PROSPECTIVE EVALUATION OF CORRELATION OF DEPTH OF DEXMEDETOMIDINE SEDATION AND CLINICAL EFFECTS FOR RECONSTRUCTIVE SURGERIES UNDER REGIONAL ANAESTHESIA

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Abstract

This study evaluated the correlation of efficiency and depth of dexmedetomidine sedation, parameters of haemodynamics and breathing, and the time and quality of recovery under regional anaesthesia. 32 ASA I-II patients who received dexmedetomidine sedation under regional anaesthesia during reconstructive surgeries were assessed in this prospective study. The loading dose of dexmedetomidine was 1 μg/kg over 10 min intravenously (IV) followed by a continuous infusion of 0.1-0.6 μg/kg/h until the end of the surgery. Standard monitoring was used. The depth of the sedation was measured with Narcotrend electroencephalogram (EEG) index and Richmond Agitation Sedation Scale (RASS). The time and quality of the recovery were evaluated. Dexmedetomidine did not cause any significant haemodynamic instability and did not induce bradycardia while EEG index was 20-80. According to RASS the level of sedation was 0 to -3 during all surgeries. Dexmedetomidine provided fast and good quality of recovery without impaired cognitive and psychomotor functions. The loading dose of dexmedetomidine 1 μg/kg over 10 min IV followed by 0.1-0.6 μg/kg/h provided sufficient sedation according to EEG index 50-70 during reconstructive surgeries under regional anaesthesia maintaining spontaneous breathing.

Keywords: dexmedetomidine, regional anaesthesia, sedation

Introduction

The result of the surgery under regional anaesthesia can be affected by fear and anxiety of the patient and discomfort from lying on the operating table [1]. In order to reduce

the patient's stress of being awake during the surgery under regional anaesthesia and to increase surgeon's and anaesthetist's satisfaction of the surgery sedation is widely used [1, 2, 3, 4]. For surgeries under regional anaesthesia midazolam and propafol are the most common sedatives [4].

Dexmedetomidine is a selective α-2 receptor agonist with an anxiolytic, sedative and analgesic effect, and is not associated with respiratory depression [4, 5, 6, 10]. Compared to sedatives we have used so far, dexmedetomidine causes the 'natural sleep' through inhibition of neuronal firing in the locus coeruleus in the brain stem which means the patient is easily arousable on verbal stimulation without impaired cognitive abilities and psychomotor functions [4, 7, 8, 9, 10, 13]. Dose dependent bradycardia and hypotension are the most frequently reported adverse reactions of dexmedetomidine [4, 6, 14, 16].

The purpose of this study was to investigate correlation of the efficiency and depth of dexmedetomidine sedation, parameters of haemodynamics and breathing, and the time and quality of recovery under regional anaesthesia.

Methods

32 ASA I-II patients scheduled for reconstructive surgeries under regional anaesthesia (RA) with dexmedetomidine sedation were enrolled in a prospective study, after an ethical committee's approval and receiving written consent from all patients. The following inclusion criteria were used: men or women over the age of 18, normal liver and renal function and no acute diseases. And the following exclusion criteria were used: second or third degree heart block, bradycardia and arrhythmia, uncontrolled hypotension, mechanical ventilation, history of sleep apnea, liver failure, acute cerebrovascular accident, psychiatric disorder or currently being on psychotropic medication, pregnancy and coagulation disorders.

All patients received premedication with tablet of 7.5 mg midazolam before regional anaesthesia. Intravenous catheter (IV) was inserted in the non-operated arm and a 5 ml/kg/h infusion of 0.9% NaCl solution was given. Standard monitoring was used – noninvasive systolic (SBP) and diastolic (DBP) blood pressure, heart rate (HR), respiratory rate (RR), peripheral oxygen saturation (SpO_2) was recorded before and after regional anaesthesia was administered and recording continued until the end of the surgery. The respiratory depression was defined as oxygen saturation <90% or RR under 12 breaths/min. HR <50 beats/min for more than 5 minutes was considered to be bradycardia and patients received a solution of 0.5 mg atropine IV. HR >100 beats/min for more than 5 minutes was considered to be

tachycardia. SBP >180 mmHg was considered to be hypertension and SBP <90mmHg was considered to be hypotension.

EEG monitoring with EEG monitor Narcotrend - Compact M was used during sedation. After regional anaesthesia was performed, three self-adhesive disposable electrodes were placed on the forehead using electrode gel, the patient's leads were connected with Narcotrend - Compact M monitor and the EEG recording was started monitoring the depth of sedation or hypnotic status of the patient during sedation. The monitor automatically classified EEG stages on a scale from stage A (conscious) to stage F (very deep sedation), this division refers explicitly to a range of EEG indexes: EEG stage A – awake (EEG index 95-100); EEG stage B, C – light sedation (EEG index 65-94); EEG stage D – moderate sedation (EEG index 37-64); EEG stage E, F – deep sedation (EEG index < 36) [11].

Patients were divided into 3 groups depending on their type of RA to be used which again depends on the type of reconstructive surgery they would have had planned. Axillary brachial plexus blockade was done for reconstructive surgeries in hands, this was performed while patients were in the supine position with the upper arm abducted and flexed 90 degrees at the elbow. A solution of 20 ml 0.5% bupivacaine and a solution of 20 ml 1% lidocaine was used for axillary brachial plexus blockade. Spinal anaesthesia (SA) was done for reconstructive surgeries in legs, this was performed with a 25 gauge needle in L3-L4 interspace while patients were sitting on the operating table placing feet on a stool, head flexed and arms hugging a pillow providing maximum flexion of the lumbar spine. A solution of 4 ml 0.5% levobupivacaine was used for spinal anaesthesia. Axillary brachial plexus blockade and spinal anaesthesia was done for free flap microvascular surgeries not exceeding the maximum recommended doses of local anaesthetics. After confirmation of successful regional anaesthesia, loading dose of dexmedetomidine 1 μg/kg over 10 min was administered IV followed by a continuous infusion of 0.1-0.6 μg/kg/h until the end of the surgery. To provide an efficient sedation during surgery the continuous infusion of dexmedetomidine was adapted by EEG index maintaining a definite target EEG index of 50-70 (complies with EEG stage C_2 – D_1).

An independent observer rated the level of sedation of the patients using RASS. Measurements were obtained before and after the loading dose and then every 20 minutes until the end of the surgery. The sedation was considered too deep when RASS was -4 or -5 [12]. The time and quality of the recovery were evaluated at the end of each surgery. In the

recovery room at 30 minutes patients' satisfaction with the quality of sleep was assessed by the use of handed out questionnaires.

Statistical analysis was performed with Microsoft Excel 2010 and SPSS (Statistical package for social sciences) 20. Data was evaluated with ANOVA (Analysis of variance) and Student's t-test. Results with p values of <0.05 were considered statistically significant.

Results

The demographic data and surgical characteristics were similar in all patients (Table 1). Types of RA used: 24/32 had an axillary brachial plexus blockade (75.0 %) for reconstructive surgeries in hand, 5/32 had a spinal anaesthesia (15.6 %) for reconstructive surgeries in leg, 3/32 – SA with plexus blockade (9.4 %) for free flap microvascular surgery.

Table 1. Demographic data and surgical characteristics

Gender (F/M)	14 (43.8 %) female	18 (56.2 %) male
Age (years)	46.44 ± 16.88 (20 to 74)	
Weight (kg)	75.00 ± 14.11 (50 and 120)	
Height (cm)	172.85 ± 8.31 (163 and 185)	
Type of surgery	28 (87.5 %) elective	4 (12.5 %) acute
Duration of surgery (minutes)	89.38 ± 67.46 (min 20, max 300)	
Duration of sedation (minutes)	102.81 ± 67.52 (min 35, max 310)	

Cardiovascular and Respiratory Measurements

The mean HR during sedation was 62.86 ± 7.90 beats/min. After dexmedetomidine loading dose the mean HR decreased by 8.44 ± 7.16 beats/min (p = 0.000) (before loading dose 73.75 ± 10.34 beats/min). We observed bradycardia below 50 beats/min requiring a single minimum dose of atropine in 2/32 patients (6.3 %), 5/32 patients (15.6 %) had a temporary bradycardia that does not require treatment and in 25/32 cases (78.1%) sedation with dexmedetomidine did not cause bradycardia. After the loading dose bradycardia did not appear in any of the patients while EEG index was 20-80 (Table 2). 2 patients with

bradycardia requiring atropine had a Narcotrend EEG stage A – awake (EEG index of 95-100). Out of those two patients – one patient was a 28-year-old professional athlete, he had bradycardia during loading dose when EEG index was 98, other patient was a 71-year-old man who had an acute surgery and bradycardia occurred 20 minutes after the start of continuous infusion at EEG index 96.

When comparing all types of RA used, HR was similar in all three RA groups after the loading dose (Table 3).

Table 2. Changes of HR after loading dose according to EEG index (20-80).
The number printed on bars indicates the number of patients in current group of EEG index.

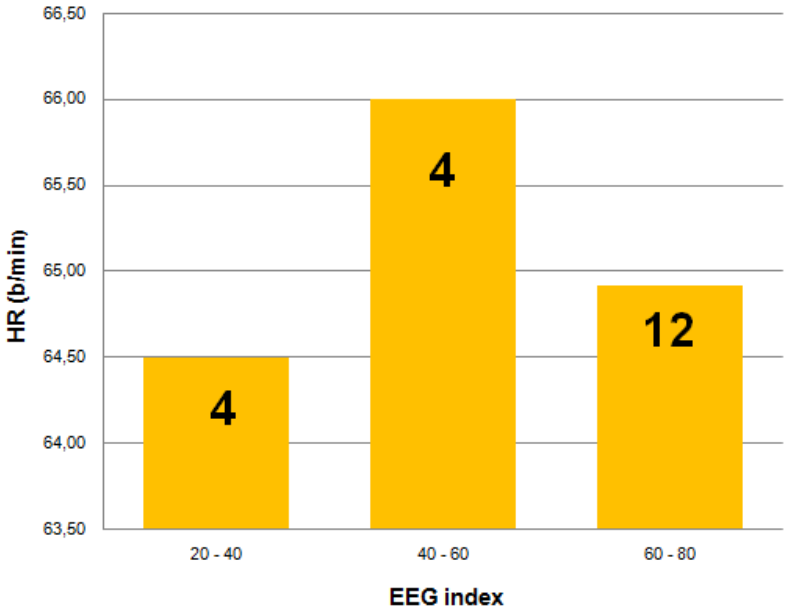
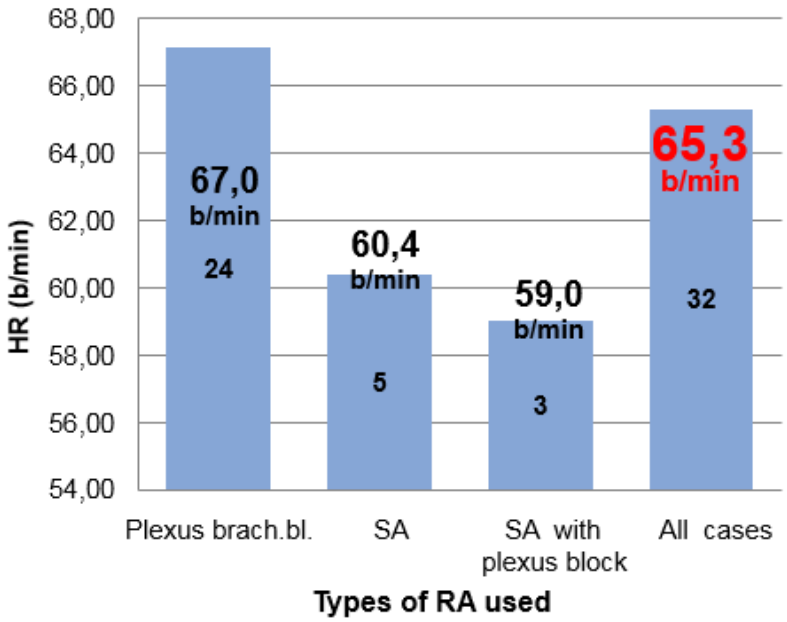


Table 3. Changes of HR after loading dose according to types of RA used.



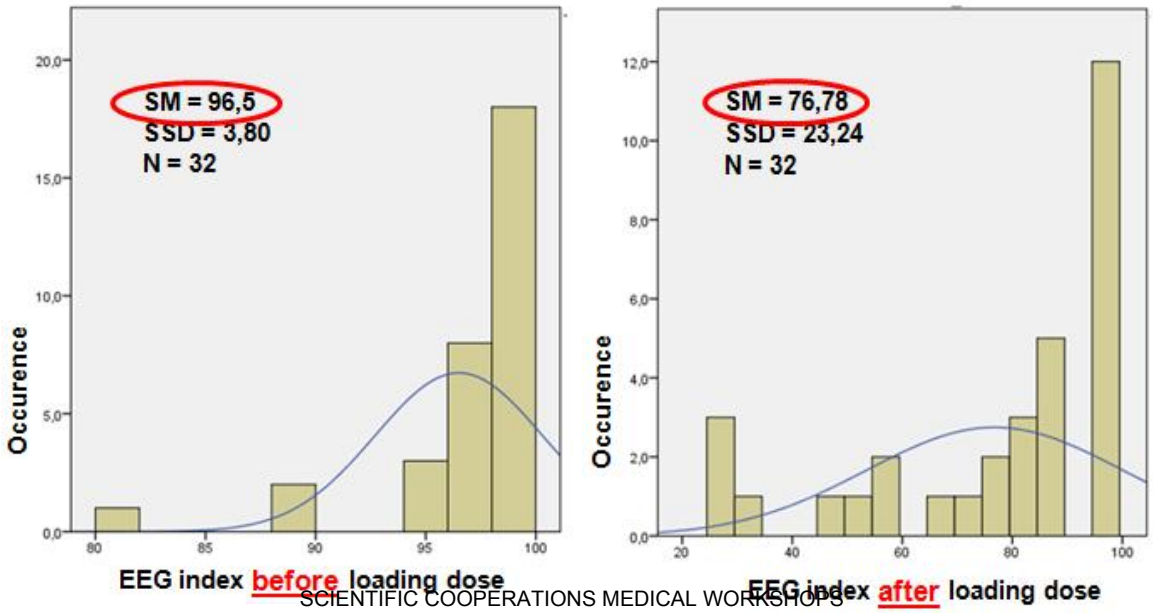
We did not observe any significant changes in SBP and DBP after dexmedetomidine loading dose was administered – the mean SBP decreased by 7.31 ± 12.03 mmHg (p = 0.002) and the mean DBP decreased by 4.75 ± 7.15 mmHg (p = 0.001). The mean SBP during the sedation was 119.39 ± 15.16 mmHg, the mean DBP was 71.99 ± 9.83 mmHg. Results showed that sedation with dexmedetomidine caused neither of the following in any of the patients: hypotensia, the need to stop the continuous infusion or add other sedatives.

We observed minimal decrease in SpO_2 levels after the loading dose (1.28 ± 2.37 %, p = 0.005) without the need to use assisted ventilation or any airway device. All patients had adequate spontaneous breathing during their sedation.

Sedation Measures

The mean EEG index after loading dose decreased by 19.72 ± 23.85 (p = 0.000) indicating light to moderate sedation (Table 6). During dexmedetomidine sedation the mean EEG index was 68.53 ± 21.70 which was within the target EEG index rage. The target level of sedation was reached 10 minutes after the start of continuous infusion. The mean lowest recorded EEG index was 53.10 ± 25.00 after a continuous infusion of 30 minutes. The environment had a significant negative impact to the quality of dexmedetomidine sedation. Increased noise levels rose the EEG index during surgery therefore the patients woke up. However, those patients were able to quickly fall back asleep. According to RASS the level of sedation during surgery was from 0 to -3. We observed that at the end of the surgery all patients were promptly arousable with verbal stimulation without impaired cognitive abilities and psychomotor functions. According to answers from their questionnaires all patients were satisfied with the sedation they received.

Table 6. Changes of EEG index before and after loading dose of dexmedetomidine.



Discussion

The aim of the study was to investigate correlation of the efficiency and depth of dexmedetomidine sedation, parameters of haemodynamics and breathing, and the time and quality of recovery under regional anaesthesia. We found that low doses of dexmedetomidine (loading dose 1 μg/kg/10 min, a continuous infusion 0.1-0.6 μg/kg/h) during reconstructive surgeries under RA sedation did not cause any significant haemodynamic instability and bradycardia was not seen while EEG index 20-80. Similar results were reported by Arain S. R. at al. and Kilic N. et al. using dexmedetomidine loading dose of 1 μg/kg over 10 minutes followed by a continuous infusion of 0.4-0.7 μg/kg/h and 0.2-0.7 μg/kg/h providing efficient sedation [***34***, 15]. Ok H. G. et al. study results showed that dexmedetomidine loading dose of 1 μg/kg over 10 minutes is sufficient for surgeries up to 60 minutes long. A continuous infusion of dexmedetomidine of 0.2 μg/kg/h is sufficient for surgeries up to 80 minutes long and a continuous infusion of 0.4 μg/kg/h provides efficient sedation for surgeries up to 120 minutes long under spinal anaesthesia [4].

The incidence of bradycardia and hypotension is the most frequently reported dexmedetomidine adverse hemodynamic response associated with increased dosage and concentration [4, 6, 14, 16]. A study by Ok H. G. et al. reported that the frequency of bradycardia and hypotension does not increase when a low dose of dexmedetomidine is administered IV for sedation under spinal anaesthesia. In our study the incidence of bradycardia requiring atropine was low (2 out of 32 patients) in addition – hypotension was never recorded.

Authors report dexmedetomidine as a useful sedative for procedures because of its minimal effects on the respiratory system [15, 17]. Belleville J.P. et al. reported a study of examined ventilatory effects of a 2 minute intravenous four different dose level of dexmedetomidine infusion. Results showed that right after the maximum infusion of 2.0μg/kg irregular breathing with periods of apnea were noticed. However, the authors also report that there was no significant arterial oxygen desaturation below 90% [19].

In this study the level of sedation was assessed by RASS (the level was from 0 to -3 during sedation) and the depth of sedation or hypnotic status was measured by Narcotrend EEG monitor maintaining the pre-set target level EEG index between 50 and 70. Authors emphasize that there are some limitations using assessment scales like Richmond Agitation Sedation Scale, Ramsay Sedation Scale or Observer's Assessment of Alertness/Sedation scale. Assessment scales are subjective interpretations by the observers of patients' alertness.

The quality of sedation is compromised because the assessments require the patient to be awaken every time an assessment is done [4]. Therefore authors recommend using Bispectral Index System (BIS) or Narcotrend EEG monitoring for measuring the depth of the sedation instead of the assessment scales [4, 20]. BIS and Narcotrend EEG monitoring provide real time assessment and the quality of sedation is not compromised by external stimulation [20]. Ekin A. et al. in a study measuring the depth of sedation with BIS reported that environmental stimuli and the application of tourniquet increase values of BIS, although it does not affect the patient's satisfaction with his sedation [3].

There are reports about dexmedetomidine's advantages of providing fast recovery after procedures, patients are easily arousable on verbal stimulation and able to perform the psychomotor testing without impaired cognitive abilities and psychomotor functions [10, 15, 18]. In our study at the end of each surgery all patients were promptly arousable with verbal stimulation.

Conclusion

The loading dose of dexmedetomidine of 1 μg/kg administered intravenously over 10 minutes and a continuous infusion of 0.1-0.6 μg/kg/h until the end of the surgery provides safe management of sedation according to pre-set target for Narcotrend electroencephalogram index of 50-70 during reconstructive surgery under regional anaesthesia.

After the loading dose of dexmedetomidine bradycardia did not appear while Narcotrend electroencephalogram index was 20-80, all patients maintained spontaneous breathing and sedation did not cause any significant haemodynamic instability. Dexmedetomidine sedation under regional anaesthesia provides fast and good quality recovery and ensures a high patient satisfaction rate of sleep quality during reconstructive surgery.

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