PRETREATMENT WITH REMIFENTANIL IS ASSOCIATED WITH LESS SUCCINYLCHOLINE-INDUCED FASCICULATION

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Abstract

Background: Succinylcholine is a popular muscle relaxant and one of its most common side effects is muscle fasciculation. The purpose of this study was to evaluate the efficacy of remifentanil in preventing succinylcholine-induced fasciculation in patients undergoing general anesthesia.

Methods: In a prospective, double blind study, 60 ASA I & II patients were randomly assigned into two groups (30 each) to receive either remifentanil1 μg/kg (Group R), or saline 3 ml (Group S) as a pretreatment agent, one minute before induction of general anesthesia by propofol, fentanyl, and 1.5 mg/kg succinylcholine. The duration and the intensity of fasciculation were assessed using a four-point rating scale. Data were analyzed by Mann-Whitney *U*-test, Fisher exact test and Student-t-test using SPSS software.

Results: In the remifentanil group the duration ($p<0.001$) and the intensity ($p<0.001$) of fasciculation were lower compared to the saline group. However the incidence of bradycardia was higher in the remifentanil group in comparison to the group which received normal saline.

Conclusions: Our findings indicate that remifentanil can reduce the duration and the intensity of succinylcholine induced fasciculation. However, it induces greater bradycardia.

Key words: remifentanil, succinylcholine, propofol, fasciculation.

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Introduction

Succinylcholine survives into its sixth decade (1952 to the present) by distinctive advantages, namely, low cost, fast onset of action, fast recovery, excellent muscular relaxation, and nontoxicity of its metabolites[1]. However, it has some undesirable side effects, such as fasciculation and postoperative myalgia.

Numerous methods have been used to alleviate or attenuate fasciculation[2,3]. Although these methods were helpful to a certain extent, each one had drawbacks of its own.

Remifentanil is a synthetic and esterase-metabolized opioid with a rapid onset, an ultra-short duration of action and a stable, short context-sensitive half time compared with other opioids[4,5]. Recent studies have suggested that propofol in combination with remifentanil may have muscle relaxant properties and could provide adequate conditions for laryngoscopy and tracheal intubation without using muscle relaxants[6,7].

We designed a prospective double blind, randomized study to evaluate the effectiveness of remifentanil in preventing fasciculation following succinylcholine injection in patients anesthetized with propofol, fentanyl, and succinylcholine.

Methods

After approval by our institutional Ethics Committee and procurement of patients' written informed consent, we studied 60 adult patients, ASA physical status I or II, scheduled for ambulatory urological or gynecological surgery under general anesthesia. This study was carried out in the Be'sat Hospital, Keshavarz St. Sanandaj, Iran. Exclusion criteria included known allergy to the pretreatment agent arrhythmia, hypo-or hypertension, dehydration, hyperkalemia, increased intraocular pressure, increased intracranial pressure, history of malignant hyperthermia, presenting a difficult airway, pregnancy, treatment with any drug known to interact with neuromuscular function, and significant renal, neuromuscular, or hepatic disease.

The observer and the patients were unaware of the pretreatment used and patients were randomized using computer-generated random numbers into two groups (30 each) in accordance to the pretreatment designed: NaCl 0.9% (control), and remifentanil 1μg/kg (study) that were always adjusted to a 3-mL volume. Standard monitoring included ECG, non-invasive oscillometric blood pressure, pulse oximetry, and end-tidal carbon dioxide levels.

No agent was given for premedication. The induction regimen was standardized for all patients and consisted of the following:

At time 0, injection of fentanyl 1 μg/kg together with the pretreatment designed for each group;

2 min later, anesthesia was induced with propofol 2 mg/kg IV and succinylcholine 1.5 mg/kg. Following succinylcholine, the patient was observed by an observer who was unaware of patient's group and fasciculation was graded according to a 4-point rating scale[8]:

no fasciculation = 0.

mild, fine fasciculation of the eyes, neck, face or fingers without limb movement = 1.

moderate fasciculation occurring at more than two sites or obvious limb movement = 2.

vigorous or severe, sustained, and widespread fasciculation = 3.

Changes in the cardiac rhythm or blood pressure following induction of anesthesia were also recorded.

Patients were ventilated via face mask and none of them intubated. Anesthesia was maintained with a mixture of N_2O/O_2 60%/40% with isoflurane1-1.3%.

Sample-size calculation was performed based on the pilot study, in that, the incidence of fasciculation was 96%, and we aimed at detecting a decrease to less than 50% with remifentanil pretreatment. With a power of 80% and type 1 error of 5%, we calculated that 30 subjects were required per group.

Statistical analysis was performed using SPSS 14.0 for Windows. Demographic data were analyzed by using the Mann-Whitney *U*-test. The incidence and the intensity of fasciculation were analyzed using Fisher's exact test and Student-t-test. Student's *t*-test was used to analyze bradycardia and arrhythmia between the two groups. A value of $P < 0.05$ was considered statistically significant.

Results

Demographic data showed there was no ststistical difference balance Groups R & S (Table 1).

Table 1
Demographic data and duration of surgery in Groups R-S

	Group R (n = 30)	Group S (n = 30)	P
Age (years)	31.3 ± 11.7	37.8 ± 13.7	0.6
Weight (kg)	67.4 ± 10.9	69.4 ± 12	0.5
Gender ratio (m/f)	16:14	19:11	0.6
Duration of surgery (min)	7 (2.4)	8 (3.1)	0.9

Group R: Remifentanil. Group S: Saline 0.9%
Values are mean ± sd or numbers (gender ratio).

The duration and the intensity of muscle fasciculation were significantly reduced by pretreatment with remifentanil as compared to that of saline: (P<0.05) (Table 2).

Table 2
The duration and the intensity of muscle fasciculation in Group R & S

Pretreatment	Group R (n = 30)	Group S (n = 30)	Differeces (95% CI)
Intensity			
0(n)	4*	1	
1(n)	20*	12	
2(n)	5*	10	
3(n)	1*	7	
Duration(second)	21.4(17.8)	41.9(20.6)*	20.5(10.2-30.9)

Group R: Remifentanil. Group S: Saline 0.9%
* P<0.05 compared with Group NS.

Baseline MAP and HR values were not significantly different between the two groups. However, after induction of anesthesia, MAP decreased significantly in group remifentanil compared to baseline values (P<0.05). The percentage decrease in MAP values from baseline was significantly higher in Group remifentanil than in Group saline (16.6% ± 11.8 *vs.* 6.3% ± 10.7); (P<0.05). Ephedrine was not used in any patient.

Following induction of anesthesia, HR decreased in Group remifentanil compared to baseline (P<0.05); whereas, HR in Group saline did not show significant changes compared to baseline. Also, the percentage change from baseline HR values was significantly higher in Group remifentanil than in Group saline (19.2% ± 9.7 *vs.* 2.9% ± 12.4). In Group remifentanil, eight patients developed a decrease of HR by more than 20% from baseline necessitating the use of atropine, while in Group saline none of the patients required atropine (P<0.05).

Discussion

Succinylcholine is the relaxant of first choice for endotracheal intubation and for short operative procedures requiring good muscular relaxation. However, its use is associated with considerable fasciculation.

Fasciculation have been attributed to a prejunctional depolarizing action of succinylcholine, resulting in repetitive firing of the motor nerve terminals and antidromic discharges that manifest as uncoordinated muscle contractions[9]. To solve this problem, several preventive methods had been tried including: pre-treatment with a small dose of non-depolarizing muscle relaxant[10], Pre-treatment with lignocaine[11], diazepam[12], magnesium sulphate[13], high-dose Propofol[14], and self-timing of succinylcholine-induced fasciculation[15].

Few studies have been designed to evaluate the effect of pretreatment with opioids on succinylcholine induced fasciculation, none of them used remifentanil.

Lindgren and colleagues designed[16] a prospective study to compare the effects of tubocurarine, alcuronium, pancuronium, and fentanyl on muscle fasciculation associated with succinylcholine in 171 children undergoing otolaryngological surgery. They concluded that the most effective pre-treatment was fentanyl (2.0 µg/kg) followed, in order, by alcuronium, fentanyl (1 µg/kg), tubocurarine and pancuronium. In another study with a different design, the same authors evaluated the change in intragastric pressure after the administration of succinylcholine in 32 children pretreated with physiological saline or alfentanil 50 µg/kg. anesthesia was induced with thiopentone 5 mg/kg. They concluded that alfentanil 50 µg/kg effectively inhibits the incidence and the intensity of succinylcholine induced muscle fasciculation, moreover, intragastric pressure remains in control values[17].

Yli-Hankala and colleagues[18] studied the effects of alfentanil on succinylcholine induced muscle fasciculation, in a double blind study in 34 children and

30 adults. They concluded that alfentanil significantly decreased the intensity of visible fasciculation caused by succinylcholine. In children the duration of muscle fasciculation was shorter in the alfentanil group than in the control group. In adults, the intensity rather than the duration of fasciculation was attenuated by alfentanil. The inhibition of fasciculation caused by alfentanil was demonstrated in children in electromyogram recorded on the biceps muscle.

Our results demonstrated the efficacy of 1 μg-kg remifentanil in reducing both the incidence and the intensity of fasciculation. All patients of our study received fentanyl as premedication, and propofol as anesthesia inducing agent, so fentanyl and/or propofol could not here influenced the results.

The mechanism of the inhibitory action of remifentanil on succinylcholine induced muscle fasciculation is unclear. Remifentanil is a new synthetic μ opioid agonist that is characterized by a rapid onset of action due to a short blood-effect site equilibration half-time and a rapid offset of action due to its high clearance by nonspecific blood and tissue esterases[19]. On the other hand, Propofol has been shown to decrease muscle tone in a dose-dependent manner in clinical use, and this effect is attributed not only to the central nervous system depression but also to a block in the skeletal muscle sodium channels[14]. Additionally, the administration of propofol 3.5 mg/kg may attenuate both the incidence and the intensity of muscle fasciculation[14]. All patients in our study received an induction dose of propofol (2 mg kg^{-1}), that did not attenuate fasciculation[20,21].

Propofol and remifentanil are both short-acting anesthetic agents that complement each other pharmacodynamic profiles (*i.e.*, hypnosis, analgesia and return of consciousness)[19]. In a report, the pharmacodynamics of remifentanil and its interaction with propofol were investigated. The authors reported that propofol reduces remifentanil requirements to suppress responses to laryngoscopy, intubation, and intra-abdominal surgical stimulation in a synergistic manner[19]. Remifentanil combined with propofol is therefore a promising combination for preventing succinylcholine induced muscle fasciculation.

There are some limitations with this study. First, the study design was observational, and we measure a subjective variable (fasciculation) rather than objective variables (increase in potassium, myoglobin, and CPK).The objective variables are not as easy to measure as fasciculation[22]. Second: We evaluated only remifentanil; therefore, comparisons to other drugs especially non depolarizing muscle relaxants, cannot be made.

In conclusion, we believe that remifentanil 1 μg/kg administered for induction of anesthesia is capable of reducing the incidence and the intensity of succinylcholine-induced fasciculation, however, it can concomitantly induce bradycardia.

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