SUXAMETHONIUM: A NEW LOOK AT PRETREATMENT

S. A. MASEY, C. W. GLAZEBROOK AND V. A. GOAT

SUMMARY
Fifty patients were pretreated with either suxamethonium 10 mg or gallamine 20 mg before an injection of suxamethonium 1 mg kg⁻¹. The effect of the pretreatment upon neuromuscular transmission was monitored by recording the mechanical response of the adductor pollicis muscle to indirect stimulation, using a 2-Hz train-of-four stimulus repeated every 12 s. The pretreatment injection of suxamethonium caused fasciculation in one-quarter of the patients studied. Significant neuromuscular blockade occurred during pretreatment in 16 of the 25 patients investigated. Pretreatment with gallamine 20 mg predictably decreased the efficacy of the intubating injection of suxamethonium, making intubation more difficult. The frequency of muscle pain was similar in both groups.

Since its introduction into anaesthetic practice, the use of suxamethonium has been accompanied by certain side-effects including muscle fasciculation and muscle cramps (Churchill-Davidson, 1954; Prince-White, 1957) and various pretreatment regimens have been devised in an attempt to decrease the frequency of these problems. For example, sub-paralysing amounts of a non-depolarizing neuromuscular blocking drug have been given before injection of suxamethonium (Foster, 1960; White, 1962). Most of the non-depolarizing agents have been used with varying degrees of success, but interactions between these drugs and suxamethonium have caused further problems, of which the most frequent is a decrease in the neuromuscular blocking activity of suxamethonium (Freud and Rubin, 1972; Brodsky, Brock-Utne and Samuels, 1979).

Interest in pretreatment, using suxamethonium itself, arose after observations that this technique decreased the frequency and the severity of muscle fasciculation (Baraka, 1977; Brodsky and Brock-Utne, 1979). Further studies (Siler, Cook and Ricca, 1980; Wilson and Dundee, 1980) failed to show any decrease in the frequency of muscle pain.

The response of an individual to neuromuscular blocking drugs varies considerably and, since premature paralysis could be unacceptable in the conscious patient, it was decided to monitor the effect of small doses of suxamethonium on neuromuscular transmission during the pretreatment period, and to compare this with the effect of a pretreatment injection of gallamine.

PATIENTS AND METHODS
Fifty healthy patients (ASA Grade 1) aged between 18 and 45 yr took part in the study. Informed consent was obtained, and the trial was conducted with the approval of the local Ethics Committee. All the patients were undergoing minor surgical dental treatment and required intubation of the trachea. None was on regular medication apart from the contraceptive pill.

The patients were alternatively allocated to receive either suxamethonium 10 mg (group A) 1 min before the intubating injection of suxamethonium (1 mg kg⁻¹) or gallamine 20 mg (group B) 3 min before a similar injection of suxamethonium.

It was decided to pretreat patients in group A with suxamethonium 10 mg, since this was the dose used by previous workers without reported problems (Baraka, 1977; Wilson and Dundee, 1980; Siler, Cook and Ricca, 1980). The choice of the dose of gallamine for the patients in group B was more difficult, since doses ranging from 5 mg (White, 1962) to 40 mg (Churchill-Davidson, 1954) have been used previously. Miller and Way (1971) demonstrated that a pretreatment injection of gallamine 20 mg had no significant effect upon the

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neuromuscular blockade produced by suxamethonium. Therefore, this intermediate amount was selected for this trial. The timing of the administration of the pretreatment drugs was chosen on the basis of previous work by many investigators.

All patients received papaveretum and hyoscine as premedication approximately 1 h before surgery.

Before anaesthesia was induced, a modified Elcomatic transducer (Armstrong, Goat and Loach, 1977) was attached to the patient's dominant hand to measure the contraction of the adductor pollicis muscle. Anaesthesia, induced with thiopentone 5 mg kg\(^{-1}\) plus fentanyl 3 μg kg\(^{-1}\) i.v., was maintained with nitrous oxide in oxygen. Respiration was assisted using a face-mask.

The ulnar nerve was stimulated at the wrist using a Grass S48 stimulator and isolation unit. The stimulating current was applied over the nerve by disposable ECG electrodes and the duration of the stimulus was 0.2 ms.

Once it was certain that the stimulus applied was supramaximal, a 2-Hz train-of-four stimulus was applied to the nerve, and repeated once every 12 s throughout the procedure. The mechanical response of the adductor of the thumb to this stimulation was measured by the transducer and displayed on a recorder (Elcomatic).

Once the response to a control train-of-four stimulus had been obtained, the pretreatment drug was injected; the start of the injection was coincident with the first response of a train. One minute (group A) or 3 min (group B) later, the intubating dose of suxamethonium 1 mg kg\(^{-1}\) was administered; again the start of the injection coincided with the first response of a train.

Laryngoscopy and nasal tracheal intubation were attempted as soon as full peripheral neuromuscular blockade had been achieved. Full peripheral blockade was assumed to coincide with the total abolition of a motor response to any of the stimuli within the train-of-four.

The occurrence of muscle fasciculation, and the ease of intubation, were noted by observing the vocal cords, and noting the response to intubation. Monitoring of neuromuscular transmission was continued until the response of the first twitch in the train had recovered to 80% of its original height.

All patients were given halothane during surgery, but this was not added until the completion of the neuromuscular monitoring.

The first twitch in the train-of-four is in itself an unconditioned twitch as long as it is not preceded by any other nerve stimulation in the preceding 10 s (Lee and Katz, 1980). This first unconditioned twitch was used to ascertain the maximum twitch depression during pretreatment, by measuring the height of the most depressed first twitch during pretreatment, and expressing it as a percentage of the control first twitch. In addition, the fade within each train-of-four was measured and expressed as the ratio of the fourth twitch response to the first.

All patients were interviewed at approximately 24 h following anaesthesia, and asked specific, direct questions regarding muscle pain. The site of discomfort was noted. Pain in the neck and jaw was considered to be of surgical origin. Pain in sites other than neck and jaw were classified as: mild = requiring no analgesia; moderate = requiring analgesia but not interfering with normal activity; severe = requiring analgesia and causing disability — for example, unable to get out of bed.

RESULTS

Depression of the response of the first twitch (table I) occurred to a variable degree in those patients given suxamethonium 10 mg. In one patient total paralysis occurred. The height of the first twitch was decreased to values of less than 70% of control in 13 of the 25 patients, before the intubating dose of

<table>
<thead>
<tr>
<th>Table I. Neuromuscular blockade occurring during pretreatment.</th>
<th>*P = 0.001 (Student's unpaired t test)</th>
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</thead>
<tbody>
<tr>
<td>Pretreatment drug</td>
<td>Suxamethonium</td>
</tr>
<tr>
<td>Mean age (yr)</td>
<td>22.1</td>
</tr>
<tr>
<td>Male : Female</td>
<td>7:18</td>
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<tr>
<td>Depression of first twitch of the train-of-four</td>
<td></td>
</tr>
<tr>
<td>Mean depression (as a percentage of control) (SD ± 35)*</td>
<td>61.9%</td>
</tr>
<tr>
<td>No. of patients with depression of twitch to less than 70% of control</td>
<td>13</td>
</tr>
<tr>
<td>Fade of the train-of-four</td>
<td></td>
</tr>
<tr>
<td>Maximal fade (4/1 ratio)</td>
<td>0.67</td>
</tr>
<tr>
<td>(SD ± 0.14)*</td>
<td></td>
</tr>
<tr>
<td>No. of patients with 4/1 ratio less than 0.7</td>
<td>16</td>
</tr>
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suxamethonium was given. Pretreatment with gallamine produced minimal depression of the first twitch response. This remained greater than 90% of control in all patients. There was an initial increase in twitch response in some subjects in both groups following the pretreatment drug.

Fade within the train-of-four (table I) was observed in both the gallamine and suxamethonium groups during the pretreatment period. The fade was expressed as the ratio of the height of the fourth twitch to that of the first and the mean values were 0.67 after suxamethonium (group A) and 0.84 after gallamine (group B). Sixteen patients who received the pretreatment injection of suxamethonium had a fade ratio of less than 0.7, compared with three amongst the group who received gallamine.

Time to complete myoneural blockade was more rapid in those patients who received additional suxamethonium (0.69 min SD ± 0.41) compared with those subjects who received gallamine (1.04 min SD ± 0.22). The duration of total neuromuscular blockade was also longer in group A (7.6 min SD ± 1.4) compared with 5.23 min (SD ± 0.94) in group B.

Fasciculation. Five patients pretreated with gallamine fasciculated after the intubating injection of suxamethonium. Of the 25 patients pretreated with suxamethonium 20 fasciculated at some time during induction: 12 patients after the pretreatment injection of suxamethonium, 14 patients following the intubating dose, and six individuals fasciculated after both the pretreatment and intubating injections of suxamethonium.

Intubation was less smooth in those patients who had received gallamine. Ten patients moved or coughed during intubation, but none required any additional neuromuscular blockade to effect intubation.

The frequency of muscle pain at 24 h was similar in both groups; 11 patients in group A and nine in group B complained of moderate to severe muscle cramps. There was no difference between the groups in the severity of the muscle pain.

DISCUSSION
Muscle pain has been a frequent and unpleasant accompaniment to the use of suxamethonium. However, it is important that any pretreatment regimen, devised to decrease the frequency of this complication should not only work, but be totally safe. It is well documented that the use of subparalysing doses of non-depolarizing neuromuscular blockers decreased the neuromuscular blocking activity of suxamethonium (Cullen, 1971; Freud and Rubin, 1972), and this occurred in this small series also.

Pretreatment with suxamethonium does not decrease the efficacy of the intubating injection, and this must be one of the major attractions to its use, but in this small series, an unacceptable degree of neuromuscular blockade occurred during pretreatment.

Sixteen of the 25 patients showed evidence of partial neuromuscular blockade, demonstrated by either a decrease in the first twitch response of the train-of-four to less than 70% of control, or a fade within the train-of-four to values less than 0.7. This degree of neuromuscular blockade is considered by many workers to be clinically significant (Ali and Savarese, 1976). None of the patients demonstrated prolonged blockade, so it is unlikely that their cholinesterase concentrations were low or abnormal, although these were not measured.

Fasciculation was observed in 12 patients following the pretreatment injection which, if given to the conscious subject would be at the very least, unpleasant.

Depolarization of skeletal muscle fibres occurs after the administration of suxamethonium i.v. in man. This is usually accompanied by muscle fasciculation and sometimes associated with a transient increase in the tension of the muscle contraction. This was observed in some of our patients (fig. 1), and is associated with repetitive firing of the muscle fibres (Standaert and Adams, 1965; Bowman, 1980). One of the characteristics of the depolarization block which follows is that the mechanical response to tetanic stimulation (30–50 Hz) is well sustained. This is also true of the response to a train-of-four stimulus, the ratio T4/T1 being greater than 0.7. This was not so in 16 of the patients studied, and the mean T4/T1 value was 0.67 (fig. 2).

Recovery from the effects of the drug followed the accepted pattern for depolarizing blockers (Durant and Katz, 1982), all four twitches of the train being of equal size.

It is possible that the fade observed was a result of the rapid and continued progression of paralysis. To see if this was so, a train-of-six stimulation was carried out in two patients. This showed that there was a levelling of the response at the fourth twitch. It is also possible that a Phase II block was occurring, but this is unlikely following suxamethonium 10 mg.
Pretreatment with gallamine produced minimal effects on neuromuscular transmission, as shown by both the response of the single twitch and the train-of-four. However, intubation was rendered more difficult, and the onset of neuromuscular blockade produced by suxamethonium was delayed.

CONCLUSION

The technique of "self-taming" with suxamethonium is not only ineffective in preventing fasciculation and muscle pain, but is potentially dangerous, producing significant blockade in over one-half the subjects studied.
SUXAMETHONIUM: PRETREATMENT

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tions, 1st edn, p. 76. Bristol: John Wright & Sons Ltd.

Cinquante patients ont été prétraité soit par l'injection de 10 mg de suxamethonium, soit par l'injection de 20 mg de gallamine avant de recevoir de suxamethonium 1 mg·kg⁻¹. Les effets du prétraitement sur la transmission neuromusculaire ont été surveillés en enregistrant la réponse mécanique du muscle adducteur
du pouce à une stimulation indirecte, utilisant un stimulus de train de quatre de 2 Hz répété toutes les 12 s. L'injection de suxamethonium, en prétraitement, entraînait des fasciculations chez le quart des patients étudiés. Un bloc neuromusculaire net est survenu chez 16 patients sur 25 étudiés, à la suite du prétraitement. Le prétraitement par 20 mg de gallamine diminuait, comme prévu, l'efficacité de l'injection de suxamethonium faite pour l'intubation, ce qui rendait cette dernière plus difficile. La fréquence des douleurs musculaires était la même dans les deux groupes.

SUXAMETHONIUM: EINE NEUE SICHT BEI DER PRÄMEDIKATION

ZUSAMMENFASSUNG


SUXAMETONIO: UNA NUEVA CONSIDERACION DEL PRETRATAMIENTO

SUMARIO

Se premedicaron cincuenta pacientes, bien con 10 mg de suxa-
metonio o con 20 mg de gallamina, antes de administrar una inyección de 1 mg·kg⁻¹ de suxametonio. El efecto de la pre-
medicación sobre la transmisión neuromuscular se vigiló registran-
do la respuesta mecánica del músculo aductor bajo la esti-
mulación indirecta, usando una serie de cuatro estímulos de
2 Hz que se repitieron cada 12 segundos. El pretratamiento mediante inyección de suxametonio ocasionó la separación de las fibras muscular en la cuarta parte de los pacientes analizados. En 16 de los 25 pacientes analizados se observó un bloqueo neuromuscular significativo durante la premedicación. La premedicación con 20 mg de gallamina disminuyó, como era predecible, la eficacia de la inyección de suxametonio tendente a la intubación, lo que hizo que ésta fuera más difícil. La frecuencia de dolor muscular fue similar en ambos grupos.