INTRAOPERATIVE ASSESSMENT OF ATRACURIUM-INDUCED NEUROMUSCULAR BLOCK USING DOUBLE BURST STIMULATION†

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SUMMARY
Paired train-of-four (TOF) and double burst stimuli (DBS) were administered to the ulnar nerve at the wrist in 25 patients (group 1) paralysed with atracurium 0.5 mg kg⁻¹; responses were measured mechanically (except every third DBS response which was manually evaluated). Another 30 patients (group 2) received a DBS every 60 s. A post-tetanic count (PTC) was performed when the first response (D1) was palpated. There was a significant correlation between the twitch heights of the first TOF response (T1) and D1 and likewise between the twitch heights of both second responses (r = 0.9; P < 0.001), but there was a significant difference in regression coefficients of these two correlations (P < 0.001). D1 was palpable first with a median PTC of 7. Our results showed that palpation of a single response implied a satisfactory level of paralysis. DBS may be useful for intraoperative clinical monitoring of neuromuscular block.

KEY WORDS

Train-of-four (TOF) peripheral nerve stimulation with tactile assessment of response is used widely for monitoring neuromuscular block. However, it is inaccurate for identifying residual block [1] and has been shown recently not to influence the total dose of relaxant used or the incidence of postoperative residual neuromuscular block [2].

Double burst stimulation (DBS) is the most reliable clinical method of detecting residual paralysis [3], but its suitability for quantifying profound and intermediate levels of neuromuscular block is not clear. We have therefore investigated its potential for this use.

PATIENTS AND METHODS
The study was approved by the Hospital Research Ethics Committee, but in view of the routine nature of neuromuscular monitoring, patient consent was not sought. We studied 55 healthy adult patients, none of whom was receiving any medication which may have influenced neuromuscular transmission.

All patients were anaesthetized in a standard manner. After premedication with papaveretum and hyoscine, anaesthesia was induced with propofol 2–3 mg kg⁻¹ i.v. and maintained with 1% enflurane (after an initial overpressure period of 3 min with 5% enflurane) and 66% nitrous oxide in oxygen. Neuromuscular block was produced with atracurium 0.5 mg kg⁻¹ and subsequent increments of 0.2 mg kg⁻¹ were given according to clinical need. Fentanyl 50–100 μg i.v. was administered for analgesia as required. Normocapnia (based on end-tidal carbon dioxide measurement) was maintained throughout the study using positive pressure ventilation via a tracheal tube or laryngeal mask airway. The ulnar nerve was stimulated at the wrist with a Rutter...
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MkV programmable nerve stimulator via surface electrodes on the side opposite to which i.v. access and an arterial pressure cuff were sited.

The patients were allocated to two groups. In group 1 the force of the isometric adductor pollicis contraction was measured using a Grass FT-10 force displacement transducer [4], Lectromed MX 216 amplifier and chart recorder. After a stabilization period of 3–5 min after induction, the supramaximal point and control values were established using a 1-Hz stimulus. Thereafter, a set stimulus sequence was delivered to the patient every 120 s for the remainder of the study. This consisted of a TOF stimulus followed 20 s later by a DBS [3]. Before every third DBS, the thumb mount was disconnected from the transducer and one of five observers (each familiar with the use of a nerve stimulator) palpated the thumb response to stimulation. This response was recorded as no response, single response or double response. The same observer was used throughout any single patient study. The recorded level of block was concealed from the observer, who was also unaware of whether or not any incremental dose of atracurium had recently been administered. A 200-g resting abducting tension on the thumb was maintained throughout the study and this was confirmed before each recording and after reconnection. Readings taken during the 6 min following administration of incremental doses of atracurium were discounted.

After completion of an individual patient study, the amplitude of the first twitch of each TOF response (T1) was measured from the paper record and expressed as a fraction of the measured control value (T1/C). T1/C values of more than 0.55 were considered to lie outside the range of adequate surgical relaxation and were excluded. Each T1/C value before and after palpation was compared. Measured values where T1/C was less than 0.03 were excluded from the data, because of their low signal-to-noise ratio. The first, third and fifth readings occurring subsequently were selected from each patient’s data, in order to include a wide range of block and to exclude bias towards those patients undergoing longer operations. These were compared with their respective first and second DBS (D1 and D2) twitch height measurements. In each case the following comparisons were made: T1/C with the ratio D2:D1; D1 with T1 twitch heights; and D2 with T2 twitch heights (where present). The first, median and last palpated DBS responses were also selected and compared with their paired T1/C values.

In group 2, the supramaximal point was established by palpation by one of two observers. A similar DBS pattern to that used previously was delivered every 60 s and a PTC was performed 20 s after the first D1 response became palpable. The median PTC and range of the 30 data points were computed.

Data were expressed as mean (SD) or median (range). The relationships of twitch heights of T1 with D1 and T2 with D2 were compared using linear regression analysis. The difference between regression coefficients was evaluated with reference to tables of normal distribution. P < 0.05 was considered significant.

RESULTS

Twenty-five patients were studied in group 1. The mean age was 46.5 yr (range 17–74 yr), the male:female ratio 1.4:1 and the median duration of each study was 39 (17–65) min. Because of a prolonged period of profound block (no response to DBS or TOF) or short operative time, insufficient palpation data were gained from six patients and insufficient measurement data from five patients. These patients were excluded from the relevant data groups. D1 always returned before T1 on 18 occasions when profound block was achieved. All T1 readings taken after palpation were 2–8 % greater than the T1 reading taken before palpation. From the 60 measured readings selected, a significant linear correlation between D1 and T1 (fig. 1) was evident (r = 0.9; P < 0.001; regression coefficient $\hat{\beta} = 100$).

D2 twitch height (mm) vs T1 twitch height (mm)

**Fig. 1.** Relationship between the measured twitch heights of T1 and D1, showing the line of best fit.
There was a similar degree of correlation between D2 and T2 twitch heights \((n = 57; r = 0.9; \text{regression coefficient 0.93})\) (fig. 2). The two data set regression coefficients differed significantly \((P < 0.001)\). Figure 2 shows that when no T2 response was present there was a particularly wide scatter of D2 twitch heights.

There was poor correlation between D2:D1 and T1/C \((r = 0.3)\), with data points particularly widely scattered through the range of T1/C 0–0.1 (fig. 3).

Fifty-seven palpated DBS responses were selected, of which 27 were perceived as a single response and 30 as a double response. The relationship between these responses and different levels of neuromuscular block is indicated in figure 4. Only one double response was palpated when T1/C was <0.05 and two responses were always palpated when T1/C >0.20. Thus palpation of a single response implied a T1/C of <0.20 \((P = 1)\), but palpation of a double response implied only a 0.66 chance of T1/C ≥0.20. Palpation of a double response did, however, suggest a 0.97 chance of T1/C ≥0.05. The sensitivity of this technique in identifying a T1/C value above or below 0.20 was 0.73 and the specificity was 1. The arrowed data points in figures 2–4 were derived from the same three patients and illustrate an earlier and relatively more powerful initial return of D2. There was no common observer or demographic factor link between these patients.

The mean age of the 30 patients studied in group 2 was 45.3 yr (range 20–77 yr) with the male:female ratio 1:1.3. Data from this group indicated a median PTC when D1 was first palpated of 7 (3–12).
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DISCUSSION

The three elements of the D1 stimulus produced a more powerful response than the single T1 response by a factor of almost 2 (fig. 1); this would suggest easier and earlier recognition of the D1 DBS response. This is confirmed by our other results: D1 always returned before T1 and the median PTC when D1 was first palpated was 7 (compared with a PTC of 8-14 using the TOF [5, 6]). Our PTC result probably overestimates the true value, as a 60-s interval elapsed between assessments and our D1 response was palpated, not visualized as in the study by Bonsu and colleagues [5]. This result is also consistent with other published work which has shown that D1 returns 2.2 min earlier than T1 [7].

The relationship between T2 and D2 differed significantly from that between T1 and D1 (as shown by the slopes of the regression lines in figures 2 and 3). Despite the greater power of the D2 electrical stimulus, the D2 response was similar in force to T2, although D2 did return at an earlier stage in recovery of neuromuscular function. The reason for this is unclear, but may reflect enhanced fade after the D1 stimulus.

The poor correlation between D2:D1 and T1/C (fig. 3) may reflect the fact that these parameters quantify different aspects of the effect of atracurium on neuromuscular function (in a manner analogous to the relationship between T4/T1 and T1/C). Fade is a presynaptic phenomenon and attenuation of a single response has a postsynaptic basis [8]. The scatter is particularly evident in the region of profound block, which may also partly reflect a reduced signal-to-noise ratio. The palpated responses mirror the wide interpatient measured variations in initial D2 recovery. In figures 2-4 the data points where D2 returned relatively early or more powerfully (indicated by arrows) were derived from the same three patients in whom D2 response was palpated at a relatively early stage in recovery of neuromuscular function (fig. 4). These patients appear to represent the extremes of the spectrum, rather than a discrete group and have contributed to the reduced sensitivity of the DBS response with profound block.

Our palpated results indicated satisfactory specificity, but less satisfactory sensitivity for DBS as a test to identify a T1/C of less than 0.05 or more than 0.20. Identification of these points is of particular clinical value: a T1/C value of less than 0.20-0.25 is compatible with adequate intraoperative relaxation when a volatile agent is used [9] and excellent conditions for tracheal intubation are present with a T1/C value of less than 0.05 [10]. In addition, antagonism of atracurium-induced paralysis may be accomplished reliably from this latter point in less than 9.6 min [11]. Nevertheless, despite limitations of sensitivity, palpation of a single response implies a T1/C value < 0.20 and palpation of a double response a T1/C value ≥ 0.05 with a high degree of certainty.

The clinical use of the TOF stimulus pattern (and likewise DBS) during operation is based on a fade-induced reduction in the number of responses relating reliably to the degree of attenuation of T1 [12]. This close relationship between the pre- and postsynaptic effects has been shown to be present with atracurium and an anaesthetic technique similar to our own [13]. However, the same workers in another study using vecuronium have shown a considerably wider variation in visual assessment of T2 return (T1/C of 0.16 (SD 0.1)) compared with measured assessment [13, 14]. This discrepancy may result from difficulty in interpreting up to four responses and could account for the limited impact of TOF usage in clinical practice [2].

DBS used for the quantification of the attenuated T1 response is based probably on the same pre- and postsynaptic mechanisms, but may be complicated by enhanced D2 fade (see above), resulting in more interpatient variation than TOF. Nevertheless, it is possible that the simplicity of the double DBS response may offer enhanced clinical accuracy in comparison with TOF.

Validity of data could have been impaired by variations in neuromuscular junction temperature, changes in the resting tension of the adductor pollicis muscle or alterations in the neuromuscular effects of enflurane (compared with initial control value). Although temperature was not measured, the effect of this was likely to be very limited as surgery was of a minor nature, all i.v. infusions were delivered through the opposite arm and the duration of the studies was relatively short. The resting tension was confirmed as being unchanged throughout the study and the 2-8% increase in T1 values after reconnection of the thumb almost certainly reflects spontaneous recovery of block over the 2-min period between consecutive readings. The neuromuscular effect of enflurane is related to blood concentration and period of exposure [15]. The effect of consistent over-
pressuring at the outset and the short duration of each study would thus have limited the influence of this variable.

In conclusion, our data and the results of others show that DBS may be used as a universal stimulus pattern throughout the full range of neuromuscular block. Palpation of a single response may reliably indicate adequate intraoperative relaxation, but palpation of a double response does not necessarily imply adequate relaxation. DBS, however, may detect initial return of neuromuscular function earlier than TOF. Measurements of DBS response confirmed an enhancement of D1 response compared with T1, but showed an unexpected relative impairment of D2 response compared with T2. This study suggests that the simpler double response of DBS may offer a clinical advantage in comparison with TOF in the accuracy of monitoring neuromuscular function at levels of block suitable for intraoperative use.

REFERENCES