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Original Article

Ketamine versus Dexmedetomidine for Postoperative Cognitive Dysfunction after Cataract Surgery: A retrospective Study

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ABSTRACT

Introduction and aim: Postoperative cognition is an important issue after different surgeries. Some anesthetic drugs suggested to protect against postoperative cognitive dysfunction (POCD) and others lead to increased POCD. With high rate of cataract in geriatric populations, it is essential to protect against POCD. The current work aimed to compare retrospectively between ketamine dexmedetomidine for protection against POCD.

Methodology: We retrospectively analyzed data of patients over the age of 60 years, with physical status (ASA II or III), between June 2019 and July 2020, who were submitted to cataract extraction. We included three equal groups (each 25 patients). Control group received normal saline; ketamine group received 0.3 mg/kg/h of ketamine by continuous infusion, and dexmedetomidine group received 0.5 μg/kg/h of dexmedetomidine by continuous infusion. All were adequately assessed preoperatively, and standard monitoring was prepared. A simple objective computer-based test battery was used to assess the postoperative (PO) cognition, while PO pain was assessed by Numeric Rating Scale (NRS), and PO analgesia was assessed by Ramsay sedation score. In addition, hemodynamics and intraocular pressure were measured and documented.

Results: Patients of the three groups were comparable regarding patient characteristics, surgery duration and hemodynamics. POCD was significantly higher among control than ketamine or dexmedetomidine groups (56% versus 28.0% or 16.0%). The sedation score was significantly higher in K- and D- groups when compared to control group directly post-surgery, and at 2 and 4-hours postoperatively. The PO pain was lower in K and D-groups directly postoperative and at 2 hours. Otherwise, there was no significant differences between groups regarding intraocular pressure (IOP) and postoperative complications.

Conclusion: The intravenous infusion of ketamine or dexmedetomidine in cataract surgery significantly reduces the POCD. This was achieved with preserved hemodynamic parameters and IOP. In addition, no significant complications were recorded. .

Keywords: Ketamine; Cataract Extraction; Dexmedetomidine; Cognition

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INTRODUCTION

Postoperative cognitive dysfunction (POCD) defined by the new decline in cognitive function, while perioperative neurocognitive disorders describes the pre-existing and postoperative cognitive dysfunction within one year after anesthesia or surgery [1-3].

In geriatric populations, cataract surgery is the most common eye surgery under local anesthesia with or without sedation. There is a higher risk of postoperative dizziness and unconsciousness with the use of sedation. The POCD after cataract surgery is related to anesthesia or sedation rather than cataract surgery [4,5].

Dexmedetomidine exerts its analgesic and sedative effects by stimulation of alpha-2 adrenergic receptors. Its main advantage is the absence of any respiratory depression [6]. In addition, it did not induce delirium when used for short term sedation, as in cataract surgery [7]. However, its role in reduction of POCD remains controversial.

Ketamine can be used for sedation, as a N-methyl-d-aspartate (NMDA) receptor antagonist. In addition, it has anti-inflammatory and neuroprotective effects. It may reduce POCD by its anti-inflammatory actions [8-10].

Here, we aimed to evaluate the effects of ketamine or dexmedetomidine on the POCD, hemodynamics and intraocular pressure in cataract extraction surgery under local anesthesia.

PATIENTS AND METHODES

We retrospectively analyzed data of patients over the age of 60 years, with physical status (ASA II or III), between June 2019 and July 2020, who were submitted to cataract extraction.

Exclusion criteria: Patients with a score less than 24 on the "Mini Mental State Examination" for screening of dementia, and those receiving antipsychotic or antidepressant medications, those with chronic medical diseases were excluded.

Patients were assigned to one of three groups: Group C (control group) included patients who did not receive any active medication (they received normal saline by continuous infusion). The second group is Group K (ketamine group), where patient received 0.3 mg/kg/h of ketamine by continuous infusion, and the third group was Group D (Dexmedetomidine group) where patient received 0.5 µg/kg/h of dexmedetomidine by continuous infusion. Each group included 25 patients.

Methods

Adequate preoperative clinical assessment was performed by history taking and detailed clinical examination. Intravenous access was achieved on the day of surgery. In addition, each patient was monitored by a standard system (pulse oximetry, non-invasive blood pressure and 5-leads electrocardiography).

The preparation of drugs was performed by a resident not included in the study. A uniform syringe were used for this purpose.

Dexmedetomidine was prepared through dilution of 250 µg in 50 ml syringe to obtain (5 µg/ml).

Ketamine on the other side, was prepared by dilution of 150 mg in 50 ml syringe (3 mg/ml).

The infusion was started 10 minutes before starting surgery on a rate of 0.1 ml/kg/h and continued through the whole surgery.

The sedation was achieved by midazolam 0.01 mg/kg and fentanyl (0.5µg/kg).

Peribulbar anesthesia was completed through the single- injection technique using 5-7 mL of a local anesthetic solution (lidocaine 2% and levobupivacaine 0.5% along with 5 U/mL of hyaluronidase). Nasal cannula was used for oxygenation at a rate of 2-3 L/min.

We aimed to assess different aspects of brain function by incorporating tests for the assessment of problem-solving skills, speed to process information, flexibility, short-term memory, and reaction time measured.

The cognitive function was assessed by a neuropsychiatrist blinded to used drugs or patient assignment group. He used a simple objective computer-based test battery as described by Moller *et al.* [11].

The tests were presented in Arabic language and help to complete them was provided by the neuropsychiatrist.

This assessment was performed one day before surgery and postoperative re-assessment was performed with the usual postoperative follow up visits at the ophthalmology clinic, one week and three months postoperatively. The neuropsychiatrist assigned patients as to have or not postoperative POCD.

The Intraocular pressure (IOP) was measured just before the peribulbar block, immediately after the block, before starting surgery, and directly after surgery.

Postoperative analgesia was assessed by the Numeric Rating Scale (NRS) (metric score of 0–10, with 0 = no pain and 10 = the most severe pain) directly after surgery. Then, every 2 h during the first 6-h after surgery. With NRS of 4 or more, 15 mg/kg of paracetamol was injected intravenously.

The sedation was assessed by Ramsay sedation score at the beginning and end of surgery, followed by every 2 h for 4 h after surgery. The hemodynamics (heart rate, respiratory rate, oxygen saturation, and mean arterial blood pressure) were recorded before the peribulbar block, directly after the block, at the start of surgery, directly postoperative, and 2 h after surgery.

Data analysis:

The statistical package for social science software (version 16) was used to perform all statistical tests (SPSS Inc., Chicago, IL, USA). Qualitative (categorical) data were presented as numbers and percentages. Continuous parametric variables were presented by their mean and standard deviation. The Chi square and one-way analysis of variance and Tukey's post-hoc test were used for analysis according to the type of data. The *P* value ≤ 0.05 was considered statistically significant.

RESULTS

Table (1) presented patient characteristics. Patients age ranged between 61 to 73 years, with male sex predominance. Most of the patients were of ASA class-II. Phacoemulsification was performed for the majority of patients in all groups with mainly equal distribution of right and left eye-surgery. The surgery duration ranged between 15 and 34 minutes. There was no significant differences between groups regarding patient demographics, side of operation or surgery duration.

In addition, there was no significant differences between studied groups regarding any of hemodynamic variables (heart rate, mean arterial pressure, oxygen saturation and respiratory rate) before block, directly after block, at the start or end of the surgery and 2 hours after surgery (Table 2).

Regarding primary outcome, POCD was significantly higher among control than ketamine or dexmedetomidine groups (56% versus 28.0% or 16.0%). However, the difference between ketamine and dexmedetomidine groups was statistically non-significant. The sedation score was significantly higher in k and D- groups when compared to control group directly post-surgery, and at 2 and 4-hours postoperatively. However, at the 6th hour after surgery, no significant difference was observed between groups. The post operative pain was lower in K and D-groups directly postoperative and at 2 hours. But, at the 4th hour postoperatively, the NRS was significantly lower in K and D-groups than the control group. Otherwise, there are no significant differences between groups regarding IOP and postoperative nausea and vomiting (Table 3).

Table (1): Patient characteristics, surgery type and duration among study population

Variable		C-Group	K-Group	D-Group	Test	*P*
Age (years)	Mean±SD	65.80±2.75	66.12±2.49	65.48±2.89	0.347	0.708
	Min. – Max.	62-71	62-70	61-73		
Sex (n,%)	Male	17 (68.0%)	16(64.0%)	20 (80.0%)	1.672	0.433
	Female	8 (32.0%)	9 (36.0%)	5 (20.0%)		
ASA-Class (n,%)	II	19(76.0%)	17 (68.0%)	21 (84.0%)	1.754	0.416
	III	6 (24.0%)	8 (32.0%)	4 (16.0%)		
Surgery type (n,%)	ECCE	8 (32.0%)	6(24.0%)	5(20.0%)	0.987	0.611
	Phaco-emulsification	17(68.0%)	19(76.0%)	20(80.0%)		
Side (n,%)	Right	13(52.0%)	11 (44.0%)	12 (48.0%)	0.321	0.852
	Left	12(48.0%)	14 (56.0%)	13 (52.0%)		
Surgery duration (min)	Mean±SD	22.76±4.62	22.36±4.57	21.96±2.49	0.248	0.781
	Min. - Max.	15-33	16-34	18-29		

Table (2): Hemodynamics characteristics among study population

		Control		Ketamine		Dex		Test	p
		Mean	SD	Mean	SD	Mean	SD		
HR (beat/min)	Before block	74.48	3.23	73.60	2.43	73.12	2.35	1.631	0.203
	Directly after block	75.84	2.39	75.36	2.34	75.76	2.92	0.251	0.778
	At the start of surgery	76.72	2.94	75.20	2.29	75.52	2.82	2.209	0.117
	At the end of surgery	76.52	1.81	75.92	2.43	76.12	3.02	0.383	0.683
	2H after surgery	73.52	2.45	74.40	3.44	74.92	3.25	1.322	0.273
MAP (mmHg)	Before block	104.32	5.13	106.00	3.50	105.40	4.80	0.883	0.418
	Directly after block	110.80	3.89	112.32	4.53	113.08	4.12	1.917	0.154
	At the start of surgery	115.16	4.78	116.84	4.20	117.00	3.58	1.460	0.239
	At the end of surgery	113.16	4.26	113.60	4.26	113.40	3.77	0.072	0.931
	2H after surgery	105.80	3.93	106.40	3.04	107.24	3.67	1.030	0.362
O2 saturation	Before block	94.88	0.83	94.88	0.93	95.00	1.12	0.128	0.880
	Directly after block	97.16	1.18	97.12	1.20	97.32	1.07	0.211	0.810
	At the start of surgery	97.60	0.87	97.72	0.89	97.64	0.76	0.132	0.876
	At the end of surgery	97.08	1.08	97.36	1.04	96.96	0.93	1.017	0.367
	2H after surgery	95.64	0.99	95.96	1.06	96.04	1.06	1.038	0.359
RR (cycle/min)	Before block	14.88	1.39	14.76	1.13	14.92	1.66	0.087	0.917
	Directly after block	15.32	1.11	15.04	1.27	15.64	1.50	1.328	0.271
	At the start of surgery	13.92	1.08	14.28	1.14	14.64	1.32	2.318	0.106
	At the end of surgery	13.68	0.85	13.08	1.15	13.20	1.12	2.289	0.109
	2H after surgery	12.68	0.75	12.56	0.65	12.72	0.74	0.341	0.712

Table (3): Outcome among study population

Variable			C-Group	K-Group	D-Group	Test	P
POCD			14(56.0%)	7(28.0%)	4(16.0%)	***9.48***	***0.009****
IOP (mmHg)	Before Block	Mean±SD	17.24±1.36	17.00±1.68	16.80±1.89	0.440	0.646
		Min. – Max.	16-20	15- 22	14-23		
	Directly after Block	Mean±SD	23.32±2.46	23.48±2.27	24.28±2.31	1.194	0.309
		Min. - Max	19-28	19-27	20-28		
	Directly before Surgery	Mean±SD	18.96±2.30	19.20±1.78	19.00±1.61	0.112	0.894
		Min. - Max	16-25	16-24	17-23		
	Directly after Surgery	Mean±SD	19.00±1.54	19.16±0.89	19.28±0.94	0.491	0.614
		Min. - Max	17-21	18-21	18-21		
PO sedation score	Directly po	Mean±SD	1.36±0.57	2.40±0.82	2.16±0.85	***12.98***	***<0.001****
		Min. - Max	1-3	1-4	1-4		
	2 hours	Mean±SD	1.24±0.52	2.08±0.70	1.64±0.70	***10.53***	***<0.001****
		Min. - Max	1-3	1-4	1-3		
	4 hours	Mean±SD	1.16±0.37	1.28±0.54	1.68±0.80	***5.16***	***0.008****
		Min. - Max	1-2	1-3	1-4		
	6 hours	Mean±SD	1.08±0.28	1.16±0.37	1.12±0.33	0.367	0.694
		Min. - Max	1-2	1-2	1-2		
Postoperative pain (NRS)	Directly postoperative	Mean±SD	1.32±0.69	1.16±0.68	1.16±0.62	0.478	0.622
		Min. - Max	0-3	0-2	0-2		
	2 hours	Mean±SD	3.60±1.61	3.36±1.70	3.40±1.26	0.175	0.840
		Min. - Max	0-6	0-6	1-6		
	4 hours	Mean±SD	4.20±1.35	2.12±0.78	1.92±0.81	***38.52***	***<0.001****
		Min. - Max	2-7	1-4	1-4		
PONV			3 (12.0%)	4(16.0%)	2 (8.0%)	0.758	0.685

DISCUSSION

Results of the current work proved the effective role of continuous ketamine or dexmedetomidine infusion to reduce POCD with higher sedation score in patients undergoing cataract surgery and enhanced the postoperative level of sedation, without significant changes in hemodynamics, IOP or incidence of postoperative complications. Both drugs were comparable in their effects with slight improved actions of dexmedetomidine over ketamine.

The action of local anesthetics on the cognitive function had been studied previously after different surgeries. For example, Chen *et al.* [12] studied the effects of ketamine on cognitive function and concluded that, it does not impair cognitive function, it even could improve the cognitive functions postoperatively. However, **Fathy *et al.*** [13] reported contradictory results, as the use of lignocaine or bupivacaine can cause POCD after cataract extraction surgery. This could be attributed to different inclusion criteria, different batteries for neurocognitive assessment and short duration of follow up (one week).

Ketamine exerts neuroprotective effects by reducing the release of proinflammatory cytokines, and prevents the formation of micro-thrombosis, preserving the blood supply to the brain [14]. Th increased blood supply to the brain by ketamine is responsible for preservation of cognitive function, was reported in a previous study [15].

In recent years, dexmedetomidine gained wide acceptance in the anesthetic field. One of its advantages is the reported reduction of the POCD risk. However, its POCD reduction is still debatable. Its effect on cognitive function is attributed to the sedative, analgesic and neuroprotective action, especially the POCD is attributed to the reduction of brain-derived neurotrophic factor [16,17].

The findings of this study are consistent with **Rascon-**Martinez *et al.* [18] who reported that, the IV administration of ketamine (0.3mg/kg) in different ophthalmological surgeries significantly preserved the postoperative cognition with stable hemodynamic parameters and IOP. However, their study follow up period was shorter than the current one. In addition, Hovaguimian *et al.* [8] reported that ketamine protective effects against POCD could be attributed by the reduction of apoptosis, inflammation and micro-thrombus formation.

Poorzamany *et al.* [19] compared the effects of remifentanil and dexmedetomidine after cataract extraction surgery. They reported that dexmedetomidine by its sedative effects reduced the POCD with preserved hemodynamics. However, they used a loading dose of dexmedetomidine (0.5 μg/kg) followed by 0.2 μg/kg/h as a a maintenance dose. Mansouri *et al.* [20] conducted a clinical trial to compare the effects of preoperative administration of midazolam or dexmedetomidine on the prevention of cognitive dysfunction after cataract extraction surgery. They reported significant reduction of POCD with dexmedetomidine or midazolam than the control group with preserved hemodynamics. The difference between both drugs was statistically non-significant.

To sum up , the current work proved that the IV infusion of ketamine or dexmedetomidine in cataract surgery significantly reduces the POCD. This was achieved with preserved hemodynamic parameters and IOP. In addition, no significant complications were recorded.

Conflict of interest disclosure: None to disclose.

Financial disclosure: None.

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