ORIGINAL ARTICLE

Dexmedetomidine for monitored anesthesia care in patients undergoing liberation procedure for multiple sclerosis: An observational study

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ABSTRACT

Background: It has been postulated that Multiple sclerosis (MS) stems from a narrowing in the veins that drain blood from the brain, known medically as chronic cerebrospinal venous insufficiency, or CCSVI. It has been proposed that balloon angioplasty should alleviate the symptoms of MS. This procedure is also known as "The Liberation Procedure." Accordingly, a clinical study was undertaken to determine the effects of dexmedetomidine in patients undergoing the liberation procedure. **Aims:** To assess the effectiveness of dexmedetomidine in providing adequate sedation and pain relief for patients undergoing the liberation procedure. **Settings and design:** A prospective, nonrandomized observational study of 60 consecutive adult patients undergoing the liberation procedure under monitored anesthesia care (MAC) who will receive dexmedetomidine as an anesthetic agent. **Methods:** A total of 60 adult patients were enrolled in the study. Dexmedetomidine was administered to all patients in a loading dose of 1 mcg/kg, which was followed by a maintenance dose of 0.2–0.5 mcg/kg/h. The evaluation of quality of sedation was based on Ramsay Sedation and the quality of analgesia was assessed using the visual analog scale. The following parameters were measured continuously: heart rate, mean arterial pressure and hemoglobin oxygen saturation. Patients were asked to answer the question, "How would you rate your experience with the sedation you have received during surgery?" using a seven-point Likert-like verbal rating scale. **Statistical analysis:** Repeated measurements were analyzed by repeated measures ANOVA for HR and BP. **Results:** Most of our patients were satisfied with their sedation. In most of the patients, MAP and HR dropped after the bolus dose of dexmedetomidine, and the drop was statistically significant. **Conclusions:** Dexmedetomidine can be used as a sole sedative agent in patients undergoing the liberation procedure.

Key words: *Dexmedetomidine, monitored anesthesia care, multiple sclerosis liberation procedure*

INTRODUCTION

Multiple sclerosis (MS) is a disease in which the fatty myelin sheaths around the nerve fibers of the brain and spinal cord are damaged. Depending on which nerves are involved, this leads to eventual impairment in sensation, movement, cognition or other functions. It has been postulated that MS stems from a narrowing or blockage in the veins that drain blood from the brain, known medically as chronic cerebrospinal venous insufficiency (CCSVI).[1] This impaired flow of blood from the brain builds up pressure, and thus the resulting collection of blood may cause MS symptoms. Blood that remains in the brain too long creates a deposition of iron, which in turn damages the brain tissue. It has been proposed that percutaneous transluminal balloon angioplasty, a common technique for widening blood vessels should alleviate the symptoms of MS.[2] As it frees the blood flow, the procedure is also known as "The Liberation Procedure." The liberation procedure is most frequently performed under monitored anesthesia care (MAC). The Interventional neuroradiologist wants a calm, sedated but cooperative patient who lies still while this complex procedure is going on, and the neuroanesthetist wants this with minimal respiratory or hemodynamic compromise

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during MAC in a dark and remote Digital Subtraction Angiography (DSA) lab. Several drugs can be used for sedation during this procedure, including propofol, benzodiazepines and opioids. However, propofol may cause oversedation and disorientation,[3] benzodiazepines may result in confusion, particularly when administered to elderly patients,[4] and opioids are associated with increased risk of respiratory depression and oxygen desaturation.[5] All these untoward effects may hamper the patients' cooperation during the procedure, and would make these agents less than ideal for the intraoperative management of sedation. In contrast, dexmedetomidine is a highly selective a_2-adrenoceptor agonist with both sedative and analgesic properties, and is devoid of a respiratory depressant effect. It has been used to premedicate and sedate patients undergoing day care procedures without adverse effects, and patients, typically, remain cooperative although being sedated.[6] These properties along with its relatively short elimination half-life of 2 h (compared with 3–4 h for midazolam) makes dexmedetomidine an attractive agent for sedation during MAC for the liberation procedure. Accordingly, this clinical study was undertaken to determine the effects of dexmedetomidine in providing adequate sedation and pain relief in patients undergoing the liberation procedure.

METHODS

After Institutional Ethics Committee approval for an observational study, a total of 60 adult patients were enrolled in the study. All had normal renal and hepatic function and no history of allergy or chronic use of medical therapy.

Inclusion criteria

- All patients of MS scheduled for the liberation procedure.

Exclusion criteria

1. Severe cardiac disease such as valve stenosis or regurgitation
2. Advanced heart block
3. Severe coronary artery disease
4. Deranged renal or hepatic function
5. In patients who are already hypotensive and/or hypovolemic.

All patients received no premedication and were monitorized by noninvasive blood pressure, electrocardiogram (ECG) and pulse oximetry on arrival to the DSA lab. Dexmedetomidine was administered to all patients in a loading dose of 1 mcg/kg over 10 min, which was followed by a maintenance dose of 0.2–0.5 mcg/kg/h. Infusions were further decreased or appropriate intervention carried out if one of the following adverse events was observed: apnea longer than 20 s, hemoglobin oxygen saturation (SpO_2) lower than 90%, decrease of heart rate (HR) (below 20% of the initial value) or mean arterial pressure (MAP) below 30% of the initial value. The evaluation quality of sedation was based on a six-point Ramsay Sedation Score (RSS)[7] (1 = anxious or restless, 2 = cooperative, 3 = responds to commands, 4 = brisk response to auditory stimulus, 5 = sluggish response, 6 = no response) and, accordingly, the infusion dose was titrated to maintain a sedation score of 3. The quality of analgesia was assessed by using a 10 cm visual analog scale (VAS), in which 0 represents no pain at all and 10 represents maximal pain. If the patient reported pain exceeding 3 cm on the scale, intravenous fentanyl in doses of 50 mcg was administered. Similarly, if RSS is 1 despite infusion, midazolam in increments of 1 mg was given. Oxygen was administered by a face mask at 5 L/min to all patients throughout the procedure. Administration of any medication apart from the study protocol and occurrences of complications and side-effects were recorded. Sedation and monitoring were performed by the anesthesiologist in all cases. The following parameters were measured continuously: HR, MAP and SpO_2. The recorded data were analyzed and averaged over the following time intervals: before injection of study drug (baseline) and every 10 min thereafter till the end of the procedure (at which the infusions were discontinued). RSS and VAS was recorded during the intraoperative period and at the post anesthesia care unit at the 30^{th} and the 60^{th} minutes. The patients were transferred to the ward when RSS was 2 point. Patients were asked to answer the question, "How would you rate your experience with the sedation (or analgesia) you have received during surgery?" using a seven-point Likert-like verbal rating scale.[8] This assessment of patient's satisfaction with sedation and analgesia was performed just before recovery room discharge to minimize the effects of sedation on patients' judgement.

Statistical analysis

A sample size of 60 patients was calculated on the basis of the parameters at a statistical power of 95%, with a confidence level of 95% (i.e., at the 5% level of significance). This is a cross-sectional observational study. The parameters of interest are blood pressure (BP) and HR. It is hypothesized that there will be sharp decline in the values of the parameters after sedation up to 20 min, and will almost stabilize thereafter.

Accordingly, the assumptions made are: d = 1 (difference of 1 will be interpreted that the parameter values have almost stabilized) s (SD value of difference in parameter) = 4 and $z_\alpha = 1.96$ (for confidence level 95%).

Formula used:

$$n = \frac{z^2_{\alpha} * \sigma^2}{d^2}$$

The sample size

calculated is = (1.96*1.96*4*4)/1 = 61.5

Rounded to 60, statistical testing was conducted with the statistical package for the social science system version SPSS 17.0 (Chicago, IL, USA). HR and BP are expressed as mean±SD and VAS scores as median (min - max). Repeated measurements were analyzed by repeated measures ANOVA for HR and BP. $P<0.05$ was considered statistically significant.

RESULTS

Demographic profile is shown in Table 1. HR is significantly lower than the baseline at all end points as shown in Figure 1 and Table 2. The MAP values during sedation were significantly lower than those at baseline ($P<0.05$) at all time points as shown in Figure 2 and Table 3. Deep sedation causing hypotension, bradycardia or respiratory depression ($SpO_2<90\%$) were not encountered in any patient. None of our patients had any episode of desaturation. All the patients achieved RSS of 3 with titrated infusion of dexmedetomidine. Rescue sedation was not required in any patient. Ten patients required boluses of fentanyl at the time of balloon dilatation. Rest of the patients tolerated the procedure well, with a VAS score of less than or equal to three. No patient had a delayed stay in post anaesthesia care unit post-anesthesia care unit and they achieved RSS of 2 within 60 min. Most of our patients (55) were satisfied with their sedation, with a median satisfaction score of 6 (range 5–7).

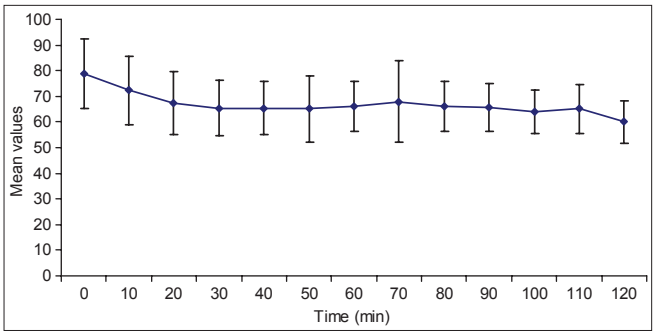

Figure 1: Heart rate changes

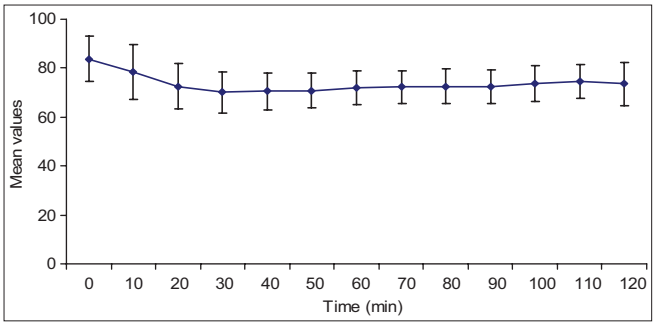

Figure 2: Blood pressure changes

Table 1: Demographic profile

Variable	
Age (in years)	
Mean	46.38
Range	32–64
Gender (n%)	
Male	33.34
Female	66.66
ASA classification (%)	
I	71.66
II	28.34

Table 2: Heart rate

Time	Mean (HR)	SD
0	78.87	13.588
10	72.29	13.33
20	67.42	12.318
30	65.38	10.899
40	65.46	10.312
50	65.1	13.01
60	66.06	9.755
70	67.94	15.889
80	65.98	9.656
90	65.77	9.357
100	64.15	8.511
110	65.05	9.38
120	60.0	8.22

$P<0.001$. Heart rate is significantly lower than that at the baseline at all end points

Table 3: Mean arterial pressure

Time	Mean (MAP)	SD
0	83.83	9.15
10	78.46	11.29
20	72.46	9.26
30	70.13	8.44
40	70.52	7.56
50	70.81	7.13
60	71.88	6.98
70	72.25	6.82
80	72.58	7.18
90	72.29	6.86
100	73.91	7.32
110	74.63	6.95
120	73.60	8.76

$P<0.001$; MAP: Mean arterial pressure

DISCUSSION

Dexmedetomidine is a highly selective α-2-adrenergic receptor agonist that has analgesic and sedative properties. This pharmacologic profile, combined with a very impressive safety margin, has made it an attractive choice for anesthesiologists and intensivists.[9] The agonistic action on the a-2-adrenergic receptors in the sympathetic ganglia modulates the release of catecholamines, resulting in sympatholytic effect, and there have been reports of bradycardia and hypotension.[10] Dexmedetomidine does not result in respiratory depression, and it appears to mimic natural sleep.[11,12]

The liberation procedure requires adequate sedation and analgesia for the following reasons:

Most of the patients of MS experience mild to severe spasm of the lower limbs; therefore, cooperation during the procedure is an issue for which the patient requires sedation.

Most of the patients of MS suffer from depression; therefore, they require sedation and anxiolysis during the procedure.

In this procedure, balloon angioplasty of the internal jugular vein and azygous vein is performed. At the time of dilatation, the patient feels moderate to severe pain requiring analgesia.

For maximal patient comfort, the most suitable drug for the liberation procedure should provide sufficient sedation, adequate analgesia, minimal side-effects and rapid recovery.

Our study demonstrates that sedation with dexmedetomidine is effective in patients undergoing the liberation procedure. The lower HR and MAP observed in our study were similar to the studies conducted by other authors on dexmedetomidine.[11-15]

In most of the patients, the MAP and HR decreased after the bolus dose of dexmedetomidine, which is statistically significant, and both gradually recovered but never reached the baseline value. Only five patients (7.3%) had a significant drop in BP that required a single bolus dose of ephedrine 6 mg to treat hypotension. Overall, dexmedetomidine caused a predictable and manageable decrease in HR and MAP. Protocol-defined hypotension was the most common adverse event in dexmedetomidine-treated patients during the infusion period; however, all cases were mild or moderate in severity and responded to intervention, when indicated. In this study, all patients received supplemental oxygen and desaturation was not reported in any case. In a study conducted by Belleville *et al*.,[16] irregular breathing patterns were noticed with short periods of apnea immediately after the maximum infusion of 2.0 mcg/kg. Decrease in minute ventilation was considered as the cause of the above side-effect. In accordance with the above study, we kept the loading dose to 1 mcg/kg. The desired level of sedation was achieved in all patients. In this study, only 10 (16.6%) patients required rescue analgesic. Dexmedetomidine has an analgesic sparing effect, significantly reducing opioid requirements both during and after surgery.[17-21] The sedative and analgesia-sparing effects of dexmedetomidine have been attributed to its action on the dorsal horn of the spinal cord and locus coeruleus.[22,23]

CONCLUSION

Dexmedetomidine is a safe sedative agent with patients easily aroused to cooperate without showing irritation in patients undergoing the liberation procedure. Dexmedetomidine, because of its analgesic properties, "cooperative sedation" and lack of respiratory depression, is increasingly being used as a sedative for MAC.

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