ORIGINAL ARTICLE

Dexmedetomidine as a Sedative in the Awake Implantation of a Neuromodulative System

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■ **Abstract**

Objective: During implantation of a neuromodulative system, high patient satisfaction is closely associated with the equilibrium between an effective analgesia and sedation regimen, and the possibility for the patient to be awake and cooperative during procedure. This study assessed the efficacy of the sedative dexmedetomidine to achieve this balance, with patient satisfaction as the primary outcome.

Methods: Ten patients undergoing implantation of a dorsal column and dorsal root ganglion stimulator received dexmedetomidine (1 mcg/kg over 10 minutes, followed by 0.6 mcg/kg/hour) in combination with remifentanil at a set dose (3 mcg/kg/hour). Sedation was titrated to a Ramsay Sedation Score of 3. Recorded were as follows: patient satisfaction score, patient comfort score, operator comfort score, pain score, rescue medication and number of adjustments of dexmedetomidine intra-operatively, as well as sedation level, hemodynamic (blood pressure and heart rate), and respiratory characteristics (SpO_2).

Results: Scores were high on patient satisfaction (median 8.5; IQR 2.0), patient comfort (3.0; IQR 1.25), and operator comfort (4.0; IQR 1.0). In all patients, intra-operative heart rate and mean arterial pressure were lower compared with baseline values. No respiratory depression or other complications related to anesthesia were reported. Moments of incident pain were effectively treated in 6 patients requiring an extra bolus of remifentanil.

Conclusion: In this study group, dexmedetomidine combined with remifentanil provided a high level of patient satisfaction and comfort, as well as operator comfort, without any clinically relevant adverse events. All patients were highly cooperative and instructable; incident pain needs to be closely monitored. ■

Key Words: sedation, dexmedetomidine, neuromodulation, chronic pain

INTRODUCTION

To place neurostimulation leads, most of the currently available systems require the cooperation of the patient. The overlap between neurostimulation-induced paresthesia and the pain area can only be specified by the patient. For patients, the procedure can be frightening, uncomfortable (due to the prolonged prone position), and sometimes painful due to inadequate analgesia. Therefore, adequate information and guidance is essential. In addition, besides local anesthesia, the use of anxiolytics, sedatives, and more general analgesics can be helpful. However, a potential disadvantage of these adjuvants is that, due to the sedative effect of these drugs, patients may be insufficiently cooperative with the instructions and questions posed by physicians and nurses.

A promising analgosedative is dexmedetomidine, a highly selective, long-lasting presynaptic $\alpha 2$-receptor agonist with sedative, anxiolytic, and analgetic

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properties. With dexmedetomidine, there is no decline of cooperation or of cognitive skills. Due to its pharmacologic profile, dexmedetomidine acts on the α2 receptors in the locus coeruleus, in contrast to other sedatives which act on GABA receptors/cerebral cortex (eg, midazolam and propofol), and there is no respiratory depression. Furthermore, in combination with intravenous opioids (such as remifentanil), dexmedetomidine allows for lower doses of opioids. Earlier randomized controlled trials evaluating the use of dexmedetomidine alone during small diagnostic and therapeutic procedures showed promising results[1–3]. However, a potential disadvantage of dexmedetomidine is its hemodynamic side effects, which include hypotension and bradycardia.[4,5]

Therefore, this study aimed to examine the applicability of dexmedetomidine for the placement of neurostimulation leads for procedures in which the patient's cooperation is required. Applicability is operationalized as measurement of patient satisfaction, patient and operator's comfort, pain relief and rescue medication, the number of adjustments made to the administration of dexmedetomidine, sedation level, and hemodynamic and respiratory monitoring.

METHODS

Study Design, Selection of Patients

The study protocol was approved by the Medical Ethics Committee of Erasmus Medical Center and registered with the Netherlands Clinical Trials Registry (NL 49012.078.12).

This is a proof-of-concept, prospective observational study. After providing informed consent, we enrolled 10 consecutive patients (aged 18 to 65 years) with an indication for trial implantation of a neurostimulation system, for which cooperation of the patient during lead placement is required. Exclusion criteria included hypersensitivity to either of the drugs involved, atrioventricular block (II–III), acute cerebrovascular disease, heart rate ≤ 60 bpm, pregnancy, acute epilepsy, severe liver dysfunction, use of beta blocking agents, psychological instability, and/or a communication problem.

Study Site, Measurements

Before the procedure, all patients received standard education and were guided perioperatively by a nurse. All patients were commenced on a dexmedetomidine infusion in the operating room, using an intravenous cannula. Sedation was performed by an independent anesthesiologist not involved in the interventional procedure. Implantation of the neuromodulative system was performed by another anesthesiologist-pain specialist not involved in the sedation. An independent observer, not involved in the sedation or the interventional procedure, performed all study measurements. During each procedure, measurements were made at 7 predefined moments: a preoperative measurement, at start of dexmedetomidine, at start of remifentanil, at start of the procedure, at midline incision (incision of the skin for anchoring the lead on the subcutaneous fascia and subcutaneous tunneling of the lead), at end of the procedure, and postoperatively on the ward.

Patients were administered a loading dose of dexmedetomidine of 1 mcg/kg over 10 minutes to achieve the required level of sedation according to the Ramsay Sedation Scale[6] (score 2 to 3) (Table 1). This scale was used before the initiation of sedation and at 5-minute intervals until the end of the procedure. The dose was adjusted depending on the required level of sedation (ie, a Ramsay score of 2 when the patient is required to be cooperative, and a score of 3 to 4 when the patient requires increased sedation). The maintenance dose of dexmedetomidine is 0.1 to 1.4 mcg/kg/hour; in the present study, a maintenance dose of 0.6 mcg/kg/hour was used.

Ten minutes after commencement of the loading dose of dexmedetomidine, remifentanil infusion was started at a set dose (3 mcg/kg/hour) to achieve a high analgesic effect. Standard care involves the use of 1% lidocaine in combination with adrenaline (1:200,000) at the start of the procedure, during the midline incision, and at end of the procedure. When a patient complained of pain during the procedure, the anesthesiologist administered an additional bolus of remifentanil (25 to 50 mcg/kg/hour).

Our primary outcome parameter was patient satisfaction, as measured with a postoperative overall patient

Table 1. Details of the Ramsay Sedation Scale

Clinical Score	Level of Sedation
1	Patient is anxious and agitated or restless or both
2	Patient is cooperative, oriented and tranquil
3	Patient responds on command
4	Patient exhibits a brisk response to a light glabellar (between the eyebrows) tap or loud auditory stimulus
5	Patient exhibits a sluggish response to a light glabellar tap or loud auditory stimulus
6	Patient exhibits no response to stimulus

satisfaction questionnaire (consisting of 7 questions) (Table 2).[6] Secondary outcomes were pain relief, patient's comfort and operator's comfort (using a comfort score) (Table 3)[4], number of adjustments made during dexmedetomidine titration, scores on the Ramsay Sedation Scale, and intra-operative standard monitoring including noninvasive mean arterial pressure (MAP), heart rate (HR) via ECG, pulse oximetry (spO_2), and end tidal CO_2 ($EtCO_2$).

Data Analysis

At each measurement moment, mean values of the outcomes were collected and reported as outcome per time moment. These values differ for each measurement moment, depending on the duration of the procedure, as measurements are made every 5 minutes.

Statistical Analysis

Descriptive statistics were used to determine the frequencies of the demographic variables and the outcome parameters, and to describe measures of central tendency and of variability, depending on the shape of the distribution. All analyses were performed using IBM SPSS Statistics version 21 (Armonk, NY, USA).

RESULTS

A total of 10 patients were included (Table 4).

All patients completed the study; the median score of patients' overall satisfaction was 8.5 (IQR, 2.0) (Table 5). All patients reported to be awake during the implantation and 20% experienced the procedure as stressful. In case of a repeat procedure, all patients stated they would request the same anesthetic procedure again. None of the patients reported complications related to the anesthesia. The median score for patient comfort was 3.0 (IQR, 1.25), and for operators' perioperative comfort, it was 4.0 (IQR, 1.0).

In case of unacceptable pain management, patients received a bolus of remifentanil of 25 mcg/kg/hour. Six patients required an extra bolus of remifentanil during insertion of the Tuohy needle, or during subcutaneous tunneling. One patient needed 1 bolus of remifentanil, 3 patients received 2 boluses, and 2 patients needed ≥ 3 boluses. During the procedure, only 1 patient needed an increase of 0.2 mcg/kg/hour dexmedetomidine to achieve an adequate sedation level.

Median SBP, DBP, MAP, and mean HR decreased during the procedure (Figures 1 and 2); however, none of these changes were clinically relevant. No patient required any airway intervention.

The mean duration of the procedure was 115.4 (SD 34.84) minutes, and the median duration was 118.5 (IQR, 56.25) minutes.

Table 2. Patient Satisfaction Questionnaire

Q1	On a scale from 1 to 10 (1 least satisfied, 10 most satisfied), how satisfied were you with your anesthesia during your operation?
Q2	Do you remember awakening during the procedure?
Q3	If yes, was the experience distressful?
Q4	If you were to have the operation again, would you choose the same anesthesia?
Q5	Do you recall problems at home after discharge with anesthesia (hangover)?
Q6	Do you know of any complications from the anesthetic used?
Q7	If yes, what complications?

Table 3. Patient Comfort Score and Operator Comfort Score

Criteria	Score
Excellent	4
Good	3
Fair	2
Poor	1

Table 4. Details of the Included Patients

Variables	Patients (n = 10)
Age in years (median; IQR)	53.5; 17,75
Female gender, *n* (%)	7 (70%)
BMI (kg/m^2): mean (SD)	28.47 (4.35)

Table 5. Data on Overall Patient Satisfaction

Patient satisfaction (median; IQR)	8.5; 2.0
Awake	Yes (100%)
Stressful	Yes (20%)
Would choose same anesthesia again?	Yes (100%)
Home problems	*Not applicable*
Were there complications related to anesthesia?	No (100%)

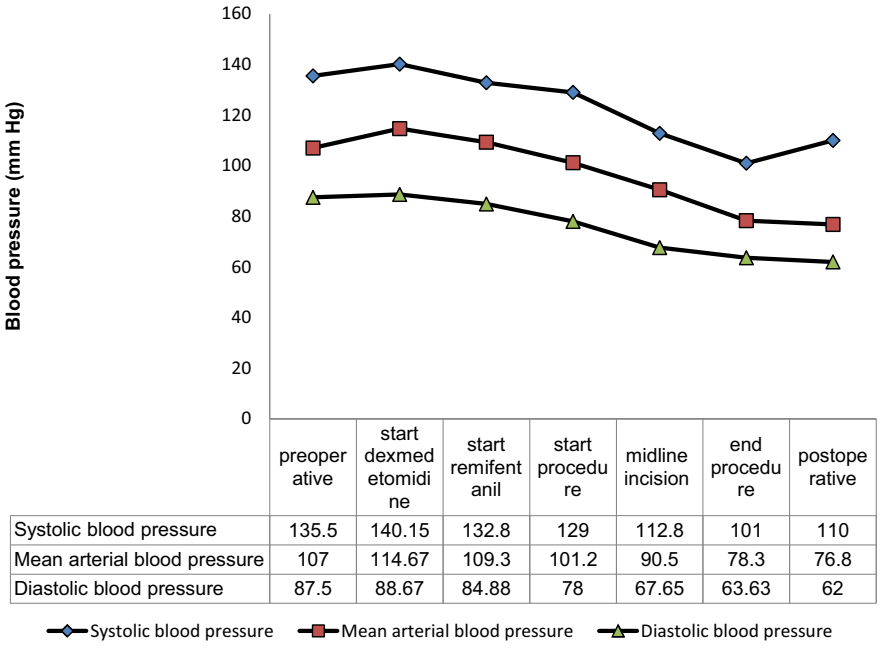
DISCUSSION

When a patient is required to be awake during a surgical procedure, this is generally experienced as a stressful and uncomfortable situation. Therefore, an effective sedo-analgesic regimen is necessary. During implantation of a neuromodulative system (classified as a small therapeutic procedure), patients need to be cooperative and able to follow instructions. Dexmedetomidine may be useful for this clinical situation, as its benefits have been

reported in various types of procedures.[7,8] In the present study, patients reported a high level of satisfaction (median 8.5; IQR 2.0). Moreover, all patients would choose the same anesthesia regimen again in case of future comparable interventions, and only 20% experienced the implantation as a stressful procedure. Patient comfort was good (median 3.0; IQR 1.25), and operator comfort was excellent (median 4.0; IQR 1.0).

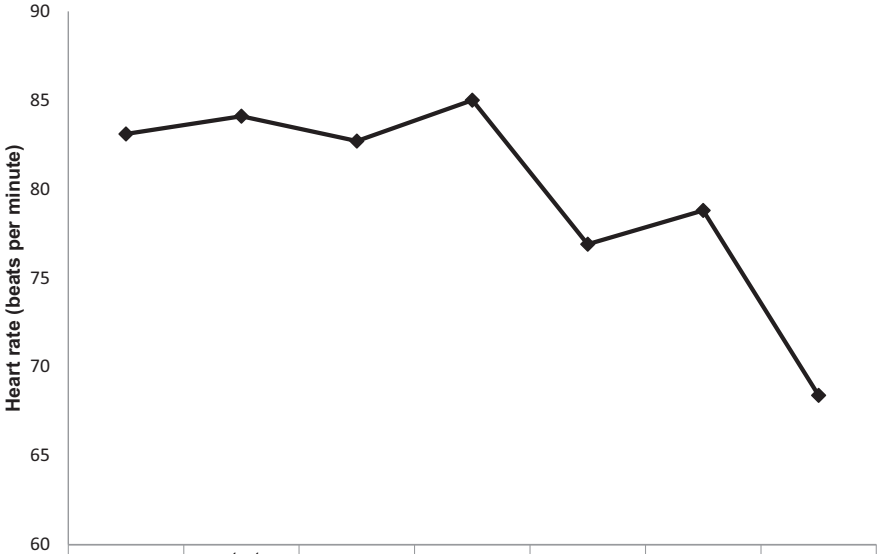
During the procedure, scores on the Numeric Rating Scale (NRS) decreased in nearly all patients, demonstrating adequate pain relief using dexmedetomidine in combination with remifentanil. However, dexmedetomidine is not suitable for incident pain. In our study, incident pain occurred during insertion of the Tuohy needle or tunneling, during which pain scores rose to 8 to 10. This was dealt with by administering a bolus of remifentanil of 25 mcg/kg/hour before the start of tunneling, or a comparable procedure.

In the postoperative period, heart rate and saturation went down (Figures 2 and 3); however, the pain score



	preoperative	start dexmedetomidine	start remifentanil	start procedure	midline incision	end procedure	postoperative
Systolic blood pressure	135.5	140.15	132.8	129	112.8	101	110
Mean arterial blood pressure	107	114.67	109.3	101.2	90.5	78.3	76.8
Diastolic blood pressure	87.5	88.67	84.88	78	67.65	63.63	62

Figure 1. Median, systolic and diastolic arterial blood pressure at each measurement.



-	preoperative	start dexmedetomidine	start remifentanil	start procedure	midline incision	end procedure	postoperative
	83.1	84.1	82.7	85	76.9	78.8	68.4

Figure 2. Mean heart rate at each measurement.

increased. This might be due to the fact that the patient was not experiencing fear any more after the procedure (HR decreased) and did not get any oxygen support (saturation). The decrease in HR and saturation were not clinically relevant. Pain score increased postoperatively probably because of pain around the wound, made during surgery. The neuromodulative system was not active at that moment.

This proof-of-concept study demonstrates that a sedation regimen of dexmedetomidine and remifentanil allows implantation of a neuromodulative without the need for airway support. Safety during a procedure depends on airway tone, and controlling this factor will potentially increase patient safety. In our study, airway stability was maintained and no respiratory depression in prone position was observed. This latter result was expected, because dexmedetomidine does not act on GABA receptors.[9]

During all procedures, hypotension and bradycardia were observed in all patients (Figures 1 and 4), but

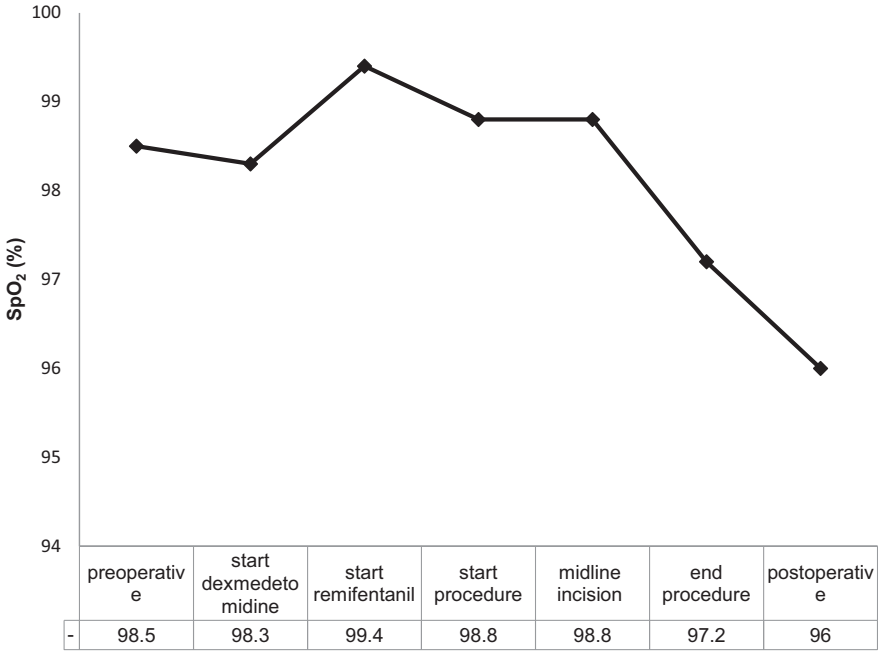


Figure 3. Median oxygen saturation level (SpO_2) at each measurement.

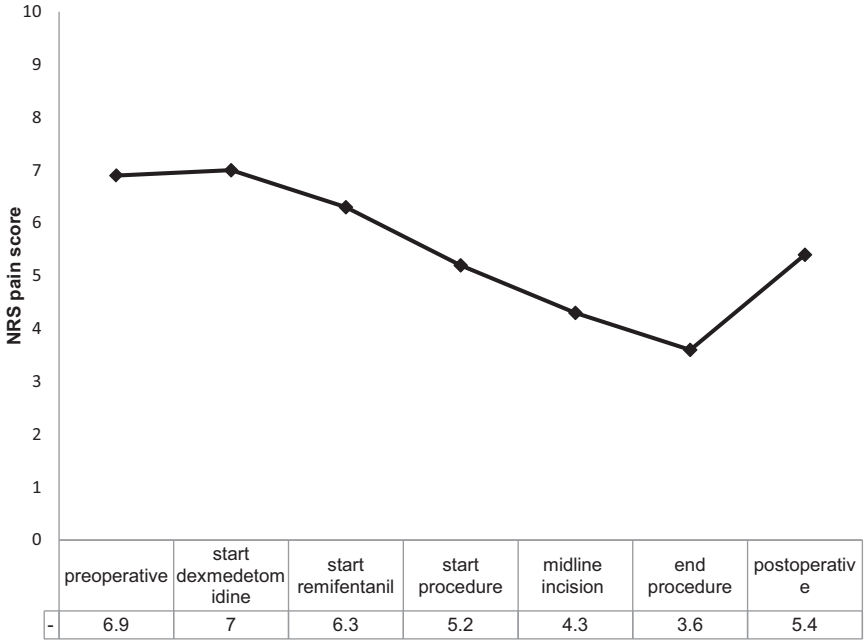


Figure 4. Mean Numeric Rating Scale (NRS) pain score at each measurement.

stayed within an acceptable range. No patient required atropine or any form of hemodynamic support. Patient cooperation and level of instructability were excellent during all procedures. Patients were asleep during the procedure but awakened immediately upon hearing a verbal command. During the procedure, patients had a Ramsay score of 2 to 3 when using a loading infusion of 1 mcg/kg/hour for 10 minutes and a maintenance dose of 0.6 mcg/kg/hour for the remainder of the procedure; this is the desired level of sedation. During the entire procedure, a set dose of remifentanil of 3 mcg/kg/hour was administered. Moreover, the use of dexmedetomidine allowed to use a lower set dose of remifentanil as compared with standard care.

The use of dexmedetomidine in neuromodulation surgery including deep brain stimulation (DBS) is well described. Outcomes show promising results, such as good surgical conditions, patient comfort, and analgesia. Furthermore, dexmedetomidine provided a comparable hemodynamic stability during DBS implantation and this trial.[10,11] A limitation of the present study is that we used an observational design with a small sample size, because our first aim was to examine the applicability of dexmedetomidine. Furthermore, we did not add the management of bradycardia in the study protocol because this is part of standard care. Any form of hemodynamic support using atropine was not necessary. A follow-up study will compare dexmedetomidine with more conventional regimens of sedation, as well as its cost-effectiveness.

CONCLUSION

In summary, in this patient group, dexmedetomidine combined with remifentanil provided a high level of patient satisfaction and comfort, as well as good operator comfort, without any clinically relevant adverse events. All patients were asleep during the procedure, but were highly cooperative and instructable when required; moreover, there was no report of respiratory depression. A randomized controlled trial is required to further investigate the role of dexmedetomidine for the implantation of a neuromodulative system.

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