Pipecuronium bromide is a bis-quaternary non-depolarizing neuromuscular blocking agent with a structure similar to that of pancuronium. It has been available in Hungary for some years; clinical trials in Western Europe and the United States have commenced only recently. An initial study from Holland suggested that its neuromuscular profile was similar to that of pancuronium [1]. However, there is no study comparing the potency of pipecuronium bromide with that of pancuronium bromide; it was thought necessary to determine its potency before commencing neuromuscular and haemodynamic studies.

**METHODS AND RESULTS**

We studied 30 adult patients (ASA grades I or II) scheduled to undergo elective surgery requiring the use of non-depolarizing neuromuscular blocking agents. Informed consent and Ethics Committee approval were obtained. Following premedication with oral diazepam 10-15 mg 1 h before operation, anaesthesia was induced with thiopentone 5-6 mg kg$^{-1}$ and maintained with 70 % nitrous oxide in oxygen and increments of fentanyl as required. Ventilation was assisted to maintain the end-tidal carbon dioxide concentration in the range 4.5—5 %. Neuromuscular monitoring was carried out by applying supra-maximal square wave stimuli of 0.2 ms duration to the ulnar nerve via cutaneous electrodes at a frequency of 0.1 Hz. The force of contraction of adductor pollicis muscle was recorded using a force displacement transducer and a neuromuscular function analyser (Myograph 2000).

The control twitch height was allowed to stabilize for a period of approximately 10 min before administration of the study drugs. Fifteen patients were allocated randomly to receive 10-µg kg$^{-1}$ increments of either pipecuronium or pancuronium, successive increments of the same agent being administered when there was no change in twitch height in response to three consecutive stimuli. Repeated increments were administered until a reduction in twitch height of at least 95 % was attained, for constructing cumulative dose–response curves. Twitch height data were subjected to arc sine transformation as described by Armitage [2] for responses involving the 0 and 100 % points on the dose–response line. Log dose–response curves were constructed after regression analysis of the data from which the ED$_{50}$ and ED$_{95}$ values (doses required for producing 50 % and 95 % block of the twitch height, respectively) were derived. These were compared for the two agents using Student's $t$ test.

It is clear from figure 1 that pipecuronium is more potent than pancuronium. The dose–response curves were significantly different in their slopes (pipecuronium slope = 132, 95 % confidence intervals 121-144; pancuronium slope = 108, 95 % confidence intervals 102-114). The regression equations were: pipecuronium arc sine of response $= -2.37 + 132 \log_{10} \text{(No. of increments)}$; pancuronium arc sine of response $= -1.95 + 108 \log_{10} \text{(No. of increments)}$.

The ED$_{50}$ values for pipecuronium and pancuronium were 24.96 (95 % confidence intervals 22.32-27.60) and 30.42 (27.54-33.30) µg kg$^{-1}$,
POTENCY OF PIPECURONIUM BROMIDE AND PANCURONIUM BROMIDE

respectively, and the ED$_{95}$ values were 44.96 (38.84–51.08) and 61.12 (54.59–67.66) µg kg$^{-1}$, respectively. Both the ED$_{50}$ and ED$_{95}$ values were significantly different between the two agents. Based on the estimates of ED$_{95}$, pipecuronium was 1.36 times as potent as pancuronium.

It was interesting to note in the present study that the dose–response curves deviated significantly from parallelism between the two drugs. This may indicate that pancuronium and pipecuronium act at different sites at the neuromuscular junction. Studies with pancuronium have shown that this drug may have predominantly postsynaptic actions in comparison with tubocurarine as judged by fade in response to a train-of-four or tetanic stimulation [5, 6]. Such information is not available at this stage for pipecuronium.

Patients who received the highest doses (40 or 50 µg kg$^{-1}$) of pipecuronium showed that the time to 25 % recovery of these doses was in the region of approximately 40–50 min, which was similar to that obtained with pancuronium given in doses of 50 or 60 µg kg$^{-1}$. Although this would indicate approximately similar durations of action of pancuronium and pipecuronium administered in equipotent doses, more detailed studies are required to assess this aspect.

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COMMENT

Our data have shown that pipecuronium is approximately one-third more potent in terms of its ED$_{95}$ than pancuronium.

The method of estimating potency has been shown to be important [3, 4]. Although these studies have shown that a single dose method of estimating potency is more accurate for relatively shorter acting neuromuscular blocking drugs, these have shown no significant difference in the case of agents with a relatively long duration of action. A previous study with pancuronium and tubocurarine showed that the ED$_{95}$ values estimated by either the single dose or the cumulative dose technique are comparable [4]. The ED$_{95}$ of approximately 60 µg kg$^{-1}$ for pancuronium is in keeping with previous studies using a cumulative dose technique [4].

REFERENCES