Egyptian Journal of Anaesthesia (2013) **29**, 47–52

Egyptian Society of Anesthesiologists

Egyptian Journal of Anaesthesia

www.elsevier.com/locate/egja
www.sciencedirect.com

Research Article

Quality of MRI pediatric sedation: Comparison between intramuscular and intravenous dexmedetomidine

Tarek F. Tammam [a,*], **Sherif S. Wahba** [b]

[a] *Department of Anesthesia, Faculty of Medicine, Suez Canal University Hospital, Egypt*
[b] *Ain-Shams University Hospital, Egypt*

Received 7 June 2012; revised 10 August 2012; accepted 23 August 2012
Available online 18 October 2012

KEYWORDS

Procedure;
MRI;
Population;
Pediatrics;
Sedation;
Dexmedetomidine

Abstract *Objective:* The study was designed to compare the efficacy of dexmedetomidine whether given intramuscular or intravenous for pediatric MRI sedation.
Subjects and methods: Ninety children between the ages of 2 and 8 years with ASA physical status I–II, scheduled for elective MRI, were enrolled in a double blind, comparative randomized study. Patients assigned into two equal groups. Group DV, sedation was performed using IV dexmedetomidine hydrochloride; a loading dose of 1 μg/kg administered over 10 min followed by a continuous infusion at 1 μg/kg/h. Group DM where the patient received IM dexmedetomidine 3 μg/kg. Primary endpoints included incidence of failed sedation and the requirement of midazolam supplementation. Secondary endpoints were time to sedation, duration of sedation, discharge time, and hemodynamic status.
Results: The sedation failure rate was significantly higher in the DV group (40%) in comparison with the DM group (20%) ($P = 0.04$). Also, the use of rescue midazolam was significantly higher in the VD group (0.37 ± 0.47 mg) in comparison to the DM group (0.17 ± 0.35 mg) ($P = 0.025$). The onset of satisfactory sedation was significantly shorter in DV group in comparison to DM group (7.93 ± 0.884 vs. 16.87 ± 4.49). Also, the discharge time was significantly less in the DV group (32.27 ± 3.04 min) in comparison to DM group (41.87 ± 5.80 min). Patients in DV group had significantly lower MBP compared to patients in DM group after receiving dexmedetomidine ($p < 0.05$). Although the HR decreased in both groups during the MRI study, the decrease was statistically significant in the DV group compared to the DM group in the period extended from the 2nd to 35th min ($p < 0.05$).

* Corresponding author. Address: Department of Anesthesia and Intensive Care, Suez Canal University Hospital, Egypt. Tel.: +2096599631041.
E-mail address: tarek1367@hotmail.com (T.F. Tammam).

Peer review under responsibility of Egyptian Society of Anesthesiologists.

ELSEVIER **Production and hosting by Elsevier**

http://dx.doi.org/10.1016/j.egja.2012.08.002

Conclusion: In pediatric MRI sedation, although IM dexmedetomidine does have a late sedation onset; it reduces the sedation failure rate, the need for supplement sedation and the incidence of hemodynamic instability associated with IV dexmedetomidine.

1. Introduction

Dexmedetomidine is a potentially effective agent for sedation during non-invasive procedures such as magnetic resonance imaging (MRI) [1,2]. It has several potential beneficial effects over older sedatives including its fast onset of action, minimal respiratory depression, and an option for repeated administration when needed for special procedures [3]. The risks of its sedation are in part related to the inherently unpredictable response to medication and to the route of administration. There is a varied response in sedation to IV dexmedetomidine; it should be titrated for successful sedation [2]. The needs for titration are practically difficult and interfere with the continuity of MRI procedure. The most frequently seen adverse effects of IV dexmedetomidine that has been reported are hypotension and bradycardia [4–7]. The ideal sedative should be administer by a simple and non-sophisticated technique, and produces adequate sedation conditions while minimizing the incidence of adverse events. Intramuscular dexmedetomidine administration might avoid the most serious risks and complications associated with IV dexmedetomidine and might reduce the need for titration which is essential for IV sedation. The study was designed to compare the efficacy of dexmedetomidine whether given Intramuscular or intravenous for pediatric MRI sedation.

2. Patients and methods

After obtaining approval of the hospital's Research Ethics Committee and written informed consent from parents for the sedation, 90 children between the ages of 2 and 7 years with ASA physical status I–II, scheduled for elective MRI were enrolled in a double blind, comparative, randomized study. The study was conducted from June 2009 to March 2012. Patients with a history of cardiovascular, active respiratory tract, hepatic, or renal diseases and by reason of parents' refusal were excluded. Patient demographics, type of MRI study performed and its imaging time, as well as patient's ASA physical status were recorded. Imaging time refers to the duration of imaging study from initiation of scan till the radiologist confirms completion of successful MRI study.

Patients were randomized to one of two groups for sedation: In Group DV ($n = 45$), sedation was performed with dexmedetomidine hydrochloride (Precedex®, Abbott, 200 μg/ml) intravenously, a loading dose of 1 μg/kg administered over 10 min, followed by a continuous infusion at 1 μg/kg/h for the duration of the procedure. In Group DM ($n = 45$), the dexmedetomidine 3 μg/kg was delivered as a single IM injection in the lateral cranial thigh muscle group; using a 25 gauge needle, with the child on the parent's knee or lying on the trolley 20 min before the procedure. Every child had IM injection (dexmedetomidine/saline) and IV infusion (dexmedetomidine/saline) prepared by dedicated nurse, sedation was given by anesthesiologists blinded to the group assignment. The patients were randomly assigned on a one-to-one ratio. Randomization was performed by means of a computer-generated random-numbers table. Parents were instructed to make their children NPO for solids 6 h and to give clear liquids up to 2 h prior to their scheduled appointment. EMLA cream was applied 1 h before the procedure to the places of IM injection and IV cannulation. Before each procedure, an IV access and standard monitoring of electrocardiogram (ECG), non-invasive arterial blood pressure (NIABP), and peripheral oxygen saturation (SpO2), were established. Heart rate (HR) and rhythm were displayed continuously by using a lead II ECG. All values of vital signs (NIABP, HR, SPO2, and RR) were recorded every 2 min during the 1st 10 min and at 5-min intervals throughout the procedure.

The sedation levels were consecutively assessed with Ramsay sedation score (RSS) [8]. Primary endpoints included incidence of failed Sedation and the requirement of midazolam supplementation. Secondary endpoints were time to sedation, duration of sedation, discharge time, and hemodynamic status. The level of radiologist satisfaction regarding the quality of sedation and the incidence of adverse events were also recorded.

The time to sedation is defined as the time in minutes (min) from administration of sedative to achievement of adequate sedation (RSS 4). Duration of sedation is defined as the time from onset to offset of sedation (RSS 2). Time to discharge is the time from giving sedation to point at which patient meets the discharge criteria (Alderete score of 8 or greater) [9]. The sedation was classified as failed if RSS is less than 4 or if unacceptable motion artifacts lead to inability to complete the imaging study. Supplemental sedation was provided by using titrated doses of midazolam IV 0.05 mg/kg every 4 min.

Adverse events, including airway complications, oxygen desaturation less than 92%, emesis, and unplanned admission were recorded. Bradycardia was identified as rates less than 60 beat min^{-1} and was treated with IV atropine 20 μg/kg. Hypotension was identified as a 20% decrease in the mean blood pressure (SBP) and was treated with fluids administration (10 ml/kg) and IV ephedrine 0.1 mg/kg. The need of head repositioning, jaw thrust, and oral airway placement in a state of airway obstruction were recorded. Radiologist satisfaction was evaluated using a 10-cm visual analog scale (VAS) scores (0, not satisfied and 10, totally satisfied) at the end of procedure.

Statistical analyses: EPI-INFO program was used for sample size calculation by using incidence of sedation failure as the primary outcome of this study. The α-error level was fixed at 0.05 and power was set at 80% while the expected change to be detected was 10%. Qualitative data were analyzed with pearson Chi-square test. Quantitative data, expressed as 'mean ± standard deviation (SD)', were analyzed by one way ANOVA test. A probability value of less than 0.05 was considered statistically significant. All analyses were done by using the statistical package for social sciences (SPSS).

Table 1 Patient demographics and the clinical characteristics.

Parameters	Group		
	Group DV (n = 45)	Group DM (n = 45)	Significance (P value)
Age (yr)	3.70 ± 1.57	3.93 ± 1.46	NS
Weight (kg)	16.10 ± 3.57	15.70 ± 2.79	NS
ASA I/II	6/12	7/11	NS
Gender (F/M)	10/8	9/9	NS
Imaging time (min)	14.21 ± 3.4	14.86 ± 3.8	NS

Abbreviation: M; male, F; female, No; number as mean ± SD (M ± SD).
Values are expressed as M ± SD or absolute numbers.
NS = No significant differences between the groups $P > 0.05$.

Table 2 The clinical outcome characteristics.

Parameters	Group		
	Group DV (n = 45)	Group DM (n = 45)	Significance (P value)
Onset of sedation	7.93 ± 0.88	16.87 ± 4.49	0.002
Duration of sedation	22.93 ± 2.31	24.27 ± 2.99	NS
Time to discharge	32.27 ± 3.04	41.87 ± 5.80	0.001
Sedation failure rate	18 (40%)	9 (20%)	0.04
Midazolam (mg)	0.37 ± 0.47	0.17 ± 0.35	0.025
Radiologist satisfaction (VAS)	7.10 ± 0.51	8.77 ± 0.74	0.001

Abbreviation: VAS; visual analog scale.
Values are expressed as M ± SD or absolute numbers.
NS; $P > 0.05$.

Table 3 Type of MRI examination.

Type of MRI examination n (%)	Group DV (n = 45)	Group DM (n = 45)	Significance
Head or neck	27	29	NS
Spine	8	7	NS
Thorax	3	3	NS
Abdomen	4	3	NS
Extremity	3	3	NS

NS = $P > 0.05$.

3. Results

There was no significant difference between the DM and DV groups with respect to patient's characteristics, type and duration of the imaging study ($p > 0.05$, Tables 1 and 3). The duration of MRI averaged 14.21 ± 3.4 min vs. 14.86 ± 3.8 min in DV group and DM group respectively. The onset of satisfactory sedation was significantly shorter in the DV group in comparison with the DM group (7.93 ± 0.884 vs. 16.87 ± 4.49 min), Table 2. The patients in the DV group had sedation duration of 22.93 ± 2.31 min, while it was 24.27 ± 2.99 min in the DM group with no significance difference between them. On the contrary, the discharge time was significantly less in the DV group (32.27 ± 3.04 min) in comparison to the DM group (41.87 ± 5.80 min), Table 2.

Although all the patients completed the MRI studies, the sedation failure rate was significantly higher in the DV group (40%) in comparison with the DM group (20%) ($P = 0.04$, Table 2). Also, the use of rescue midazolam was significantly higher in the VD group (0.37 ± 0.47 mg) in comparison to the DM group (0.17 ± 0.35 mg) ($P = 0.025$; Table 2). Regarding using the dexmedetomidine as a sedative during the MRI study in pediatrics, the radiologist satisfaction was significantly higher in the DM group in comparison to the DV group (8.77 ± 0.74 vs. 7.10 ± 0.51) ($P = 0.001$; Table 2).

Patients in the DV group had significantly lower MBP compared to patients in DM group in the intervals extended from the 6th to 20th min after receiving dexmedetomidine ($p < 0.05$, Table 4). Although the HR decreased in both groups during the MRI study, the decrease was statistically significant in the DV group compared to the DM group in the intervals extended from the 4th to 35th min ($p < 0.05$, Table 5).

During the MRI procedure, the incidence of bradycardia and hypotension that led to intervention was higher in the DV group (22.2% and 15.6% respectively) in comparison to the DM group (6.67% and 6.67%); Table 6. All cases of bradycardia and hypotension that have been reported were treated with IV atropine and ephedrine respectively in addition to fast IV fluid administration in case of hypotension. While

Table 4 Shows the mean blood pressure values of the two groups.

Time	Group		
	Group DV (n = 45)	Group DM (n = 45)	Significance
Baseline	63.20 ± 5.13	63.00 ± 4.54	NS
2 min	64.24 ± 4.45	62.50 ± 4.32	NS
4 min	61.20 ± 4.77	61.80 ± 3.68	NS
6 min	55.80 ± 5.27	61.27 ± 4.28	0.03
8 min	53.66 ± 4.12	60.60 ± 4.10	0.006
10 min	52.87 ± 2.83	58.73 ± 5.06	0.001
15 min	52.20 ± 3.23	55.73 ± 4.50	0.020
20 min	51.00 ± 3.76	55.33 ± 5.04	0.012
25 min	56.40 ± 3.58	57.73 ± 5.96	NS
35 min	58.20 ± 4.62	59.27 ± 5.06	NS
45 min	61.07 ± 4.20	60.73 ± 4.38	NS

Values are expressed as mean ± SD (M ± SD).
NS = $P > 0.05$.

Table 5 Shows that the mean heart rate values of the two groups.

Time	Group		
	Group DV (n = 45)	Group DM (n = 45)	Significance (P value)
Baseline	100.00 ± 3.928	99.67 ± 4.25	NS
2 min	95.40 ± 4.26	99.20 ± 3.098	NS
4 min	84.60 ± 2.17	97.67 ± 3.498	0.001
6 min	84.20 ± 2.48	91.93 ± 4.65	0.001
8 min	84.07 ± 2.52	88.33 ± 4.07	0.002
10 min	80.13 ± 7.21	86.00 ± 3.93	0.010
15 min	79.53 ± 9.46	84.47 ± 7.49	NS
20 min	81.73 ± 2.92	85.60 ± 3.996	0.005
25 min	82.60 ± 2.75	85.13 ± 2.997	0.023
35 min	86.07 ± 3.15	89.87 ± 3.58	0.005
45 min	94.00 ± 4.26	95.53 ± 2.42	NS

Values are expressed as mean ± SD (M ± SD).
NS = $P > 0.05$.

Table 6 Incidence of adverse events of the two groups.

Variables	Group		
	Group DV (n = 45)	Group DM (n = 45)	Significance (P value)
Bradycardia	10 (22.2%)	3 (6.67%)	0.037
Hypotension	7 (15.6%)	3 (6.67%)	NS
Oxygen desaturations	3 (6.67%)	1 (2.2%)	NS
Vomiting	2 (4.44%)	1 (2.2%)	NS

NS = $P > 0.05$.

the incidence of Oxygen desaturation and vomiting was (6.67% and 4.44%) in the DV group, it was (2.2% and 2.2%) in the DM group ($p > 0.05$, Table 6). In case of oxygen desaturation, patients responded to head repositioning and assisted mask ventilation.

4. Discussion

There are various possible uses of dexmedetomidine for pediatric sedation, it appears to be a potentially effective agent for sedation during non-invasive procedures [1,2]. Dexmedetomidine has several potential beneficial effects aside from sedation, such as mild analgesia, anxiolysis, and its minimal respiratory effects [1]. However, there are many unanswered questions directed towards the significance of its side effects and the wide varied sedative response to IV dexmedetomidine use in pediatrics. Mason et al. reported that only 9.7% of sedated patients using IV dexmedetomidine were able to complete the CT imaging study during the loading dose while 90.3% of patients required the maintenance infusion of dexmedetomidine ± 2nd bolus dose [2]. Due to the regular need for dose titration and the instant onset of adverse events, patients may rapidly move from conscious sedation to deep sedation with increased risk of cardiovascular instability, or

can inadvertently pass from a deep level of sedation to shallow one, with increased risk of unacceptable motion artifacts. Patients' movement was noted to be a significant problem on using IV dexmedetomidine for pediatric sedation [10], the addition of rescue of another sedative was necessary for MRI rescanning. The sedative effect of dexmedetomidine is dose-dependent, further dosing acts to lengthen the duration of sedation and increase the risk of adverse effects [11]. For MRI study, the ideal sedative should make by a non-sophisticated method and produce adequate sedation conditions while minimizing the incidence of adverse events.

In this study, IM dexmedetomidine had lower sedation failure rate and lesser adverse events, but had a significantly delayed onset of adequate sedation compared with IV dexmedetomidine. Although the onset of sedation was shorter in IV dexmedetomidine, it is expected due to the route of drug administration. Scheinin et al. have reported that time to maximal effect of IM dexmedetomidine given to adult patients occurred between 60 and 150 min, depending on the dosage of dexmedetomidine administered [12]. While IM dexmedetomidine had steady sedation state and needed less rescue doses, the requirement for supplemental sedation is essential for successful sedation in the IV dexmedetomidine. IM dexmedetomidine may allow a 'depot' of drug to be established such will be released gradually into the systemic circulation over a period of time, allowing sound sedation in children, reducing the possible adverse events and the possible need for titration which is sensibly difficult to practice during the MRI procedure. Dexmedetomidine is a sedative with limited experience in pediatric patients [2]. There are a limited number of studies regarding using IM dexmedetomidine in children. Mason et al. reported successful MRI on using IV dexmedetomidine in 97.6% of children [13], and the cardiovascular side- effects were seen in 16% of patients [13]. The most common adverse effects experienced on using dexmedetomidine are hypotension and bradycardia [6,7], while hypertension is only frequent with the administration of the loading dose [7]. In our study, the mean arterial pressure values decreased when using both IM and IV dexmedetomidine. However the mean arterial pressure was significantly lower after drug administration in the DV group, when compared with that of the DM group. Also, there was higher incidence of hypotension and bradycardia during IV dexmedetomidine administration in comparison to IM dexmedetomidine. The hemodynamic changes were steady in the IM dexmedetomidine in comparison to the IV dexmedetomidine. The most frequently seen adverse effects of IV dexmedetomidine that has been reported are hypotension and bradycardia [5,7,9]. Dexmedetomidine has been shown to produce dose-dependent decreases in blood pressure and heart rate as a result of its alpha2 agonist effect on the sympathetic ganglia with resulting sympatholytic effects [14]. Although IV dexmedetomidine was found effective for pediatric non-invasive procedural sedation, statistically significant changes in hemodynamic state were reported [15]. It was observed that the low doses of dexmedetomidine (0.25–1 $\mu g\ kg^{-1}$) were associated with a decrease in MBP, while the higher doses (1–4 $\mu g\ kg^{-1}$) of dexmedetomidine were reported to increase transiently the MBP and decrease significantly the HR [16,17]. On the other hand, at the most IM dexmedetomidine moderately suppresses BP and HR depending on the dosage [12]. As premedication, the IM dexmedetomidine produces mild hypotension and bradycardia in patients undergoing arthroscopic knee surgery [18]. In this study, the transient increase in MBP associated with IV loading dose of dexmedetomidine might be attributed to vascular smooth muscle constriction and direct stimulation of peripheral alpha-receptors, likely alpha 1 [14]. This effect was not noted with the IM dexmedetomidine administration. The most common effect noted with alpha-2 agonists is an initial hypertension, which results in a baroreceptor-mediated reflex bradycardia. As the peripheral effects diminish, central alpha-2 actions predominate, leading to decreased blood pressure and cardiac output [14]. The incidence of vomiting and peripheral oxygen desaturation was more noted with IV dexmedetomidine administration as compared to IM dexmedetomidine. As evaluation of dexmedetomidine with respect to its side effect profile reveals that it is well tolerated [19,20]. Nausea, discomfort and agitation noted as rare side effects observed after dexmedetomidine administration [19,20]. Dexmedetomidine can even decrease the need for antiemetics [21]. Also, the effect of dexmedetomidine on the respiratory system is bare minimum [22], which explains the comparable low incidence of adverse respiratory events in the IV and IM dexmedetomidine in the current study. Taghinia et al. [21] reported that dexmedetomidine decreased the incidence of oxygen desaturation and reduced the amounts of narcotic and anxiolytic requirement. Similarly, Ebert et al. did not observe any apnea, airway obstruction and hypoxemia with bolus doses of dexmedetomidine [17]. Also, Belleville et al. [23] correlate the irregular ventilation and apnea episodes with dexmedetomidine 1–2 $\mu g\ kg^{-1}$ administrated in 2 min, to the deep sedation, not to the 2α adrenergic agonists which have no active role on the respiratory center1 [17]. The radiologist satisfaction was significantly higher with the use of IM dexmedetomidine in pediatric MRI sedation compared to IV dexmedetomidine. The IM dexmedetomidine can reduce the most serious risks and complications associated with IV dexmedetomidine and frequent titration for sedation is not necessary. Although the study encourages the use of IM dexmedetomidine in pediatric sedation, the optimal dose and the concurrent use of IM dexmedetomidine with other agents as dissociative agents needs further study.

Conclusion, in pediatric MRI sedation, although IM dexmedetomidine does have a late sedative onset; it reduces the sedative failure rate, the need for supplement sedation and the incidence of hemodynamic instability associated with IV dexmedetomidine.

References

[1] Phan Hanna, Nahata Milap C. Clinical uses of dexmedetomidine in pediatric patients. Pediatr Drugs 2008;10(1):49–69.
[2] Mason Keira P, Zgleszewski Steven E, Dearden Jennifer L, et al. Dexmedetomidine for pediatric sedation for computed tomography imaging studies. Anesth Analg 2006;103:57–62.
[3] Powers Karen S, Nazarian Emily B, Tapyrik Sarah A, Kohli Susan M, et al. Bispectral index as a guide for titration of propofol during procedural sedation among children. Pediatrics 2005;115:1666–74.
[4] Arain SR, Ebert TJ. The efficacy, side effects and recovery characteristics of dexmedetomidine versus propofol when used for intraoperative sedation. Anesth Analg 2002;95:461–6.
[5] Hammer GB, Drover DR, Cao H, Jackson E, et al. The effects of dexmedetomidine on cardiac electrophysiology in children. Anesth Analg 2008;106(1):79–83.
[6] Martin E, Ramsay G, Mantz J, et al. The role of the alpha2-adrenoceptor agonist dexmedetomidine in postsurgical

sedation in the intensive care unit. J Intensive Care Med 2003;18(1):29–41.
[7] Herr DL, Sum-Ping STJ, England M. ICU sedation after coronary artery bypassgraft surgery: dexmedetomidine-based versus propofol-based sedation regimens. J Cardiothorac Vasc Anesth 2003;17:576–84.
[8] Ramsay MA, Savege TM, Simpson BR, et al. Controlled sedation with alphaxalone–alphadolone. Br Med J 1974;2:656–9.
[9] Aldrete J. Discharge criteria. Bailliere's Clin Anaesthesiol 1994;8:763–73.
[10] Heard CMB, Joshi P, Johnson K. Dexmedetomidine for pediatric MRI sedation: a review of a series of cases. Pediatr Anesth 2007;17:888–92.
[11] Bhana NL, Goa KL, McClellan KJ. Dexmedetomidine. Drugs 2000;59:263–8.
[12] Scheinin H, Karhuvaara S, Olkkola KT, et al. Pharmacodynamics and pharmacokinetics of intramuscular dexmedetomidine. Clin Pharmacol Ther 1992;52:537–46.
[13] Mason K, Zurakowski D, Zgleszewski S, et al. High dose dexmedetomidine as the sole sedative for pediatric MRI. Paediatr Anaesth 2008;18:403–11.
[14] Talke P, Lobo E, Brown R. Systemically administered alpha2-agonist-induced peripheral vasoconstriction in humans. Anesthesiology 2003;99:65–70.
[15] Berkenbosch JW, Wankum PC, Tobias JD. Prospective evaluation of dexmedetomidine for noninvasive procedural sedation in children. Pediatr Crit Care Med 2005;6:435–9.
[16] Bloor BC, Ward DS, Belleville JP, et al. Effects of intravenous dexmedetomidine in humans. II. Hemodynamic changes. Anesthesiology 1992;77:1134–42.
[17] Ebert T, Hall JE, Barney JA, et al. The effects of increasing plasma concentrations of dexmedetomidine in humans. Anesthesiology 2000;93:382–94.
[18] Karaaslan D, Peker TT, Alaca A, et al. Comparison of buccal and intramuscular dexmedetomidine premedication for arthroscopic knee surgery. J Clin Aneth 2006;18(8):589–93.
[19] De Wolf AM, Fragen RJ, Avram MJ, et al. The pharmacokinetics of dexmedetomidine in volunteers with severe renal impairment. Anesth Analg 2001;93:1205–9.
[20] Dyck JB, Maze M, Haack C, et al. The pharmacokinetics and hemodynamic effects of intravenous and intramuscular dexmedetomidine hydrochloride in adult human volunteers. Anesthesiology 1993;78:813–20.
[21] Taghinia AH, Shapiro FE, Slavin SA. Dexmedetomidine in aesthetic facial surgery: improving anesthetic safety and efficacy. Plast Reconstr Surg 2008;121:269–76.
[22] Nguyen D, Abdul-Rasool I, Ward D, et al. Ventilatory effects of dexmedetomidine, atipamezole, and isoflurane in dogs. Anesthesiology 1992;76:573–9.
[23] Belleville JP, Ward DS, Bloor BC, et al. Effects of intravenous dexmedetomidine in humans. Anesthesiology 1992;77:1125–33.