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Original Article

Dexmedetomidine versus remifentanil sedation for obese patients undergoing cataract surgery

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Abstract: Introduction: The prevalence of obesity has increased all over the world and it is closely correlated to multiple medical comorbidities. The aim of this study is to compare dexmedetomidine sedation and remifentanil sedation with respect to safety and effectiveness for obese patients undergoing cataract surgery with peribulbar anesthesia. Methods: Eighty ASA II-III patients scheduled for cataract surgery were randomly assigned to receive an infusion of either 0.4 mcg/kg/min dexmedetomidin or 0.05 mcg/kg/min remifentanil. Body mass indexes of all patients were between 30-40 kg/m^2. Infusion drug doses were applied according to patients' ideal body weights. Primary outcome was to assess respiratory depression and analgesia by peripheral oxygen saturation and bispectral index scores respectively. Results: There was no significant deifference in demographic variables of the patients. In the first 25 minutes peripheral oxygen saturation levels were higher in dexmedetomidine group and it was higher in remifentanil group after 35th minute. BIS scores were lower in dexmedetomidine group throughout the operation. Conclusion: Sedation for obese patients has several clinical challenges. Both dexmedetomidine and remifentanil can be accepted as appropriate drug preferences for sedation of obese patients, while dexmedetomidine provided a safer and more effective analgesia in our study.

Keywords: Cataract, dexmedetomidine, obesity, remifentanil, sedation

Introduction

The prevalence of obesity has increased all over the world. Nowadays greater numbers of obese patients are encountered in intensive care units and anesthetic surgeries [1]. Nevertheless, obesity is closely correlated to multiple medical comorbidities. Especially the rates of diabetes mellitus, hypertension, coronary artery disease, obstructive sleep apnea and complications related to these diseases increase in obese patients [2]. Clinical challenges presented by obese patients are well known and the principles of good practice/risk reduction are established [3].

Dexmedetomidine is a highly selective alpha 2-adrenoceptor agonist with sedative and analgesic effects. It has great advantages such as not causing respiratory depression during sedation [4] and relatively short elemination half-life which makes it favorable for sedation during cataract surgery [5].

Remifentanil is the newest synthetic opioid derivative which is introduced into the clinical use in 1996 [6]. It's molecular configuration and rapid metabolism result in rapid onset of action, easy titration by continuous infusion, and rapid elimination across all age groups [7]. Although it's respiratory depressant effect and potency is twice that of fentanyl, significantlly shorter elemination half-life makes it attractive for day care procedures [8].

The aim of this study is to compare dexmedetomidine sedation and remifentanil sedation with respect to safety and effectiveness for obese patients undergoing cataract surgery with peribulbar anesthesia.

Methods

After institutional Ethics Committee approval (Medical, Surgical and Drug Research Ethics Committee of Hacettepe University Medical Faculty, n◦ HEK 09/59-19), 80 ASA II-III patients

Table 1. Demographic variables of patients

	Group D	Group R
Age	58 ± 5.7	57 ± 5.8
Male:Female	22:18	24:16
IBW (kg)	69 ± 7.7	72 ± 11.2
Height (cm)	160 ± 4	161 ± 5.9
Operation time (min)	24 ± 11.7	23 ± 17

were participated into the study. The study was conducted in accordance with the Helsinki declaration. Written informed consent was taken from all patients. Patients were between 40-80 years of age and undergoing elective cataract surgery with peribulbar anesthesia. Body mass indexes (BMI) of all patients were between 30-40 kg/m^2. The exclusion criterias were history of allergy to local anesthetics or study drugs, advanced cardiac, hepatic or renal failure, chronic use of sedatives, opioids, beta blockers, history of alcohol or drug abuse and BMI under 30 or above 40 kg/m^2. Patients were randomized into two groups by using a computer-generated randomization schedule. Each group included 40 patients; one group was planed to receive dexmedetomidine (Group D) and the other group remifentanil (Group R) for sedation. All patients were taken to operation room un-premedicated. In the operating room, 22 gauge venous line was inserted and 8 mg of ondansetron was applied to all patients preoperatively. Oxygen was administered at 2 liters/minute. Standard monitorization included EKG, non invasive arterial pressure, pulse oximeter and bispectral index (BIS).

The study drug solutions were prepared into 50-ml identical syringes. The constant infusion rate for each patient was calculated and labeled on the syringes by an anesthetist who did not participate in the study. The investigator and patients were blinded to group allocation. In group D, dexmedetomidine infusion was applied with 0.4 mg/kg/hour and in group R, 0.05 μg/kg/minute remifentanil infusion was applied as analgesic-sedative dose. At the end of 10 minute infusion of each drug, peribulbar block was performed using 5 ml of lidocaine 1% and bupivacaine 0.25% mixture by the same ophthalmologist. Previously remifentanil was reported to be best dosed using patients' ideal body weight for obese patients [9]. Whereas best dosing of dexmedetomidine at obesity is still contraversial. It is known that administration of dexmedetomidine according to total body weight of an obese patient will result in over dose application [10]. So, both of the drug doses were applied according to patients' ideal body weight (IBW). IBW of patients were calculated according to this formula:

Males: IBW = 50 kg + 2.3 kg for each inch over 5 feet Females: IBW = 45.5 kg + 2.3 kg for each inch over 5 feet.

"Modified Observer's Assessment of Alertness/Sedation" (OAA/S) scale was used to determine intraoperative and postoperative sedation levels of patients. According to this scale, "0" means "no response to stimulus" and "6" means "completely awake, agitated". To determine the pain scores of patients, Verbal Rating Scale (VRS) was used intraoperatively and postoperatively. Throughout the operation at every 10 minute, heart rate (HR), mean arterial blood pressure (MAP), pulse oximeter, BIS score, OAA/S score and VRS score of patients were recorded. Adverse events including respiratory depression (<10/min), bradycardia (<50/min), and hypotention (20% decrease of the basal blood pressure) were recorded. Sedation levels and VRS scores of patients were also assessed at 15th, 30th and 60th minutes postoperatively.

Statistical analysis

All statistical procedures were performed using SPSS statistical software, version 15.0 for Windows. Demographic variables (age, sex, IBW, operation time) were analysed using x^2 and Fisher's exact test. For comparison of heart rate, mean arterial pressure, pulse oximeter, BIS and VRS scores between groups, repeated measures analysis of variance (ANOVA) and Friedman test were used. For comparison of categorical variables (respiratory depression, bradycardia, hypotension) between groups, chi-square test was performed. A P value<0.05 was considered to be significant. Sample size calculation was based on a pilot study. According to this, a sample size of 39 patients in each group would provide 0.8 power with 5% missing data to detect a significant difference for peripheral oxygen saturation between groups.

Results

Eighty-eight patients were screened and 8 of them were excluded due to intraoperative addi-

Table 2. Peripheral oxygen saturation of patients

SpO2	Group D (mean ± SD)	Group R (mean ± SD)	*P* value
Before induction	96.70 ± 1.20	96.27 ± 1.32	0.136
After induction			
1. min	94.97 ± 2.0	93.56 ± 2.69	0.014*
5. min	95.50 ± 2.13	92.84 ± 4.56	0.001*
10. min	95.52 ± 2.57	92.65 ± 3.31	0.000*
15. min	96.02 ± 2.27	93.34 ± 4.08	0.001*
20. min	95.95 ± 2.43	92.78 ± 4.15	0.000*
25. min	95.18 ± 3.77	94.09 ± 3.19	0.196
30. min	94.62 ± 3.72	95.54 ± 5.24	0.108
35. min	93.14 ± 4.71	97.0 ± 1.63	0.002*
40. min	94.29 ± 3.94	97.08 ± 1.13	0.027*
45. min	93.92 ± 4.17	97.42 ± 1.51	0.048*

*: p< 0.05.

Table 3. VRS scores of patients

VRS	Group D (mean ± SD)	Group R (mean ± SD)	*P* value
Before induction	0	0	
After induction			
1. min	1.17 ± 0.84 (0-3)	1.38 ± 0.98 (0-3)	0.370
5. min	0.90 ± 0.70 (0-3)	1.33 ± 1.15 (0-3)	0.133
10. min	0.67 ± 0.69 (0-2)	1.78 ± 1.68 (0-3)	0.016*
15. min	0.57 ± 0.59 (0-2)	1.15 ± 1.0 (0-3)	0.008*
20. min	0.52 ± 0.55 (0-2)	1.16 ± 1.04 (0-3)	0.006*
25. min	0.54 ± 0.60 (0-2)	1.12 ± 1.02 (0-3)	0.015*
30. min	0.54 ± 0.56 (0-2)	1.13 ± 1.02 (0-3)	0.023*
35. min	0.42 ± 0.50 (0-1)	1.09 ± 0.99 (0-3)	0.024*
40. min	0.41 ± 0.51 (0-1)	0.94 ± 0.89 (0-2)	0.118
45. min	0.25 ± 0.46 (0-2)	0.84 ± 0.89 (0-2)	0.123

*: p<0.05.

Table 4. OAA/S scores of the patients

OAA/S	Group D (mean ± SD)	Group R (mean ± SD)	*P* value
Before induction	5.02 ± 0.15 (5-6)	5.02 ± 0.15 (5-6)	1.00
After induction			
1. min	3.45 ± 0.74 (2-5)	3.82 ± 0.93 (1-5)	0.012*
5. min	2.72 ± 0.59 (2-4)	2.79 ± 0.89 (1-4)	0.583
10. min	2.62 ± 0.70 (1-5)	2.73 ± 0.86 (1-4)	0.717
15. min	2.50 ± 0.71 (1-4)	2.84 ± 0.97 (1-5)	0.135
20. min	2.77 ± 0.86 (1-6)	3.05 ± 1.14 (1-6)	0.322
25. min	3.13 ± 1.08 (1-5)	3.11 ± 1.06 (2-6)	0.815
30. min	3.48 ± 1.28 (1-5)	3.44 ± 1.08 (2-5)	0.825
35. min	3.68 ± 1.05 (2-5)	4.09 ± 1.22 (2-6)	0.269
40. min	4,00 ± 1.04 (2-5)	3.35 ± 1,11 (2-5)	0.116
45.min	4.00 ± 0.46 (2-5)	3.30 ± 1.18 (2-5)	0.003*

*: p<0.05.

tive anesthetic requirements or incomtability to VRS and OAA/S scoring. There were no differences between groups with respect to demographic characteristics and operation time (**Table 1**).

MAP and HR of patients didn't differ significantly amoung groups throughout the operation (p>0.05).

Peripheral oxygen saturation (SpO2) of patients were significantly different amoung groups at several time points. It was higher in Group D at first, fifth, 10th, 15th and 20th minutes of operation, while it was higher in Group R at 35th, 40th and 45th minutes (p<0.05) (**Table 2**).

VRS scores of patients were statistically significantly different from 10th to 35th minutes of operation. They were higher in remifentanil group (p<0.05) (**Table 3**).

VRS scores at postoperative period did not differ significantly between groups (P>0.05).

OAA/S scores of patients were very close amoung groups throughout the operation. Although they were lower in group D at all time points, the difference was significant only at first and 45th minutes of the operation (**Table 4**).

BIS scores of patients were recorded throughout the operation. BIS scores of group D were lower in all time points after induction, but the difference was statistically significant from first to 20th minutes and at the end of the operation (**Table 5**).

When we assess the adverse effects, the number of respiratory depression was significantly high in Group R (P<0.05). Bradycardia and hypotension epidoses were not significantly different between groups (**Table 6**).

Discussion

In the present study we aimed to compare dexmedetomidine and remifent-

Table 5. BIS scores of patients

BIS	Group D (mean ± SD)	Group R (mean± SD)	*P* value
Before induction	99.2 ± 3.17	99.67 ± 3.11	0.850
After induction			
1. min	86.1 ± 14.07	91.95 ± 7.72	0.024*
5. min	79.92 ± 8.03	88.76 ± 7.23	0.000*
10. min	76.92 ± 6.30	84.35 ± 8.59	0.000*
15. min	76.77 ± 5.94	83.39 ± 7.29	0.000*
20. min	76.67 ± 6.17	82.76 ± 6.81	0.000*
25. min	79.4 ± 9.18	82.09 ± 6.95	0.177
30. min	82.09 ± 11.15	84.62 ± 7.54	0.533
35. min	84.95 ± 8.65	86.84 ± 9.91	0.524
40. min	86.11 ± 10.4	87.66 ± 7.16	0.660
45. min	87.3 ± 8.4	94.25 ± 1.75	0.017*

*: p<0.05.

Table 6. Adverse Effects of Infusions

Adverse Effects	Group D	Group R	*P* value
Respiratory Depression	0 (0%)	10 (25%)	0.02*
Bradycardia	0 (0%)	2 (5%)	0.494
Hypotension	4 (10%)	8 (20%)	0.348

*: p<0.05.

anil sedations on obese patients undergoing day care cataract surgery. We found that dexmedetomidine was more effective and safer providing deeper sedation with higher peripheral oxygen saturation for obese patients. Secondly, dexmedetomidine infusion resulted in more analgesic effect intraoperatively than remifentanil infusion.

The prevalence of obesity has increased significantly in the last decades. In the recent studies from United States, 32.2% of adult men and 35.5% of adult women were reported to be obese [11]. But these patients have distinct clinical challenges for anaesthesiologists both in the perioperative management and in the intensive care units. Probably the most common problems seen during follow-up of obese patients are respiratory function alterations. It is well known that obese patients have impaired function of respiratory muscles, diminished functional residual capacity due to decreased chest wall compliance [12], increased oxygen consumption, increased production of carbon dioxide and increased work of breathing [13], increased upper airway resistance, propensity to obstructive sleep apnea syndrome (OSAS) [14] and many other deteriorations which complicate the management of obese patients during interventions with anaesthesia. These respiratory problems undoubtedly conduce sedation preference of obese patients more important than normal BMI population.

Dexmedetomidine is a potent a2-adrenoceptor agonist that has eight times greater specificity for a2 receptor than clonidine does [15]. The most important advantage of dexmedetomidine is proving anxiolysis and analgesia without respiratory depression [16]. So it has been studied for sedation of different patient groups for six years. Chen et al conducted a study to compare dexmedetomidine and remifentanil on children undergoing foreign body removal [17]. They combined either dexmedetomidine or remifentanil with propofol intravenous anaesthesia and their primary aim was to estimate the effect of study drugs on spontaneous ventilation. Although both of the drugs provided an effective anaesthesia for endoscopy procedure, respiratory function of dexmedetomidine group remained more stable. In the current study, both dexmedetomidine and remifentanil provided enough sedation and analgesia for cataract surgery while peripheral oxygen saturation remained higher in dexmedetomidine group. Respiratory depressant effect of remifentanil has been reported to occur above 0.2 μg/kg/min or with 0.1 μg /kg/min in combination with propofol [18]. In our study we applied remifentanil infusion as low as 0.05 μg/kg/minute, so none of the patients required mask ventilation according to respiratory depression, even so peripheral oxygen saturation of patients remained lower than dexmedetomidine group.

The traditional approach to anaesthetic management of cataract surgery is local anaesthesia combined with monitored anaesthesia care and sedation. But need for cooperation and spontenous ventilation during surgery conduce the intraoperative management more complicated [19]. Alhashemi compaired dexmedetomidine and midazolam sedation during cataract surgery. He didn't report any advantages of dexmedetomidine for day care sedation, despite a beter patient satisfaction [5]. Hu et al recently compared dexmedetomidine with remifentanil sedation during awake fiberoptic intubation. They stated that dexmedetomidine sedation provided beter conditions for intubation [20]. In our study, BIS and OAA/S scores

were lower in dexmedetomidine group when compared to remifentanil. Dexmedetomidine provided better sedation conditions intraoperatively. BIS score differences were significant from first minute to 20th minute and at 45th minute after induction. Although rapid onset of action and potency are favorable properties for dexmedetomidine, remifentanil has the advantage of extremely short elemination half-life. So it is not suprising that BIS scores of remifentanil group were higher at the 45th minute after sedation. Remifentanil provided a more rapid recovery after surgery.

Chen et al also compared the hemodynamic parameters of dexmedetomidine and remifentanil groups in their previous study [17]. Dexmedetomidine caused a decrease in HR while causing an increase in MAP. On the other hand, Hu et al found no significant difference in hemodynamic parameters between dexmedetomidine and remifentanil groups [20]. In the present study, there was no significant difference between the groups either. It is well know that dexmedetomidine prevents hemodynamic responses by decreasing noradrenaline release and sympathetic tone [21]. However, peripheral vasoconstriction can result in increased systolic arterial pressure with high doses of dexmedetomidine [22]. In our study, the dose of dexmedetomidine was constant and the mean operation time was as short as 24 minutes. So the hemodynamic parameters remained stable.

Both dexmedetomidine and remifentanil are well known potent analgesic agents for adult sedation procedures [23]. Although VRS scores of dexmedetomidine group were significantly lower for 25 minutes in our study, mean VRS scores of both groups remained lower than “2” throughout the operation. So we can suggest that both of the drugs provided enough analgesia for cataract surgery.

There are two important limitations in this study; First, investigator verbally stimulated the patient at every 5 minute intraoperatively in order to assess OAA/S score. This stimulus may have effected BIS scores of patients. Secondly, the sedation quality is estimated by intraoperative BIS, OAA/S and VRS scores. A questionnaire could be held to patients at postoperative period.

In conclusion, sedation for obese patients has several clinical challenges. Both dexmedetomidine and remifentanil can be accepted as appropriate drug preferences for sedation of obese patients, while dexmedetomidine provided a safer and more effective analgesia than remifentanil in our study.

Disclosure of conflict of interest

None.

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