RECOVERY OF SPONTANEOUS BREATHING FOLLOWING NEUROMUSCULAR BLOCKADE WITH ATRACURIUM

G. H. HACKETT, R. HUGHES AND J. P. PAYNE

Atracurium is a competitive neuromuscular blocking agent of intermediate duration of action, with a unique metabolic degradation which proceeds independently of hepatic and renal function (Payne and Hughes, 1981).

Once recovery from neuromuscular blockade has begun, the recovery phase develops rapidly, and is linear throughout that phase when plotted logarithmically (Madden, Hughes and Payne, 1983). Despite extensive investigation of the properties of atracurium, the recovery of respiration following its use has not been studied fully. This study was undertaken to determine the pattern of recovery of spontaneous breathing following neuromuscular blockade with atracurium.

PATIENTS AND METHODS

Studies were performed on 11 patients aged 25–64 yr (mean age 43.8 yr) who had given their informed consent, and who were about to undergo elective urological surgery. Approval was also obtained from the Ethics Committee of the hospital. No premedication was given. In all patients anaesthesia was induced with thiopentone 400–500 mg given i.v. and maintained with 70% nitrous oxide in oxygen supplemented with 1–2% halothane until neuromuscular and arterial monitoring had been established. Halothane was then withdrawn for a period of 10 min before the administration of atracurium 0.3 mg kg⁻¹. After endotracheal intubation was achieved, anaesthesia was continued with 60–66% nitrous oxide in oxygen using intermittent positive pressure ventilation. The minute volume was adjusted to obtain an end-tidal carbon dioxide concentration between 5 and 6%. A polyethylene cannula was placed in a radial artery to allow the intermittent sampling of blood for blood-gas analysis, and the monitoring of arterial pressure which was displayed continuously, as was the ECG. Simultaneous recordings of the contraction of the adductor pollicis muscles.

SUMMARY

Atracurium 0.3 mg kg⁻¹ was given to two groups of patients to compare the recovery of spontaneous breathing with that of peripheral neuromuscular function. Anaesthesia was maintained in one group (n = 6) with an infusion of etomidate (mean flow rate 24 µg kg⁻¹ min⁻¹) and in the other group (n = 5) with 0.5% halothane. From the time of discontinuing ventilation, about 5 min after the reappearance of the tetanic response, spontaneous breathing returned in an average time of 135 s (range 18–300) in the patients given etomidate and in 68 s (range 0–123) in the patients who received halothane (ns). The duration of action of atracurium was not significantly prolonged by halothane, probably because of the low concentration used. Adequate recovery of respiratory muscle function occurred within 30 min of administration of atracurium at a time when there was less than 25% recovery of the tetanic response of the adductor pollicis muscle. It was concluded that recovery of the muscles of respiration from neuromuscular blockade by atracurium occurred more rapidly than recovery of the muscles of the hand, but an adequate tidal volume in the absence of other clinical signs should not be regarded as a reliable indicator of complete return of neuromuscular function.
were obtained by stimulating an ulnar nerve supramaximally at the wrist every 12 s with tetanic bursts of 50 Hz for 1 s.

End-tidal carbon dioxide, halothane and oxygen concentrations were measured by mass spectrometry. The probe of the mass spectrometer was situated between the endotracheal tube and the catheter mount. A thermistor located distally to the mass spectrometer probe was used to detect the onset of spontaneous breathing and the change in respiratory pattern.

In the first group of six patients, anaesthesia was supplemented by an infusion of etomidate at a rate which was adjusted according to the patient's requirements, but which averaged 24 μg kg⁻¹ min⁻¹. The total dose of etomidate administered varied between 75 and 90 mg, with the exception of one patient who required 140 mg. In the second group of five patients, 0.5% halothane was used throughout.

Ventilation was discontinued immediately after the first evidence of tetanic recovery was seen, at which stage a 6-litre flow of 100% oxygen was delivered through the endotracheal tube. The first attempts to breathe spontaneously were detected by the thermistor (fig. 1). Manual ventilation was undertaken if the arterial carbon dioxide tension increased to more than 8 kPa. This was calculated on the basis of the last reading of the carbon dioxide from the mass spectrometer and on the assumption that carbon dioxide concentration increases at the rate of approximately 0.53 kPa min⁻¹.

The time from discontinuing ventilation to the onset of spontaneous breathing was recorded, as was the time from the administration of atracurium to: (1) the return of the tetanic response; (2) the termination of ventilation; (3) the first spontaneous breath; and (4) 95% recovery of the tetanic responses. Adequacy of respiration was assessed by measuring the tidal volume with a Wright's respirometer. The average of four determinations was recorded at 0–5, 15–20 and 30–35 min after the return of spontaneous breathing and measurements of the arterial oxygen and carbon dioxide tensions were made concurrently. The results were expressed as mean ± SEM and compared using the Mann–Whitney U test for unpaired data.

RESULTS

Figure 1 shows a typical tracing obtained from a patient in the study. Five minutes after the return of respiration, the arterial carbon dioxide tension was 6.27 kPa and the tidal volume was 300 ml, at which point there was less than 25% recovery of neuromuscular function. After 15 min of spontaneous breathing, the tidal volume had increased to 325 ml and the arterial carbon dioxide tension had decreased to 5.47 kPa—a value which confirmed the adequacy of respiration.

The relationship between the termination of ventilation and the return of spontaneous breathing is shown in table I, together with the time to the first appearance of the tetanic response after blockade, and the time to 95% recovery of the tetanic response. In the group of patients receiving etomidate (group I), the time from discontinuing

![Fig. 1. Tetanic response of the adductor pollicis muscle following administration of atracurium 0.3 mg kg⁻¹ to a patient anaesthetized with halothane.](image-url)
ventilation to the return of spontaneous breathing averaged 135 s (range 18–300). This was compared with the halothane group (group II), in which spontaneous breathing returned after 68 s (range 0–123), but the difference was not significantly shorter. Similarly, there were no significant differences in the time to return of the tetanic response or the time to 95% recovery of neuromuscular function between the two groups.

Measurements of blood-gas tensions taken at 0–5, 15–20 and 30–35 min after the return of spontaneous breathing are shown in table II. The mean arterial carbon dioxide partial pressure remained within acceptable limits in both groups, although in those patients given etomidate the mean value at each stage was consistently higher than the corresponding value for the halothane group. However, there was no statistical difference between the two groups. Arterial oxygen tension was consistently greater than 13.3 kPa with an inspired oxygen concentration between 35 and 40% with the exception of patients K.S. and C.B. in group I at 15–20 min.

Measurements of tidal volume taken concomitantly with the blood-gas measurements are shown in table III. In group II the mean tidal volume increased from 335 ± 23.2 ml at 0–5 min to 365 ± 12.8 ml at 30–35 min, and in group I it increased from a value of 375 ± 73.9 ml at 0–5 min to 383 ± 44.1 ml at 30–35 min. No statistical difference was found.

**DISCUSSION**

Early studies undertaken to equate neuromuscular blockade with respiratory function have used sustained headlift as an indication that neuromuscular transmission was sufficient to maintain adequate ventilation in the post-anaesthetic period (Dam and Guldmann, 1961). Johansen, Jorgensen and Molbech (1964) found respiratory muscle power to be relatively well preserved when
curarization was carried to the point where the subject was almost unable to raise the head and strength in the hand grip was substantially weakened. This sparing effect of neuromuscular blocking drugs on the muscles of respiration, first described by Paton and Zaimis (1951), was demonstrated for atracurium in the present study. Respiration was shown to be adequate as assessed by measurements of tidal volume and blood-gas tensions 30 min after the administration of atracurium, when there was less than 25% recovery of peripheral neuromuscular function. However, there are quantitative differences between drugs. In a recent study of alcuronium, recovery of neuromuscular function was found to be delayed and adequate respiration could not be assumed until 60 min after the administration of the drug, at which time the recovery of the tetanic response in the six patients studied varied between 17 and 58% of the initial height (Astley, Hughes and Payne, 1983).

Another factor to be considered is the potentiating effect of certain anaesthetic techniques on the action of neuromuscular blocking agents. In particular, the potentiating effect of halothane on the action of atracurium has been demonstrated previously (Payne and Hughes, 1981). However, in the concentration used in the current study (0.5%), halothane is unlikely to have had any marked effect either on the extent or on the duration of the blockade produced by atracurium. This is borne out by the fact that there was no significant difference in the behaviour of atracurium when the halothane group was compared with the group of patients given etomidate. Etomidate used to supplement inhalation anaesthesia has been reported to have little effect on respiration (Morgan, Lumley and Whitwam, 1977). Those patients given halothane followed a recovery pattern similar to those given etomidate. Indeed, in the case of the etomidate group, the recovery of spontaneous breathing from the time of discontinuing ventilation was slightly longer, but the difference was not clinically important. It may, however, be relevant that the patient who received the largest dose of etomidate (140 mg) also achieved the highest arterial carbon dioxide tension.

In conclusion, it has been shown that, following the administration of atracurium 0.3 mg kg⁻¹, spontaneous breathing returned within 8 min of the reappearance of the tetanic response. Respiration was adequate within a further 5 min and within 30 min of the administration of the drug. Thus recovery of the muscles of respiration from atracurium-induced neuromuscular blockade occurs more rapidly than that of the small muscles of the hand. However, an adequate tidal volume in the absence of other clinical signs should not be regarded as a reliable indication of complete return of neuromuscular function.

ACKNOWLEDGEMENTS
We are indebted to Miss V. A. Bishop, s.r.n., and Mr A. Harman for skilled technical assistance, to our surgical and nursing colleagues for their tolerance and patience, and to our volunteers without whom this study would not have been possible.

REFERENCES