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CLINICAL REPORT

A high dose of dexmedetomidine using the BIS monitor™ for diagnostic and interventional cardiac catheterization in a toddler with congenital heart disease

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Abstract Dexmedetomidine (DEX) for sedation in diagnostic and interventional cardiac catheterization (DICC) has been reported to require other drugs or rescue drugs because of its insufficient sedative effect when used alone. We administered DEX and adjusted its dose according to the bispectral index (BIS) monitor™ for DICC in a toddler; consequently, a high dose of DEX had to be administered. The patient was a 1-year and 4-month-old boy who was scheduled to undergo DICC after intracardiac repair. We used DEX alone as the sedative because this was expected to avoid oxygen supply and mechanical ventilation and to produce a safe situation for procedures around the neck. DEX was administered at the dose of 1–15 μg/kg/h according to BIS monitor™; administration of cardiovascular drugs or oxygen supply or assist ventilation, except chin lift, were not needed. The maximum predicted plasma concentration (pCp) of DEX and mean pCp were calculated as 6.1 and 4.1 ng/mL, respectively. A high dose of DEX may be required for DICC sedation, as for MRI sedation, in many cases. Although further studies should be conducted to reveal the merits and demerits of DEX in cardiac catheterization, a high dose of DEX may be useful in some cases.

Keywords Dexmedetomidine · Diagnostic and interventional cardiac catheterization · Congenital heart disease

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Introduction

Previous studies have indicated the usefulness of dexmedetomidine (DEX) for diagnostic cardiac catheterization (DCC) in children; however, ketamine as combined or supplemental drugs or propofol as rescue drugs were required because of the insufficiency of the sedative effect of DEX alone [1–4]. A high dose of DEX is used for sedating many pediatric patients undergoing MRI [5, 6]. We thought that DEX could provide desirable sedation for DCC in a pediatric patient if a higher dose of DEX than the standard dose based on the package insert (initial dose 1 μg/kg over 10 min; maintenance dose 0.2–0.7 μg/kg/h) was used, as is the case for MRI sedation in pediatric patients or sedation of adult patients for invasive procedures [6–8]. We administered DEX and adjusted the dose of DEX according to the bispectral index (BIS) value and brain activity waveform obtained by use of a BIS monitor™ (Aspect, BIS Monitor A-2000; Nihon Kohden, Tokyo, Japan) to perform diagnostic and interventional cardiac catheterization (DICC) in a toddler; therefore, a high dose of DEX had to be administered.

Case report

Use of DEX for sedation during DICC was approved and monitored by the Research Ethics Committee of Asahikawa Medical College, and informed consent was obtained from the patient's parent.

The patient was a 1-year and 4-month-old boy (height 71 cm and weight 9.3 kg) who had undergone internal cardiac repair for total anomalous pulmonary vein (PV) return immediately after birth and additional cardiac repair for consequent pulmonary venous obstruction at the age of 6 months. He had developed cyanosis at a percutaneous pulse oxygen saturation (SpO_2) of 78% during inspiration of room air (90–95% with 3 L/min oxygen supplied via nasal cannula) a month previously. Therefore, he was scheduled for DCC to evaluate the morphological features of the PV. Moreover, he had atrial flutter (AF) with 2:1 atrioventricular conduction at a heart rate (HR) of 150 beats per minute (bpm) the day before DCC; therefore, the cardiac catheterization also involved an intervention to treat AF. He was treated with furosemide (28 mg/day) and spironolactone (20 mg/day). Transthoracic echocardiography revealed normal contraction of the left ventricle, but it did not provide any detailed information about the PV. Institutional standard sedation using midazolam is a simple technique that can be performed by pediatric cardiologists and does not need anesthesiologists. However, the pediatric cardiologists asked us to perform anesthetic management for two reasons.

1. They had to use the internal jugular vein to approach his heart because of femoral vein occlusion, and hence, they wanted us to secure the patient's airway.
2. They wanted the patient to be immobile during the intervention for defibrillation of AF.

We selected DEX as the sedative for two reasons.

1. DEX was believed to be safer than other drugs while performing a procedure around the neck, because it has little effect on spontaneous breathing.
2. Supply of oxygen and mechanical ventilation can be avoided during morphological assessment of the PV.

He did not receive any particular premedication except daily medication. Standard monitoring was performed after the patient was brought into the catheter room. Administration of DEX was started at a dose of 15 μg/kg/h (with reference to the initial dose reported by Mason et al. [6]) so that the BIS value decreased from 98 to 60 and the Ramsay sedation score increased from 1 to 5 (Fig. 1). Mild glossoptosis occurred, but it was easily treated by chin lift. Administration of DEX was continued at the same dose because he responded to stimuli such as positioning the body for DICC or chin lift. However, the dose of DEX was reduced to 5 μg/kg/h after 30 min because he stopped

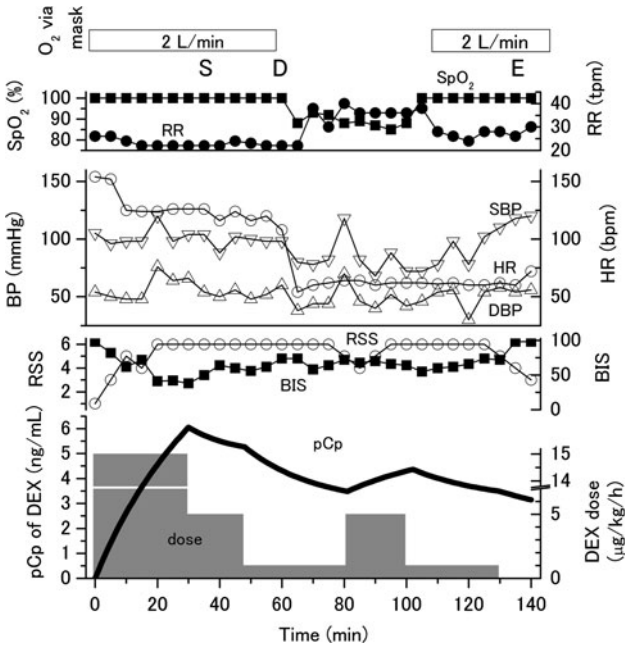

Fig. 1 Vital sign, dexmedetomidine dose, and predicted plasma concentration of dexmedetomidine (DEX). DEX was administered continuously, and the bispectral index (BIS) value and Ramsay sedation score (RSS) changed according to the dose of DEX. Because the hemodynamics were stable, no cardiovascular drugs were administered. The HR dropped because of defibrillation. Consequently, the blood pressure and percutaneous oxygen saturation decreased and respiratory rate increased; however, these were not critical. Predicted plasma concentration of DEX temporarily increased to 6.1 ng/mL after initiating the administration of DEX and stabilized at approximately 4.1 ng/mL. *SpO_2* percutaneous oxygen saturation, *BP* blood pressure, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *HR* heart rate, *bpm* beats per minute, *O_2* oxygen supply, *DEX* dexmedetomidine, *DEX dose* dose of dexmedetomidine, *pCp* predicted plasma concentration, *BIS* bispectral index, *RSS* Ramsay sedation score, *RR* respiratory rate, *tpm* times per minute, *S* start of the procedure, *D* defibrillation, *E* end of the procedure

responding to stimuli when the BIS value was 38, RSS was 6, and the brain wave was mainly composed of high-amplitude δ waves (Fig. 2). The dose of DEX was adjusted:

1. to maintain the BIS value between 40 and 70;
2. to prevent the appearance of the β waveform in the BIS monitor; and
3. to keep the patient immobile.

The typical brain wave of the patient during the procedure is shown in Fig. 2; the brain wave is composed of α and θ waves. Although oxygen supply was discontinued 5 min before initiating the hemodynamic evaluation and the intervention, the SpO_2 was maintained above 100% for 10 min. After defibrillation, normal sinus rhythm returned and the HR dropped from 108 to 54 bpm. Immediately, blood pressure (BP) and SpO_2 decreased slightly; however, because the decreases were not critical, morphologic

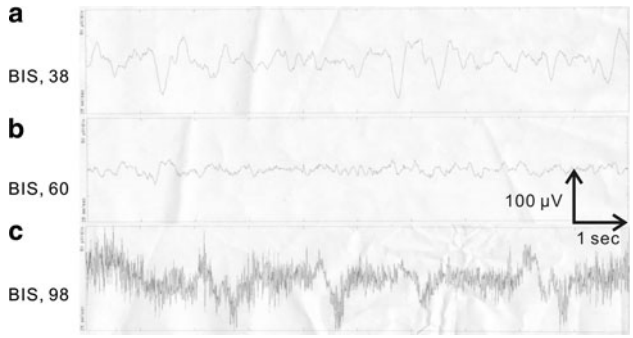

Fig. 2 Brain waveforms. The raw brain waveform in the bispectral index (BIS) monitor™ when **a** the BIS value was 38, 30 min after starting administration of dexmedetomidine (DEX), **b** the BIS value was 60, 45 min after starting administration of DEX, and **c** the BIS value was 98, 8 min after stopping the administration of DEX. **a** The brain wave is mainly composed of high-amplitude δ waves, which resemble the brain waves seen at sleep stage 4. **b** The brain wave is composed of α and θ waves, which resemble the brain waves seen at sleep stage 1. **c** The brain wave is mainly composed of β waves together with waves corresponding to muscular activity

assessment of the PV was continued. DCC revealed pulmonary hypertension with pressure of 43/7 mmHg, right upper PV occlusion and severe left upper PV stenosis. The procedure was smoothly performed, and administration of DEX was discontinued at the end of the procedure. He cried temporarily 8 min after DEX administration was discontinued, when the BIS value was 98 and the brain waveform was mainly composed of β waves together with waves corresponding to muscular activity, and was transferred to the pediatric ward. He became alert 3 h after discontinuation of DEX. Because the hemodynamics were stable, no cardiovascular drug had to be administered. The maximum predicted plasma concentration (pCp) of DEX and mean pCp during the procedure, which were calculated after the procedure by use of TIVAtrainer™ (available at: http://www.eurosiva.org/; accessed on May 1, 2010) with Potts's parameter [9], were approximately 6.1 and 4.1 ng/mL, respectively.

Discussion

Mason et al. [5, 6] reported that a high dose of DEX was required for MRI sedation and that the dose was larger than that required for CT sedation, which suggests that the dose of DEX should be increased according to the intensity and/or type of stimuli. Munro et al. [3] reported that only 40% of catheterizations could be performed by administering DEX alone, despite use of a moderate dose of DEX (0.6–2.0 μg/kg/h), and that ketamine was supposed to be used from the beginning in other procedures [1, 2]. Therefore, a high dose of DEX was considered to be necessary while performing cardiac catheterization. In this case, the dose of DEX could be freely increased according to the BIS values, brain activity, and status of the patient; therefore, a high dose of DEX was required. This finding suggests that the stimuli were as large as MRI. We also found a case in which a high dose of DEX was used for DICC in a pediatric patient similar to MRI in pediatric patients or DCC in adult patients [6, 8]. The mean pCp of DEX during the procedure was calculated to be 4.1 ng/mL. This value is higher than the value in previous case studies in which a high dose of DEX was used for sedation for an invasive procedure in adult patients [7, 8]. The reason for this may be the difference in sensitivity between adults and children, accuracy of simulation, or difference in the degree of invasiveness of the procedure. However, we cannot mention the above reason because all of these were only case reports and the real concentrations of DEX were not measured in any of the cases. Further study is needed to reveal the optimum concentration for sedation.

The most important concern about the use of DEX in DCC is the effect of DEX on the hemodynamic data. The importance of this is believed to depend on the type of diagnosis. In this case, the main purpose of diagnostic catheterization was morphological assessment of the PV. We wanted to avoid oxygen supply or mechanical ventilation because these can affect the pulmonary venous flow. The fact that the assessment could be performed under spontaneous breathing in room air was one of the merits of this method. However, if DCC was being used for another purpose, for example measurement of cardiac output, vascular resistance, and Q_p/Q_s (ratio of pulmonary to systemic blood flow), then indication for DEX must be given due consideration [8]. If the catheterization is used for intervention, then great care need not be taken regarding the effect of DEX on the hemodynamics. However, because great care need not be taken regarding the effect of other sedative drugs or general anesthesia, the advantage of DEX cannot be shown. The abovementioned concerns may be some of the reasons why DEX is not widely used in cardiac catheterization, unlike in MRI. Further studies should be conducted to verify the usefulness of DEX in cardiac catheterization.

Accuracy of the BIS value during sedation using DEX may still be controversial. First, the BIS value has been calculated on the basis of data acquired by monitoring brain waves during administration of midazolam, isoflurane, propofol, etc., but not DEX [10]. Second, because DEX enables novel sedation when the patient remains cooperative and can be aroused by stimuli, the BIS value can easily change because of stimuli under sedation induced by low-dose DEX [11]. Therefore, the BIS value during DEX sedation cannot be used to completely predict the response to stimuli, and the utility of the BIS value to predict the response to stimuli during DEX sedation was

lower than that during sedation using other drugs. Third, the BIS values during DEX sedation were significantly lower than those during propofol sedation at Observer's Assessment of Alertness and Sedation (OAA/S) responsiveness scores of 2, 3, and 4 [12]. In contrast, many studies have shown a correlation between sedative depth and BIS value not only in adults [13, 14] but also in children [15, 16]. In our case also, because the BIS value reflected the sedation status well, we could use the BIS value as a criterion for adjusting the dose of DEX according to the brain waveform, as supported by many reports [17–20].

Mason et al. [5, 6] reported that a high dose of DEX was safe for use in pediatric patients. Although the incidence of bradycardia was 16%, no treatment was required; concomitant mean arterial BPs were within 20% of the age-adjusted normal range, and oxygen saturation was 95% or higher [6]. Although hypertension occurred in 4.9% of the patients, no treatment was required, and no adverse sequelae attributable to hypertension were identified [5]. In our patient, because the hemodynamics were stable, administration of cardiovascular drugs was not required; this finding was in agreement with those of previous reports. A high dose of DEX may be safely administered; however, strict monitoring is still required because DEX can affect the hemodynamics. In our case, chin lift was sometimes required because glossoptosis developed during the procedure; similarly, a previous study had reported the need for repositioning of the airway [1]. However, glossoptosis could be easily treated, without the occurrence of apnea and the need for assisted ventilation. If the need for chin lift, which disturbs the procedure, had continued, an airway device such as a laryngeal mask airway would have been needed.

We have administered DEX to sedate patients undergoing DICC. The dose of DEX was adjusted according to the BIS value, brain waveform, and immobilization of the patient; consequently, a high dose of DEX was needed. We encountered a case in which a high dose of DEX was required for DICC sedation, similar to the high dose of DEX required for MRI sedation in many cases. DEX was found to be useful because the morphological assessment could be performed without the need for oxygen supply or mechanical ventilation and because no respiratory trouble occurred despite the procedure being performed around the neck. However, because DEX can affect the vascular resistance or cardiac output, it is unclear whether DEX is suitable in all cardiac catheterizations. Although further studies should be conducted to reveal the merits and demerits of DEX in cardiac catheterization, we experienced a case in which a high dose of DEX was the only sedative in DICC.

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