receptor, and that it blocked neurotransmission in a voltage-dependent manner.

The precaution that amantadine should not be given to patients with renal disease was not observed in this case, as the prescribing physician was unaware of the patient's renal insufficiency. The inability to excrete the drug produced toxic levels with the production of serious muscular paresis and respiratory difficulty.

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REFERENCES


Pulse Oximetry Monitoring in Stable Patients

To the Editor:

While providing an interesting observation of oxygenation changes in ventilated patients with pneumonia, the article by Solis and colleagues in the February 1993 issue of Chest (103:554-56) suggests that arterial blood gas analysis should be performed following changes in the fraction of inspired oxygen (FIO2). Several studies, recently reviewed in a meta-analysis, have demonstrated the utility and accuracy of pulse oximetry for monitoring changes in oxygenation in otherwise stable patients. The routine sampling of arterial blood in stable patients whose FIO2 has been changed and who are properly monitored with pulse oximetry should be abandoned.

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REFERENCE


To the Editor:

The primary objective of our study was to assess the efficiency of gas exchange (ie, time course of change in PaO2 relative to a change in FIO2) in mechanically ventilated patients with severe hypoxic respiratory failure due to pneumonia. Clearly, pulse oximetry may be substituted for an arterial blood gas analysis in a stable patient whose oxygen saturation is greater than 90 percent. However, we believe that this policy is unsafe in unstable, critically ill patients with substantial desaturation because, for any given O2 saturation, differences in hemoglobin-oxygen affinity (engendered by a little, in part by a change in pH or PCO2) might result in substantial variations in PaO2. Assessment of arterial pH and PCO2, therefore, is invaluable in "fine-tuning" the management of such a patient.

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The Potential of Nosocomial Transmission of Pseudomonas cepacia Exists at Cardiopulmonary Transplant Centers

To the Editor:

We read with interest in the February 1993 issue of Chest (103:466-71), the important observations made by the Toronto