Muscular relaxation adequate to allow abdominal surgery is associated with a depression of the single evoked twitch response in excess of 75 percent of its control value (DeJong, 1966). An alternative quantitative assessment of residual neuromuscular blockade is provided by a train-of-four stimuli delivered in 2 s at 10-s intervals (Ali, Utting and Gray, 1971). The train-of-four ratio has its own internal control, and has been found to be a more sensitive index of the intensity of blockade than is the single twitch (Lee, 1975; Lee, Barnes and Katz, 1976; Ali and Savarese, 1976; Ali et al., 1981). At apparent full recovery of the single twitch, the T4:T1 ratio (ratio of the height of the fourth twitch to the first) can still be decreased. In 1975, using tubocurarine, Lee (1975) demonstrated that the disappearance and reappearance of each twitch of the train-of-four correlated with specified degrees of blockade. During recovery, the second twitch appears at 90% blockade of T1, the third at 80% blockade, and the fourth at 75% blockade. As a result, counting the number of responses to a train-of-four stimuli has become a clinically useful method for the intraoperative monitoring of neuromuscular blockade.

The purpose of this study was to examine the intensity of neuromuscular blockade present at the time of reappearance of the second, third and fourth twitches following blockade induced with atracurium or vecuronium, and to compare these with the values associated with tubocurarine-induced neuromuscular blockade.

SUMMARY

The characteristics of train-of-four recovery after atracurium or vecuronium were studied, under enflurane anaesthesia, and compared with those associated with tubocurarine-induced blockade. Ten patients each received vecuronium 0.1 mg kg\(^{-1}\), atracurium 0.5 mg kg\(^{-1}\) or tubocurarine 0.5 mg kg\(^{-1}\). Neuromuscular blockade was calculated as the percent depression of the first twitch, and was determined at the time of reappearance of the second, third and fourth twitches of the train-of-four. The pattern during recovery from blockade induced by the three neuromuscular blocking agents was similar, with T2, T3 and T4 reappearing at approximately 93%, 89% and 86% residual blockade, respectively. These results are different from those previously reported by Lee (1975) indicating that, under enflurane anaesthesia, the train-of-four count may give an incorrect estimate of the degree of neuromuscular blockade.

PATIENTS AND METHODS

Seventeen males and 13 non-pregnant females (ASA physical status I or II) scheduled for elective operative procedures requiring neuromuscular blockade for intubation only, entered the study. The study was approved by the Institutional Review Board of Northwestern University, which granted permission to conduct the study without written informed consent. The procedures all lasted long enough to allow for spontaneous recovery of the fourth twitch. Patients were aged 20–60 yr and within 25% of ideal body weight (Bray, 1976).

The patients had no known renal, hepatic or
neuromuscular disease, nor were they receiving drugs known to affect neuromuscular transmission in the preoperative period.

Patients were premedicated with a narcotic or a belladonna alkaloid, or both. Anaesthesia was induced with thiopentone 3–5 mg kg⁻¹ i.v. and maintained with increments of fentanyl 50–100 μg and 1–2% enfurane (delivered concentration) in 50% nitrous oxide in oxygen, according to surgical requirements. Ventilation to normocarbia was maintained as measured by end-tidal carbon dioxide tension (Datex CO₂ monitor, Puritan-Bennett Corp.).

Each patient was randomly assigned to receive vecuronium 0.1 mg kg⁻¹, atracurium 0.5 mg kg⁻¹ or tubocurarine 0.5 mg kg⁻¹. The drugs were injected over 60 s to minimize the potential for hypotension with tubocurarine and atracurium.

Before the administration of the neuromuscular blocker, a Grass S48 stimulator provided supra-maximal stimuli of 0.2 ms duration to the ulnar nerve at the elbow to obtain a steady control value. Train-of-four was recorded continuously from the thumb via a linear force transducer (Devices ST-10) and displayed on a Hewlett-Packard 7754B chart recorder.

The percent depression of the first twitch (control – T1/control) was then determined at the time of reappearance of the second, third and fourth twitches (T2, T3, T4), for each patient. The height of the first twitch was monitored during the remainder of the anaesthetic to ensure that the twitch height returned to control.

Mean values ± standard deviations for each agent, at each degree of train-of-four recovery, were calculated. Significance was determined by two-way analysis of variance (Snedecor and Cochran, 1967).

RESULTS

The mean ages, heights, and weights for each group are listed in table I. There were no statistically significant differences between these values in the three groups.

The mean durations of anaesthesia for the atracurium, vecuronium and tubocurarine groups were similar: 164 ± 126 min, 127 ± 78 min, and 197 ± 86 min, respectively.

The measured intensity of blockade at the times of reappearance of the second, third and fourth twitches for each agent are shown in table II. The mean percent blockade at the times of reappearance of T2, T3 and T4 were all found to be different from each other by the Newman–Keuls test (P < 0.01).

The mean times to the onset of blockade (first depression of T1 (below control), to the maximum degree of blockade and to the reappearance of each twitch in the train-of-four are listed in table III.

There were no significant changes in end-tidal carbon dioxide concentration or temperature during the study. Delivered enfurane concentrations remained stable at 1–2% throughout the study.

DISCUSSION

The times to the onset of blockade and to recovery to 90% blockade (the time to reappearance of T3 in our study) are similar to previously reported values (Watts and Dillon, 1968; Hilgenberg, 1983; Bencini and Newton, 1984; Hunter, Jones and Utting, 1984; Miller et al., 1984).
The train-of-four data show a similar recovery pattern for atracurium, vecuronium and tubocurarine, with T2, T3 and T4 reappearing at approximately 93%, 89% and 86% residual neuromuscular blockade, respectively.

These results, however, are different from those of Lee (1975) (T2, T3, T4 reappearing at 90%, 80% and 75%). In that study, Lee used a number of agents which are now known to affect neuromuscular blockade. Some, but not all, of the patients received diazepam for premedication. Diazepam has been shown (Feldman and Crawley, 1970) to increase neuromuscular blockade. In addition, intubation was with the aid of suxamethonium in that study and, although 30 min elapsed before the administration of the non-depolarizing drug, it is probable that the prior dose of suxamethonium augmented the blockade (Katz, 1971). Blockade was antagonized in some of the patients in Lee's study, but times of the administration of the reversal agent were not detailed. Donati, Ferguson and Bevan (1983) have shown that, in antagonizing neuromuscular blockade, different reversal agents alter the characteristics of train-of-four and tetanic fade. It has been suggested that this occurs by differential binding of the anticholinesterase inhibitors to a presynaptic receptor (as yet unidentified).

Recent studies of neuromuscular blocking agents have indicated that train-of-four fade is the result of a presynaptic effect, and that neuromuscular blocking agents have different affinities for pre- and post-synaptic receptors (Blaber, 1973; Glavinovic, 1979; Williams, Webb and Calvey, 1980; Rang, 1981; Donati, Ferguson and Bevan, 1983; Jones et al., 1984; Robbins et al., 1984; Stanec and Baker, 1984). Bowman (1980), and Day and colleagues (1983), have indicated that vecuronium may have less of a presynaptic effect than previously available non-depolarizing drugs such as tubocurarine. As a result, vecuronium might be expected to cause less fade during onset and recovery than tubocurarine. Our results could not detect this effect.

It is possible that the use of different volatile anaesthetics could explain the difference between our results and those of Lee (1975). Lee (1975) used halothane; in this study we used enflurane. Rupp, Miller and Gencarelli (1984) have shown that enflurane has a more marked potentiating effect on vecuronium-induced neuromuscular blockade than halothane. Both in vitro (Kennedy and Galindo, 1975; Waud and Waud, 1975a, b) and in vivo (Lebowitz, Casey and Walts, 1970; Stanski et al., 1980) studies have shown that enflurane, even in low concentrations, potentiates the neuromuscular blocking effect of tubocurarine. This effect is thought to occur post-synaptically. If train-of-four fade is caused by a presynaptic effect, enflurane may affect twitch height more than fade. Whether halothane and enflurane affect fade to different degrees is not known.

Recently, Ham and Redpath (1985) reported, in abstract form, a similar train-of-four study with halothane anaesthesia using tubocurarine, atracurium, pancuronium, metocurine and gallamine, but not vecuronium. On recovery they found train-of-four characteristics similar to those of Lee's (1975) study with all of the neuromuscular blocking agents used. In their study, however, the train-of-four response was considered “absent” when it was diminished to 1–2% of control. This difference in criteria for complete blockade as well as the use of halothane might account for the difference between our results and those of Ham and Redpath.

In summary, the measured fade observed on train-of-four recovery was similar for the three drugs studied, and under enflurane anaesthesia occurred at greater degrees of blockade than reported previously. It is possible that, by counting the observed twitchs in the train-of-four, the actual degree of blockade is incorrectly estimated.

REFERENCES


