

COMPARISON OF FAZADINIUM AND SUXAMETHONIUM FOR ENDOTRACHEAL INTUBATION IN MALAYSIAN PATIENTS

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INTRODUCTION

Prevention of regurgitation and active vomiting with the resulting aspiration of the gastric contents into the tracheobronchial tree is of cardinal importance at the time of induction of anaesthesia. Death during induction of anaesthesia is most often due to aspiration of vomitus or regurgitated material especially in an emergency situation (Dinnick, 1964). It is for this reason that crash induction and rapid intubation is practiced especially when a patient has a full stomach.

Rapid intubation is facilitated by the use of a depolarising muscle relaxant, the commonly used being suxamethonium. Suxamethonium is considered to be the drug of choice since it acts fast and provides excellent muscle relaxation for rapid intubation (Boulton, 1972). Suxamethonium is a depolarising muscle relaxant of short onset and duration of action and rapidly hydrolysed by serum cholinesterase. However, its use is associated with post-anaesthetic muscle pains. (Bourne *et al.*, 1952; Churchill-Davidson, 1954). This has been attributed to the muscle fasciculation caused by depolarisation which in addition elevates the plasma potassium level. This elevation may be harmful and cardiac arrest has been reported (Roth and Wuthrick, 1969). The other disadvantages include dysrhythmias, bradycardia, (Luppriant *et al.*, 1960; Perez, 1970) elevation of intraocular pressure (Dilion *et al.*, 1957), and elevation of intragastric pressure (Andersen, 1962; Roe, 1962). Furthermore, suxamethonium is known to induce malignant hyperpyrexia (Leading article, British Medical Journal, 1971). Prolonged apnoea may occur in the presence of atypical serum cholinesterase or when the level of serum cholinesterase is decreased (Hunter, 1966).

The adverse effects of suxamethonium may be attributed to the depolarisation which occurs before the paralysis of muscle fibres. Consequently, a search for a rapidly acting non-depolarising muscle relaxant began. Commonly used non-depolarising muscle relaxants are slower in onset of action compared to suxamethonium and, therefore, unsuitable for rapid intubation in patients with full stomach.

Fazadinium (AH 8165, Fazadon) is an azobis-arylimidazo-pyridinium derivative which has competitive neuromuscular blocking activity. It was the most potent of nine related compounds tested by Bolger *et al.*, (1972). Initial animal studies showed that fazadinium had rapid onset, short duration, and non-depolarising mode of action (Brittain and Tyres, 1972, 1973). Simpson *et al.*, (1972) did studies on human volunteers using isolated limb techniques and followed it with clinical trials. They showed that although paralysis was produced rapidly the duration of action was much longer than in animals and was similar to that of pancuronium. Coleman *et al.*, (1973) found that the speed and ease of endotracheal intubation following the injection of fazadinium was comparable in every respect to those following suxamethonium.

This study was undertaken to compare the ease of intubation following the administration of suxamethonium and fazadinium at predetermined times in Malaysian patients.

METHOD

The investigation involved study of intubating conditions in 72 adult patients of both sexes in the age group of 18 – 35 years. All these patients were undergoing elective surgery requiring muscle relaxation. All patients chosen had normal respiratory and cardio-vascular functions and belonged to the grades 1 to 3 of the American Society of Anaesthesiologist's classification of physical fitness (1963). Patients in whom any difficulty in intubation (due to deformities of the head and neck or other causes) was anticipated were excluded from the study. The patients were randomly allocated to one of two groups

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according to the muscle relaxant used for intubating.

Group 1. Suxamethonium chloride 1.0 mg/kg.

Group 2. Fazadinium 1.0 mg/kg as bromide.

A standard premedication of Pethidine 1 mg/kg and Promethazine 0.5 mg/kg to a maximum of 25 mg was administered to all cases one hour prior to the induction of anaesthesia.

Before induction of anaesthesia, oxygen was administered to all patients for 5 minutes at a flow rate of 6 litres/minute. Anaesthesia was then induced by administering sodium thiopentone 4 mg/kg as a 2.5% solution. As soon as loss of consciousness occurred the muscle relaxant was given intravenously and a stop watch started immediately on completion of the injection. Thirty seconds after the injection of muscle relaxant laryngoscopy and intubation were attempted in both the groups of patients. The intubating conditions were classified according to Lund and Stovner (1970) classification which is summarised in Table I.

Table I
CLASSIFICATION OF INTUBATING CONDITIONS
(LUND AND STOVNER 1970)

Grade 3	-	Well separated cords, not moving. No bucking on the tube.
Grade 2	-	Slight movement of the cords when touched. Only slight bucking for a short period after insertion of the tube.
Grade 1	-	Conditions less favourable than in the previous two categories but permitting intubation.
Grade 0	-	Impossible to intubate.

If the intubating condition was not grade 3, the endotracheal tube was removed. Laryngoscopy was then done at intervals of 15 seconds (i.e. 45, 60, 75 & 90 seconds after injection of the muscle relaxant) and movement of vocal cords used to grade the condition of intubation. Reintubation was done only when the vocal cords were well separated and motionless (grade 3 intubating condition) except in 2 patients in group 2 who were intubated at 90 seconds with grade 2 intubating conditions. All intubations were performed by the same anaesthetists (SD) and any patients in whom intubation was difficult for any reasons other than the degree of relaxation were excluded from the trial.

In the group 1 patients further muscle relaxation required for surgery was maintained by any one of the non-depolarising muscle relaxant (i.e. pancuronium alcuronium or tubocurarine). At the end of surgery, residual neuromuscular block by the non-depolarising compounds was reversed by a standard dose of atropine 1.2 mg and neostigmine 3.75 mg.

RESULTS

The distribution of patients in the two groups was comparable as shown in Table II. The intubating conditions obtained and the number of patients in each grade at various time intervals is shown in Table III.

All patients in group 1 who received suxamethonium reached grade 3 intubating conditions in 45 seconds. In group 2, (i.e. patients who received fazadinium) 35 out of 37 patients reached grade 3 intubating condition between 60 to 90 seconds and 2 patients took more than 90 seconds.

Table II
DISTRIBUTION OF PATIENTS WITHIN THE STUDY

Group	Sex		Mean age in years + s.d. (Range)	Mean weight in kg + s.d. (Range)
	F	M		
1. Suxamethonium 1 mg/kg	17	18	26.97 + 4.88 (18 - 33)	54.08 + 8.34 (36 - 72)
2. Fazadinium 1 mg/kg	18	19	27.37 + 4.30 (18 - 33)	54.39 + 7.27 (39 - 73)

s.d. = standard deviation

In most clinical situations grade 2 conditions may also be considered satisfactory. Therefore, grade 3 and grade 2 were considered acceptable and grade 1 and 0 not acceptable. Test of significance (Chi-square) was then done for these two subgroups at various intervals of time. The results showed that suxamethonium was significantly superior to fazadinium at 30, 45 and 60 seconds ($p < 0.001$), and there was no significant difference at 75 and 90 seconds ($p > 0.5$).

DISCUSSION

Patients with full stomach presenting for emergency surgery are at risk of aspirating the vomitus

Table III
TIMES AND INTUBATING CONDITIONS AFTER ADMINISTRATION OF THE TWO
MUSCLE RELAXANTS

Time	Group	(No. of Patients)			
		Grade 3	Grade 2	Grade 1	Grade 0
30 sec.	1	26	8	1	0
	2	0	0	1	36
45 sec.	1	9	0	0	0
	2	0	2	35	0
60 sec.	1	—	—	—	—
	2	3	18	16	0
75 sec.	1	—	—	—	—
	2	15	18	1	0
90 sec.	1	—	—	—	—
	2	17	2	0	0

Group 1 = Suxamethonium 1 mg/kg

Group 2 = Fazadinium 1 mg/kg

or regurgitated material. In such situations rapid intubation is essential but conditions for smooth intubation like adequate muscle relaxation, absence of vocal cord movements and bucking after intubation may also be equally important. Suxamethonium has been the drug of choice in such situations. However, use of suxamethonium is not without serious hazards. The initial fasciculation may lead to a rise in intragastric pressure and thus induce regurgitation before intubation is accomplished.

Non-depolarising muscle relaxants like tubocurarine, alcuronium and pancuronium are not suitable because of slower onset of action. Fazadinium was claimed to have a more rapid onset of action than suxamethonium (Simpson, *et al.*, 1972). However, later studies have not substantiated this claim. Young *et al.*, (1975) found suxamethonium 1 mg/kg gave superior conditions for intubation to those of fazadinium 1.25 mg/kg at predetermined times. Hartley and Fidler (1977) found that fazadinium 1 mg/kg was not significantly different in times to intubation from suxamethonium although the latter gave a highly significant greater number of patients with excellent conditions.

The results in our study in Malaysian patients tend to confirm those of Young *et al.*, (1975). Suxamethonium 1 mg/kg produces better intubating conditions at 30, 45 and 60 seconds than fazadinium 1 mg/kg. However, at 75 and 90 seconds there is no significant difference.

Among the non-depolarising muscle relaxants, fazadinium has been found to provide better intubating conditions than pancuronium, alcuronium or tubocurarine (Corral *et al.*, 1977; Hartley and Fidler, 1977). Therefore, in non-emergency situation where regurgitation is not so much of a hazard, fazadinium could be used for intubation in patients who are going for surgery requiring muscle relaxation. This also avoids the use of an additional drug, namely suxamethonium, as commonly practised. Fazadinium does not produce any adverse effects on the cardiovascular system (Savege *et al.*, 1973). In fact it provides cardiovascular stability similar to pancuronium.

Neuromuscular blockade can be promptly antagonised by the usual standard dose of neostigmine (Cane and Sinclair, 1976; Arora *et al.*, 1973). Buckley

et al., (1974) concluded that the action of fazadinium was antagonised as easily as that of tubocurarine and from our experience with the drug we tend to concur with their view.

From the results of our study we are of the opinion that in situations where rapid intubation and excellent intubating conditions are of prime importance (e.g. obstetric and other emergency practice) suxamethonium is still the drug of choice.

However, in non-emergency practice anaesthetists who use suxamethonium followed by a non-depolarising muscle relaxant may like to consider fazadinium as an alternative to these combinations. Such a change in technique, of course, will mean a greater caution in the pre-anaesthetic assessment of the patient to weed out those who may turn out to be cases of "difficult intubation". The obvious advantages of using fazadinium are avoidance of using several drugs, elimination of adverse effects of suxamethonium, cardiovascular stability and easy reversal of the neuromuscular blockade by neostigmine.

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