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Original Contribution

Influence of dexmedetomidine on cognitive function in volunteers☆,☆☆

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Abstract

Study objective: Some outpatient procedures are performed under sedation with dexmedetomidine, although the effect of dexmedetomidine on cognitive function remains unclear. This study investigated the effect of dexmedetomidine on cognitive function in healthy volunteers.

Design: Observation study in volunteers.

Setting: University-affiliated teaching hospital.

Patients: Six healthy volunteers.

Interventions: After infusion of a 6-μg/kg per hour loading dose of dexmedetomidine for 10 minutes, a maintenance infusion of 0.4 μg/kg per hour was administered for 4 hours.

Measurements: Cognitive function was evaluated before infusion (baseline) and at 2, 4, 6, and 8 hours after infusion. Cognitive function, response speed, accuracy, and consistency were measured by CogHealth. Depth of sedation was evaluated at 1-hour intervals by evaluating the Bispectral Index. Data are presented as the change from baseline.

Main results: The Bispectral Index value was significantly lower from 10 minutes to 6 hours after infusion versus the pre-infusion value. Response speed was also significantly lower at 2 hours and 4 hours after infusion (92 ± 8%, $P< .0001$; 93 ± 6%, $P< .0001$), as was consistency (96 ± 7%, $P= .0009$; 96 ± 5%, $P= .0003$). Response accuracy was unaltered by the infusion.

Conclusions: Dexmedetomidine slightly reduced response speed and consistency, but did not affect response accuracy. Cognitive function was restored to pre-administration values 2 hours after the infusion of dexmedetomidine was discontinued.

1. Introduction

Dexmedetomidine is widely used as a sedative agent in patients under critical care [1,2]. Some outpatient procedures are also performed under sedation with dexmedetomidine because it has almost no effect on the respiratory system [3–5]. Dexmedetomidine has also been used for sedation during pediatric magnetic resonance imaging [6]. In fact, the Japanese Ministry of Health, Labor and Welfare recently approved the use of

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dexmedetomidine for non-intubated patients who have undergone surgery. However, an important consideration in using this agent is not only its respiratory and hemodynamic effects, but also its effects on cognitive function in outpatients after sedation. Although a few studies on cognitive function in volunteers or patients who received dexmedetomidine have been published, the effect of dexmedetomidine on cognitive function remains unclear [7–9]. The package leaflet for dexmedetomidine indicates that patients receiving this agent should avoid driving until the sedative effect disappears, it does not note how long it takes for the sedative effect to disappear.

CogHealth software (previous generation software of Cogstate, Melbourne, Australia) is a computer-based screening tool for cognitive function [10–12]. We suggest anesthesiologists should observe their patients after administering dexmedetomidine until their cognitive function and vital signs have recovered. An understanding of the effect of dexmedetomidine on cognitive function is necessary to improve outpatient safety. This study characterized the effect of dexmedetomidine by using CogHealth software to evaluate cognitive function in healthy volunteers.

2. Materials and methods

2.1. Ethics statement and study protocol

The ethics committee of Kochi Medical School hospital approved the study (ID 23–63). Written informed consent was obtained from the participants, who were healthy volunteers aged 20 years or older. Subjects who were undergoing medical treatment, had a history of serious adverse reaction or allergy to any drug, or abnormal electrocardiogram were excluded from the study. This study was performed in our intensive care unit for participant safety. Before administration of dexmedetomidine, vital sign monitoring was initiated and included electrocardiogram, non-invasive blood pressure, and hemoglobin oxygen saturation. After infusion of a 6-μg/kg per hour loading dose of dexmedetomidine (Precedex, Hospira Japan, Osaka, Japan) for 10 minutes, a maintenance infusion of 0.4 μg/kg per hour was performed for 4 hours. Cognitive function was evaluated before the infusion (baseline) and at 2, 4, 6, and 8 hours after. Depth of sedation was evaluated at 1-hour intervals by evaluating the Bispectral Index (BIS) (BIS Covidien; Boulder, CO).

2.2. Cognitive function

Cognitive function was evaluated using CogHealth, Japanese edition. The brief computerized test battery consists of 5 tests and provides a reliable measure of cognitive function [13]. The tests measure psychomotor function (Detection task: "Has the card turned over?"), attention (Identification task: "Is the card red?"), visual memory (One Card Learning task: "Have you seen this card before in this task?"), working memory (One Back task: "Is the card the same as the previous card?"), and visual attention function (Monitoring task: Does a moving card touch either one of the lines?"), and require approximately 15 minutes to complete [11,14]. One of the advantages of this tool is that it can be used repeatedly because there are no learning effects [11]. All participants received standard instructions before the administration of dexmedetomidine.

2.3. Statistical analysis

We evaluated cognitive function in the context of speed, accuracy, and consistency. The values for these 3 parameters in each of the 5 tasks were reported by CogHealth and averages were calculated. Cognitive function data are presented as the change from baseline. Statistical analyses were performed using a statistical software package (JMP 9; SAS Institute Japan, Tokyo, Japan). Changes in the BIS value and cognitive function were assessed by repeated-measures analysis of variance. $P < .05$ were considered statistically significant.

3. Results

3.1. Vital signs

Six healthy volunteers were enrolled; 3 were women (Table 1). The mean age was 29 ± 2 years (mean ± SD), and the mean body mass index was 22 ± 2 kg/m^2. Average heart rate at baseline was 82 ± 7 beat/min and minimum heart rate was 49 ± 7 beat/min at 5 hours after infusion (Table 2 and Fig 1). Heart rate was significantly lower from 10 minutes to 8 hours after infusion versus the pre-infusion rate. The mean blood pressure at baseline was 99 ± 5 mmHg and minimum mean blood pressure was 71 ± 5 mmHg at 6 hours after infusion. The mean blood pressure was significantly lower from 1 hours to 8 hours after infusion. The hemoglobin oxygen saturation at baseline was 99 ± 1% and minimum value was 97 ± 2%. The hemoglobin oxygen saturation from 10 minutes to 3 hours after infusion was significantly lower than that before infusion. The BIS value at baseline was 99 ± 5 and minimum value was 62 ± 11 at 3 hours after infusion. The BIS value from 10 minutes to 6 hours after infusion was significantly lower than it was prior to infusion.

Table 1 Participants' background

		N = 6
Gender	F:M	3: 3
Age	years	29 ± 2
Height	cm	165 ± 7
Weight	kg	60 ± 10
Body mass index	kg/m^2	22 ± 2

Data are mean ± SD.