Pharmacokinetics and Pharmacodynamics of Pipecuronium Bromide (Arduan) in Elderly Surgical Patients

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Previous studies indicated that recovery from neuromuscular blockade produced by pancuronium, d-tubocurarine, and metocurine is prolonged in the elderly as a result of decreased plasma clearance and increased elimination half-life. To assess whether pipecuronium had different effects in elderly patients, the authors studied 10 patients under 60 yr of age and 20 aged above 70 yr who were free of disease or drug intake capable of altering response to neuromuscular blockers. All patients were induced similarly. The adductor pollicis response was measured following supramaximal stimulation of the ulnar nerve at the wrist.

After determination of baseline, each patient received a 70 μg/kg bolus of pipecuronium, and the trachea was intubated after establishment of maximal blockade. Pipecuronium plasma levels were determined periodically for 360 min after injection. The derived data were employed to calculate pharmacokinetic variables. Pharmacodynamic data determined included time to maximum blockade, depth of block, time to recovery to 10%, 25%, 50%, 75%, and 90% of baseline twitch, and recovery indices.

Older patients averaged 75 ± 4 yr and younger ones 49 ± 7 yr and total body weight as a percentage of IBW was similar between groups. Onset time was longer in older patients (6.9 ± 2.6 vs. 4.5 ± 1.5 min), but depth of block was similar, although 2 elderly patients were not totally blocked. The rate of spontaneous recovery was not different between groups and recovery indices at 10%, 25%, and 75% were not different. There was no difference between groups for neuromuscular junction sensitivity. Mean plasma concentration versus time curves for pipecuronium were not different for the 2 groups.

In view of the primary renal path of excretion of pipecuronium and the known decrease in renal function with age, the elimination and action of the drug were not expected to be similar. The pharmacokinetic similarity between the 2 groups might involve a nonrenal pathway for elimination of pipecuronium, compensating for the age-related deterioration in renal function. In addition, once recovery began there were no pharmacodynamic differences between groups.

Comment: While this is a fascinating study, it should be remembered that this study was done in healthy elderly persons. Furthermore, I can't find in the paper any male versus female breakdown, and it is in the female elderly that the greatest variations and sensitivity in muscle relaxants occur. Would these data have been similar if they had used all female elderly versus all male elderly? We can't answer that because we have no idea of how many females versus males were included in this study. One would hope that I had just missed these analyses in reading the paper, but after reading it three times I still can't find them. I wonder if the defect is in the journal editors who allowed such a publication to be published without insisting on a detailed analysis of males versus females.

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