ORIGINAL RESEARCH

Comparative evaluation of dosages and plasma concentrations of dexmedetomidine in clinically ill patients: An observational study

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ABSTRACT

Background: This study was conducted to assess the comparison between dosages and plasma concentrations of dexmedetomidine in clinically ill patients.**Material and methods**: Using a single-blind method, ultra performance liquid chromatography coupled with tandem mass spectrometry was used to measure the plasma dexmedetomidine concentrations of 65 samples taken from 50 patients who had been in an intensive care unit for a period of two months. Additionally, the correlation coefficient between dosages and plasma concentrations was calculated. The criteria for exclusion included individuals who were less than 15 years old and samples acquired from patients whose dosage of dexmedetomidine was altered within a period of three hours. SPSS software was used for evaluation of the results. **Results**:Among the patients, 30 (60%) of the 50 were given dexmedetomidine at a dosage range of 0.22–0.85μg/kg/h. Furthermore, in the 50 samples that were administered dexmedetomidine, this occurred for a median length of 17.9 hours, with a range that extended from three to eighty-seven hours. Dexmedetomidine plasma concentrations ranged from 0.25 to 2.58 ng/ml throughout the investigation. **Conclusion**:Patients were able to achieve an effective concentration of dexmedetomidine ranging from 0.25 to 2.58 ng/ml by administering a dosage of 0.22 to 0.85μg/kg/h.

Keywords: dexmedetomidine, dosages, plasma concentration.

INTRODUCTION

Dexmedetomidine is a highly selective central α2-agonist with anesthetic and analgesic properties used in critically ill pediatric patients.[1, 2] Dexmedetomidine has been used in children with heart disease,[3- 6] those undergoing mechanical ventilation,[7] and as part of an early extubation strategy.[8] A long duration of administration may be required.[5] In clinical settings, we administer dexmedetomidine in intensive care units at a dosage of 0.2–0.7 μg/kg/h because there is no commercially available blood concentration simulator. In Japan, a dosage of 0.2–0.7 μg/kg/h was used because medical insurance approved doses within this range. There is little information about the relationship between dosage and plasma concentration during long drug infusions of dexmedetomidine in critically ill patients.[9, 10]Hence, this study was conducted to assess the comparison between dosages and plasma concentrations of dexmedetomidine in clinically ill patients.

MATERIAL AND METHODS

Using a single-blind method, ultra performance liquid chromatography coupled with tandem mass spectrometry was used to measure the plasma dexmedetomidine concentrations of 65 samples taken from 50 patients who had been in an intensive care unit for a period of two months. Additionally, the correlation coefficient between dosages and plasma concentrations was calculated. The criteria for exclusion included individuals who were less than 15 years old and samples acquired from patients whose dosage of dexmedetomidine was altered within a period of three hours. For the purpose of conducting statistical analyses, the computer program Statistical Package for the Social Sciences (SPSS 19.0) was utilized. Utilizing either Pearson's r or Spearman's ρ, the correlation coefficient was determined based on the type of distribution being considered. There are no two-tailed P values found. We judged the P values to be significant if they were less than 0.05.

RESULTS

A total of 50 subjects were enrolled. Among them, 40 were males and 10 were females. Among the patients, 30 (60%) of the 50 were given dexmedetomidine at a dosage range of 0.22–0.85µg/kg/h. Furthermore, in the 50 samples that were administered dexmedetomidine, this occurred for a median length of 17.9 hours, with a range that extended from three to eighty-seven hours. Dexmedetomidine plasma concentrations ranged from 0.25 to 2.58 ng/ml throughout the investigation.

Table 1: Characteristics of the patients.

Characteristic	Value
Number of subjects	50
Gender Males Females	 40 10
Mean age (years)	68.3

Table 2: Details of administration of dexmedetomidine and sedation

Variable		Number
Duration of infusion (hours)		17.9
Plasma concentration (ng/ml)		1.13
Dosage (µg/kg/h)		0.38
Combination drug	No drug	20
	One drug	25
	Two drugs	3
	Three drugs or more	2
Intubation	33 subjects	
RASS	≥1	0
	0	21
	-1	12
	-2	8
	-3	5
	-4	2
	-5	2

DISCUSSION

Sedation plays a key role in the management of agitation and anxiety in the intensive care setting. The usual goal of sedation in the intensive care unit (ICU) is a calm, co-operative patient who is easy to rouse and who is able to communicate their needs, particularly for analgesia.[11, 12]

Guidelines recommend the use of dexmedetomidine, propofol and benzodiazepines (most commonly midazolam and lorazepam) for sedation in an intensive care setting, and suggest that nonbenzodiazepine agents may be preferred over benzodiazepines. Maintaining a light level of sedation in ICU patients is recommended, when possible, given that light sedation is associated with improved outcomes, including a shorter duration of ventilation and a shorter ICU stay.[13]Hence, this study was conducted to assess the comparison between dosages and plasma concentrations of dexmedetomidine in clinically ill patients.

In this study, a total of 50 subjects were enrolled. Among them, 40 were males and 10 were females. Among the patients, 30 (60%) of the 50 were given dexmedetomidine at a dosage range of 0.22–0.85µg/kg/h. Furthermore, in the 50 samples that were administered dexmedetomidine, this occurred for a median length of 17.9 hours, with a range that extended from three to eighty-seven hours. Dexmedetomidine plasma concentrations ranged from 0.25 to 2.58 ng/ml throughout the investigation. In the study conducted by Fujita Y et al[14], patients admitted to the PICU at Nagoya City University Hospital, Japan, between November 2012 and March 2013 were eligible for inclusion in the study. Plasma dexmedetomidine concentration was measured by ultra-performance liquid chromatography coupled with tandem mass spectrometry. They measured the plasma dexmedetomidine concentration in 203 samples from 45 patients. Of these, 96 samples collected from 27 patients < 2 years old were included in this study. All patients received dexmedetomidine at 0.12–1.40 µg/kg/h. The median administration duration was 87.6 hours (range: 6–540 hours). Plasma dexmedetomidine concentration ranged from 0.07 to 3.17 ng/ml. Plasma dexmedetomidine concentration was not correlated with the administered dose ($r = 0.273$, $P = 0.007$). The approximate linear equation was $y = 0.690x + 0.423$. In infants, plasma dexmedetomidine concentration did not exhibit any correlation with administered dose, which is not a reliable means of obtaining optimal plasma concentration.Eren G et al[15]compared the efficacy and

effects of dexmedetomidine and midazolam in preoperative sedation. A total of 125 patients in American Society of Anaesthesiologists (ASA) I-II were divided into three groups: Group I (n = 40) for controls, Group II (n = 40) for Dexmedetomidine (1 μg/kg), and group III was the midazolam group (n = 45). Group III was further divided into three subgroups according to the doses of midazolam: Group IIIA (n = 15) received 0.02 mg/kg, group IIIB (n = 15) received 0.04 mg/kg, and group IIIC (n = 15) received 0.06 mg/kg of midazolam. Drugs were infused over a 10-minute period with appropriate monitoring. Ramsay and visual analog scores, for sedation and anxiety, respectively, and mean arterial pressure, heart rate, and SpO2 measurement, including respiratory rates were recorded, every 5 minutes for 30 minutes following infusion. There was marked sedation and a decrease in anxiety in groups II and IIIC ($P < 0.01$). Mean arterial pressure (MAP) and heart rate (HR) decreased significantly in group II ($P < 0.01$ and $P < 0.05$, respectively), but there was no associated hypotension (MAP <60 mm Hg) or bradycardia (HR <50 bpm) ($P < 0.05$). Respiratory rates and SpO2 values decreased in groups II, IIIA, IIIB, and IIIC. The differences in respiratory rates were not significant ($P > 0.05$); however, decrease in SpO2 was significant in group IIIC ($P < 0.01$). Dexmedetomidine was as effective as higher doses of midazolam in sedation. The hemodynamic and respiratory effects were minimal. Although dexmedetomidine caused significant decrease in the blood pressure and heart rate, it probably just normalized increased levels caused by preoperative stress.

CONCLUSION

Patients were able to achieve an effective concentration of dexmedetomidine ranging from 0.25 to 2.58 ng/ml by administering a dosage of 0.22 to 0.85μg/kg/h.

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