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Case Series

OPIOID-FREE ANESTHESIA IN OPHTHALMIC SURGERIES

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ABSTRACT

Introduction: Opioid-free anesthesia (OFA) is an alternative to Opioid based anesthesia (OBA) which uses multimodal analgesia to replace opioids. However, its feasibility, safety, and exact recommended combination remain debatable. **Case Series**: We administered OFA in 5 types of elective ophthalmic surgeries under general anesthesia in ASA 1-2 adult patients (evisceration, ocular exenteration, periosteal graft, scleral buckling, vitrectomy, and dacryocystorhinostomy) to assess the feasibility of OFA. We gave preoperative Paracetamol and Pregabalin with Dexmedetomidine as a loading dose (1 mcg/kg in 10 minutes) and maintenance at 0.7 mcg kg^{-1} per hour. Induction was performed using Propofol 1-2 mg kg^{-1}, Lidocaine 1-1.5 mg kg^{-1} IV, and Rocuronium. Before the incision, Dexamethasone and Ranitidine were given. Maintenance was done using Dexmedetomidine and Sevoflurane. Fentanyl was used as rescue analgesia if required. Dexmedetomidine was stopped 15-30 minutes before the procedure ended. Metoclopramide and Ketorolac were given as postoperative management. Throughout the procedure, our patients had stable hemodynamics, did not experience life-threatening bradycardia, and did not require rescue analgesia. All patients regained full consciousness and did not experience postoperative nausea and vomiting, emergency delirium, or coughing. **Conclusion:** Multimodal analgesia was an excellent intraoperative OFA regimen as an alternative to OBA and provided controlled hypotension in ocular surgery. Safe OFA is possible with combined analgesia regimens, strict intraoperative monitoring, and adequate anesthesia depth.

Keywords: Feasibility; Ophthalmic surgery; Opioid-free anesthesia; Multimodal analgesia; Safety

ABSTRAK

Pendahuluan: *Opioid free anesthesia (OFA)* merupakan alternatif untuk *opioid based anesthesia (OBA)* menggunakan analgesia multimodal untuk menggantikan opioid. Kelayakan, keamanan dan kombinasi tepat yang dianjurkan masih menjadi perdebatan. **Serial kasus:** Kami menggunakan OFA dalam 5 jenis operasi mata elektif dengan anestesi umum pada pasien dewasa ASA 1-2 (eviscerats, eksenterasi okular, cangkok periosteal, buckling scleral dan vitrektomi serta dakriosistorhinostomi) untuk menilai kelayakan OFA. Pemberian parasetamol dan pregabalin pra operasi dengan dexmedetomidine, diberikan sebagai dosis muatan (1mcg/kg dalam 10 menit) dan dosis pemeliharaan 0,7 mcg/kg^{-1}per jam. Induksi dilakukan dengan propofol 1-2 mg/kg^{-1}per jam, lidokain 1-1.5mg/ kg^{-1}per jam, dan rocuronium. Sebelum insisi, akan diberikan deksametason dan ranitidine. Pemeliharaan dilakukan dengan menggunakan dexmedetomidine dan sevoflurane. Jika diperlukan fentanyl akan diberikan untuk membantu obat analgesia utama. Dexmedetomidiin akan dihentikan 15-30 menit sebelum prosedur berakhir. Metoclorperamide dan ketorolac diberikan sebagai manajemen pasca operasi. Selama prosedur berlangsung, hemodinamik pasien dalam keadaan stabil, tanpa bradikardia, dan tidak memerlukan analgesia tambahan. Pasca operasi semua pasien kembali sadar, tidak mengalami gejala mual dan muntah, penurunan kesadaran , maupun batuk. **Kesimpulan:** Analgesia multimodal bekerja sebagai rejimen OFA intraoperatif yang sangat baik dan memberikan alternatif untuk OBA, dan memberikan hipotensi terkontrol pada operasi mata. Regimen kombinasi analgesia, pemantauan intraoperatif yang ketat, dan kedalaman anestesi yang adekuat dapat mencapai keamanan prosedur OFA.

Kata kunci: Kelayakan; Operasi mata; *Opioid-free anesthesia*; Analgesia multimodal; Keselamatan

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INTRODUCTION

Opioid-free anesthesia has been gaining popularity in recent years. However, debates regarding the safety of opioid-free regimens have been the center for discussion, with trials showing increased risk for bradycardia and hypotension, likely due to the use of Dexmedetomidine (DEX) as a replacement for opioid agents such as remifentanil (1). The added benefits of an opioid-free regimen include a lower incidence of postoperative nausea and vomiting, reduced incidence of delirium, and lower incidence of hyperalgesia.

DEX is an alpha agonist commonly used for the controlled hypotension (2) technique in maxillofacial, ear, nose, and throat, as well as ocular surgery. With this in mind, we administered opioid-free anesthesia (OFA) in 5 elective ophthalmic surgery patients with Dex to evaluate the feasibility of OFA in this population (3). We gave a standardized regiment using 1 gram of oral paracetamol (PCT) and 75 mg Pregabalin (PGB), given 2 hours before surgery, DEX (1 mcg kg^{-1} in 10 minutes, followed by 0.7 mcg kg^{-1} per hour), Lidocaine (LD) IV 1-1.5 mg kg^{-1}, and Ketorolac 30 mg IV for postoperative analgesia (3,4). All patients were given Propofol 1-2 mg kg^{-1}, Sevoflurane (SEV) 1 MAC, and Rocuronium 0.4 mg kg^{-1} for induction. Baseline heart rate and blood pressure were monitored closely throughout the protocol at seven distinct time points; before starting Dexmedetomidine (T0), before induction (T1), after the insertion of the airway device and induction (T2), following incision (T3), before stopping Dexmedetomidine (T4), at the end of the procedure (T5), and the recovery room (T6). Rescue analgesia (Fentanyl 50 mcg) was administered if there was an increase in heart rate or blood pressure of over 20% of the baseline.

CASE SERIES

Case 1: Ocular evisceration and dermofat graft from the abdomen

A 25-year-old male was referred to our hospital due to a periosteal cyst and retinal detachment of the right eye. The ophthalmology department planned to eviscerate the right eye to maintain globe integrity. The patient was assessed by the American Society of Anesthesiologists (ASA) 1 and had no airway difficulties. Two hours before surgery, he was given paracetamol and pregabalin. Upon arrival at the operating theater (OT), he was placed on standard ASA monitoring tools, and his baseline values were recorded. Induction was performed following preoxygenation using Lidocaine 1.5 mg kg^{-1} IV bolus, Propofol 1-2 mg given as titrated dosing, SEV at 1 MAC, and muscle relaxation was achieved using 0.4 mg kg^{-1} Rocuronium. A supraglottic airway device (LMA, Unique) was inserted. During draping, the patient was given Ranitidine 50 mg and Dexamethasone (DEXA) 5 mg IV bolus. SEV was increased to 1.1-1.2 MAC and was maintained throughout the procedure. Dexmedetomidine was stopped 15 minutes before the procedure ended while maintaining SEV at 1 MAC. Ketorolac 30 mg and Metoclopramide 10 mg were given 15 minutes before the procedure ended.

The SGA was removed while the patient was deeply anesthetized while maintaining spontaneous breathing. The patient had a stable range of vital signs throughout the procedure (68 minutes), with heart rate and blood pressure variations falling within 20% of the baseline. The anesthesia duration was 90 minutes. The patient experienced bradycardia but was still within a tolerable range (>50 beats per minute). He did not experience any desaturation throughout and after the procedure. After 15 minutes in the

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recovery room (RR), he regained full consciousness with a Numerical Rating Scale (NRS) of 0-1. There was no PONV, coughing, delirium, or desaturation.

Case 2: Mass exenteration of the left eye

A 32-year-old male was referred to our center due to invasive intraocular squamous cell carcinoma extending to the superior-lateral-inferior rectus and left lacrimal gland. He was scheduled for mass exenteration of the left eye. The patient was assessed with ASA 2 and had no airway difficulties. Similarly, he was given PCT and PGB preoperatively and was placed on standard ASA monitoring. He was administered DEX 10 minutes before induction. Induction was performed using a combination of LD, Propofol, and Rocuronium while maintaining DEX at 0.7 mcg/kg/hour. This patient had a baseline heart rate of 100-110 bpm, possibly due to the tumor, and was unresponsive to fluid challenge. Upon insertion of LMA and incision, there were no significant changes to the heart rate and blood pressure. His heart rate gradually decreased following mass exenteration, further supporting our initial hypothesis. Dexmedetomidine was stopped 30 minutes before the procedure's completion, and ketorolac was administered 15 minutes before the procedure ended. Sevoflurane was stopped upon procedural completion. The patient recovered spontaneous breathing after 15 minutes and was fully awake 25 minutes after his transfer to the RR. Similarly, there was no PONV, coughing, delirium, or desaturation.

Case 3: Periosteal graft of the left eye

A 33-year-old female was scheduled for a periosteal graft due to left ocular perforation caused by a corneal ulcer. She was assessed with ASA 2, with leukocytosis 12,170, and had no airway difficulties. She had experienced constant ocular pain of NRS 1-2, controlled with routine PCT (3x1 gram). Similar to previous cases, she was administered PGB and an extra dose of PCT preoperatively. She had an NRS of 0-1 when she reached the OT. She was started on Dexmedetomidine for 10 minutes before induction. Induction was performed using lidocaine, propofol, and rocuronium. Upon insertion of the LMA and incision, there was no significant increase in pulse or blood pressure. The intraoperative patient was stable. The procedure was completed after 45 minutes, and anesthesia was administered for 80 minutes. DEX was stopped 30 minutes before the procedure ended, while SEV was decreased to 1 MAC and was stopped 15 minutes before the procedure's completion. As we had experienced a delayed return of spontaneous breathing, we started giving assisted manual ventilation to trigger spontaneous breathing 15 minutes prior. The patient recovered spontaneous breathing 5 minutes after the procedure's completion and was transferred to the RR. She regained consciousness after 30 minutes. There was no PONV, coughing, delirium, or desaturation.

Case 4: Scleral buckling, vitrectomy, endolaser, and silicone oil insertion of the right eye

A 22-year-old female experienced retinal detachment of the right eye with proliferative vitreoretinopathy. She was scheduled for scleral buckling, vitrectomy endolaser, and silicone oil insertion of the right eye. She was assessed with ASA 2, with nodular opacity in her chest x-ray. Clinically she did not experience dyspnea or tachypnea and had no signs of increased work of breathing, cough/fever, and airway difficulties. She was given PCT, PGB, and DEX for 10 minutes

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before induction. Induction was performed with Propofol, LD, Rocuronium, and SEV. LMA was inserted. Before the incision, she was given Dexamethasone and Ranitidine. Throughout the procedure, she had stable hemodynamics. Oculocardiac reflex (OCR) occurred twice throughout the procedure but did not confer hemodynamic instability. The operator was asked to pause until the heart rate recovered before resuming the procedure. The procedure was completed after 150 minutes, and the anesthesia duration was 180 minutes. DEX was stopped 20 minutes before the procedure ended. The patient recovered spontaneous breathing 10 minutes after the procedure ended. Following the deep removal of the airway device, she was transferred to the RR. She regained full consciousness without PONV, delirium, desaturation, bradycardia, or coughing. She had a well-controlled pain score of 0-1.

Case 5: External dacryocystorhinostomy of the left eye

A 43-year-old female was admitted to our center due to nasolacrimal duct obstruction. She was planned for an external dacryocystorhinostomy. She was assessed with ASA 2, with controlled diabetes mellitus on Metformin 3x500 mg, and had no airway difficulties. We administered general anesthesia with endotracheal intubation with the previously described opioid-free regiment and a combination of PCT, PGB, DEX, LD, propofol, SEV, and Rocuronium. However, we did not give Dexamethasone to this patient. Following intubation, the patient's vital signs remained stable and smooth intubation was performed without using Fentanyl. Intraoperative, the patient maintained stable vital signs. DEX was stopped 30 minutes before the end of the procedure. The procedure was completed after 85 minutes, and the anesthesia duration was 120 minutes. She recovered adequate spontaneous breathing 5 minutes after the procedure ended and was transferred to the RR, where she regained consciousness. There was no PONV, coughing, or delirium, with adequate analgesia (NRS 0-1).

Table 1. Doses and Agents Used During the Procedure

Case No (Body weight)	2 hours prior		10 minutes prior	Induction					Before incision			Before procedure ends (dose in mg)		Airway device
	Pct (mg)	Pregabalin (mg)	Dex (mcg)	Lidocaine (mg)	Propofol (mg)	Sev (MAC)	Dex (mcg/hour)	Rocuronium (mg)	Dexa (mg)	Ranitidine (mg)	Sev (MAC)	Ketorolac (mg)	Metoclopramide (mg)	
Case 1 (50 kg)	1000	75	50	60	100	1	35.0	50	5	50	1.2	30	10	LMA
Case 2 (55 kg)	1000	75	50	60	100	1	38.5	30	5	50	1.2	30	10	LMA
Case 3 (72 kg)	1000	75	70	80	100	1	50	20	5	50	1.2	30	10	LMA
Case 4 (54 kg)	1000	75	54	60	100	1	37.8	20	5	50	1.1	30	10	LMA
Case 5 (52 kg)	1000	75	52	80	100	1	36.4	20	5	50	1.1	30	10	ETT

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Table 2. Changes in Vital Signs During the Procedure

Case Number	Parameters	Time points						
		T0	T1	T2	T3	T4	T5	T6
Case 1	Heart rate (beat per minute)	82	62	60	72	70	62	58
	Blood pressure (mmHg)	132/83	116/68	94/58	105/66	110/71	101/72	97/62
	Respiratory Rate (times per minute)	16	18	NA	NA	NA	18	18
	Peripheral Oxygen Saturation (%)	99%	99%	99%	99%	99%	99%	99%
	Numeric Rating Scale	1	1	NA	NA	NA	NA	0-1
Case 2	Heart rate (beat per minute)	88	104	100	110	90	80	75
	Blood pressure (mmHg)	132/78	120/67	94/63	109/77	100/58	102/57	98/64
	Respiratory Rate (times per minute)	18	18	NA	NA	NA	18	18
	Peripheral Oxygen Saturation (%)	99%	99%	99%	99%	99%	99%	99%
	Numeric Rating Scale	1-2	1	NA	NA	NA	NA	0-1
Case 3	Heart rate (beat per minute)	91	88	80	82	81	78	74
	Blood pressure (mmHg)	141/100	120/79	115/71	128/79	130/80	118/78	116/70
	Respiratory Rate (times per minute)	18	18	NA	NA	NA	18	18
	Peripheral Oxygen Saturation (%)	99%	99%	99%	99%	99%	99%	99%
	Numeric Rating Scale	0-1	0-1	NA	NA	NA	NA	0-1
Case 4	Heart rate (beat per minute)	92	75	79	72	78	76	81
	Blood pressure (mmHg)	130/75	127/77	87/57	93/62	84/50	98/57	106/64
	Respiratory Rate (times per minute)	18	18	NA	NA	NA	18	18
	Peripheral Oxygen Saturation (%)	98%	99%	99%	99%	99%	99%	99%
	Numeric Rating Scale	0	0	NA	NA	NA	NA	0
Case 5	Heart rate (beat per minute)	80	78	72	68	69	61	76
	Blood pressure (mmHg)	125/80	130/81	110/72	112/64	104/60	100/58	118/71
	Respiratory Rate (times per minute)	18	18	NA	NA	NA	18	16
	Peripheral Oxygen Saturation (%)	99%	99%	99%	99%	99%	99%	99%
	Numeric Rating Scale	1	1	NA	NA	NA	NA	0-1

DISCUSSION

To our knowledge, this is the first case series that evaluated the feasibility of opioid-free anesthesia in different types of ocular surgeries. In this series, we showed that opioid-free anesthesia is possible and beneficial in a wide range of ocular surgeries through LMA or even intubation.

We used a combined regiment of preemptive analgesia with oral paracetamol and pregabalin 2 hours before the procedure. This provided sufficient time to hit plasma level (1) and ensured hydration. The use of intravenous lidocaine and Dexmedetomidine allows for sufficient analgesia and sympathetic blunting throughout the surgery. We did not use topical lidocaine as patients were sedated with Dexmedetomidine before induction. Nonetheless, using IV lidocaine 1-1.5 mg bolus and Dexmedetomidine confer analgesia during the administration of propofol and insertion of airway device and surgical incision. The sedative nature of Dexmedetomidine gave anti-anxiolytic properties before induction and reduced the need for propofol during induction (2).

The use of Dexmedetomidine brings the added benefit of controlled hypotension, which is preferable in ocular surgery. Controlled hypotension also provided optimal visualization of the operating field and resulted in less bleeding. Intraoperative, the patients had stable hemodynamics, which indicates an added benefit of stable intraocular pressure. Controlled hypotension is easily reversed with Dexmedetomidine, bringing adequate surgeon satisfaction and excellent procedural efficiency.

There were concerns about bradycardia and desaturation following the use of

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Dexmedetomidine. However, we anticipated this pulse reduction and thus selected patients with a baseline heart rate of > 70 bpm and systolic blood pressure of > 100 mmHg. We also screened possible candidates to be < 55 years of age without any cardiac problems. Some patients experienced stable bradycardia without significant changes to blood pressure or saturation. None of these cases had bradycardia < 40 bpm, even in procedures with a high oculocardiac reflex (OCR) risk. Dexmedetomidine was associated with less emergence agitation and post-operative vomiting without increasing the incidence of OCR (3). We did not experience severe OCR that requires rescue atropine as they were easily managed by stopping the stimulus. In all patients, there was no emergence of delirium or PONV.

Close intraoperative monitoring allows for rapid management of any hemodynamic instability. However, in our cases, we found little changes to the heart rate, blood pressure, and oxygen saturation throughout the procedure. We postulated that the combined use of Dexmedetomidine, propofol, and lidocaine reached the deep anesthesia plane enough to ameliorate possible sympathetic response to nociception during incision. The combined Dexmedetomidine and Sevoflurane 1.1-1.2 MAC could maintain deep anesthesia and blunts nociception-induced responses (4,5).

We also found that we could use less Rocuronium for these patients, as little as 0.4 mg/kg for procedures lasting for 1-2 hours. The return of spontaneous breathing was slower in these cases, which contributed to the increased time for LMA removal. The use of Dexmedetomidine was associated with an increased duration of action of Rocuronium in Sevoflurane anesthesia (6,7). However, this disadvantage can be easily solved with the use of sugammadex. In our center, the use of sugammadex is expensive and is not the standard regimen for general anesthesia. Thus, we used neostigmine, an acetylcholine esterase inhibitor, for the reversal. We also observed that our use of atropine for the reversal regimen did not confer significant tachycardia in our patients. Adequate breathing was achieved in all cases.

Despite the use of Sevoflurane (MAC 1-1.2), we had zero cases of PONV, agitation, or coughing. This is beneficial in patients with ocular surgery as these adverse effects might lead to increased intraocular pressure and possible dislodging of the implant (8–10). We did not use Ondansetron or Propofol at the end of the procedure.

CONCLUSION

Safe opioid-free anesthesia in ophthalmic surgery is possible with careful patient selection and close intraoperative monitoring. The added benefits of opioid-free anesthesia include less PONV, coughing, and emergency delirium. The use of Dexmedetomidine allows the use of controlled hypotension while maintaining stable hemodynamics.

Limitations of the Study

The main limitation of this study is the lack of nociceptive monitoring tools, such as Connox or ANI. Thus, the direct relationship between our regiments and the nociceptive index could not be directly assessed. Although the main effect of sympathetic activation due to nociception is rapidly increased heart rate and blood pressure, such observations might be masked using medications such as beta-blockers. Hence, we did not include patients with cardiac comorbidities and arrhythmias. Tachycardia can also be caused by a multitude of etiologies, such as hypovolemia and ocular pain. Therefore, we used preoperative

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analgesia. We also asked the subjects to maintain adequate fluid intake and encouraged fluid intake 2 hours before the procedure by instructing the patients to take the medication orally.

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Conflict of Interest
There is no conflict of interest.

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None

Authors' Contribution
Conception and design of the case series: ART, HA; Informed consent and performed the anesthesia: ART, HA; Interpretation and data analysis: ART, HA, RF; Drafting the manuscript: ART, HA, TC, INT; Final approval of the manuscript: ART, RF

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