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Pancuronium Bromide Requirement during Anesthesia for the Morbidly Obese

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The relationship of dose to body size for the nondepolarizing muscle relaxants, which are highly ionized molecules with low fat solubility, may not apply in obese patients, where the excess body weight is mostly due to adipose tissue. To examine the above impression, we studied prospectively the dose requirements of pancuronium bromide in morbidly obese patients.

METHODS

Fourteen unpremedicated patients, ASA Class 1 or 2, were studied. Gastric bypass (95 per cent gastric exclusion and *roux-en-y* gastrojejunostomy) was performed for morbid obesity in seven patients, and gastrectomy was performed for peptic ulcer disease in the remaining seven patients, who were not obese. In the obese group, mean height was 166 ± 4 cm, mean weight, 137 ± 10 kg, and mean body surface area 2.4 ± 0.1 m^2. In the non-obese group, mean height was 167 ± 2 cm, mean weight, 65 ± 6 kg, and the mean surface area, 1.7 ± 0.1 m^2. Ages ranged from 22 to 46 years. None of the patients was taking any drug known to have neuromuscular effects. Bowel preparation with antibiotics was not performed.

Anesthesia was induced with thiopental, 350 ± 21 mg, and maintained with halothane and nitrous oxide–oxygen (3:3 l/min flow). The trachea was intubated without the use of muscle relaxants. Inspired halothane concentrations ranged from 0.5 to 1.0 per cent during maintenance. Halothane had been administered for at least 30 min before injection of pancuronium bromide in nonobese patients and for one hour in obese patients. Ventilation was controlled to maintain a constant arterial carbon dioxide partial pressure at 36 ± 3 torr.

To quantitate muscle relaxation, the ulnar nerve was stimulated with a supramaximal square-wave bipolar pulse delivered by a Grass S-4 stimulator at 0.3 Hz for 0.1 msec. The resultant force of thumb abduction was transduced (FT-10) and recorded on a Grass polygraph. After a bolus injection of pancuronium bromide, 1/mg/m^2, intravenously, 0.2 mg/ml pancuronium was infused continuously via a Harvard pump to produce a constant 90 per cent depression of twitch tension. The amount of pancuronium needed was recorded every 30 min. Data were analyzed using Student's t test for paired data.

RESULTS

Obese patients needed significantly more pancuronium than non-obese patients to maintain a constant 90 per cent depression of twitch height. The amounts of pancuronium (mean ± SE) required in the nonobese and obese patients were: 2.75 ± 0.21 and 3.66 ± 0.25 mg* for the first 30 min; 0.81 ± 0.12 and 1.17 ± 0.11 mg for the second 30 min; 0.57 ± 0.08 and 0.91 ± 0.07 mg* for the third 30 min; 0.45 ± 0.04 and 0.75 ± 0.06 mg* for the fourth 30 min; 0.43 ± 0.02 and 0.71 ± 0.06 mg* for the fifth 30 min, respectively (asterisk indicates $P < 0.05$).

When the amounts of pancuronium were corrected for the body surface area, however, there was no difference between the amounts of pancuronium needed

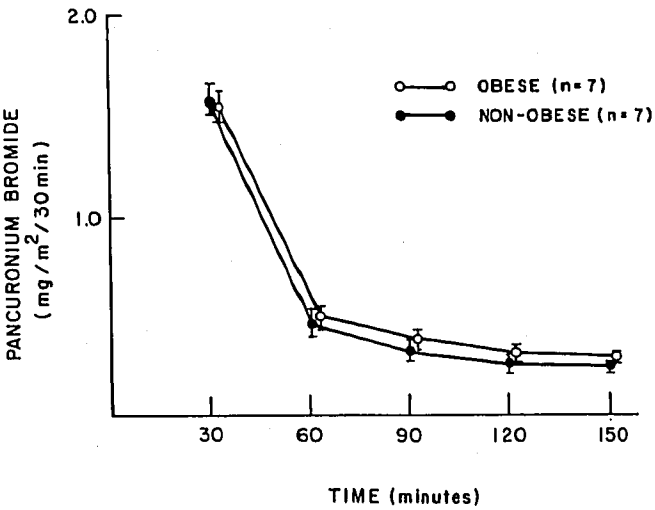

FIG. 1. Dose requirements of pancuronium bromide (mg/m^2/30 min) for constant 90 per cent depression of twitch tension in the obese and non-obese patients.

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to produce constant 90 per cent depression of twitch height in the two groups (fig. 1).

Discussion

Pancuronium bromide is a competitive muscle relaxant with three-compartmental distributional characteristics.[1,2] A short plasma half-life ($T_{1/2}$ less than 5 min) in the initial phase of the plasma concentration curve suggests that the drug is distributed rapidly between plasma and the extracellular fluid space. The rapid onset of drug action indicates that its site of action is located in the central compartment. The second slower phase ($T_{1/2}$ approximately 10 min) probably reflects both drug distribution to acceptor tissue compartments and elimination. The third phase in the plasma concentration curve ($T_{1/2}$ about two hours) probably represents renal and biliary drug elimination after equilibrium among the plasma, liver and acceptor tissue compartments is attained.

In the obese subject, both blood volume and cardiac output increase as body weight increases.§ The values for blood flow through adipose tissue in the non-obese subject range from 2 to 7 ml/100 g/min.[3,4] Although the values per unit adipose tissue tend to decrease with increasing obesity, the total flow through adipose tissue in markedly obese subjects would be considerable. Since no major alteration in the blood flow through other organs has been demonstrated, the increase in blood volume in the obese probably reflects increased vascular space supplying adipose tissue.

The greater pancuronium requirement observed in our obese patients was directly proportional to body surface area. Although there is no specific study in the literature concerning the relationship between extracellular fluid volume and body surface area in the morbidly obese, available data do indicate that blood volume and extracellular fluid increase in proportion to body surface area.§[,5] The lipid solubility of pancuronium is very low.[6] It seems reasonable, therefore, to assume that the greater amount of pancuronium necessary to produce clinically adequate muscle relaxation in obese patients is probably related to the increase of extracellular fluid space that occurs with increasing obesity.

The inspired halothane concentration in our obese patients was lowered gradually to the maintenance level over a period of at least an hour before the administration of pancuronium. It is, however, possible that the alveolar concentration was significantly lower than the inspired concentration due to the high fat–blood partition coefficient for halothane. This would place the alveolar halothane concentration of our patients above minimum alveolar concentration but less than 1 per cent. At high concentrations, halothane potentiates the neuromuscular blockade produced by nondepolarizing muscle relaxants.[7,8] However, in lower concentrations, 0.5 to 1.0 per cent as in our patients, halothane does not appear to potentiate significantly the neuromuscular blockade produced by *d*-tubocurarine or pancuronium.[9,10] We believe the influence of halothane on the amount of pancuronium needed to produce 90 per cent depression of muscle twitch height was not significant in our study.

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