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Effect of narcotic pretreatment on pain after rocuronium injection: a randomized, double-blind controlled comparison with lidocaine

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Abstract
Various strategies have been studied to reduce the discomfort of rocuronium pain. These studies have shown fentanyl and lidocaine to be effective in reducing the incidence of pain on rocuronium injection. This prospective, randomized, and double-blind study was carried out on 80 neurosurgical patients for whom pain on rocuronium injection was assessed after pretreatment with lidocaine, fentanyl, sufentanil, or normal saline. The 80 neurosurgical patients were randomly allocated to anyone of the groups to receive lidocaine, fentanyl, sufentanil, or normal saline prior to being given rocuronium. The patients were asked about any discomfort in the hand, and also to rank that discomfort on a 5-point scale. In the normal saline group, the incidence of pain was 95%, of which 90% had very severe pain. In the lidocaine group, only 10% of patients reported pain, which was mild in nature. In the fentanyl group, 95% of patients had pain, of whom 25% had severe to very severe pain. In the sufentanil group, 85% of patients reported pain, of whom 25% fell into the severe to very severe group. We found that lidocaine was best at decreasing the incidence of pain on intravenous (i.v.) injection of rocuronium. Although the incidence of pain on injection of rocuronium with both fentanyl and sufentanil was high, the intensity was definitely reduced, with most patients falling in the mild pain group.

Key words Rocuronium · Pain · Narcotics · Neurosurgical patients

The fact that rocuronium bromide injection causes pain in both awake and anesthetized patients is now well established [1,2]. The incidence is high (50%–80%) [3], and the pain is at times severe and burning [1–4]. Various strategies have been studied to reduce the discomfort [5–9], but to date, no study has evaluated the effect of sufentanil on this pain. The purpose of this study was to determine the effect of sufentanil, and compare it with that of fentanyl and lidocaine in patients undergoing neurosurgical procedures. Earlier studies have shown that both fentanyl and lidocaine are effective in reducing the incidence of pain on rocuronium injection [5–9].

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Material and methods

This prospective, randomized, and double-blind study was carried out after obtaining approval from Institution Ethics Committee and informed patient consent. Eighty patients, aged between 20 and 75 years, of both sexes, belonging to American Society of Anesthesiologist (ASA) physical status 1 or 2, and posted for elective neurosurgery were enrolled in the study. The patients were randomly allocated to one of four groups of 20 patients each. In group 1, patients received 5 ml normal saline intravenously before 1 ml (10 mg) rocuronium bromide, while in groups 2, 3, and 4, patients received 1 mg/kg 2% lidocaine, 1 μg/kg fentanyl, and 0.5 μg/kg sufentanil, respectively, all diluted to 5 ml in normal saline. All patients were premedicated with 0.2 mg intramuscular glycopyrrolate 1 h prior to the induction of anesthesia. After electrocardiography, and noninvasive blood pressure and pulse oximetry monitoring, an 18-gauge i.v. cannula was inserted on the dorsum of the hand. The test drug was prepared by independent anesthetists according to a computer-generated randomization chart. A blinded investigator recorded the responses to drug injection.

We excluded all patients with difficult venous access, thin dorsal veins, those requiring rapid sequence, the presence of an allergy to any of the anesthetic medication, and those unable to provide informed consent. Patients were informed that they would be receiving a

Table 1. Assessment of pain and scoring [10]

Pain score	Severity of pain	Patient's response
0	None	No pain or discomfort reported when questioned
1	Mild	Pain or discomfort reported by the patient to be mild when questioned
2	Moderate	Pain or discomfort reported by the patient to be moderate when questioned
3	Severe	Pain or discomfort reported spontaneously by the patient and stated to be severe
4	Very severe	Pain or discomfort associated with a strong vocal response, hand or arm withdrawal, facial grimacing, or crying, and reported to be very severe

Table 2. Demographic characteristics of the patients (mean ± SD)

	Weight (kg)	Age (years)	Sex (M:F)
Group 1	55.5 ± 10.9	40.7 ± 14.2	11:9
Group 2	61.3 ± 11.9	38.4 ± 11.4	16:4
Group 3	60.0 ± 11.1	40.7 ± 11.4	15:5
Group 4	52.4 ± 13.7	34.4 ± 14.6	9:11

drug at the start of the anesthetic that may or may not cause pain. They were also told about the scoring system of their pain. Pain, if any occurred, was graded as shown in Table 1 [10].

A pneumatic tourniquet was applied on the upper arm and inflated to 70 mmHg to produce venous occlusion. The test drug was then injected. One minute later, the tourniquet was released and 10 mg rocuronium bromide, at room temperature, was injected over 10–15 s. During this period, the patients were asked about any discomfort in the hand, and also to rank the discomfort on the 5-point scale. Immediately thereafter, general anesthesia was induced with fentanyl and thiopentone sodium. The observations were tabulated, and the syringes were decoded. One-way analysis of variance (ANOVA) was used for a comparison of mean age, sex, and weight among the groups. The χ^2 test was used for a comparison of the grades of pain among the different groups. A value of P less than 0.05 was considered significant.

Results

The demographic data were comparable in all groups (Table 2). In the normal saline group, the incidence of pain was 95% (19 patients), of whom 90% (18 patients) had very severe pain, and 5% (1 patient) had severe pain. In lidocaine group, only 10% (2 patients) reported pain, which was mild in nature. In the fentanyl group, 95% (19 patients) had pain, of whom 25% (5 patients) had severe to very severe pain, and the remaining 70% (14 patients) complained of only mild to moderate pain. In the sufentanil group, 85% (17 patients) reported pain, of whom 25% (5 patients) had pain of a severe to very severe degree, and the rest (12 patients) had pain of mild to moderate degree (Table 3).

Discussion

The pain on injection of rocuronium is significant, both in incidence [1–3] and intensity. It has been described as a "burning" sensation [1–4]. Pain has been found to occur immediately on injection, in both awake and anesthetized patients [1–5].

Rocuronium is an important addition to anesthetic practice because of its rapid onset of action. It is also one of the best precurarizing agents [11]. The mechanism by which rocuronium causes pain is the subject of speculation. It has been attributed to its low pH [12], but a study by Borgeat and Kwiatowksi [2] showed that patients receiving i.v. saline adjusted to pH 4.0 reported no pain. Tuncali et al. [13] showed that the osmolalities of undiluted (10 mg/ml) rocuronium and of that diluted to 1 or 0.5 mg/ml with 0.9% NaCl did not differ significantly but undiluted rocuronium still caused significant pain on injection as compared with the diluted preparations. These studies validate the fact that pH and osmolality are not the major causes of pain during i.v. administration.

Joshi and Whitten [6] showed that pretreatment with midazolam and 100 mcg of i.v. fentanyl prevented the pain associated with the injection of a defasciculating dose of rocuronium in adults. Borgeat et al. [8] found 2 mcg/kg of fentanyl to be effective in reducing pain on the injection of rocuronium. Shevchenko et al. [5] found that using lidocaine pretreatment causes a significant decrease in the incidence of withdrawal on rocuronium administration in children and adolescents. Cheong and Wong [7] found that 10 and 30 mg i.v. lidocaine significantly reduced the incidence and severity of pain on injection of rocuronium, and that the larger dose was more effective. Reddy et al. [14] demonstrated that ondansetron was effective in reducing the pain of

Table 3. Distribution according to intensity of pain

	Pain score				
	None (0)	Mild (1)	Moderate (2)	Severe (3)	Very severe (4)
Group 1 (n = 20) normal saline	1 (5.0%)	0 (0.0%)	0 (0.0%)	1 (5.0%)	18 (90.0%)
Group 2 (n = 20) lidocaine	18 (90.0%)	2 (10.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Group 3 (n = 20) fentanyl	1 (5.0%)	9 (45.0%)	5 (25.0%)	3 (15.0%)	2 (10.0%)
Group 4 (n = 20) sufentanil	3 (15.0%)	11 (55.0%)	1 (5.0%)	3 (15.0%)	2 (10.0%)

n, number of patients
P value for group 1 vs 2 < 0.001; group 1 vs 3 < 0.001; group 1 vs 4 < 0.001; group 2 vs 3 < 0.001; group 2 vs 4 < 0.001; group 3 vs 4 = 0.424

rocuronium, but not as effective as lidocaine. Memis et al. [9] found that ondansetron, lidocaine, tramadol, and fentanyl were all effective in minimizing the pain caused by the injection of rocuronium, and that lidocaine was the most effective. In another study by Turan et al. [15] comparing magnesium sulfate, lidocaine, sodium bicarbonate, and alfentanil, magnesium sulfate and sodium bicarbonate were found to be effective. Chiarella et al. [10] demonstrated that mixing 10 mg rocuronium with 8.4% sodium bicarbonate reduced the pain during i.v. administration of rocuronium. Tuncali et al. [13] showed that the dilution of 10 mg/ml rocuronium to 1 mg/ml with 0.9% NaCl reduced the incidence and intensity of pain, whereas dilution to 0.5% mg/ml completely prevented the pain associated with i.v. rocuronium injection. Dalgleish et al. [16] suggested the use of larger veins to inject rocuronium.

We conducted this study using sufentanil because to date no study has been conducted using sufentanil to attenuate the pain of rocuronium injection. In addition, our choice of neurosurgical patients sets this study apart because narcotics as analgesics are used in neurosurgical procedures. Therefore, the use of sufentanil and fentanyl before rocuronium injection, if found to be effective in reducing the pain, would not add to the co-administered drugs. They would also serve their intended purpose of providing analgesia.

Neurosurgical patients are usually on long-term phenytoin and steroids, which have been shown to have some analgesic and anti-inflammatory properties. Thus, any confounding influence that these drugs might have could also be uncovered and subjected to further evaluation.

The results of our study were in accordance with earlier studies conducted on nonneurosurgical patients. We found that lidocaine was the best at decreasing the incidence of pain on i.v. injection of rocuronium. Although the incidence of pain on injection of rocuronium with either fentanyl or sufentanil was high, the intensity was definitely reduced, with most patients falling into the mild pain group.

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