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Original Contribution

Dexmedetomidine reduces pain associated with rocuronium injection without causing a decrease in BIS values: a dose-response study☆

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Abstract

Study Objectives: To examine whether dexmedetomidine reduces the injection pain of propofol and rocuronium and to investigate whether the decrease in injection pain is associated with the known sedative action of dexmedetomidine.

Design: Randomized, double-blind, placebo-controlled clinical comparison study.

Interventions: Patients undergoing general anesthesia with intubation received 40 mg of 1% lidocaine (lidocaine group; n = 28), 0.25 μg/kg of dexmedetomidine (low-dose group; n = 27), 0.5 μg/kg of dexmedetomidine (subclinical dose group; n = 28), 1.0 μg/kg of dexmedetomidine (clinical dose group, n = 27), or normal saline (saline group; n = 28) before anesthetic induction.

Measurements: Pain associated with propofol and rocuronium injection was assessed using a 10-point verbal analog scale (VAS) and a 4-point withdrawal movement scale, respectively. The BIS value was measured 60 seconds after administration of the study drug, and at the time of rocuronium injection and intubation.

Main Results: The overall incidence of withdrawal movements due to rocuronium decreased significantly as the dose of dexmedetomidine increased (92.8%, 85.2%, 78.6%, and 51.9% in the saline, low-dose, subclinical dose, and clinical dose groups, respectively; P = 0.001). There was no significant difference in BIS values among the groups 60 seconds after study drug administration or at the time of rocuronium injection.

Conclusions: Dexmedetomidine reduced pain associated with rocuronium injection in a dose-dependent manner. This effect was not associated with the decrease in BIS value.

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☆ The authors have no conflicts of interest to report.

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1. Introduction

Propofol and rocuronium cause pain on intravenous (IV) injection, with incidences of 20% to 100% and 22% to 84%, respectively [1-3]. Dexmedetomidine is a highly selective alpha-2 adrenoreceptor agonist with potent sedative, analgesic, and sympatholytic effects [4]. Although there are reports that dexmedetomidine reduces the pain associated with injection of propofol and rocuronium, the optimal dose and underlying mechanisms remain unclear.

The effect of dexmedetomidine at various doses in reducing injection pain was studied. A secondary aim was to investigate whether the decrease in injection pain was associated with the known sedative action of dexmedetomidine.

2. Materials and Methods

With approval of the Institutional Review Board of Catholic Medical Center (approval no. KC11MISI0584) and written, informed consent, we studied 150 ASA physical status 1 and 2 patients (aged 19-64 yrs), scheduled to undergo elective surgeries during general anesthesia from August to December, 2011. Patients who were allergic to the study drugs; those with diabetes mellitus, hypertension, ischemic heart disease, arrhythmias, or vascular disease; and those who had an infection at the injection site were excluded from the study. Patients were allocated to 5 groups using double-blind block randomization: saline group = normal saline, lidocaine group = 1% lidocaine, low-dose group = dexmedetomidine 0.25 μg/kg, subclinical dose group = dexmedetomidine 0.5 μg/kg, and clinical dose group = dexmedetomidine 1 μg/kg. All study drugs were prepared in 4 mL dilute saline solutions.

On arrival at the holding area, a 16-gauge angiocatheter was inserted into a vein on the dorsum of the hand. In the operating room (OR), electrocardiogram, noninvasive blood pressure (BP), heart rate (HR), pulse oximetry, and Bispectral Index (BIS; Aspect Medical Systems, Norwood, MA, USA) monitors were attached. The preassigned study drug was administered slowly over two minutes. At 60 seconds after administration of the study drug, BIS was recorded and 50 mg (5 mL) of propofol was injected. Pain was evaluated using a 10-point scale verbal analog score (VAS). The remaining propofol dose (total 2 mg/kg) was injected. Rocuronium 0.9 mg/kg was injected over 5 seconds and withdrawal movements related to rocuronium injection were graded according to a 4-point scale (grade 0 = no movement, grade 1 = movement at the wrist only, grade 2 = movement involving the upper arm and shoulder of the injected arm, and grade 3 = generalized movement or withdrawal in more than one extremity) [5]. After manual mask ventilation with 100% oxygen for one minute, tracheal intubation was performed. Aside from patient movement, the maximum BIS was recorded at the point of rocuronium injection and endotracheal intubation.

To compare hemodynamic changes, systolic (SBP), diastolic (DBP), and mean arterial pressures (MAP), and HR were recorded immediately after arrival at the OR and on intubation. All vital signs, 10-point VAS, and 4-point withdrawal movement scores after rocuronium injection were recorded by an anesthesiologist who was not involved in the study.

Because the 10-point VAS showed a normal distribution as a continuous variable in a pilot study, a *t*-test was performed to evaluate differences between the saline and clinical dose groups. The Δ [$\Delta = (u2 - u1)/\sigma$] of the 10-point VAS was 0.8, and the difference in mean values between the groups was 3.0, with a standard deviation of 3.75. The sample size required at a level of significance of 5% (2-sided $\alpha = 0.05$) and a power of 80% ($1 - \beta = 0.8$) was 26 patients per group; thus, we included 30 patients in each group. All data were analyzed using SigmaStat software (version 2.03; Systat, San Jose, CA, USA). To compare demographic data, a chi-squared test and one-way analysis of variance (ANOVA) were used. Hemodynamic variables were subjected to repeated-measures ANOVA, and Tukey's *post hoc* test was used if significance existed. The 10-point VAS and BIS score at the time of propofol injection were subjected to one-way ANOVA, and the 4-point withdrawal movement scores at the time of rocuronium injection were compared among groups using a chi-squared test. A P-value < 0.05 was considered to indicate statistical significance.

3. Results

There was no significant difference in demographic characteristics among the groups (Table 1). The clinical-dose and low-dose groups showed lower VAS scores than the saline group at the time of propofol injection, although the difference was not statistically significant (Fig. 1). The 4-point withdrawal movement score after rocuronium injection decreased significantly as the dose of dexmedetomidine increased (Table 2). No significant difference was noted in BIS among the groups at 60 seconds after drug administration, or on rocuronium injection or endotracheal intubation (Fig. 2).

With regard to hemodynamic variables immediately after arrival in the OR and after endotracheal intubation, the subclinical-dose and clinical-dose groups showed significantly lower HRs than the saline or lidocaine groups (Table 3).

4. Discussion

Dexmedetomidine premedication reduced the pain associated with rocuronium injection in a dose-dependent

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