Open Journal of Anesthesiology, 2013, 3, 237-242
http://dx.doi.org/10.4236/ojanes.2013.34054 Published Online June 2013 (http://www.scirp.org/journal/ojanes)

Dexmedetomidine Causes Increased Hypotension in Older Adults When Used for Cataract Surgery Compared to Propofol

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Received March 4th, 2013; revised April 10th, 2012; accepted May 17th, 2013

ABSTRACT

Purpose: This study evaluated the hemodynamic effects, suitability and safety of dexmedetomidine (DEX) compared with propofol (PRO) in older adults having outpatient cataract surgery under monitored anesthesia care. The patients, surgeon and the anesthesia staff evaluated satisfaction for both drugs. **Method:** This prospective, single blind, randomized study was conducted using forty-seven patients ≥55 years old undergoing cataract surgery. The two patient groups received either i.v. dexmedetomidine 1 μg/kg over 10 min; followed by maintenance i.v. infusion at 0.2 - 0.7 μg/kg/hr (DEX group, N = 24), or propofol infused between 25 - 120 μg/kg/min (PRO group, N = 23). Both agents were titrated to patient comfort. **Results:** Patients' mean arterial pressures (SEM) at baseline were 104.7 (2.6) and 107.5 (2.7) mmHg for the DEX and PRO groups, respectively ($p = 0.45$). At discharge the pressures were 78.1 (2.5) and 98.1 (2.6) mmHg in DEX and PRO groups, respectively ($p < 0.05$). Patients' heart rates (SEM) at baseline were 74.8 (3.0) for the DEX group and 73.2 (2.8) bpm for the PRO groups ($p = 0.71$). At the time of discharge following surgery, the mean heart rate for the DEX group was 61.5 (2.2) bpm vs. 69.1 (2.3) bpm ($p < 0.05$) for the PRO group. Three patients in the DEX group developed complications precluding discharge or requiring readmission while none of the patience in the PRO group had complications ($p = 0.08$). Patient and surgeon satisfaction scores were similar between the groups. **Conclusion:** Dexmedetomidine is a less suitable sedative compared with propofol use in older patients undergoing cataract surgery due to the decrease in hemodynamic parameters and noted increases in complication rates.

Keywords: Cataract Surgery; Dexmedetomidine; Monitored Anesthesia Care; Propofol

1. Introduction

Cataract surgery is one of the most frequently performed surgical procedures worldwide with an estimated three million cases performed each year in the United States. The majority of procedures are performed on an outpatient basis in elderly patients with significant co-morbidities [1]. Sedation and topical anesthesia are used to provide anesthesia in the vast majority of these procedures [2]. Each class of sedative drugs has a different combination of anxiolytic, hypnotic, amnestic, and analgesic effects, and the selection of the most appropriate medication for a specific patient requires consideration of many factors. Potential drug interactions, pharmacokinetics and pharmacodynamics of each medication must therefore be weighed.

Sedation with propofol (PRO) has limitations which may include respiratory depression, disorientation, and excitation [3]. Since PRO has no analgesic component, an opioid is often given to prevent the unintentional reflex to painful stimuli, and thus may result in a higher incidence of confusion, excessive sedation, disorientation or respiratory depression. Since most patients undergoing cataract surgery are elderly, these effects can be serious. According to the American Society of Anesthesiologists Closed Claims database, overdose of sedative or opioid leading to respiratory depression was the most common (24%) in monitored anesthesia care claims, and 40% of these resulted in permanent brain damage or death [4].

Dexmedetomidine (DEX) (Precedex, Hospira, Lake Forest, IL) is a selective, centrally acting $\alpha 2$ receptor agonist that produces sedation and analgesia without causing respiratory depression [5]. It produces only mild

cognitive impairment [6] and allows patients to respond to verbal commands during the sedation [7]. DEX has been used in various clinical fields, such as sedation in the intensive care unit [8], shockwave lithotripsy [9], awake intubation [10], endoscopic examination [11], pediatric patients [12], and as an adjuvant to anesthetics [13-15]. Because of its analgesic properties, "cooperative sedation", and lack of respiratory depression, DEX is increasingly being used as a sedative for MAC [16,17]. DEX has recently been suggested as an alternative agent for cataract surgery. However, conflicting results have been reported regarding safety and delay in recovering among this patient population to whom DEX in was administered [18,19]. This randomized single-blind clinical study was undertaken to evaluate the suitability and safety of DEX compared with PRO in older adults having outpatient cataract surgery under MAC.

2. Method

Forty-seven patients were enrolled into this prospective, single-blind, randomized IRB approved study. A study investigator obtained written informed consent for all patients and determined patient eligibility for the study. To be included in the study, the patients had to be: ≥55 yrs; have an ASA physical status of I-III; and be administered MAC anesthetic for their cataract surgery performed under topical anesthesia. Patients were excluded if they had: received general anesthesia within 7 days before study entry; any experimental drug within 30 days prior to the study drug administration; or an alpha-2-agonist or antagonist within 14 days before the scheduled procedure. Patients were also excluded if they had any of the following: acute unstable angina; first or second degree heart block; liver disease; active seizure disorder; or history of or current use of sedatives, narcotics, alcohol or illicit drugs.

2.1. Surgical Procedure

Patients arrived in the operating room without premedication and were positioned on the operating table. A nasal cannula (MAC-SAFE™, Vital Signs, Inc., Totowa, NJ) was connected to a capnograph to measure expired CO_2. An oxygen flow rate of 2 L/min was supplied to all patients. Other standard monitors such as ECG, noninvasive arterial pressure and pulse oximeter were also applied. All patients received intravenous fentanyl 50 μg and midazolam 1mg immediately before randomization to an infusion of the DEX or PRO. The infusions for both drugs were administered according to a computer generated randomization schedule provided to the investigational pharmacist by the Cooper University Hospital Biostatistical Group. DEX was bolused at 1 μg/kg over 10 min, followed by a maintenance infusion at 0.2 - 0.7 μg/kg/hr during surgery as per package insert while PRO was infused between 25 - 120 μg/kg/min. Both agents were titrated to patient comfort which was assessed by the anesthesia care giver by asking the patient appropriate questions. The same surgeon performed all the surgeries but was blinded to which group each patient was randomized by covering the infusion bags with aluminum foil. Ramsay score and BIS monitoring were used to assess agitation and adequacy of sedation. The Ramsay score defines the conscious state from a level 1: the patient is anxious, agitated or restless, through the continuum of sedation to a level 6: the patient is completely unresponsive. Vital signs were monitored throughout the procedure and post recovery period. Following the procedure, the study drugs were discontinued and the patients were transferred to a phase II outpatient recovery area (PACU).

Immediately after transfer to the PACU, the surgeon assessed surgical procedure difficulty based on patient compliance and cooperation using a satisfaction assessment scale (SAS). The SAS scores range from 1 (excellent) to 4 (poor) and were recorded by a study-blinded observer. The anesthesia provider, who was not blinded, evaluated the ease and quality of the sedation based on the same 4 point SAS scale. Patient satisfaction was evaluated immediately prior to discharge by a visual analog patient satisfaction scale (PSS). The PSS scores ranges from 1 (excellent) to 4 (poor). Complications prior to PACU discharge were monitored and recorded. Once stable, patients were discharged to home if they met the following hemodynamic and respiratory criteria: a systolic blood pressure within 20 mmHg of their preoperative value without symptoms of orthostatic hypotension and a respiratory rate between 10 and 30 breaths per min. Discharge time was recorded and compared between groups. Safety was evaluated by monitoring adverse events, cardiac hemodynamic variables, laboratory tests, vital signs, and rescue medications required (IV midazolam).

2.2. Statistical Analyses

Descriptive statistics were used to summarize data at baseline and during the procedure in tables with means (SD). Quantitative variables such as demographic data, surgical and recovery times, vital signs, and BIS data were analyzed by ANOVA with repeated measures for interval measurements. Nonparametric data: surgeon, anesthetist, and patient satisfaction rating scales were analyzed using the Kruskal-Wallis test. For all tests, a $p < 0.05$ was considered statistically significant. For the observed difference between MAP in the DEX and PRO groups following surgery, actual power of this study was

99% with 23 & 24 patients per group. A difference of 15% was considered to be the smallest detectable difference that would be clinically significant in this setting and was based on the clinical experience of the investigators. Power analysis was set for a one way fixed effects analysis of variance with repeated measures at 2 levels. The criterion for significance (alpha) was 0.05 and the analysis of variance was non-directional.

3. Results

3.1. Patients

47 ASA class I-III patients participated in this study. Patient characteristics were similar in the groups. There were no statistically significant differences between the two patient groups with respect to age, gender distribution, height, weight, BMI and ASA status (**Table 1**).

3.2. Hemodynamics

Baseline mean (SEM) hemodynamic measurements of MAP for the DEX and PRO groups were 104.7 (2.6) and 107.5 (2.7) mmHg, respectively ($p = 0.45$). Patient mean (SEM) arterial pressures at discharge were 78.1 (2.5) and 98.1 (2.6) mmHg in the DEX and PRO groups, respectively ($p < 0.05$). Patients receiving DEX had significantly lower MAP compared to the PRO group post-op and at discharge (**Figure 1**). This represents 25% and 26% drops in MAP from baseline at post-op and at discharge, respectively.

Patient mean (SEM) heart rates were similar in both groups at baseline [74.8 (3.0) bpm DEX, 73.2 (2.8) bpm PRO]. Patient heart rates at discharge for the DEX and PRO groups were 61.5 (2.2) and 69.1 (2.3) bpm respectively ($p < 0.05$) **(Figure 2)**. This represents 11% and 8% drop in HR from baseline post-op and at discharge, respectively.

Table 1. Patient characteristics.

	DEXMEDETOMIDINE N = 24	PROPOFOL N = 23	p value
Age (years)			
Mean (SD)	69.5 (8.8)	69.5 (9.7)	NS
Range	55 - 85	55 - 90	
Gender, n (%)			
Male	13 (54)	9 (39)	NS
Height (cm)			
Mean (SD)	167.9 (10.3)	165.4 (13.3)	NS
Range	152 - 185	130 - 188	
Weight (kg)			
Mean (SD)	82.7 (22.6)	76.5 (21.5)	NS
Range	50 - 125	34 - 117	
BMI			
Mean (SD)	29.4 (7.7)	28.2 (9.7)	NS
ASA status			
I/II/III	1/9/14	0/8/15	NS

NS = not statistically significant; SD = standard deviation.

3.3. Surgery and Post-Op Statistics

Mean (SD) surgical times and duration of study drug infusion for the DEX and PRO groups were 44 (19) and 38 (12.4) min, respectively (**Table 2**). None of the patients in either group required rescue sedation with midazolam. Intraoperative Ramsay scores were 2.56 (0.84) and 3.08 (0.90) in the DEX and PRO groups, respectively. By the end of the surgery, Ramsay scores were 2.27 (0.46) and 2.25 (0.44) in the DEX and PRO groups, respectively. Intra-op BIS values, respiration rates and SPO_2 values were similar in both groups (**Table 2**).

No significant differences were found in surgeon and patient satisfaction ratings between the groups (**Table 2**). Results from the anesthesiologists' assessment showed a significant difference favoring the DEX group compared with the PRO group for ease of maintenance of sedation (1.16 vs. 1.62, respectively; $p = 0.003$).

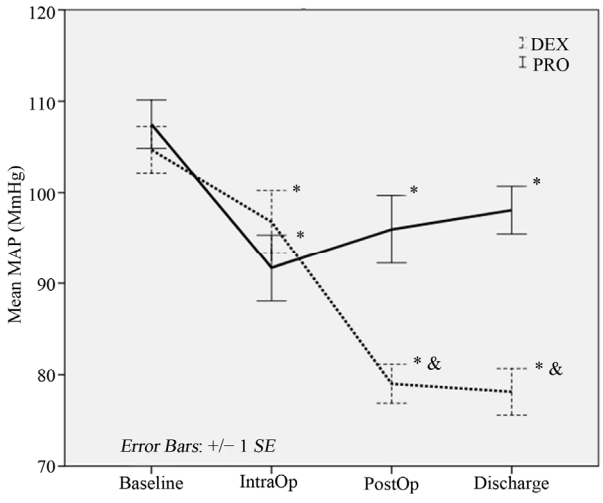

Figure 1. Mean Arterial Pressures (MAP), MAP at baseline, during the cataract surgery (IntraOp), at the end of the cataract surgery (Post-Op) and at discharge from the phase II outpatient recovery area. The dotted line represents the Dexmedetomidine group and the solid line represents the Propofol group. Error bars represent +/−1 standard error of the mean (SEM). [&] = $p < 0.05$ comparing DEX with PRO. [*] = $p < 0.05$ comparing baseline with IntraOp, post-op and discharge.

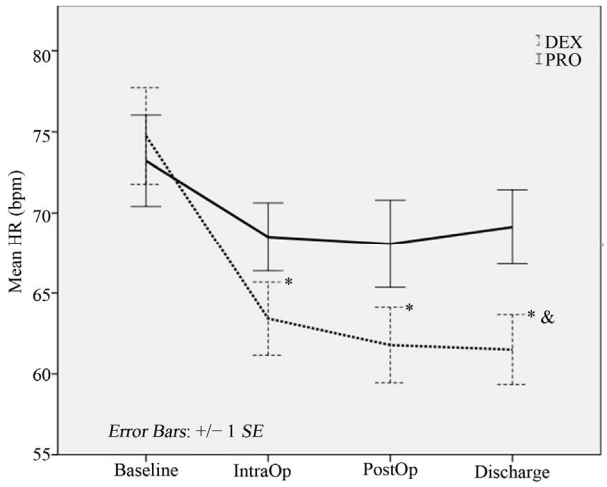

Figure 2. Mean Heart Rates, Mean heart rates at baseline, during the cataract surgery (IntraOp), at the end of the cataract surgery (Post-Op) and at discharge from the phase II outpatient recovery area. Dotted line represents the Dexmedetomidine group and the solid line represents the Propofol group. Error bars represent +/−1 standard error of the mean (SEM). [&] = p < 0.05 comparing DEX with PRO. [*] = p < 0.05 comparing baseline with IntraOp, post-op and discharge.

The number (%) of patients discharged from the PACU in greater than 90 min for the DEX and PRO groups were 6 (25%) and 2 (9%), respectively (p = 0.11) (**Table 2**). One subject in the DEX group was identified as at outlier (Durbin-Watson D statistic and the first-order autocorrelation) with a PACU time of 815 min. Removal of that data point reduced the mean DEX PACU time to 57 (59) min with P value increased to 0.42. Oxygen saturations were above 97% for both groups. Three subjects (11%) in the DEX group had complications precluding discharge or requiring readmission compared to zero in the PRO group (p = 0.08). All of the complications were cardiovascular with two patients experiencing hypotension requiring treatment. The third patient experienced ectopy requiring observation and was assigned to a monitored bed. The required prolonged post-operative monitoring explains the longer mean PACU stay and high variability in the DEX group which did not reach statistical significance.

4. Discussion

The most suitable agents for conscious sedation during cataract procedures are still being investigated. Studies comparing DEX to other sedating agents have also increased in number. However, the number of studies comparing PRO sedation to DEX in this specific population appears to be limited. This prospective, randomized, single-blinded investigation was conducted to compare PRO and DEX to produce adequate levels of analgesia during cataract surgery with monitored anesthesia care.

Table 2. Surgery and post-op statistics.

	DEX N = 24	PRO N = 23	p value
Surgical Time (min)			
Mean (SD)	45.7 (19.6)	38.1 (12.4)	NS
Range	23 - 116	19 - 65	
Respiration (bpm)			
IntraOp	15.6 (8.1)	15.7 (3.6)	NS
Post-Op	19.0 (11.1)	15.9 (2.9)	NS
SPO_2 (%)			
IntraOp	99.0 (1.5)	98.8 (1.7)	NS
Post-Op	97.1 (2.7)	97.7 (2.1)	NS
Ramsay Scores			
IntraOp	2.56 (0.84)	3.08 (0.90)	0.048
Post-Op	2.27 (0.46)	2.25 (0.44)	NS
BIS			
Mean (SD)	83.8 (9.4)	76.0 (18.3)	NS
Satisfaction Scores[a]			
Surgeon SAS	1.25 (0.44)	1.45 (0.67)	NS
Anesthetist SAS	1.14 (0.35)	1.62 (0.59)	0.003
Patient PSS	1.13 (0.34)	1.23 (0.53)	NS
Time in PACU (# pts)			
≥90 min	6 (25%)	2 (9%)	0.11
PACU Complications			
N (%)	3 (13%)	0 (0%)	0.08

[a]Satisfaction was measured using the Satisfaction Assessment Scale (SAS). The SAS scores range from 1 (excellent) to 4 (poor). Surgeon assessed surgical procedure difficulty based on patient compliance and cooperation. The anesthesia provider evaluated the ease and quality of the sedation (they were not blinded). Patient satisfaction was evaluated immediately prior to discharge by a visual analog patient satisfaction scale (PSS). The PSS scores ranges from 1 (excellent) to 4 (poor). DEX = Dexmedetomidine, PRO = Propofol, NS = not statistically significant, SD = standard deviation, PACU = phase II outpatient recovery area.

Cataract surgery is usually performed under topical anesthesia administered via ophthalmic solution, thereby eliminating needle injection of local anesthesia [2]. While the technique of topical anesthesia minimizes complications, it may result in inadequate anesthesia and require deeper levels of sedation for optimal patient satisfaction.

Furthermore, patients who undergo cataract surgery are usually elderly and have significant co-morbidities [1] and lasting reduction in their hemodynamic stability should be avoided.

The major findings of this research are as follows:

PRO and DEX provided similar levels of sedation as determined by the intraoperative Ramsay and BIS scores and no patient in either group required rescue midazolam. We noted significant decreases in intraoperative MAP and HR which persisted in the DEX group until the patients were discharged. This 25% drop in MAP and 11% drop on HR present a potential problem in this patient population. A rather disturbing consequence of the fall in MAP and HR was that a prolonged recovery and delayed discharge was noted in 13% of the DEX patients.

The lower HR and MAP observed in the DEX group could be explained by the decreased sympathetic outflow and circulating levels of catecholamines as well as its sympatholytic and vagal mimetic effects [20]. Similar hemodynamic changes have been reported by others [21-24]. The persistent effects of DEX in the PACU can be partly explained by the relatively long half-life of DEX which is reported to be 100 - 150 min compared to 30 - 60 min for PRO [25].

The drug regiment used may also explain some of the hemodynamic effects of DEX. In this study, a loading dose of DEX (1 μg/kg over 10 min) was used and the infusion was stopped when the surgery was complete. Stopping the DEX infusion when surgery was complete, instead of careful titration to surgery end, may have contributed to the residual hemodynamic effects we observed. Alhashemi [15] who used a similar regiment with similar results postulated that the relatively high loading dose and infusion rate might have caused the observed cardiovascular suppression. Some studies have shown that omitting the loading dose of DEX resulted in appropriate sedation and stable hemodynamics [19,23,24].

Patient and surgeon satisfaction scores were similar between the PRO and DEX groups. However, the anesthesia provider satisfaction scores were significantly different, favoring DEX sedation for ease of maintenance over PRO. The reason for this was not totally obvious in that respiratory depression was not seen with either medication. Because of the non-blinding of the caregiver, personal bias could have been a factor. Respiratory end points (RR and SPO_2) were similar between treatment groups throughout the entire study period.

While the study was designed to evaluate recovery parameters in this older patient population, an area of concern in this population is the increased prevalence of orthostatic hypotension with age reaching almost 50% of nursing home individuals. The delayed return to baseline hemodynamics and potential side effects noted may make DEX a less than ideal medication for MAC anesthesia in this elderly population. Decreases in hemodynamic parameters and increases in complication rates may warrant consideration of other drugs or an alternative dosing regimen for DEX. Further evaluation of DEX and possible orthostatic changes in elderly patients warrants further study.

REFERENCES

[1] P. B. Greenberg, J. Liu, W. C. Wu, *et al.*, "Predictors of Mortality within 90 Days of Cataract Surgery," *Ophthalmology*, Vol. 117, No. 10, 2010, pp. 1894-1899. doi:10.1016/j.ophtha.2010.02.009

[2] D. V. Leaming, "Practice Styles and Preferences of ASCRS Members 2003 Survey," *Journal of Cataract & Refractive Surgery*, Vol. 30, No. 4, 2004, pp. 892-900. doi:10.1016/j.jcrs.2004.02.064

[3] P. R. Janzen, A. Christys and M. Vucevic, "Patient-Controlled Sedation Using Propofol in Elderly Patients in Day-Case Cataract Surgery," *British Journal of Anaesthesia*, Vol. 82, No. 4, 1999, pp. 635-636. doi:10.1093/bja/82.4.635

[4] S. M. Bhananker, K. L. Posner, F. W. Cheney, *et al.*, "Injury and Liability Associated with Monitored Anesthesia Care: A Closed Claims Analysis," *Anesthesiology*, Vol. 104, No. 2, 2006, pp. 228-234. doi:10.1097/00000542-200602000-00005

[5] A. T. Gerlach and J. F. Dasta, "Dexmedetomidine: An Updated Review," *The Annals of Pharmacotherapy*, Vol. 41, No. 2, 2007, pp. 245-252. doi:10.1345/aph.1H314

[6] R. Venn, C. Bradshaw, R. Spencer, *et al.*, "Preliminary UK Experience of Dexmedetomidine, a Novel Agent for Post-operative Sedation in the Intensive Care Unit," *Anaesthesia*, Vol. 54, No. 12, 1999, pp. 1136-1142. doi:10.1046/j.1365-2044.1999.01114.x

[7] J. E. Hall, T. D. Uhrich, J. A. Barney, *et al.*, "Sedative, Amnestic, and Analgesic Properties of Small-Dose Dexmedetomidine Infusions," *Anesthesia and Analgesia*, Vol. 90, No. 3, 2000, pp. 699-705. doi:10.1097/00000539-200003000-00035

[8] J. A. Tan and K. M. Ho, "Use of Dexmedetomidine as a Sedative and Analgesic Agent in Critically Ill Adult Patients: A Meta-Analysis," *Intensive Care Medicine*, Vol. 36 No. 6, 2010, pp. 926-939. doi:10.1007/s00134-010-1877-6

[9] K. Kaygusuz, G. Gokce, S. Gursoy, *et al.*, "A Comparison of Sedation with Dexmedetomidine or Propofol during Shockwave Lithotripsy: A Randomized Controlled Trial," *Anesthesia and Analgesia*, Vol. 106, No. 1, 2008, pp. 114-119. doi:10.1213/01.ane.0000296453.75494.64

[10] S. D. Bergese, B. Khabiri, W. D. Roberts, *et al.*, "Dexmedetomidine for Conscious Sedation in Difficult Awake Fiberoptic Intubation Cases," *Journal of Clinical Anesthesia*, Vol. 19, No. 2, 2007, pp. 141-144. doi:10.1016/j.jclinane.2006.07.005

[11] S. Muller, S. M. Borowics, E. A. Fortis, *et al.*, "Clinical Efficacy of Dexmedetomidine Alone Is Less than Propofol for Conscious Sedation during ERCP," *Gastrointestinal Endoscopy*, Vol. 67, No. 4, 2008, pp. 651-659. doi:10.1016/j.gie.2007.09.041

[12] C. Chrysostomou, "Dexmedetomidine: Should It Be Stan-

dard after Pediatric Cardiac Surgery?" *Pediatric Critical Care Medicine*, Vol. 13, No. 6, 2012, pp. 696-697. doi:10.1097/PCC.0b013e31825b84f4

[13] A. Bekker, M. Sturaitis, M. Bloom, *et al.*, "The Effect of Dexmedetomidine on Perioperative Hemodynamics in Patients Undergoing Craniotomy," *Anesthesia and Analgesia*, Vol. 107, No. 4, 2008, pp. 1340-1347. doi:10.1213/ane.0b013e3181804298

[14] N. M. Bulow, N. V. Barbosa and J. B. Rocha, "Opioid Consumption in Total Intravenous Anesthesia Is Reduced with Dexmedetomidine: A Comparative Study with Remifentanil in Gynecologic Videolaparoscopic Surgery," *Journal of Clinical Anesthesia*, Vol. 19, No. 4, 2007, pp. 280-285. doi:10.1016/j.jclinane.2007.01.004

[15] J. A. Alhashemi, "Dexmedetomidine vs Midazolam for Monitored Anesthesia Care during Cataract Surgery," *British Journal of Anaesthesia*, Vol. 96, No. 6, 2006, pp. 722-726. doi:10.1093/bja/ael080

[16] T. J. Ebert, J. E. Hall, J. A. Barney, *et al.*, "The Effects of Increasing Plasma Concentrations of Dexmedetomidine in Humans," *Anesthesiology*, Vol. 93, No. 2, 2000, pp. 382-394. doi:10.1097/00000542-200008000-00016

[17] A. Apan, N. Doganci, A. Ergan, *et al.*, "Bispectral Index-guided Intraoperative Sedation with Dexmedetomidine and Midazolam Infusion in Outpatient Cataract Surgery," *Minerva Anestesiologica*, Vol. 75, No. 5, 2009, pp. 239-244.

[18] M. Erdurmus, B. Aydin, R. Usta, *et al.*, "Patient Comfort and Surgeon Satisfaction during Cataract Surgery Using Topical Anesthesia with or without Dexmedotomidine Sedation," *European Journal of Ophthalmology*, Vol. 18, No. 3, 2008, pp. 361-367.

[19] H. S. Na, I. A. Song, H. S. Park, *et al.*, "Dexmedetomidine Is Effective for Monitored Anesthesia Care in Outpatients Undergoing Cataract Surgery," *Korean Journal of Anesthesiology*, Vol. 61, No. 6, 2011, pp. 453-459. doi:10.4097/kjae.2011.61.6.453

[20] H. Scheinin, S. Karhuvaara, K. T. Olkkola, *et al.*, "Pharmacodynamics and Pharmacokinetics of Intramuscular Dexmedetomidine," *Clinical Pharmacology & Therapeutics*, Vol. 52, No. 5, 1992, pp. 537-546. doi:10.1038/clpt.1992.182

[21] S. R. Arain and T. J. Ebert, "The Efficacy, Side Effects, and Recovery Characteristics of Dexmedetomidine versus Propofol When Used for Intraoperative Sedation," *Anesthesia and Analgesia*, Vol. 95, No. 2, 2002, pp. 461-466.

[22] J. A. Alhashemi, "Dexmedetomidine vs Midazolam for Monitored Anaesthesia Care during Cataract Surgery," *British Journal of Anaesthesia*, Vol. 96, No. 6, 2006, pp. 722-726. doi:10.1093/bja/ael080

[23] P. Jalowiecki, R. Rudner, M. Gonciarz, *et al.*, "Sole Use of Dexmedetomidine Has Limited Utility for Conscious Sedation during Outpatient Colonoscopy," *Anesthesiology*, Vol. 103, No. 2, 2005, pp. 269-273. doi:10.1097/00000542-200508000-00009

[24] K. A. Candiotti, S. D. Bergese, P. M. Bokesch, *et al.*, "Monitored Anesthesia Care with Dexmedetomidine: A Prospective Randomized, Double-Blind, Multicenter Trial," *Anesthesia and Analgesia*, Vol. 110, No. 1, 2010, pp. 47-56. doi:10.1213/ane.0b013e3181ae0856

[25] R. M. Venn and R. M. Grounds, "Comparison between Dexmedetomidine and Propofol for Sedation in the Intensive Care Unit: Patient and Clinician Perceptions," *British Journal of Anaesthesia*, Vol. 87, No. 5, 2001, pp. 684-690. doi:10.1093/bja/87.5.684

