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Pretreatment with remifentanil to prevent withdrawal after rocuronium in children

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Background. Pain from rocuronium injection is a common side-effect reported to occur in 50–80% of the patients. This randomized, double-blind, placebo-controlled study was designed to evaluate the efficacy of pretreatment with i.v. remifentanil on prevention of withdrawal response during rocuronium injection in paediatric patients.

Methods. After obtaining parental consents, 70 paediatric patients were randomly allocated into two groups to receive either i.v. remifentanil 1 $\mu g\ kg^{-1}$ (remifentanil group, n=35) or i.v. saline 5 ml (saline group, n=35). Anaesthesia was induced with thiopental sodium 2.5% (5 $mg\ kg^{-1}$) and the test drug was injected over 30 s. One minute after the test drug injection, rocuronium 1% (0.6 $mg\ kg^{-1}$) was injected over 5 s and the response was recorded. Mean arterial pressure (MAP) and heart rate were recorded on arrival in the operating theatre, before and 1 min after the tracheal intubation.

Results. The overall incidence of withdrawal movements was significantly higher in the saline group (33 patients; 94%) than that in the remifentanil group (8 patients; 23%) (P<0.001). No patient in the remifentanil group showed generalized movement, whereas 51% of patients in the saline group did. Remifentanil prevented significant increase in MAP after intubation.

Conclusion. This study demonstrated that pretreatment with remifentanil 1 $\mu g\ kg^{-1}$ provided a safe and simple method for reducing the incidence of rocuronium-associated withdrawal movement with haemodynamic stability in children.

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Pain on rocuronium injection is a common side-effect reported in 50–80% of the patients.[1–3] Even after loss of consciousness during induction of anaesthesia, rocuronium injection is associated with withdrawal of the arm or generalized movement and such movements are presumed to be secondary to pain at the site of injection.[2 3]

Pretreatment or mixing with a variety of drugs such as fentanyl and lidocaine has been suggested to attenuate the withdrawal movements related to rocuronium injection pain.[4–9] Fentanyl was more effective in the prevention of withdrawal response than lidocaine.[7] Although withdrawal movements have a tendency to occur more frequently in younger patients,[4] previous studies were focused mostly on adult patients,[4–7] and a few studies were on children.[3 8]

Compared with other opioids such as fentanyl, remifentanil has the advantage of shortening the induction time and maintaining stable haemodynamics during anaesthesia induction owing to its faster onset and shorter duration.[10] However, there have been no reports on the use of remifentanil for reduction of withdrawal movements on rocuronium injection in children. This randomized, double-blind,

placebo-controlled study was designed to evaluate the efficacy of pretreatment with i.v. remifentanil to prevention of withdrawal response during rocuronium injection in paediatric patients.

Methods

This study was approved by the institutional review board, and informed parental consent was obtained. The study was conducted prospectively on 70 patients aged between 3 and 10 yr, ASA physical status I or II, undergoing general anaesthesia for elective surgery. Patients were randomly allocated into two groups to receive either i.v. remifentanil 1 $\mu g\ kg^{-1}$ (remifentanil group, n=35) or i.v. saline 5 ml (saline group, n=35) using a sealed envelope system. Patients with known allergy to opioids, asthma, neurological deficits, those who received analgesics or sedatives within the previous 24 h, and crying children on arrival in the operating theatre were excluded from this study. Patients, anaesthesia providers and investigators who scored the movements were blinded to the treatment group and an independent researcher prepared the study solution consisting of 5 ml mixture of remifentanil (Ultiva, GlaxoSmithKline®, UK) 1 $\mu g\ kg^{-1}$ and normal saline in the remifentanil group and 5 ml of normal saline in the normal saline group. The study syringes were stored in ambient temperature.

No premedication was administered before surgery. Before arrival at the operating theatre, a 24-gauge cannula was inserted in the dorsum of the hand, and its position was confirmed by a free flow of dextrose/saline infusion by gravity. All patients were monitored with electrocardiogram, pulse oxymeter, non-invasive arterial pressure, capnography and end-tidal sevoflurane monitor on arrival at the operating theatre. Mean arterial pressure (MAP) and heart rate (HR) were recorded on arrival at the operating theatre (baseline), before and 1 min after the tracheal intubation. All drugs were administered through the rubber port connected to the i.v. cannula with a free flow of i.v. fluid. After preoxygenation, anaesthesia was induced with 2.5% thiopental sodium 5 $mg\ kg^{-1}$ followed by free flow of i.v. fluid until loss of consciousness, which was assessed by loss of eye reflex. Mask ventilation was initiated with oxygen, $F_{I_{O_2}} = 1$, once the patient became unconscious and apnoeic. Ten seconds later, the test drug was injected over 30 s by the blinded investigator. One minute after the test drug injection, rocuronium 1% (0.6 $mg\ kg^{-1}$) was injected over 5 s. Patient response was graded by the investigator according to the following scale proposed by Shevchenko and colleagues:[3] 1=no response, 2=movement at the wrist only, 3=movement/withdrawal involving arm only (elbow/shoulder) and 4=generalized response, movement/withdrawal in more than one extremity. The investigator also recorded the incidence of coughing and breath holding.

Sevoflurane was started after rocuronium injection and its end-tidal concentration was adjusted to maintain 2.5 vol% in 100% oxygen. The trachea was intubated 2 min after rocuronium injection and their lungs were mechanically ventilated to maintain normocarbia. Anaesthesia was maintained with sevoflurane (end-tidal concentration of 2–4 vol%) in oxygen/nitrous oxide ($F_{I_{O_2}}$=0.5). Intubation time, which was defined as the time from mouth opening to obtaining an appropriate capnograph trace, was measured in all patients.

Statistical analyses were performed using the statistical package (SPSS 11.0 for windows, SPSS Inc., Chicago, IL, USA). Data are presented as mean (SD) or number of patients. Patients' characteristics were compared with Student's t-test or Fisher's exact test where appropriate. Incidence of withdrawal movement was analysed with Fisher's exact test. Haemodynamic variables were analysed using repeated measures ANOVA. To detect a 50% difference in the incidence of withdrawal movement on rocuronium injection at a significant level of 5% and a probability power of 80%, this study required at least 32 patients per group on the basis of power analysis estimating the incidence of 80%. Statistical significance was defined as $P \leqslant 0.05$.

Results

There was no significant difference in patient characteristics between the two groups (Table 1). Five patients coughed during the induction of anaesthesia only in the remifentanil group, but the difference was not statistically significant.

The incidence and grade of withdrawal movement are listed in Table 2. The overall incidence of withdrawal movements was significantly higher in the saline group

Table 1 Patient characteristics. Values are mean (SD) or number of patients. ET Sevo, end-tidal sevoflurane concentration just before intubation; coughing, coughing patients during the induction of anaesthesia. No significant differences between the groups were noted

	Remifentanil (n=35)	Saline (n=35)
Sex (M/F)	25/10	23/12
Age (yr)	7.2 (4–10)	6.7 (4–10)
Weight (kg)	25.8 (8.0)	23.2 (6.1)
ET Sevo (%)	2.6 (0.3)	2.6 (0.2)
Intubation time (s)	17.3 (3.0)	16.3 (3.6)
Coughing (n)	5	0

Table 2 Incidence and grade of withdrawal movements associated with rocuronium injection. Values are number of patients (percentage). *P<0.05 compared with saline group

Grade of withdrawal movements	Remifentanil (n=35)	Saline (n=35)
1 (No withdrawal)	27 (77%)*	2 (6%)
2 (Wrist withdrawal)	6 (17%)	2 (6%)
3 (Arm only)	2 (6%)*	13 (37%)
4 (Generalized movement)	0 (0%)*	18 (51%)