RELATION OF PRECURARIZATION TO SUXAMETHONIUM TO PROVIDE EASE OF INTUBATION AND TO PREVENT POST-SUXAMETHONIUM MUSCLE PAINS

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SUXAMETHONIUM is the relaxant of choice in anaesthetic practice where one desires quick muscle relaxation of short duration. As a depolarizing agent its inherent side effects of post-operative muscle pain,¹⁻⁴ increase in gastric pressure,^{5,6} rise in intraocular tension^{7,8} and dangerous hyperkalaemia in catabolic states⁹⁻¹¹ have led to the use of various prophylactic measures, one of which is pretreatment with a small, sub-paralyzing dose of non-depolarizing muscle relaxant.^{12-14,15}

Although this method of precurarization prevents or lessens the side effects of suxamethonium, it creates the problem of difficult tracheal intubation, and the dose requirement of suxamethonium increases.¹⁶⁻¹⁹

The present study was aimed at finding the ideal dose combination on a body weight basis of suxamethonium with d-tubocurarine, gallamine, and pancuronium which is suitable for tracheal intubation, yet effective in appreciably reducing the post-operative muscle pains.

MATERIALS AND METHOD

Two hundred and ten young healthy adults of American Society of Anesthesiologists status I, who were undergoing minor surgical procedures (tonsillectomies, dilatation and curettage, tubal ligation, herniorrhaphy and repair of hydrocele), and who were similar in age and weight (Table I) were included and were assigned at random to 21 groups of ten patients each. Premedication was avoided to permit better assessment of post-operative muscle pain and intubating conditions. Ease of tracheal intubation, visible muscle fasciculations and post-operative muscle pains were assessed by the senior author while the drugs were injected by the other author. The code was broken at the end of the study and then analyzed.

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Suxamethonium was investigated at three dose levels of 1, 1.5 and 2 mg·kg⁻¹ alone as controls, or in combination with tubocurarine (0.05 and 0.07 mg·kg⁻¹), gallamine (0.2 and 0.4 mg·kg⁻¹) or pancuronium (0.01 and 0.02 mg·kg⁻¹). These small doses of non-depolarizing muscle relaxants were given intravenously three minutes before suxamethonium. Induction of anaesthesia was with thiopentone 2.5 per cent (5 mg·kg⁻¹ body weight) given intravenously two minutes after precurarization, that is one minute before suxamethonium. Intubation was attempted 45 seconds after the suxamethonium injection and ease of intubation was graded as listed in Table II. Visible muscle fasciculations were graded as absent, mild, moderate, or severe (Table III).

Anaesthesia was maintained with nitrous oxide 60 per cent in oxygen and further doses of the non-depolarizing muscle relaxant were used, depending upon surgical requirements. Ventilation was controlled. For post-operative analgesia, metamizole 1-1.5 g was administered by intramuscular injection.

Post-operative suxamethonium pains were assessed at 6, 24 and 48 hours according to a set questionnaire and assigned to four different grades (Table IV). As the intensity of muscle pains was maximal at 24 hours, chi square (χ^2) statistical analysis was only done for pains at that time.

RESULTS

Visible muscle fasciculations

All patients in the three control groups (Figure 1) had mild to severe muscle fasciculations but pretreatment with non-depolarizing muscle relaxants reduced the incidence significantly to 10 to 20 per cent with tubocurarine ($\chi^2 = 12.93$ and 10.21 , $P = <0.001$ and <0.01). Only one group in the gallamine series (gallamine 0.2 mg·kg⁻¹ and suxamethonium 1.5 mg·kg⁻¹) had a 10 per cent incidence of moderate fasciculations ($\chi^2 = 12.93$, $P = <0.001$). Pancuronium at 0.01 mg·kg⁻¹ was much less effective than tubocurarine, gallamine or pancuronium 0.02 mg·kg⁻¹, and as the dose of suxamethonium was increased, the incidence of

TABLE I
PATIENT DATA OF AGE AND WEIGHT, MEAN $\pm$ SD IN THE 21 DRUG GROUPS (CONTROL 3 AND TRIAL 18).
EACH GROUP OF 10 PATIENTS

CONTROL GROUPS						
Drug	Dose		Mean age yrs $\pm$ SD		Mean weight kg $\pm$ SD	
Suxamethonium (Suxa 1)	1 mg·kg ⁻¹		30 $\pm$ 6.1		48 $\pm$ 7.9	
Suxamethonium (Suxa 1.5)	1.5 mg·kg ⁻¹		31 $\pm$ 7.7		52 $\pm$ 6.9	
Suxamethonium (Suxa 2)	2 mg·kg ⁻¹		32 $\pm$ 6.8		47 $\pm$ 7.2	
TRIAL GROUPS						
	Tubocurarine		Gallamine		Pancuronium	
	0.05 mg·kg ⁻¹		0.2 mg·kg ⁻¹		0.01 mg·kg ⁻¹	
	Age (yrs)	Weight (kg)	Age (yrs)	Weight (kg)	Age (yrs)	Weight (kg)
Suxa 1	31 $\pm$ 8.4	50 $\pm$ 5.4	29 $\pm$ 7.7	50 $\pm$ 5.7	31 $\pm$ 6.6	55 $\pm$ 5.5
Suxa 1.5	32 $\pm$ 9.5	56 $\pm$ 9.2	31 $\pm$ 9.3	54 $\pm$ 6.4	28 $\pm$ 7.3	47 $\pm$ 6.6
Suxa 2	31 $\pm$ 5.5	49 $\pm$ 6.6	30 $\pm$ 7.8	45 $\pm$ 7.7	28 $\pm$ 7.7	49 $\pm$ 7.0
	Tubocurarine		Gallamine		Pancuronium	
	0.07 mg·kg ⁻¹		0.4 mg·kg ⁻¹		0.02 mg·kg ⁻¹	
Suxa 1	28 $\pm$ 6.8	50 $\pm$ 5.2	28 $\pm$ 7.8	44 $\pm$ 4.6	32 $\pm$ 8.5	51 $\pm$ 5.3
Suxa 1.5	30 $\pm$ 8.6	54 $\pm$ 7.9	26 $\pm$ 6.0	50 $\pm$ 6.5	28 $\pm$ 6.2	49 $\pm$ 5.0
Suxa 2	28 $\pm$ 5.9	49 $\pm$ 5.6	30 $\pm$ 7.0	52 $\pm$ 5.3	32 $\pm$ 9.0	48 $\pm$ 7.0

TABLE II
GRADING OF DIFFICULTY OF TRACHEAL INTUBATION

I	Easy and no reaction
II	Vocal cord movements present
III	Vocal cord movements and moderate reaction
IV	Impossible without supplementation

TABLE III
GRADING OF MUSCLE FASCICULATIONS

Nil	Absent
Mild	Fine fasciculations of the eyes, face, neck or fingers without movement of the limbs
Moderate	Fasciculations of greater intensity than mild occurring at more than two sites or movements of limbs
Severe	Vigorous, sustained and widespread fasciculations

muscle fasciculations also rose from 10 to 100 per cent (Figure 1). Pancuronium 0.02 mg·kg⁻¹ completely prevented visible muscle fasciculations after suxamethonium.

Ease of tracheal intubation

Intubating conditions at 45 seconds after

TABLE IV
GRADING OF POST-OPERATIVE MUSCLE PAINS

Nil	Absence of pains
Mild	Muscle stiffness or pains on specific questioning in the nape of neck, shoulders and lower chest on deep breathing
Moderate	Muscle stiffness and pains complained of by the patient spontaneously, requiring analgesia
Severe	Incapacitating generalized muscle stiffness or pain

suxamethonium were the best (100 per cent success) when suxamethonium was used alone at the 2 mg·kg⁻¹ dose level (Figure 2).

Precurarization caused a higher incidence of difficult tracheal intubations. Ideal conditions could only be achieved at higher doses of suxamethonium (2 mg·kg⁻¹) in combination with tubocurarine, (0.07 mg·kg⁻¹, $\chi^2 = 0.56$, $P > 0.1$) gallamine (0.2 mg·kg⁻¹, $\chi^2 = 0.56$, $P > 0.1$) and pancuronium (0.01 mg·kg⁻¹, $\chi^2 = 4.27$, $P < 0.05$ and 0.02 mg·kg⁻¹, $\chi^2 = 7.27$, $P < 0.01$). Conditions for intubation became impossible if the suxamethonium dose was kept at 1.0 or 1.5 mg·kg⁻¹ after pretreatment with tubocurarine at

FIGURE 1 Showing percentage incidence of visible muscle fasciculations in control groups with suxamethonium 1.0, 1.5 and 2 mg/kg and pretreatment groups of tubocurarine (0.05 and 0.07 mg/kg), gallamine (0.2 and 0.4 mg/kg) and pancuronium (0.01 and 0.02 mg/kg). Grades of fasciculations are presented as severe ■, moderate ▨, mild □, and nil □.

FIGURE 2 Showing percentage incidence of difficulty of tracheal intubation in control groups with suxamethonium 1.0, 1.5 and 2 mg/kg and pretreatment groups of tubocurarine (0.05 and 0.07 mg/kg), gallamine (0.2 and 0.4 mg/kg) and pancuronium (0.01 and 0.02 mg/kg). Grades of difficulty in intubation are represented as severe ■, moderate ▨, mild □, and nil □.

FIGURE 3 Showing percentage incidence of different grades of post-suxamethonium muscle pains at 24 hours after anaesthesia in three control groups of suxamethonium 1.0, 1.5, 2 mg/kg dose levels and after pretreatment with tubocurarine (0.05 and 0.07 mg/kg), gallamine (0.2 and 0.4 mg/kg) and pancuronium (0.01 and 0.02 mg/kg). Grades of pains: severe ■, moderate ▨, mild □, and nil □.

0.05 mg/kg and 0.07 mg/kg ($\chi^2 = 10.21$, $P < 0.01$), gallamine at 0.2 mg/kg and 0.4 mg/kg at suxamethonium 1.0 mg/kg dose ($\chi^2 = 10.21$, $P < 0.01$) and suxamethonium 1.5 mg/kg ($\chi^2 = 4.27$, $P < 0.05$) and pancuronium at 0.02 mg/kg dose levels ($\chi^2 = 10.21$, $P < 0.01$ and $\chi^2 = 7.27$, $P < 0.01$).

Post-suxamethonium muscle pains

Marked reduction in the incidence of post-suxamethonium muscle pains was observed in the trial groups (Figure 3). Pains were completely abolished in most of the non-depolarizing and suxamethonium combinations. Mild to moderately severe pains were seen in 10–30 per cent of cases in only five of a total of 18 trial groups.

DISCUSSION

This study emphasizes the directly opposite effects of precurarization on the ease of tracheal intubation and post-suxamethonium muscle pains. Although the patients benefit significantly as far as pains are concerned, the anaesthetist's task of intubation is made more difficult at the conventional dose level of 1.0 mg/kg body weight of suxamethonium. Cullen and Freund, *et al.*,^{18,19} have suggested a 50 to 70 per cent increase in the dose of suxamethonium if "precurarization" exists, but the present work suggests the increase of the dose to be 100 per cent (to 2 mg/kg) if ideal intubating conditions are to be obtained.

The best combinations of small doses of non-depolarizing agents and suxamethonium for ideal conditions of tracheal intubation and simultaneously the least post-suxamethonium muscle pain are tubocurarine 0.07 mg/kg or gallamine 0.2 mg/kg or pancuronium 0.02 mg/kg followed three minutes later by suxamethonium 2 mg/kg. The three minute time lag is very important^{18,20–22} as it takes this time for the proper and even distribution of curare molecules in all the neuromuscular junctions before suxamethonium arrives, and it prevents the sudden surge of generalized depolarizing potentials which are probably represented as visible muscle fasciculations.

There seems to be a correlation between the intensity and incidence of visible muscle fasciculations and post-suxamethonium muscle pains. This becomes apparent in figures 1 and 3. The incidence of fasciculations was 100 per cent in the control group and of muscle pains 70 to 100

per cent. Precurarization reduced the incidence of fasciculations by 10 to 40 per cent ($\chi^2 = 12.93$ and 8.57 , $P = <0.001$ and <0.01) and of muscle pains to 10–30 per cent ($\chi^2 = 12.93$ and 7.91 , $P = <0.001$ and <0.01) except for the combination of pancuronium $0.01 \text{ mg} \cdot \text{kg}^{-1}$ and suxamethonium $2 \text{ mg} \cdot \text{kg}^{-1}$, where the incidence of muscle fasciculations was 100 per cent (similar to that of control group).

Certain factors must be kept constant if maximal advantage of precurarization is to be achieved. (1) The time interval of three minutes between non-depolarizing agent and suxamethonium. (2) The non-depolarizing muscle relaxant dose on a body weight basis. (3) Suxamethonium dose twice the conventional dose of $1 \text{ mg} \cdot \text{kg}^{-1}$ to achieve ideal intubating conditions.

SUMMARY

Tubocurarine 0.05 and $0.07 \text{ mg} \cdot \text{kg}^{-1}$, gallamine 0.1 and $0.2 \text{ mg} \cdot \text{kg}^{-1}$ and pancuronium 0.01 and $0.02 \text{ mg} \cdot \text{kg}^{-1}$ given three minutes before suxamethonium 1.0 , 1.5 and $2 \text{ mg} \cdot \text{kg}^{-1}$ in groups of 10 patients each (total 210 patients) to compare ease of tracheal intubation and incidence of post-suxamethonium muscle pain. These were compared with a control group of suxamethonium 1.0 , 1.5 and $2 \text{ mg} \cdot \text{kg}^{-1}$ given alone after thiopentone $5 \text{ mg} \cdot \text{kg}^{-1}$. On analysis, tubocurarine $0.07 \text{ mg} \cdot \text{kg}^{-1}$ and suxamethonium $2 \text{ mg} \cdot \text{kg}^{-1}$ was the ideal combination with the best intubation conditions and the lowest incidence of post-suxamethonium muscle pains. The second best combination was gallamine $0.2 \text{ mg} \cdot \text{kg}^{-1}$ and suxamethonium $2 \text{ mg} \cdot \text{kg}^{-1}$. Pancuronium $0.01 \text{ mg} \cdot \text{kg}^{-1}$ and $0.02 \text{ mg} \cdot \text{kg}^{-1}$ in combination with suxamethonium $2 \text{ mg} \cdot \text{kg}^{-1}$ were satisfactory, although less efficient than the combination with either tubocurarine or gallamine.

RÉSUMÉ

Le but du travail était d'évaluer l'influence de la tubocurarine aux doses de 0.05 et de $0.07 \text{ mg} \cdot \text{kg}^{-1}$, de la gallamine (0.1 et $0.2 \text{ mg} \cdot \text{kg}^{-1}$) et du pancuronium (0.01 et $0.02 \text{ mg} \cdot \text{kg}^{-1}$) sur la facilité d'intubation et sur l'incidence des douleurs musculaires, lorsque ces agents étaient administrés trois minutes avant une injection de 1 , 1.5 et 2 mg de succinylcholine. Vingt-et-un groupes de dix malades ont été formés pour l'étude des différentes combinaisons. Les

malades des trois premiers groupes ont reçu respectivement 1 , 1.5 et $2 \text{ mg} \cdot \text{kg}^{-1}$ de succinylcholine une minute après une injection de thiopental à raison de $5 \text{ mg} \cdot \text{kg}^{-1}$, ce qui a permis d'établir les groupes contrôles.

C'est avec la tubocurarine à la dose de $0.07 \text{ mg} \cdot \text{kg}^{-1}$, associée à une dose de $2 \text{ mg} \cdot \text{kg}^{-1}$ de succinylcholine, que l'on a trouvé les meilleures conditions d'intubation tout en notant la plus basse incidence de douleurs musculaires. L'association de second choix est celle de la gallamine à $0.2 \text{ mg} \cdot \text{kg}^{-1}$ avec une dose de $2 \text{ mg} \cdot \text{kg}^{-1}$ de succinylcholine. Le pancuronium aux doses de 0.01 et de $0.02 \text{ mg} \cdot \text{kg}^{-1}$ précédant la succinylcholine à $2 \text{ mg} \cdot \text{kg}^{-1}$, a donné des résultats satisfaisants, quoiqu'inférieurs à ceux obtenus avec la tubocurarine et la gallamine.

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