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The Effect of Defasciculating Doses of Pancuronium and Atracurium on Succinylcholine Neuromuscular Blockade

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Background: A defasciculating dose of non-depolarizing muscle relaxant administered prior succinylcholine decrease its side effects including fasciculations and postoperative myalgias; however it is believed that the dosage of succinylcholine should be increased when such a pre-treatment is used.
Objectives: We hypothesized that a defasciculating dose of pancuronium as a pre-treatment could prolong its duration of effect.
Patients and Methods: Forty patients scheduled for elective orthopaedic surgery were consecutively assigned into 5 groups, a first group without pre-treatment (succinylcholine 1 mg/kg) and 4 subsequent groups of pretreatment with atracurium 0.05 mg/kg + succinylcholine 1 or 1.5 mg/kg and pancuronium 7.5 μg/kg + succinylcholine 1 and 1.5 mg/kg. The muscle relaxant effect of succinylcholine was assessed with a force transducer using train of four stimulations every 12 seconds. Kruskall Wallis Anova test was used to compare results.
Results: The duration of succinylcholine induced paralysis (1 and 1.5 mg/kg) was significantly prolonged with pre-treatment with pancuronium but succinylcholine 1mg/kg did not reached maximum blockade after pre-treatment with atracurium. After pancuronium, full recovery after succinylcholine 1.5 and 1 mg/kg occurred respectively after 18 and 15 minutes. $P < 0.05$ vs. 12 minutes for succinylcholine 1mg/kg alone.
Conclusions: This study highlights potentiation effect of a defasciculating dose of pancuronium on succinylcholine paralysis suggesting the lack of justification to increase succinylcholine dosage.

Keywords: Succinylcholine; Atracurium; Pancuronium

1. Background

Succinylcholine is used mainly used to facilitate tracheal intubation in emergency procedures but also in elective surgery, however because of multiple side effects including fasciculations muscle damage and late postoperative myalgia, a small dose of non-depolarising muscle relaxants (NDMR) may be used to decrease these side effects (1-6). Nearly all of NMDR might be used (7, 8), however magnesium sulphate is also reported to be efficient for this purpose (9). In addition, it's generally believed that the dose of Succinylcholine should be enhanced because of receptor competition with the NMDR (10-13).

2. Objectives

A defasciculating dose of Pancuronium might have different pharmacokinetic profile, because of serum anticholinesterase activity (14, 15). In previous works we investigated different effect of low dose of pancuronium on mivacurium pharmacodynamics, suggesting that the potentiation of mivacurium effect would mostly be the result of the anti-cholinesterase activity of a low dose of pancuronium although a receptors competitive action cannot be totally excluded (16-18). Succinylcholine, like mivacurium is eliminated by plasma cholinesterase (BChe) (19, 20), therefore we hypothesized the same pharmacokinetic effect of low dose of pancuronium (18) could enhance the duration of neuromuscular blockade of succinylcholine.

3. Patients and Methods

After ethical committee approval and informed consent 40 consecutive patients ASA I-III scheduled for elective orthopaedic surgery (bone marrow grafting of hip osteonecrosis) were assigned into 5 groups successively (n = 8 per group). The study was prospective open labelled. Exclusion criteria were age less than 18 or more than 90 year, possible difficult airway, oesophageal reflux and hiatal hernia, allergy to muscle relaxants, renal insufficiency and Body Mass Index (BMI) higher than 33 and a proven history of deficit in cholinesterase activity. After the insertion of IV line, and standard operating room monitoring and pre-oxygenation, the following anaesthetic sequence was used for each group:

- Group sux 1: sufentanil 5-15 μg + followed 2 minutes later by propofol 2-3 mg/kg followed by succinylcholine, 1 mg/kg
- Group sux 1: sufentanil 5-15 μg + pancuronium 7.5 μg/kg followed 2 minutes later by propofol 2-3 mg/kg followed by succinylcholine, 1 mg/kg
- Group sux 1.5: sufentanil 5-15 μg + pancuronium 7.5 μg/kg followed 2 minutes later by propofol 2-3 mg/kg followed by succinylcholine, 1.5 mg/kg
- Group Atra sux 1: sufentanil 5-15 μg + atracurium 0.05 mg/kg followed 2 minutes later by propofol 2-3 mg/kg followed by succinylcholine, 1 mg/kg
- Group Atra sux 1.5: sufentanil 5-15 μg + atracurium 0.05 mg/kg followed 2 minutes later by propofol 2-3 mg/kg followed by succinylcholine, 1.5 mg/kg

After the injection the non-depolarizing muscle relaxant (NDMR), any complaint in relation to their side effects (weakness, blurred vision difficulty in breathing or swallowing, desaturation) was noted.

Monitoring neuromuscular blockade was performed by a force transducer with a 300 g preload attached to a Gould® monitor, and train of four stimulation every 12 second yielded by a classic nerve stimulator on the adductor pollicis muscle (ulnar nerve). Tracheal intubation was performed when maximum succinylcholine neuromuscular blockade at the adductor pollicis was reached. Anesthesia was maintained with isoflurane 1 MAC/ and O_2/air mixture and boluses of sufentanyl 5-10 μg as necessary.

3.1. Statistical Analysis

The sample size was designed to obtain a mean difference in full recovery of neuromuscular blockade of 3 minutes (30%) with a standard deviation of 3 minutes a power of 80 % and a confidence interval of 95%. Kruskall Wallis ANOVA was used to compare results. A p value of less than 0.05 was considered to be statistically significant. Sys-Stat V10 for windows (IL, USA) was used for data analysis.

4. Results

The mean age of patients was of 59 ± 12 year with a mean weight of 75 ± 23 kg and the mean height 167 ± 11 cm, no statistical difference was found between groups in demographic characteristics. No side effects occurred after the injection of pancuronium or atracurium.

Maximum blockade reached 100% except in Atra sux 1 group (95%).

The mean duration of Succinylcholine neuromuscular blockade (1mg/kg and 1,5 mg/kg) was significantly prolonged when it was preceded by administration of low dose pancuronium and shortened when preceded by low dose atracurium in comparison with Succinylcholine 1mg/kg alone ($P < 0.05$) (Table 1).

Table 1. Neuromuscular Characteristics of Different Combinations

	E Max [a], %	T 70 [b], Min	T 90 [b], Min	T 100 [b], Min	Significance
Atra sux 1	95	4.8 (3.3-7.4)	6.0 (4-8.5)	7.1 (4.8-9)	$P < 0.05$ vs sux 1
Panc sux 1	100	12.2 (7-21.5)	14.3 (8.8-23.7)	15.8 (11.3-26)	$P < 0.05$ vs sux1
Sux 1	100	9.1 (5.8-13.2)	11.5 (6.8-15.7)	12.4 (9.1-16.9)	-
Panc sux 1.5	100	13.3 (8.2-20.8)	15.8 (10.7-24.1)	18.2 (12.5-28.7)	$P < 0.05$ vs sux 1
Atra sux 1.5	100	8.6 (4.7-12.3)	10.4 (5.8-10.5)	12.6 (7.2-16)	$P < 0.05$ vs panc sux 1.5

[a] Emax, maximum blockade.
[b] T70,90,100 Min, Time to 70,90,100 min recovery of the first twitch height.

5. Discussion

This study shows that low dose of pancuronium prolongs the duration of action of Succinylcholine induced paralysis whereas atracurium reduces it, therefore increasing the dose of succinylcholine is not necessary in case of pancuronium pre-treatment. Traditionally the administration of a very low dose of NDMR is used to prevent succinylcholine induced side effects (mostly fasciculations and post-operative myalgias) (21), however the dose of sucinylcholine should be increased to obtain satisfactory neuromuscular paralysis and or intubation conditions described in several investigations (10, 12, 22) this was demonstrated also in the present study with atracurium followed by succinylcholine 1mg/kg since the maximum neuromuscular effect was of 95% in comparison to other combinations or alone. Nevertheless, despite multiple studies considering side effects of pretreatment very few investigated the duration of induced paralysis after such combinations.

As previously described with mivacurium, the potentiation of succinylcholine by pancuronium might be explained by the reduced hydrolysis of succinylcholine due to Bche inhibition (18). Although clear relationship between a decrease in Bche and a prolongation of effect of mivacurium could not be demonstrated (18).

We used the higher dose of pancuronium suggested for pre-treatment (21) to fulfill the purpose of the study in

order to yield a decrease in cholinesterase activity, however our timing of the propofol injection (2 minutes after injection of low dose of pancuronium or atracurium), avoided the occurrence of side effects including blurred vision, diplopia, heavy eyelids, weakness, difficulty in breathing and swallowing or desaturation.

This investigation was open labelled, and not randomized since our primary endpoint was objective assessment of dose-effect relationship in clinical practice, we also did not measured the Bche after administration of pancuronium but in accordance to our previous dose-response investigations with intubating and maintenance doses we assumed Bche would significantly decrease despite remaining within clinical range (18). In addition the sample size was not chosen to evaluate the side effect of succinylcholine but only to prove an increase in the duration of paralysis. This study confirms the result of a previous investigation using higher dose of NDMR for pre-treatment (17).

Low dose of NDMR before succinylcholine is considered to be safe provided accurate dosing and timing however we suggest to consider also the type of NDMR as pancuronium enhances the effect of succinylcholine and atracurium reduces it, therefore increasing the dose of succinylcholine is not justified when pancuronium is used as a pre-treatment.

Author's Contributions

Cyrus Motamed and Philippe Duvaldestin designed performed the study and wrote the manuscript.

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