SOME CLINICAL EXPERIENCES WITH A NEW NEUROMUSCULAR BLOCKING DRUG—PANCURONIUM BROMIDE (PAVULON NA97)*

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Introduction

PRELIMINARY studies with Pancuronium (Pavulon NA97—Organon) suggested that it was about five times as potent as tubocurarine as a neuromuscular blocking agent and had a similar duration of action. The electromyographic studies have shown the blockade to be of the non-depolarising, or curariform type reversible by neostigmine and there was a complete absence of cardiovascular side effects when the drug was used with halothane (Baird and Reid, 1967). Since pancuronium had these promising features further investigations with it were carried out in routine anaesthetic practice.

Methods and Results

The drug was administered to a series of 115 patients, unselected and anaesthetised as they occurred both in elective and emergency surgical lists. There were 54 males and 61 females in a wide age distribution. The largest age group was the "fifties" (30 patients) and the second largest age group was the "sixties" (23 patients). The oldest patient was 84 and the youngest patient was a child of 6 with a ruptured spleen. As they were unselected cases, they cover a wide range of surgical procedures. The majority of the 68 upper abdominal procedures were vagotomies and pyloroplasties with quite a few cholecystectomies as well. The majority of the 32 lower abdominal procedures were colectomies and abdomino-perineal resections of the rectum. The remaining cases comprised 6 other abdominal surgical procedures, 8 herniae and 1 laminectomy. Generally, however, tubocurarine is to be preferred for laminectomies in order to keep the systolic blood pressure down around 80 mm. Hg.

The distribution of the patients ranged throughout the seven classes of physical status. The classification is that of the American Society of Anesthesiologists. Class 1 (5 patients) comprised the patients who were otherwise fit. Classes 2 (45 patients), 3 (40 patients) and 4 (6 patients) were progressively unfit. Classes 5 (4 patients) and 6 (9 patients) were emergency surgery and Class 7 (4 patients) were the moribund. The 45 patients in Class 2 have, therefore, moderate systemic disease and the 40 patients in Class 3 have severe systemic disease. It would seem likely that any undesirable effects of the drug such as haemodynamic changes, or prolonged blockade would be more likely to be seen in those patients who have severe systemic disease.

* A paper read at the Section of Anaesthetics, Royal Academy of Medicine in Ireland, on March 6th, 1968.
While it was initially hoped that the short onset of the drug might enable intubation to be performed with a similar facility to that after suxamethonium, in practice this proved not to be so. With pancuronium, the intubation could not be performed after one circulation time as with suxamethonium. The first 25 patients were intubated at 90 seconds following the injection of pancuronium alone. Relaxation of the jaw muscles was good and direct laryngoscopy was usually easy. A small cough invariably occurred on intubation, but thereafter the patient was quickly brought under control. It seemed, however, that there was nothing to be gained by not using suxamethonium for the intubation. The remainder of the patients were therefore given suxamethonium for intubation and pancuronium bromide was given thereafter to produce muscular relaxation for the operative procedure in the same way as many people use tubocurarine or gallamine.

After an initial extension of the trial, a dose range of 4 mg. in the light female to 8 mg. in the husky male was used throughout the study. This is equivalent to a dose range of 20-45 mg. of tubocurarine. The duration of action of pancuronium still appears to be similar to tubocurarine, most cases which are completed within one hour requiring no supplementary dose. Also, as previously recorded, the reversal of the neuromuscular blockade at the end of the operation was easily accomplished with neostigmine 2.5 mg. and atropine 1.2 mg. given together. Some measure of the safety of the drug may be gained from experience in three cases to whom twice the normal dose was inadvertently given. In the first patient surgery was completed in about 40 minutes and the blockade reversed without difficulty with the normal dose of neostigmine and atropine. The second patient, a frail elderly bronchitic man who had an exploratory laparotomy completed inside 25 minutes, was slow to reverse and was sent to the Respiratory Intensive Care Unit for observation. He required to be ventilated for a short period but thereafter was able to maintain blood gas homeostasis, breathing spontaneously. The third patient, a fit young man for appendicectomy, received 16 mg. pancuronium, the equivalent of at least 80 mg. of tubocurarine and after 30 minutes of surgery the myoneural blockade was reversed within 10 minutes by incremental doses of neostigmine up to a total dose of 5 mg. None of these three patients showed any gross disturbance of heart rate or systolic blood pressure.

The initial trial suggested that there was a complete absence of cardiovascular side effects, even when the drug was used with halothane. This extended clinical experience has largely substantiated this fact. The changes in pulse rate and blood pressure which occur immediately after the initial dose of pancuronium are complicated by the effects of premedication, thiopentone, suxamethonium, intubation, I.P.P.V., and the time lag before surgery commences. A better indication of the cardiovascular responses to the drug can be obtained by studying the effects of supplementary doses by which time many of the previous complicating factors have been either eliminated or stabilised. The effect of 75 supplementary doses on the systolic blood pressure is shown in Fig. 1. The mean change represents a fall of 1.27 mm.Hg. with a scatter fairly close to the mean. It should be pointed out that 16 patients received more than one supplementary dose. The vast majority of the supplementary doses were 2 mg. of