



# IJOA

# Indian Journal of Ophthalmic Anaesthesia

Volume 2

Issue 1

Jan 2022

Official Journal of

**Association of Indian Ophthalmic Anaesthesiologists, AIOA**

Old No. 18, New No. 41, College Road, Chennai 600 006,

[www.aioa.org.in](http://www.aioa.org.in)

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Dear Friends,

I wish a very happy and healthy new year to all. The year 2022 started with the third wave of the covid pandemic which is having a huge impact on not only the well-being of each individual but has also impacted the health care facilities. Fortunately, the third wave involving the Omicron variant is not as severe as the second wave, though the infectivity and spread is quite high. There is no doubt that all of us are eagerly waiting for the day when the covid pandemic will disappear from the whole world and we can come out of the virtual world to the real one to meet and greet each other.

I am glad to inform all our members that We got our journal registered with ISSN number due to sincere efforts put forth by our Secretary Dr Jaichandran and the editorial team members. The Indian Journal of Ophthalmic Anaesthesia (IJOA) aims to include articles which are of interest to the anaesthesiologist and ophthalmologist. The current issue discusses effect of dexmedetomidine for ophthalmic surgery, anaesthesia options for laser photocoagulation in ROP and management for Klippel-Trenaunay syndrome. This issue also includes the nuances and information related to sedation in difficult airway during monitored anaesthesia care, adverse drug reactions in ophthalmic set up and importance of eye donation which is again of great use to the readers.

Any journal is of immense value only if the articles are of high quality. For this, participation and submission of articles by a large number of anaesthesiologists and ophthalmologists will be highly appreciated as it will not only bring forward the ideas and opinions of many, but also ensure a proper peer review so that the quality of the journal keeps on improving.

Again, I wish you all a very happy new year 2022 and the best of health and fortune for all your future endeavours. May you succeed in everything in life and attain great happiness and well-being.

Best regards,



**Dr Renu Sinha**

Editor

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Indian Journal of Ophthalmic Anaesthesia

The Official Journal of Association of Indian Ophthalmic Anaesthesiologists



# Effect of Dexmedetomidine on Surgical Stress in Children Undergoing Elective Ophthalmic Surgery– A Prospective, Randomized, Comparative Study

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## Abstract

**Background:** Surgical stress leads to neuro-endocrine response which causes metabolic derangements. Dexmedetomidine may attenuate stress response and pain in children undergoing ophthalmic surgeries.

**Methods:** Forty children between 8-14 years undergoing elective ophthalmic surgery were randomised into dexmedetomidine group (Group D) and saline group (Group C). After general anaesthesia, 0.5mcg/kg dexmedetomidine bolus and 0.5mcg/kg/hr infusion (Group D) or saline (Group C) was administered. Blood samples for serum cortisol and blood glucose were withdrawn a day before, 45 minutes after start of surgery and 1 hour after surgery. Intraoperative vitals, time for return of spontaneous respiration and airway device removal,

emergence delirium, postoperative nausea and vomiting and pain were noted.

**Results:** Demographic data was comparable. Heart rate in the Group D was significantly lower from 5 to 25 minutes, at 50 and 60 minutes in comparison to the Group C. Serum cortisol, blood glucose and emergence delirium were comparable. The time to regain spontaneous respiration, SGA removal and to achieve MAS score of 9 was more in the Group D as compared to control group but it was not statistically significant. Postoperative pain scores were statistically lower in the Group D in comparison to the Group C at 10, 20, 60 and 120 minutes ( $p < 0.05$ ). Requirement of fentanyl boluses in PACU was significantly less in the Group D in comparison to the Group C (3 vs 11) ( $p = 0.008$ ).

**Conclusion:** Dexmedetomidine significantly reduces postoperative pain but does not have effect on serum cortisol and blood glucose in children undergoing elective ophthalmic surgery.

**Keywords:** Ophthalmic surgery, Dexmedetomidine, Cortisol, Glucose, Pain numeric scale

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## Article History

**Received:** 18<sup>th</sup> November 2021

**Revision:** 20<sup>th</sup> November 2021

**Accepted:** 24<sup>th</sup> December 2021

**Published:** 17<sup>th</sup> January 2022

**How to cite this article:** Sangam Yadav, Renu Sinha, Bikash Ranjan Ray, Akok Kumar Ravi, Puneet Khanna, Vanlal Darlong et al. Effect of Dexmedetomidine on Surgical Stress in Children Undergoing Elective Ophthalmic Surgery– A Prospective, Randomized, Comparative Study. Indian J Ophthalm Anaesth 2022;2(1):2-12

## Introduction

Stress response to surgery leads to metabolic and physiological derangements resulting in inflammatory, hormonal and genomic responses. Stress leads to increased level of serum cortisol due to failure of feedback mechanism of serum cortisol on Adrenocorticotrophic hormone (ACTH) and Corticotropin releasing hormone (CRH) which results in increased levels of blood glucose.<sup>1</sup> Increased cortisol and glucose level lead to adverse effects like immune suppression, cardiovascular and gastrointestinal complications. Intraoperative stress also leads to impaired operative outcome, impaired organ function, increased incidence of post-operative cognitive dysfunction and prolonged hospital stay.<sup>2,3</sup> In children, stress response may cause varied degree of pain, emergence delirium (ED), emergence agitation (EA) and metabolic complications.<sup>1</sup>

Stress response can be measured by surrogate markers like serum cortisol and blood glucose. The other stress response markers are glucagon, norepinephrine, epinephrine, insulin, interleukins (IL-1, IL-6), TNF- $\alpha$ , vasopressin. It has been observed that anxiolytics, fluid, glucose, adequate hydration and nutrition reduce undue catabolism. Fentanyl, Midazolam, Etomidate and Clonidine have been used successfully to reduce surgical stress response by providing adequate depth of anaesthesia, thus blunting the surgical response.

Dexmedetomidine is selective alpha 2 receptor agonist with sedative and anxiolytic properties.<sup>4,5</sup>

It acts on locus ceruleus of brain stem and spinal cord, which is responsible for providing analgesia and haemodynamic stability during surgery as well as procedural sedation.<sup>6,7</sup> It has opioid-sparing effect, does not cause respiratory depression and reduces EA, ED and post-operative nausea and vomiting (PONV).<sup>8-12</sup> Dexmedetomidine reduces intra ocular pressure (IOP) during ocular surgeries.<sup>13,14</sup> Dexmedetomidine is administered as 0.5 - 1 mcg/kg bolus over 10 minutes followed by 0.2 - 0.7 mcg/kg/hr infusion. Although opioids and benzodiazepines have been used to reduce surgical stress, Dexmedetomidine can be an effective alternative due to its unique properties.

Thus we evaluated the effect of Dexmedetomidine on the rise of serum cortisol and blood glucose levels peri-operatively in children undergoing elective ophthalmic surgeries under conventional general anaesthesia (GA).

## Materials and Methods

After ethical committee approval, CTRI registration (CTRI/2016/01/006568) and informed parental/guardian consent, forty patients of ASA status I and II, aged 8-14 years, of either sex, scheduled for elective ophthalmic surgery under GA of more than 45 minutes duration were included. Patients were randomly divided into two groups of 20 each by computer generated random numbers. Children who had cardiac/hepatic/renal diseases, mental retardation, premedication with sedatives, surgical duration <45 minutes or whose

parent/guardian refused consent were excluded.

Pre-anaesthetic check-up was done a day prior to surgery and fasting instruction was written. Methodology, outcome and adverse effects were explained to parents and children. Blood samples were drawn for the baseline serum cortisol and blood glucose levels.

In the operation theatre, standard monitors (ECG, pulse oximetry, NIBP) were attached. Anaesthesia was induced with sevoflurane 8% in 100% oxygen at fresh gas flow of 5litre/min and intravenous cannula was inserted after achieving adequate depth of anaesthesia. Fentanyl 2 mcg/kg, Atracurium 0.5 mg/kg were administered and intermittent positive pressure ventilation was initiated for 3 minutes. Appropriate size supraglottic airway device (SGA) was inserted and secured.

Children in the group D received 0.5 mcg/kg Dexmedetomidine bolus over 10 minutes followed by 0.5 mcg/kg/hr infusion while children in the group C received normal saline at the same rates. Anaesthesiologist who was not involved in the study prepared Dexmedetomidine or normal saline in a 50 ml syringe. Anaesthesia was maintained with oxygen, air (FiO<sub>2</sub> 0.5) and Sevoflurane (MAC 0.8 to 1.0). Ringer Lactate was administered intraoperatively accordingly to standard guidelines. Atracurium boluses were administered whenever required. Intraoperative vitals were monitored at baseline, intravenous cannula insertion, SGA insertion and at 5 minutes interval till the end of surgery.

If there was any increase in heart rate (HR) or mean arterial pressure (MAP) >20%, Fentanyl 0.5 mcg/kg was administered. If there was decrease in HR below 50/min, or oculocardiac reflex occurred, surgeon was asked to remove the stimulus and topical Proparacaine (0.5%) was administered. If HR remained <50/min, intravenous Atropine 2.0 mcg/kg was administered. Intraoperatively blood samples were drawn again at 45 minutes after start of surgery and at 10 minutes before the end of surgery. At the end of surgery, Ondansetron 0.1mg/kg was administered and Dexmedetomidine infusion and Sevoflurane were stopped. At the start of spontaneous ventilation, Neostigmine 50mcg/kg with Glycopyrrolate 10mcg/kg was administered. Time taken from the switching off Sevoflurane to start of spontaneous breathing efforts was noted. Once the child had adequate spontaneous respiration, SGA were removed at MAC of 0.3. The time taken for SGA removal was also noted. Child was shifted to post anaesthesia care unit (PACU).

In PACU, EA (PAED score), PONV (PONV score), perioperative pain by Pain Numerical Rating (PNR) Scale was assessed. If PAED score was 7 to 9 (subsyndromal EA) then repeat observations were made at one hour, if the score were >10 then midazolam bolus 0.4 mg/kg not exceeding 10 mg was administered. If PONV score was three, 0.1 mg/kg Ondansetron was repeated and in case of recurrent PONV Metoclopramide 150 mcg/kg was administered. Fentanyl 0.5 mcg/kg was administered if PNR score was 4-6.

In case PNR score was  $>6$ , Fentanyl 1 mcg/kg was administered. Post-operative sample were drawn one hour after surgery. The children were discharged from PACU once modified Aldrete score  $>9$ .

### Statistical analysis

Mukhtar et al study<sup>15</sup> observed attenuation of the neuroendocrine response after administration of Dexmedetomidine in children undergoing cardiac surgery. Blood glucose was  $180 \pm 35$  mg% in control group and  $145 \pm 25$  mg% in Dexmedetomidine group after cardiopulmonary bypass. This calculation established that we required 16 patients in each group with a power of 90% and alpha error of 5%. We enrolled 20 children in each group considering dropout during study. Statistical analyses were performed using STATA14 software. The results are expressed as the mean  $\pm$  SD or percentage. A p value of  $<0.05$  was considered to be statistically significant. Statistically appropriate tests were applied to the data.

### Results

A total 40 patients were randomized in the present study. (Figure 1) Age, weight, duration of surgery, type of surgery and type of SGA were comparable in both the groups.

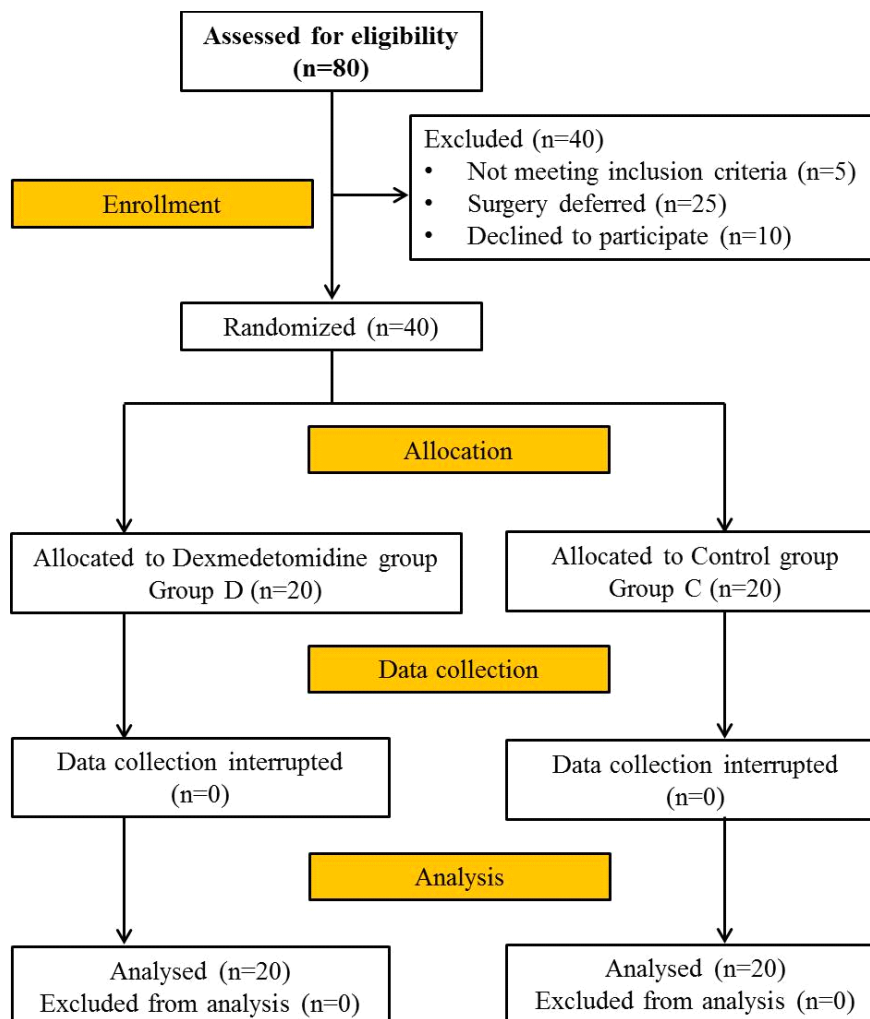


Figure 1: Consort Diagram



Male patients were more in the Group D in comparison to the Group C ( $p=0.04$ ). (Table 1)

**Table 1: Demographic data of the Group D and Group C**

Variable		Group D n=20	Group C n=20	p value
Age, years		11 $\pm$ 2.36	11.2 $\pm$ 1.98	0.77
Weight, Kg		33(22-45)	38.5(18-58)	0.28
Sex, n (%)	Male	17 ( 85 )	10 ( 50 )	<b>0.04*</b>
	Female	3 ( 15 )	10 ( 50 )	
Duration of surgery, minutes		82.5 (50-120)	65 (50-120)	0.07
Indications for surgery, n (%)	Corneal surgery	5 (25)	2 (10)	0.15
	Lid surgery	0 ( 0 )	1 (5)	
	Vitrectomy	3 (15)	7 (35)	
	Vitro – retinal	12 (60)	8 (40)	
	Glaucoma surgery	0 (0)	2 (10)	
Type of Supra Glottic Airways, n (%)	Ambu Laryngeal Mask	4 (20)	4 (20)	0.74
	Flexible Laryngeal Mask Airway	6 (30)	4 (20)	
	Air Q Intubating Laryngeal Airway	10 (50)	12 (60)	

Data are presented as mean  $\pm$  standard deviation or median [Range] or absolute numbers (with the percentage of the whole) \* $p < 0.05$  statistically significant

The blood glucose level and serum cortisol level at the pre-operative, intra-operative and post-operative period were comparable between the two groups. (Table 2)

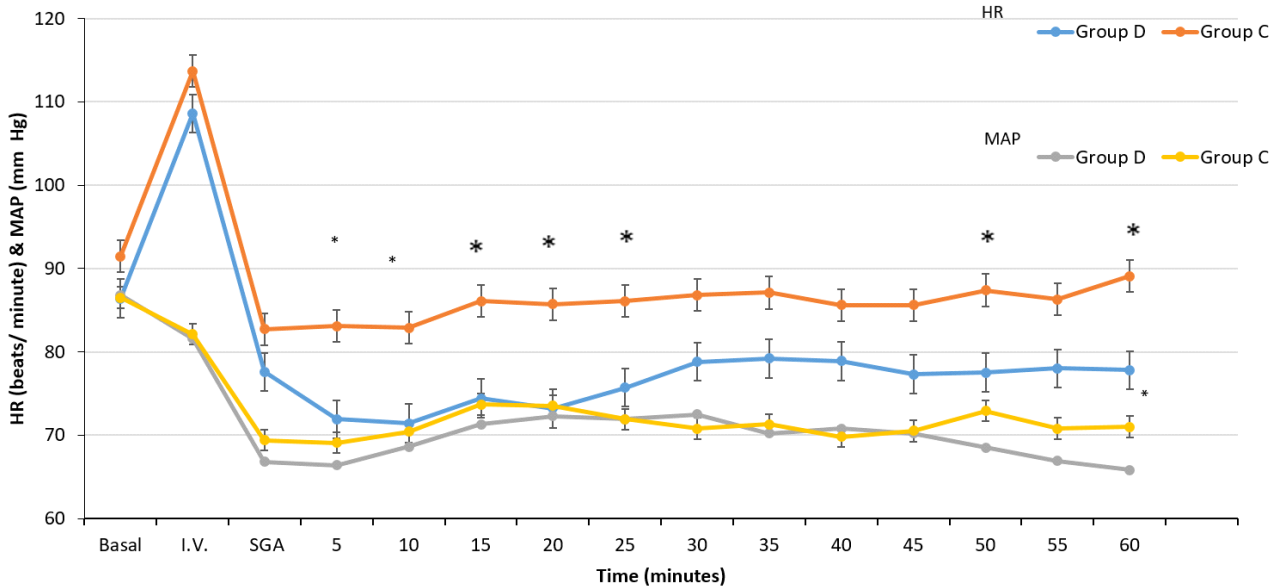
**Table 2: Blood glucose and Serum cortisol levels at different time intervals in both the groups**

		Group D, n=20	Group C, n=20	p value
Serum glucose (mg/dl)	Pre-operative	87.5 (75-122)	84 (58-115)	0.36
	Intra-operative	98 (71-117)	85.5(72-110)	0.08
	Post-operative	89 (64-117)	92(68-130)	0.22
Serum cortisol (mcg/dl)	Pre-operative	3.83 (1.52-13.07)	2.52(0.8-15.32)	0.14
	Intra-operative	7.19 (0.21-20.59)	4.55(0.56-17.67)	0.16
	Post-operative	11.66 (1.39-24.85)	12.92(0.78-23.9)	0.82

Data are presented as median (Range), n=number of patients, \* $p < 0.05$  statistically significant

In Group D, HR was significant lower from 5 to 25 minutes and at 50 and 60 minutes in comparison to the Group C. In the Group D, MAP was lower at 60 minutes in comparison to the Group C. (Figure 2)

**Figure 2. Heart rate (HR) & Mean arterial Pressure (MAP) at different time points**



The time to regain spontaneous respiration after switching off the Sevoflurane, time for SGA removal was more in the Group D as compared to control group but it was not statistically significant. PNRs scores were statistically lower in the Group D in comparison to the Group C at 10 minutes, 20 minutes, 60 minutes and 120 minutes. (Table 3)

**Table 3: Supraglottic airway removal time (SGAR), Time to regain spontaneous respiration (TS) and Pain Numeric Rating Scale (PNR)**

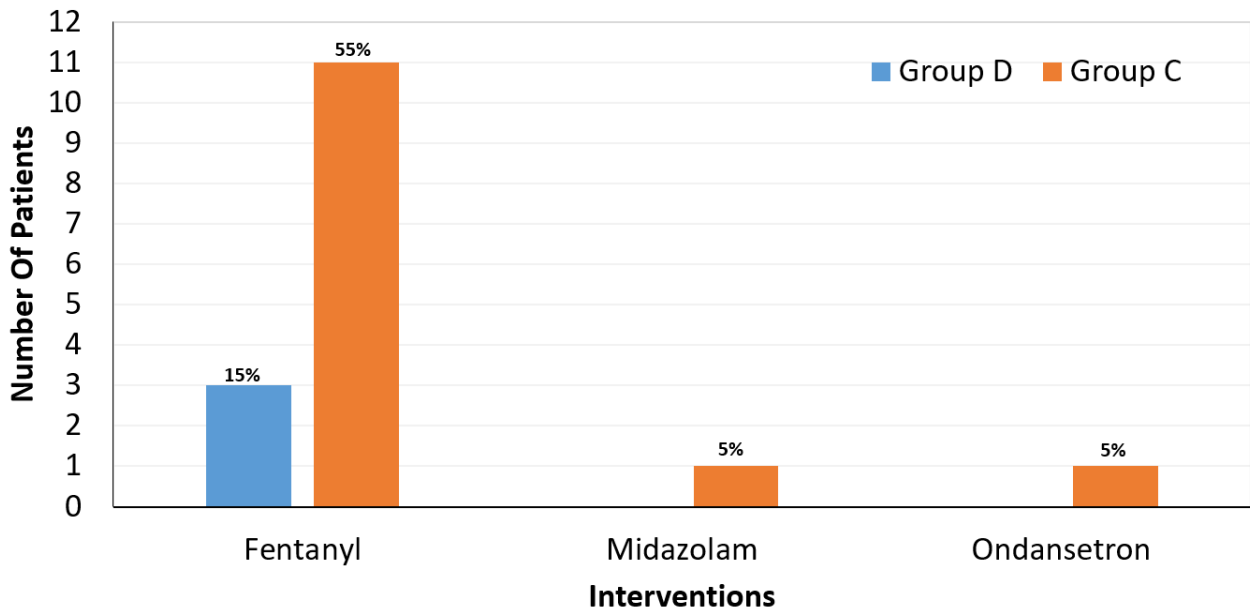
Parameters		Group D, n=20	Group C, n=20	p value
SGA removal time (minutes)		6.15 ± 1.79	5.17 ± 1.29	0.05
Time to regain spontaneous respiration (minutes)		3.92 ± 1.60	3.01 ± 1.36	0.06
PNR score	0 minutes	0 (0-3)	0 (0-6)	0.08
	10 minutes	0 (0-3)	0 (0-5)	<b>0.03*</b>
	20 minutes	0 (0-4)	2 (0-6)	<b>0.0003*</b>
	60 minutes	1.5 (0-4)	3 (0-6)	<b>0.001*</b>
	120 minutes	2 (0-3)	3 (2-4)	<b>0.01*</b>
	240 minutes	2 (1-3)	3 (1-4)	0.21

Data are presented as mean+ SD; median [Range] , n=number of patients, \*p < 0.05 statistically significant

Time to achieve MAS median score of 9 was more in the Group D as compared to control group but it was not statistically significant.

Requirement of fentanyl boluses in PACU was significantly less in the Group D in comparison to the Group C (3 vs 11) ( $p=0.008$ ). In the Group C, one child received Midazolam and another child received Ondansetron. (Figure 3)

**Figure 3. Postoperative interventions in both the groups**



## Discussion

In the present study, Dexmedetomidine infusion did not decrease serum cortisol and blood glucose level in children undergoing elective ophthalmic surgeries.

Our results are contradictory to the published studies which showed dose dependent reduction in stress response in terms of serum cortisol, blood glucose levels and norepinephrine concentration with Dexmedetomidine.<sup>16</sup> There are many factors which can lead to change in serum cortisol level like physical activity, anorexia nervosa, alcoholism, hypo/hyperestrogenism and drugs like anticonvulsants, contraceptive pills, steroid etc. Preoperative condition of the patient like sepsis, hypermetabolic state, pain, drugs intake also affects the serum cortisol and blood glucose levels. Dexmedetomidine effect on stress response has been mainly studied in cardiac, neuro and abdominal surgeries. Difference in severity of stress response with different surgeries and intraoperative hypothermia, supratentorial tumor surgery, pneumoperitoneum may affect on change in serum cortisol and blood glucose level. Dexmedetomidine has been used at variable dosage and routes in different studies including single bolus at the start or at the end of surgery, bolus followed by infusion, only infusion at different doses.<sup>17,18,19,20</sup> Variable anaesthetic techniques like use of nitrous oxide, laryngoscopy, inadequate pain relief affect the stress response.

We tried to reduce factors influencing the cortisol level by including ASA 1 and 2 children and by excluding patients who were receiving anticonvulsant, steroid. We included both male and female children as serum cortisol is not affected by the gender difference in children.<sup>21</sup> We used SGA for airway management to avoid laryngoscopy response and its contribution to stress.<sup>22</sup> Present study is done in ophthalmic surgeries which result in minimal haemodynamic variation and is less painful in comparison to cardiac and abdominal surgeries. We administered 2mcg/kg fentanyl for adequate analgesia in both the groups. The difference in preoperative condition, the type and duration of surgery, haemodynamic variation and pain stimulus might be attributed to difference in adequate stress control in the control group. In the present study, Dexmedetomidine resulted in significant reduction in the postoperative pain scores in comparison to the control group till 120 minutes. Three patients required fentanyl in the group D in comparison to 11 patients in the group C. ( $p=0.008$ ) Other studies have also shown reduction in fentanyl requirement postoperative with Dexmedetomidine.<sup>18</sup> Dexmedetomidine has analgesic property because of its effect on presynaptic  $\alpha_2$  receptors which inhibits release of norepinephrine, terminating the propagation of pain signals.<sup>23</sup> In the present study, HR and MAP were significantly lower in the Dexmedetomidine group ( $p < 0.05$ ) as compared to the control group at various

time points, but it didn't cause haemodynamic instability and didn't require any intervention. Decrease in HR and MAP with Dexmedetomidine has been observed in several studies due to its action on central as well as peripheral presynaptic  $\alpha_2$  receptors leading to decreased sympathetic tone.<sup>24</sup>

In the present study, the time to regain spontaneous respiration, SGA removal and time to achieve MAS score of 9 was more in the Dexmedetomidine group as compared to control group. Though this difference was not statistically significant, 10 minutes difference in each case may be clinically significant in a busy theatre. Sedative effects of Dexmedetomidine and continuation of infusion till the end of surgery could be contributing factors for the increased time.<sup>24</sup> The use of BIS/entropy to titrate the inhalational agent may affect the timings to regain spontaneous respiration and SGA removal.<sup>25</sup>

In the present study, PAED, PONV score were comparable in both the groups. Previous studies showed reduction of ED and EA with Dexmedetomidine, shorter duration of surgeries might be the reason for this difference.<sup>18,26,27,28</sup> We administered Ondansetron in both the groups due to high incidence of PONV in the ophthalmic surgeries.

Limitations of the present study include short duration of surgery and subjective measurement of depth of anaesthesia to titrate inhalational agent which would have affected the EA, ED and recovery time.



To conclude, Dexmedetomidine bolus followed by infusion did not decrease serum cortisol and blood glucose level in children between eight to fourteen years for elective ophthalmic surgery of 45 minutes to 120 minutes duration, however it significantly reduced postoperative pain and fentanyl requirement.

### Financial support and sponsorship

Nil.

### Conflicts of interest

There are no conflicts of interest

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# Managing the difficult airway in an Ophthalmic surgery under monitored anaesthesia care

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## Abstract

Many ophthalmic procedures are performed under local anesthesia. However, monitored anesthesia care (MAC) is often requested to ensure patient safety, particularly for high-risk and elderly patients. Some patients may fail to cooperate under local anesthesia or become agitated during the procedure requiring further management. In such situations, presence of difficult airway (DA) can worsen the outcome if not identified and managed properly. It is safer to identify the DA during pre-procedure assessment and be prepared for management than to encounter an unanticipated DA on the operating table.

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## Article History

Received: 10<sup>th</sup> November 2021

Revision: 14<sup>th</sup> November 2021

Accepted: 1<sup>st</sup> December 2021

Published: 17<sup>th</sup> January 2022

**Key Words:** Difficult airway, regional anaesthesia, monitored anaesthesia care.

## Definition and description of difficult airway

DA can be summarized as a clinical situation in which a conventionally trained anesthesiologist encounters difficulty in any technique of airway management, maintenance of oxygenation during airway management, and patient cooperation.<sup>[1]</sup> The American Society of Anesthesiologists defines a DA when "a conventionally trained anesthesiologist has trouble difficulty with facemask ventilation of the upper airway, difficulty with tracheal intubation, or both. Canadian guidelines are broader and defines it as a situation in which "an experienced provider anticipates or encounters difficulty with any or all of face mask ventilation, direct or indirect (e.g., video) laryngoscopy, tracheal intubation, supraglottic device [SGD] use, or surgical airway". Difficulty of airway management is highly variable depends on several factors including patient

**How to cite this article:** Bhavna G, Raveendra SU, Pallavi A, Anish G. Managing the difficult airway in an Ophthalmic surgery under monitored anaesthesia care. Indian J Ophthal Anaesth 2022;2(1): 13-25



characteristics, medical and surgical history, airway characteristics, clinical context for which airway management is required (including the nature of any planned surgical procedure), patient's status and vital signs.<sup>[2-4]</sup>

The range of techniques includes mask ventilation, supraglottic airway (SGAD) insertion, laryngoscopy (direct, video, or flexible video endoscopy), endotracheal intubation, surgical airway and extubation. All these represent anatomically DA. When airway management is associated with potential for compromised oxygenation, it is referred to as physiologically difficult airway. Examples include poor physical status, elderly, syndromic children with congenital heart disease, obesity and cardiorespiratory reserve for any reason. Lastly, the risk of aspiration, inability to cooperate and inability to tolerate supine position also contribute to difficulty in airway management. When the presence of DA is combined with other risk factors, the overall risk to patients is compounded (Table 1).

**Table 1- Factors that enhance the risk of complications in presence of DA**

1. Poor cardiorespiratory reserve
2. Uncontrolled diabetes and hypertension
3. Morbid obesity
4. Multiple drug therapy for co-morbidity
5. Poor effort tolerance and frailty
6. Inability/difficulty in lying down supine position

7. Anxiety, cognitive dysfunction
8. Failure to recognize difficult airway
9. Delayed gastric emptying
10. Lack of/ dysfunctional equipment
11. Difficult venous access
12. Inadequate monitoring facilities

### Spectrum of difficult airway

Diseases associated with DA management include congenital syndromes including Pierre Robin Syndrome, Treacher-Collins syndrome, Goldenhar's syndrome, mucopolysaccharidoses, achondroplasia, and acquired causes morbid obesity, acromegaly, ankylosing spondylitis, tumours involving airway, trauma, infections, previous surgical scars or deformities and old age.

In ophthalmic surgeries, DA is predominantly encountered in the elderly or obese patients. With increasing age, changes in the structure and functioning of the airways result in anatomical features of DA. Face mask seal, maintenance of a patent airway and bag mask ventilation are more difficult due to lack of upper airway muscle tone and floppy lips due to lack of teeth in edentulous elderly patients Elderly are more prone for cervical spine arthritis, which reduces neck movement and makes laryngoscopy, particularly direct laryngoscopy, more difficult. A stiffer chest wall makes ventilating with a bag-valve mask or a rescue airway more challenging (e.g., SGAD).

Many elderly patients have coexisting respiratory diseases (chronic obstructive pulmonary disease [COPD]) and might be suffering from carcinoma of lung which causes intrapulmonary shunting. All these conditions can lead to difficulty in preoxygenation, often rendering it ineffective. In elderly persons, baseline room air oxygen saturation is frequently low, and it should be recognized before induction of anaesthesia or sedation so that perioperative interpretation is more reliable. Elderly patients who are sick (ASA III or more physical status and those with trauma) desaturate more quickly than healthy, younger patients. [Table 2]

High incidence of co-morbidities in elderly is another factor which contributes to increased risk of perioperative anaesthetic complications. High prevalence of risk factors such as hypertension, diabetes, renal insufficiency, chronic heart failure, and COPD) raises the risk of perioperative myocardial ischemia to as high as 31%.<sup>[5]</sup> Anxiety is fairly prevalent in the elderly patients. Many individuals are apprehensive during ocular surgery, either because they are concerned about their eye or because they are anticipating discomfort and pain.<sup>[6]</sup>

Even patients with well-controlled hypertension at home may become acutely hypertensive on the day of surgery. Patients with diabetes, particularly those who are insulin-dependent, can experience a similar situation. Hence, ensuring patient's safety

during the perioperative period is the priority and responsibility for healthcare practitioners. It necessitates that all medical subspecialists comprehend the ophthalmic process in depth and acknowledge the additional strain on the patient's underlying co-morbidity induced by physiological changes caused by mental stress, surgery, and anaesthesia.

Presbycusis, or age-related hearing loss, is a prevalent chronic illness in older persons. It is linked to cognitive impairment, dementia, and increased risk of falls and therefore it is not surprising that hearing loss affects both the person with hearing loss (PHL) and their communication partners (family and friends). To benefit from visual cues, speak in a well-lit, quiet area. A PHL may not be able to see the speaker's face if the illumination is poor. Background noises like fans might make it harder for PHLs to perceive speech. It is better to speak slowly enough for the PHL to keep up and ask questions. Slowing down communication increases articulation and hence clarity. Use basic language, as complex or medical terminology may be difficult for a PHL to comprehend. Rather than asking "Do you understand?" specifically, give specific replies and clarifications of what was just said. Pausing between words allows PHLs to comprehend and ask questions. Pocket Talkers are portable, easy to use, and affordable. By directly amplifying a speaker's voice, these devices increase speech access. They can also be asked to wear their prescription hearing aids.

**Table 2- Difficult airway predictors in elderly – usual patient subsets encountered in eye surgeries under local anaesthesia.** <sup>[1,2,3]</sup>

<b>Risk factors of a difficult airway</b>	<b>Age-related anatomic changes</b>
Limited mandibular protrusion	TMJ disc displacement/OA, Teeth loss
Narrow dental arch	Arch width decreases
Decreased thyromental distance	Arch length decreases
Modified Mallampati class 3 or 4	Sarcopenia of the head, neck and suprahyoid pharyngeal muscles, and the overall height of cervical spines is reduced
Decreased submandibular compliance	Decreased oral soft tissue flexibility
Decreased sternomental distance	Compression of intervertebral discs
Limited head and upper neck extension and fixed cervical spine flexion deformity	Degenerative change of ligament and tendons of the intervertebral-discs, compression of the intervertebral discs, Cervical lordosis increases, Cervical spondylosis
Lack of teeth or poor dentition	Teeth-loss, Alveolar bone resorption
History of neck radiation	Possible
Reduced mouth opening	TMJ disc displacement/OA, Locked jaw
Supra- or extra-glottic pathologies (lingual tonsillar hypertrophy, neck radiation)	sarcopenia of the head, neck and suprahyoid and pharyngeal muscles, Pathologic status
Glottic and subglottic pathologies	Sarcopenia of the head, neck and suprahyoid and pharyngeal muscles, Pathologic status

Obesity might also make breathing more difficult. Because of a combination of anatomical and physiological characteristics, obesity is a strong predictor of airway difficulties. Obese individuals are twice as likely as non-obese patients to get serious airway complications. Patients with a body mass index greater than 40 (i.e., morbidly obese) are four times as likely to develop a serious complication. Physiological hazards such as decreased functional residual capacity and, more importantly, the resultant reduction in the manageable length of apnea must also be considered.

### **Preoperative identification of difficult airway**

DA is identified based on history, clinical examination, and relevant investigations. Common measurements include mouth opening, Mallampati Score, thyro-mental distance, sternomental distance and neck circumference. Once diagnosed, DA is analyzed for its impact on different airway management techniques, including patient cooperation and positioning. Anesthesiologist may ponder on following points while planning for the airway management:

1. Evaluation of affected component of airway management
2. The most suitable method of airway management in a particular patient and the backup plan
3. Ensuring appropriate facilities for the anticipated level of difficulty including expertise and equipment
4. Plan for extubation and oxygenation as well.

*Failure to prepare for failure is the most common reason for airway disasters.*

#### **Essential components of the routine airway assessment should include:**

1. Past history: Examine past medical records including any previous anaesthesia issues and talk to the patient or his or her family to ascertain disorders of the major organ systems (e.g., cardiac, renal, pulmonary, neurologic, sleep apnoea, metabolic, endocrine), adverse experience with sedation/analgesia, as well as regional and general anaesthesia, history of DA, current medications, history of smoking, alcohol intake, substance abuse, gastroesophageal reflux disease and obstructive sleep apnoea.
2. Preoperative assessment: a thorough preoperative assessment helps to provide the best possible patient preparation. Physical examination of the patient, examination of the airway, lungs. Further workup is based on patient's medical condition, physical examination, and other factors depending on impact of such findings on perioperative management will impact management of

mild sedation/analgesia. If the assessment was done several days or more than a week earlier, always re-evaluate the patient prior to the operation.

3. Educate patient or primary caregivers about the benefit, risks, and limitations of moderate sedation/analgesia, as well as feasible options, prior to the procedure, and solicit their opinions.
4. Inform patients or legal guardians about the fasting guidelines for the day of surgery
5. Assess the timing and nature from the last oral intake on the day of the procedure. When considering (1) the target level of sedation and (2) whether the procedure should be postponed, consider the risk of pulmonary aspiration of gastric contents.

#### **Ophthalmic challenges**

Ophthalmic surgeries are among most common procedures in elderly population and are rarely life-threatening. Cataract surgery can drastically improve an elderly patient's eyesight and thereby quality of life by reducing the risk of damage from falls. Many ophthalmic procedures, particularly cataract and retinal procedures, have undergone significant technical improvisation. Similarly, revolutionary technological advancements and safety initiatives have resulted in reduced incidence of major complications. Further, even patients with multiple co-morbidities also can undergo eye procedures safely.

Because of the low incidence of large volume blood loss, and the lack of major fluid shifts



or prolonged duration, ophthalmic surgical procedures are considered low risk surgery (except for some complex procedures such as complicated corneal or combined retinal surgery and corneal transplantation, which can last up to 4 to 5 hours).<sup>[4]</sup>

Ophthalmic procedures, on the other hand, are associated with distinctive complications, such as the oculo-cardiac reflex (a trigemino-vagal reflex that can cause a variety of arrhythmias, including cardiac arrest) and brain stem injection of local anaesthetics during retrobulbar block. The latter can result in not only respiratory failure requiring intubation, but also profound hypotension and tachycardia or profound hypertension needing intubation.<sup>[5]</sup>

### **Limitations in managing a difficult airway under LA in ophthalmic surgeries**

#### **Patient factors-**

- Facial drape to cover the adjacent sites.
- Apprehension and anxiety.
- Feeling of suffocation.
- Discomfort in supine position.
- Difficulty in keeping the head immobile.
- Need to manage airway while surgery is going on during emergency.
- Potential for catastrophe or complications.

### **Basic preparation for difficult airway management includes:**

(1) Decision making with patient involvement and informed consent

(2) Equipment for management of a difficult airway (i.e., portable storage unit)

(3) Assigning an individual to help as required

(4) Careful and controlled sedation, clear communication

(5) Apnoea recognition and management

(6) Know when and whom to call for help

### **Types of anaesthesia for eye surgeries**

Cataract surgery is by far the most common ocular surgery operation. Most of these procedures are done under local anaesthesia, and since the introduction of phaco-emulsion, they can be done with no or little sedation. Other eye surgical procedures, such as vitrectomy, laser surgery for retinal ablation, ocular muscle and oculoplastic surgery, require moderate sedation while performing orbital block. The trend in anaesthesia for cataract and other ophthalmic surgical procedures has shifted over time, from general anaesthesia with tracheal intubation and relaxation to laryngeal mask without paralysis, then regional blocks, intraconal (retrobulbar), extraconal (peribulbar), and sub Tenon's blocks to topical anaesthesia.<sup>[6,7]</sup>

The goals of regional anaesthesia are to render procedure painless by anaesthetizing the globe and conjunctiva, produce akinesia, and to lower the intra-orbital and intraocular pressures. The main benefit of local anaesthetic is that it has less systemic side effects, but it is also important to consider the

surgeon's preferences; some clinicians want to communicate with the patient throughout operation, while others like complete silence and total ocular immobilization.<sup>[8,9]</sup> Although topical anaesthesia does not provide as complete pain control as needle-based local techniques, it does avoid common serious complications like retrobulbar haemorrhage, globe damage, and the spread of the local anaesthetic to unusual locations, which can lead to life-threatening complications.<sup>[10]</sup>

Topical anaesthesia may cause difficulties due to uncontrolled eye movement and inadequate pain control, and this group is more likely to require sedation, but intravenous sedation has been shown to increase the risk of adverse events. Friedman and colleagues reported that 72% patients preferred a block to topical anaesthetic and two-thirds chose oral to intravenous sedation in a research on patient preference.<sup>[11]</sup> Katz and colleagues observed that while sedation alone reduced discomfort during surgery, 3.4 % of patients experienced intraoperative pain, and 2.7 % were dissatisfied. Drowsiness affected 2.7% patients, while nausea and vomiting affected 4.1% patients. The use of an opioid during surgery dramatically reduced pain, reduced sleepiness, and improved patient satisfaction.<sup>[12,13]</sup>

Sedatives and analgesics cause sleepiness and relieve fear, anxiety, and pain without impairing verbal communication.<sup>[14]</sup> Sedation must be achieved with cardiovascular stability, minimal or no respiratory depression, appropriate

operating conditions, a rapid return to the patient's baseline physical and mental state, with no residual effects. Appropriate backup facilities should be available for patients who are likely to require inpatient care or admission to ICU. If sedation is the primary plan, still the preparation must be the same as for general anaesthesia, with adequate intravenous access and a designated recovery area with monitors, resuscitation facilities and experienced staff.

Supplemental oxygen is administered through a solid tent mask, which keeps the drape from covering the face, reducing hypoxia and claustrophobia. Despite enough oxygen delivery, re-breathing can occur behind the draperies. According to a meta-analysis of RCTs, supplementary oxygen versus no supplemental oxygen is related to a lower frequency of hypoxemia during moderate sedation procedures.<sup>[9]</sup> Sedation level should be continuously monitored to prevent excessive or deep sedation which can lead to agitation, restlessness and airway obstruction rendering the patient unstable, hypoxic and difficult to manage.

### **Monitored anaesthesia care**

- Keeping a watchful eye on the patient's level of consciousness
- During moderate sedation, evaluate a patient is responding to verbal commands at regular intervals (e.g., at 5-minute intervals). Patient can be instructed preoperatively regarding the expected response from him/her during the procedure.

It can be a thumbs up sign as it is easy to understand and perform. A verbal response when the eye procedure is going on may not be feasible. Differently abled patients and those with hearing loss and cognitive dysfunction may not be able to appropriately respond. Hence clinical monitoring such as observation of breathing rate and pattern and monitoring must be used in such patients for assessing the level of sedation.

- Oxygenation of the patient should be continuously monitored with pulse oximeter. Fall in oxygen saturation can be a late phenomenon and careful observation of chest movements and EtCO<sub>2</sub> values help to anticipate and detect hypoxia early. Low flows (2 l/min) of oxygen through securely positioned nasal cannula can be continuously administered. However, the risk of hypoxic drive being abolished leading to hypercarbia in elderly with chronic obstructive lung disease must be remembered.
- Observe qualitatively clinical symptoms to monitor ventilator function constantly. Unless the nature of the patient, technique, or equipment prevents or invalidates it, continuously monitor ventilatory function by capnography. Capnography should be used for uncooperative individuals once moderate sedation has been obtained.
- Hemodynamic Monitoring- A baseline measurement of pulse rate, blood pressure and oxygen saturation breathing

room air must be obtained in every patient before initiation of sedation and subsequent changes are interpreted more meaningfully. Continuously monitor electrocardiography, blood pressure (e.g., at 5-min intervals) and heart rate during the procedure until mild sedation/analgesia has been achieved, unless such monitoring interferes with the surgery (e.g., where stimulation from the blood pressure cuff could arouse an appropriately sedated patient). Even direct arterial blood pressure monitoring may be considered in patients with poor cardiac status.

- Patients' state of awareness, ventilatory and oxygenation status, and hemodynamic variables should be recorded on a regular basis, depending on the type and amount of medication given, the length of the procedure, and the patient's overall condition. This should occur at a minimum (1) before administration of sedative/analgesic agents; (2) following the administration of sedative/analgesic agents; (3) at regular intervals during the procedure; (4) during initial recovery; and (5) immediately before discharge. Set device alerts to notify the care team of any significant changes in the patient's condition.

### **Monitoring sedation level**

A drug-induced state in which patients respond properly to verbal commands is known as minimum sedation. Cognitive and coordination abilities may be mildly impaired and respiratory and cardiovascular

systems are unchanged and airway patency is unaffected. During moderate sedation, patients respond purposefully to verbal commands, either alone or in combination with gentle tactile stimulation. The patient's airway and cardiovascular function are both preserved without the need for intervention. Airway patency and spontaneous respiration are preserved during moderate sedation. Deep sedation can be unintentionally produced during intended moderate sedation if the patient is more sensitive to sedatives and this can lead to airway obstruction and hypoxia. During deep sedation patients can develop cardiovascular instability. Maintaining sedation between a minimal and moderate level is the goal and is a challenging task that demands regular care.<sup>[10-14]</sup> The analgesic is included to alleviate patient discomfort during the block, as well as during the peri and postoperative periods. BIS monitoring improves sedative titration and reduces procedure time. The BIS measures sedation objectively, safely, and reliably, without disturbing patient or operator. When combined with other clinical signs, the BIS can help anaesthetists adjust sedation levels. This may also help lessen patient sedation. BIS monitoring improves patient care and should be used to supplement conventional evaluation.

Although having weak validity and reproducibility, clinical observation offers an approximate differentiation between appropriate, excessive, and inadequate sedation. Accurate assessment of sedation level necessitates a reliable and valid tool while also being simple to use in the operating room. The Ramsay Sedation Scale (RSS) and the Observer's Assessment of

Alertness/Sedation (OAA/S) are two clinical assessment measures that are commonly used in clinical settings.<sup>[15-17]</sup> The RSS is a simple bedside clinical technique for measuring drowsiness in ocular surgery patients. It's a single ordinal scale that determines a person's state of consciousness subjectively. (Figure 2)

Sedation Level	Score
Patient is anxious and agitated or restless, or both	1
Patient is co-operative, oriented, and tranquil	2
Patient responds to commands only	3
Patient exhibits brisk response to light glabellar tap or loud auditory stimulus	4
Patient exhibits a sluggish response to light glabellar tap or loud auditory stimulus	5
Patient exhibits no response	6

**Figure 2- RSS scoring system according to patient's response.**

### Choice of sedatives

The ideal sedative has a brief onset and duration, does not accumulate, is non-toxic, has a high therapeutic index, consistent effects, and is affordable.<sup>[18]</sup> Unfortunately, no drug currently exists that meets all these requirements. Benzodiazepines, intravenous anaesthetic induction agents (e.g. propofol), opiates, and alpha 2 agonists such as dexmedetomidine or clonidine are among the medications available. These medications can be taken orally, sublingually, intranasally, trans-dermally, trans-mucosally, rectally, intramuscularly, or intravenously, as summarised in Table 3. The drug can be given as a bolus injection, continuous infusion, or patient-controlled bolus injections (patient-controlled analgesia (PCA); patient-controlled sedation (PCS)) or a target-controlled infusion via the intravenous method (TCI)



**Table 3 Summary of drugs used for conscious sedation**

Class of drugs	Utility	Administration	Dosage and duration of action	Miscellaneous
Benzodiazepines <sup>[19]</sup>	Amnesia, Anxiolysis, Hypnosis	Orally, intravenously	Midazolam: 1 mg or 0.02-0.1 mg/kg IV. Onset- 1-2 min Duration- 30-60 min Half-life- 2 hours	In individuals over the age of 60, it is recommended that the dose be lowered by 30%.
<b>Induction agents</b>				
Propofol <sup>[20,21,22]</sup>	Sedative Induction, quick onset and a quick, obvious recovery	IV bolus, infusions, on-demand sedation via a PCA	0.5-1 mg/kg IV loading dose; may repeat by 0.5-mg/kg increments q3-5min. Infusion at 20mg/kg/hour Onset- <1 min Duration- 3-6 min	minor risk of nausea and vomiting. Respiratory depression Hypotension, Injection pain,
<b>Analgesics</b>				
Fentanyl	Powerful narcotic analgesic supplemental effects on analgesia and sedation, increasing patient comfort and surgeon satisfaction	IV injection, infusions, On-demand analgesia via a PCA	1-2 mcg/kg slow IV push. PCA with (0.5 g bolus doses with a 5-minute lockout period after an intravenous loading dose of 0.7 g /kg) Onset- 1-2 min Duration- 30-60 min	Side effects like chest wall rigidity, apnea, respiratory depression, myoclonus or hypotension
<b>Other agents (centrally acting -adrenergic agonist)</b>				
Dexmedetomidine	sedative and analgesic	No significant haemodynamic fluctuation	loading dose of 2.5 g /kg/ h over 10 minutes, followed by a 0.4 g/kg/h infusion until 30 minutes before completion the operation Onset- <1 min Duration- 3-6 min	Bradycardia, heart block, hypotension
Clonidine	sedative and analgesic, lowers sympathetic outflow	IV	0.5 to 2.0 g/kg	decrease in IOP, increased duration of akinesia

### **Intra operative conversion of cases to GA may be required in case of-**

- Excessive sedation
- Respiratory depression
- Complications secondary to local anaesthetics- LAST, anaphylaxis
- Deterioration due to co-morbidities
- Severe Agitation
- Convulsion (vascular spread)

**Figure 3- Key points in managing patients with DA undergoing ophthalmic procedures**



### **Points to be remembered in DA**

- Carefully avoid deep sedation
- Never use technique that you are not familiar with
- Don't render the patient apnoeic unless you are sure of bag and mask ventilation(Fig. 4)
- Oxygenation is always a priority, fall in saturation may be a late sign of hypoxia
- Avoid multiple attempts at intubation in case GA is necessary, consider alternates like supraglottic airway devices

## Conclusion

To summarize, adequate training, experience, risk assessment, and clinical judgement are required to estimate the difficulties of preserving and managing an airway. A skilled specialist should be able to treat a basic airway without difficulty. Advanced airway may be challenging, requiring unconventional procedures and a team with specific additional skills or equipment. However, real-world airway assessment is typically highly subjective, and even specialists have trouble anticipating which instances will be difficult. An anesthesiologist encountering such cases of difficult airways must have a clear understanding of the risks involved and a clear definition of the type and likelihood of difficulty which may be experienced. One should avoid deep sedation during monitored anesthesia care.

## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

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# Anaesthetic Options during Laser Photocoagulation for Retinopathy of Prematurity – Case Series and Review of Literature

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## Abstract

## Background

Anaesthesia for retinopathy of prematurity (ROP) is one of the most challenging in all of ophthalmic anaesthesia. A series of premature or ex-premature babies who underwent laser photocoagulation for ROP in a stand-alone ophthalmic centre between 2017 and 2020 were audited and the various risk factors, anaesthetic concerns and their management are reviewed.

## Methods

A standard protocol was followed for perioperative care. A totally inhalational technique anaesthesia was used with oxygen, air and sevoflurane via a supraglottic airway (SAD). Intravenous anaesthetic drugs were totally avoided. Enhanced recovery after surgery (ERAS), principles were followed, minimizing

preoperative as well as postoperative fasting.

Babies were fed in the recovery area when fully awake and transferred to the referring NICU for monitoring after 2-3 hours.

## Results

A total of 71 babies were studied with age ranging from 13 to 120 days (mean 38.7 + 22 days, median 30 days). Duration of the procedures ranged from 30 to 150 minutes (mean 84.5 + 30.3). Complete datasets were available for 51 babies, who comprised 31 males and 20 females. The median (range) post-conceptual age was 36 weeks (range 29-45) and the mean weight (+ standard deviation) was 1.37 + 0.43. Out of 71, 2 (3%) babies had apnoeic episodes with bradycardia, and 1 baby needed intubation (1.4%).

## Conclusion

For laser photocoagulation, it is possible to avoid endotracheal intubation with a carefully selected anaesthetic plan, avoiding all agents which may have a residual effect and predispose to post-operative apnoea and ventilatory support.

**Keywords:** Retinopathy, prematurity, anaesthesia

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## Article History

Received: 20<sup>th</sup> November 2021

Revision: 1<sup>st</sup> December 2021

Accepted: 28<sup>th</sup> December 2021

Published: 17<sup>th</sup> January 2022

**How to cite this article:** Gita Nath. Anaesthetic Options during Laser Photocoagulation for Retinopathy of Prematurity – Case Series and Review of Literature. *Ind J Ophthal Anaesth* 2022;2(1): 26-34

## Introduction

Anaesthesia for retinopathy of prematurity (ROP) is one of the most challenging in all of ophthalmic anaesthesia. In this article, the various risk factors, anaesthetic concerns and their management are summarized. We also present our experience in managing this procedure.

With the improved survival rates of extremely premature and low birth weight infants due to advances in neonatal care, greater numbers of these babies are presenting with ROP in addition to other comorbidities related to prematurity. Worldwide, almost 10% of all babies are born prematurely, defined as born before 37 weeks' gestation.<sup>1</sup> The main risk factors for ROP include gestational age, low birth weight, the APGAR score, pulmonary complications such as hyaline membrane disease, administration of supplemental oxygen and prolonged mechanical ventilation. Other factors are anaemia, blood transfusions, multiple gestations, intraventricular haemorrhage, sepsis and necrotizing enterocolitis. The incidence of ROP was found to be 33.9% in a series of 602 preterm infants.<sup>2</sup>

## Materials And Methods

We have audited 71 premature or ex-premature babies who underwent laser photocoagulation for ROP from 2017 to 2020. The procedures were performed in Pushpagiri Vitreo-Retinal Institute, Hyderabad, a stand-alone eye hospital. Babies are referred here from neonatal centres in private and government hospitals. In the pre-operative assessment, special note was made of the history in the neonatal intensive care unit (NICU) including intubation, nasal CPAP and history of apnoea.

Standard fasting instructions were given, namely breast milk 4 hours and formula feed 6 hours before the procedure. We make it a point to give clear oral fluids till 2 hours prior, by instructing the mother to give 5% dextrose solution with a syringe as tolerated.

The protocol followed was general anaesthesia (GA) with oxygen, air and sevoflurane via a supraglottic airway (SAD). Intravenous (IV) access was present for fluids and emergency drugs but no IV anaesthetic drugs were given at all. Induction and maintenance were with O<sub>2</sub>/air/Sevoflurane (FiO<sub>2</sub> 0.25) and the SAD was inserted when anaesthetic depth was adequate. 5% dextrose-normal saline was given, as it is an isotonic fluid and also contains glucose to avoid hypoglycaemia. This was given at 10 ml/kg/hr through a dial-a-flow flow controller so that excess fluid administration. Babies were well wrapped to prevent heat loss and skin temperature was monitored throughout (Figure 1). At the end of the procedure, the SAD was removed deep and baby was allowed to wake up. The baby was fed in the recovery area when fully awake and transferred to the referring NICU for monitoring after 2-3 hours.



**Figure 1. A 1.1 Kg premature baby anaesthetized with size 1 LMA**

## Results

A total of 71 babies underwent laser photocoagulation for ROP under anaesthesia during this period. Their age ranged from 13 to 120 days (mean  $38.7 \pm 22$  days, median 30 days). Complete datasets were available for 51 babies, of whom there were 31 males and 20 females. The gestational age, post-conceptional age (PCA), weight at birth and at the time of the procedure are detailed in Table 1. Duration of the procedures ranged from 30 to 150 minutes (mean  $84.5 \pm 30.3$ ).

**Table 1. Patient characteristics**

	Mean + SD	Range	Median
<b>Gestational age (weeks)</b>	31.1 + 2.8	21 - 36	32
<b>Post-conceptional age (weeks)</b>	35.6 + 3.1	29 - 45	36
<b>Weight at birth (kg)</b>	1.37 + 0.43	0.73 – 3.45	1.3
<b>Weight at time of procedure (kg)</b>	1.61 + 0.50	0.95 – 3.22	1.5

**Outcome:** All babies were monitored in the recovery area under the direct supervision of the anaesthetist. Once they were awake and alert, usually within 30 minutes, they were given fed with breast milk / formula feed. Since they were given only volatile anaesthesia, there was no residual drowsiness. After they were fed, the babies were calm and did not need further analgesics such as paracetamol. Out of 71, 3 babies had apnoeic episodes with bradycardia, and 1 of them needed intubation. All 3 were shifted back to the NICUs from which they were referred.

## Review Of Literature And Discussion

**Pathophysiology:** The intrauterine development of the retina occurs in a hypoxic environment which stimulates angiogenesis through the action of vasoactive factors, such as insulin-like growth factor (IGF-1), vascular endothelial growth factor (VEGF) and erythropoietin. These factors, along with maternally derived factors, stimulate new vessel formation. After a premature birth, the higher oxygen levels resulting from oxygen administration along with loss of placental and maternal vascular growth factors lead to vaso-oblivation. Subsequently, there is a retinal neovascularization phase which is driven by hypoxia as well as fluctuating oxygen levels as may be seen in babies with apnoeic episodes. The upregulation of VEGF and IGF-I causes abnormal vascular overgrowth into the vitreous and retina ultimately leading to haemorrhages and retinal detachment. Despite the recognition of ROP in 1942, it is a balancing act between the oxygen requirement from the pulmonary point of view versus prevention of ROP, and there is still no consensus as to the optimum oxygenation target.<sup>3</sup>

### Anaesthetic concerns

These are summarized in Table 2.

#### 1.Prematurity

Anaesthesia in the premature baby is associated with all the problems presented by term neonates, but these are further exaggerated. These include rate dependent cardiac output, increased tendency to airway closure, exaggerated hormonal response to pain and propensity to hypothermia and hypoglycaemia. The increased body water as well as the immature excretory mechanisms alter the pharmacokinetics of anaesthetic drugs. Adverse events such as hypoxia, hypotension and acidosis may reopen the

ductus arteriosus, since the circulation is still transitional<sup>4</sup>

**Table 2. Anaesthetic concerns in neonates and preterm babies**

Cardiovascular	Rate dependent cardiac output Increased parasympathetic tone Reopening of PDA
Respiratory	Increased tendency to airway closure Oxygen toxicity Respiratory distress syndrome, bronchopulmonary dysplasia Propensity to apnoea
Nervous system	Possible neurotoxicity of anaesthetic agents
Pain response	Exaggerated hormonal response to pain
General	Propensity to hypothermia, hypoglycaemia and hypocalcemia
Pharmacokinetic	Increased loading dose but prolonged action of anaesthetic drugs
Apnoea of prematurity	Hypoglycaemia Hypoxia Hypothermia Pain and stress Low gestational age Comorbidities: bronchopulmonary dysplasia necrotizing enterocolitis Apnoea at home

In addition, the premature infant is prone to *apnoea of prematurity*, defined as apnoea of >15 sec duration which may be accompanied by bradycardia. PCA of 60 weeks or more minimizes the likelihood of apnoea; but for ROP surgery, there is no option but to proceed in order to preserve the baby's vision. Other risk factors for post-operative apnoea include the history of apnoea at home, CNS morbidity and lung disease. Anaemia has been found to increase the likelihood of apnoea, but there is no evidence that pre-operative transfusion reduces the incidence. Another modifiable factor is intraoperative hypothermia. The choice of anaesthetic drugs is important and respiratory depressant drugs such as opiates increase the chances of apnoea.<sup>4</sup>

## 2. Effects of pain and stress:

It is now accepted that pain causes immediate stress response as well as long term neurological and psychological effects on the neonate.<sup>5</sup> These effects are even more pronounced in preterm babies due to inadequate maturation of the descending inhibitory pathways.<sup>6-8</sup> Painful stimuli may also lead to apnoea, and hence all efforts must be made to minimize pain in these babies.

## 3. Type of surgery

The procedures done for ROP range from examination and photocoagulation to invasive vitreoretinal surgery, and this naturally determines the type of anaesthesia required.

## 4. Effects of various anaesthetic agents:

Opiates and muscle relaxants are associated with the risk of post-operative apnoea and hypoventilation. Another issue is that of the neurodevelopmental effects of both inhalational as well as intravenous agents on the developing brain, which have been well-demonstrated in



animal studies. According to recent results from the GAS, PANDA and MASK studies, a single exposure to anaesthesia is not associated with behavioural or neurocognitive deficits, but more research is needed regarding multiple exposures or prolonged anaesthesia.<sup>9</sup>

### 5. Post-operative monitoring and discharge

Retrospective studies have reported that the first episode of post-operative apnoea occurred within 4 hours after surgery, implying that if there has been no apnoeic event during this period, it may be safe to discharge the patient.<sup>10</sup> However, 3 and 4 out of 5 apnoeic events were missed by either nursing observation or pulse oximetry alone respectively; hence a combination of these modes with electrocardiography may be necessary to detect all apnoeic episodes.<sup>11</sup> Younger preterm infants of <46 weeks PCA or those with other risk factors should be monitored for at least 12 h post-operatively. Infants of 46 and 60 weeks PCA may be monitored for a minimum of 6 hours.<sup>12</sup>

### Anaesthetic options

The possible options for anaesthetic care include the following:

- Topical anaesthesia alone
- Sedation (enteral or intravenous)
- Sedation + topical anaesthesia
- GA – supraglottic airway device
- GA – endotracheal intubation

Early studies done in the 1980's reported a number of systemic complications during cryotherapy for ROP. These included worsening cyanosis, haemodynamic disturbances like arrhythmias, bradycardia, hypertension and hypotension, seizures and even respiratory or cardiorespiratory arrest.<sup>13</sup> Hence, endotracheal intubation and monitoring was advocated by Sullivan et al, who safely treated 20 eyes in 13 babies.<sup>14</sup>

Haigh et al compared the systemic complications with 3 different anaesthetic techniques for cryotherapy for ROP. Of 30 premature infants, 12 babies were done under topical anaesthesia alone, 6 babies had GA with endotracheal intubation and the remaining 12 had GA combined with topical anaesthesia. They found more severe and protracted cardiorespiratory complications when topical anaesthesia was used alone.<sup>15</sup>

Coming to the 21<sup>st</sup> century, a postal survey of 46 ophthalmologists in the UK done in 2007 found that there was considerable variation among them, not only regarding the anaesthetic methods they used, but also in their beliefs about the severity and effect of neonatal stress during treatment.<sup>16</sup> The various methods used included the following:

- IV sedation
- Sedation + paralysis + ventilation
- Morphine + pancuronium
- Oral sedation
- Rectal chloral hydrate
- Topical in combination with above
- Topical alone was not used by any of the respondents

An editorial in the same issue discusses the various concerns regarding this procedure. First of all, they acknowledge the immense levels of stress surrounding the procedure, both for the neonate as well as for the parents. Considering this, they suggest that minimal/conscious sedation is not enough for these babies – they need deep sedation and analgesia. This in turn is associated with respiratory depression and airway obstruction, which is difficult to observe and monitor under the drapes. Hence, they suggest that neonates should be electively intubated and ventilated before laser treatment.<sup>17</sup>

Table 3 lists the different anaesthetic options which have been used for ROP surgery.<sup>18-24</sup> A comparison of intubation with long nasal prongs in 54 babies found that the 23 of 30 intubated babies were still intubated on the 3<sup>rd</sup> postoperative day.<sup>18</sup> Conscious sedation with fentanyl and midazolam was used in 15 babies, but 6 of them needed to be intubated.<sup>19</sup> Even with intravenous ketamine sedation, 2 out of 11 needed postoperative ventilatory support.<sup>21</sup> In a recent study on 61 infants who underwent 72 procedures; sevoflurane, opiates and neuromuscular blockers were used and all babies were intubated. Only 14 (19.4%) were extubated at the end of the procedure and 29 (40.3%) of them were still ventilated 24 hours later.<sup>24</sup>

**Table 3. Anaesthetic options and outcome in ROP surgery and comparison with present series**

Reference	N	Anaesthesia method	Post-operative ventilation	Post-operative apnoea and other issues
Woodhead et al, 2007 <sup>18</sup>	54	30 intubated 24 Long nasal prongs	23/30 (77%); 50% for > 2 days 1/24 (4%)	
Spector et al, 2007 <sup>19</sup>	15	Conscious sedation with fentanyl and midazolam without mechanical ventilation	6/15 (40%)	Baseline activities, feeding 17 hours after
Parulekar et al, 2008 <sup>20</sup>	10	Oral sedation + sub-tenon block		3 (30%) – Excessive movement 2 (20%) – Bradycardia 2 (20%) – Apnoea
Lyon et al, 2008 <sup>21</sup>	11	Ketamine sedation IV	2/11 (18%)	
Jiang et al, 2016 <sup>22</sup>	97			
	31	Topical anaesthesia	3 (9%)	8 (26%) - apnoea More post-op cardiorespiratory instability
	47	Fentanyl sedation, intubation, IPPV	2 (4%) for > 2 days	
	19	GA, intubation	2 (11%) for > 1 days	
Sinha et al, 2014 <sup>23</sup>	56	GA with intubation – 46		3 (5%) – apnoea IV paracetamol and topical anesthetics reduced intra-operative opioid requirement
		GA with SAD – 10	2 (3.5%)	
Kaur et al, 2020 <sup>24</sup>	72	GA with intubation		
		Sevoflurane, opiates, NMB	58 (81%)  29 (40%) for > 24 hours	
Present study	71	Volatile inhalation and maintenance, LMA	1 (1.4%)	2 (3%) – apnoea

Many of the above case series report small numbers with a significant proportion of babies needing post-operative ventilation. Prolonged or repeated invasive mechanical ventilation in premature and low birth weight babies is known to increase morbidity and can also contribute to mortality.<sup>25</sup> If the baby already requires ventilatory support for the pulmonary problems of prematurity, continuation of this support is inevitable. But if the child is currently self-ventilating, it is preferable to avoid anaesthetic techniques which may tip the balance, putting them back on the ventilator. Hence choosing an anaesthetic technique which reduces the need for post-operative ventilatory support is definitely preferable. Another issue is the upper airway problems which may be present in these babies because of previous intubation and ventilation resulting in laryngo-tracheomalacia or tracheal stenosis. Avoiding intubation if at all possible is likely to reduce the chances of airway oedema and further compromise.

The results of the present study compare favourably with previously published studies, since only 1 of our 71 patients needed post-operative ventilation (an incidence of 1.4%) and 2 out of 71 (2.8%) had apnoea and bradycardia. These are similar to the results of a study by Sinha et al, but those were a much healthier cohort of babies, with a median PCA of 56 weeks (range 36-60) and over 87% of them weighing more than 3 Kg.<sup>23</sup> In contrast, the median PCA in our series was 36 weeks (range 29-45) and the mean weight was  $1.37 \pm 0.43$ . In our series, we deliberately avoided any intravenous sedatives, opioids or neuromuscular blockers and opted for a totally inhalational technique. Thus, there were absolutely no residual effects of anaesthetic drugs which could increase the likelihood of apnoea. We also followed the principles of enhanced recovery after surgery (ERAS), by minimizing

preoperative as well as postoperative fasting. Other precautions that were taken included limiting the FiO<sub>2</sub> to 25%, ensuring continuous infusion of glucose containing fluid to avoid hypoglycaemia and keeping the baby as warm as possible by wrapping.

## Conclusion

Anaesthesia for ROP surgery is one of the most challenging situations for the neonatal anaesthesiologist, especially when conducted in a stand-alone high quality ophthalmic centre rather than a multispecialty hospital. The very fact that so many modalities are being used implies that there is no single ideal technique. The choice of anaesthetic technique depends on several factors including the set-up i.e., whether the procedure is being done in a stand-alone eye hospital or multispecialty centre; in the NICU or operation theatre. The surgical procedure is also an important deciding factor, as vitreo-retinal surgery mandates GA with endotracheal intubation.

Close monitoring of the baby is required, be it by the anaesthesiologist or neonatologist. If topical anaesthesia alone is chosen, the procedure is more challenging for the ophthalmologist, it takes longer and may be less complete. Several studies have found increased cardiorespiratory problems with solely topical anaesthesia.

Many studies recommend GA with endotracheal intubation, but for laser photocoagulation alone, it is possible to avoid this with a carefully selected anaesthetic plan, avoiding all agents which may have a residual effect and predispose to post-operative apnoea and ventilatory support.

**Acknowledgement:** My sincere thanks to the administration and staff of Pushpagiri Vitreo-Retinal Institute, Hyderabad. Special thanks to Dr Sai Kiranmayee who performed the majority of the photocoagulation

procedures in this series and also helped with data collection.

**Financial support:** Nil

**Conflicts of interest:** Nil

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# Anaesthesia management in a child with Klippel-Trenaunav Syndrome posted for examination of both eyes under general anaesthesia: A case report

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## Abstract

Klippel-Trenaunay syndrome (KTS) is a very rare congenital vascular anomaly. It is characterized by the presence of capillary malformation, venous malformation as well as limb overgrowth, generally affecting one extremity. Although clinical characteristics of KTS are well known, the epidemiology and pathophysiology still remain to be defined. Awareness of this disorder is important for anesthesiologist for managing potential complications. Here, we report a case of five-months old male baby posted for examination of both the eyes and Transscleral cyclophotocoagulation (TSCPC) under general anaesthesia.

## Key words:

general anaesthesia, Klippel-Trenaunay syndrome, examination of eyes, arterial venous malformation

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## Article History

Received: 15<sup>th</sup> November 2021

Revision: 20<sup>th</sup> November 2021

Accepted: 21<sup>st</sup> December 2021

Published: 17<sup>th</sup> January 2022

## Introduction

Over a hundred years ago, French physicians Klippel and Trénaunay described for the first time a rare congenital disorder named Klippel-Trénaunay syndrome (KTS)<sup>1</sup> with a very low incidence of about 1:100,000.<sup>2</sup> KTS is a capillary-lymphatic-venous malformation associated with soft-tissue and skeletal hypertrophy and it is clinically recognized by a triad of capillary malformations (port wine stain), atypical venous malformations and bony and/or soft-tissue hypertrophy; presence of any two of these features will confirm the diagnosis.<sup>3</sup>

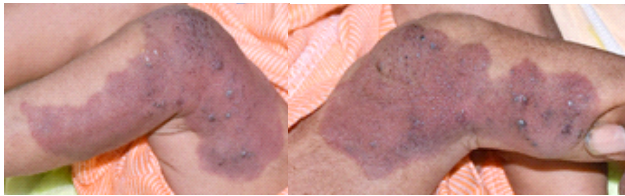
The syndrome is usually diagnosed at birth, but it can be found in older children and adults if not diagnosed in time. Extremities, particularly the lower extremities, are affected by vascular abnormalities.<sup>4</sup> Most cases of KTS are sporadic, but little has been published about family members suggesting an inherited disorder.<sup>2,5</sup>

## Case description

We report a case of five-months old baby who had with a whitish opacity over the cornea of the left eye (LE). Opacity was noted since 3 days after birth and was gradually increasing in size.

**How to cite this article:** Sirisha Senthil, Harshitha Kadava, Hari Shanker Charan, Raja Narsing Rao. Anaesthesia management in a child with Klippel-Trenaunav Syndrome posted for examination of both eyes under general anaesthesia: A case report Indian J Ophthal Anaesth 2022;2(1): 35-8

Pinkish discoloration of the skin was seen on different parts of the body associated with swelling of middle, fourth and little toes of both the feet, Figure 1 and 2. It was full-term caesarean delivered baby with birth weight of 2.4 kg and cried soon after birth.



**Figure 1. Capillary Hemangiomas involving lateral aspect of both legs**



**Figure 2. Hemangiomas involving middle, 4<sup>th</sup> and little toes of both feet with soft tissue overgrowth**

The baby underwent a thorough pre-anaesthetic evaluation by a pediatrician. On examination, both cardiovascular and respiratory system was normal. Routing blood and urine investigations were also found to be within the normal limits. Universal protocol, 4-2-1 for nil per oral was followed. On the day of surgery, the baby was shifted into the operation theater and standard monitoring ECG, peripheral oxygen saturation and non-invasive arterial blood pressure was attached. Anaesthesia was induced with 50% O<sub>2</sub>:50% N<sub>2</sub>O + 6% Sevoflurane. Intravenous line was established. Airway was secured with appropriate sized AMBU LMA and the baby was on spontaneous assisted mode of ventilation. The vitals were stable throughout the procedure. After the procedure was over, gentle suctioning was done and the baby was extubated in left lateral position.

The baby was kept under observation for one hour and handed over to the parents after uneventful adequate recovery.

## Discussion

KTS has no predilection for gender, race or geographical area and occurs sporadically.<sup>2,6</sup> Although the etiology of KTS is still unknown, damage to the sympathetic nervous system resulting in dilatation and persistence of microscopic arteriovenous anastomoses *in utero* is hypothesized to be the leading cause.<sup>7</sup> KTS has been shown to belong to a spectrum of segmental overgrowth diseases caused by mutations in the PIK3CA gene, which differentiates it from Parkes-Weber syndrome (PWS), which is caused by mutations of the RASA1.

Alteration of tight balance between angiogenesis and vasculogenesis occurs. Most patients with KTS will present with the classic triad<sup>8</sup> but some clinical variations can be seen with age (childhood and adulthood),<sup>9</sup> however, these are far less common. Few numbers or absence of lymphatic channels are leading causes of lymphedema that can be documented using ultrasound (with or without doppler) and magnetic resonance imaging (MRI).<sup>10</sup> Extremities are mostly affected, most often unilaterally (85%), sometimes bilaterally (12.5%), and only rarely crossed-bilaterally (2.5%).<sup>12</sup> The case presented in this report had right lower limbs affected. Various other limb anomalies including camptodactyly, syndactyly, clinodactyly, and congenital hip dislocation have been reported in association with KTS.<sup>10</sup>

Spectrum of PIK3CA Related Overgrowth Spectrum (PROS)<sup>8</sup>

- KTS
- CLOVES- Congenital Lipomatous Overgrowth, Vascular malformations, Epidermal nevi, Scoliosis

- MCAP- Megalencephaly Capillary Malformation
- HHML- Hemi Hyperplasia- Multiple Lipomatosis
- FAO- Fibro-adipose Overgrowth

The presence of arteriovenous fistula in PWS is the only difference with KTS, and both syndromes are generally confirmed with Doppler ultrasound and magnetic resonance angiography.<sup>10,11</sup>

These patients may require orthopaedic surgeries to correct limb discrepancies, debulking surgeries and amputations; interventions like sclerotherapy and laser therapy for vascular malformations, vascular surgeries like surgical stripping and endoscopic ligation of perforating veins, and surgical resection of the bowel in case of gastrointestinal haemorrhage.

Preoperative cardiology evaluation must be ensured as patients may have venous thrombophlebitis (50%) and pulmonary thromboembolism (22%) which may lead to pulmonary hypertension and right ventricular failure.<sup>12</sup> Arteriovenous malformations can produce high output congestive heart failure. Preoperatively, deep vein thrombosis prophylaxis must be considered. Enough packed RBC should be ready before the operation for appropriate fluid resuscitation in case of haemorrhage. In certain cases, preoperative embolisation can be carried out to reduce intraoperative bleeding. This will need close collaboration with interventional radiologists.

Reports concluded that general anaesthesia is safe for patients with KTS. Difficult intubation must be anticipated as patients may have facial anomalies, upper airway angiomas and soft tissue hypertrophy in the airway. Loss of auto-regulation in the abnormal vessels predisposes to hemorrhage, especially in the presence of

hypertension that may occur intra-operatively. Measures to obtund the hemodynamic responses to direct laryngoscopy and tracheal intubation, noxious surgical stimuli, and extubation should be performed. It is important that the patient is normotensive during induction and throughout the operation. Fluctuation of blood pressure might lead to a hypertensive state that could potentially cause rupture of multiple intracranial and peripheral arteriovenous shunts, aneurysms and capillary malformations. Other complications such as internal bleeding from vascular abnormalities and fistulas, might be exacerbated by elevated blood pressure. Maintaining a normotensive state is important if the patient is positioned prone during the surgical operation. Prone positioning is associated with predictable changes in cardiopulmonary physiology. In the prone posture, pressure on the abdomen compresses the inferior vena cava and femoral veins, diverting blood from the distal parts of the body into peri-vertebral venous plexuses. Essential part of the anaesthetic plan is the preparation for unexpected vascular complication such as hypertensive and hypotensive states. Nitroprusside sodium, dopamine hydrochloride and phenylephrine infusions should be kept ready before surgery. Excessive venous pulsation can result in inaccurately low pulse oximetry reading if the probe is placed on an affected limb. Avoidance of coughing, straining, retching, and vomiting is important to prevent rupture of the abnormal vessels. Coughing and bucking should be avoided during extubation. Central neuraxial blockade should be considered with caution due to risk of epidural hematomas in the presence of haemangiomas, spinal arteriovenous malformations and neurovascular malformation in the surrounding structure



of the spine; tendency for coagulation disorders, and venous dilation. If neuraxial blockade is planned, it is mandatory to do preoperative CT/MRI to rule out vascular malformations in the CNS and ensure absence of cutaneous lesions overlying site of needle insertion. Preoperative coagulation profile must be done in these patients.

Postoperative monitoring should be individualized depending on the surgical procedure done, the preoperative status, and the intraoperative complications.

Currently, there is no definitive treatment of KTS approved; however, a multidisciplinary management should be focused on reducing symptoms and complications associated to the disease.

### Conclusion

We presented the case of an infant with a rare congenital vascular disorder type KTS who presented with glaucoma vascular malformation on the left eye, as well as numerous port wine stains. This case serves as review of clinical features and etiology of KTS and also highlights the importance of a multidisciplinary management team and follow-up, which can help to avoid the occurrence of complications that have an impact on the prognosis of the patient.

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## Adverse Drug Reactions in an Ophthalmic Set up

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### Definition of adverse drug reaction (ADR)

The World Health Organization defines ADR as “A response to a drug that is noxious and unintended and occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease or for modification of physiological function”. The definition of an ADR is often confused with that of an adverse drug event (ADE). An ADR is a type of ADE whose cause can be directly attributed to a drug and its physiologic properties. A main distinction between ADRs and ADEs is that ADRs occur despite appropriate prescribing and dosing, whereas ADEs may also be associated with inappropriate use of the drug or medication error or other confounders that occur during drug therapy but are not necessarily caused by the pharmacology of the drug itself. A causal relationship is suspected for an ADR but is not required for an ADE.

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### Article History

Received: 10<sup>th</sup> November 2021

Revision: 20<sup>th</sup> November 2021

Accepted: 10<sup>th</sup> December 2021

Published: 17<sup>th</sup> January 2022

### Types of adverse drug reaction

Type A (Augmented) reactions result from an exaggeration of a drug's normal pharmacological actions when given at the usual therapeutic dose and are normally dose-dependent. Examples include respiratory depression with opioids or bleeding with warfarin.

Type B (bizarre) reactions are uncommon and unpredictable reaction that are not expected from the known pharmacological actions of the drug. They are independent of dose, suggesting that individual patient host factors are important. Examples include anaphylaxis with penicillin or skin rashes with antibiotics.

Type C (chronic) reactions due to cumulative long time exposure to the drug. Example includes analgesics interstitial nephritis.

Type D (delayed) reactions become apparent some time after the use of a medicine. An example is leucopenia, which can occur up to six weeks after a dose of lomustine.

Type E (end-of-use) reactions are associated with the withdrawal of a medicine. An example is insomnia, anxiety and perceptual disturbances following the withdrawal of benzodiazepines.

**How to cite this article:** Jaichandran VV. Adverse drug reactions in an Ophthalmic set up. Indian J Ophthal Anaesth 2022;2(1): 39-45

### ADR in an Ophthalmic set-up

The most important ADR is Type B reaction which can be life threatening at times. In an ophthalmic set-up such type of reactions can be encountered in outpatient clinics, operation theatre (OT) and while performing fundus fluorescein angiogram.<sup>1</sup>

Authors have reported two cases of allergic reaction to topical azithromycin eye drops.<sup>2</sup> Patient developed epiphora, eyelid edema, chemosis, conjunctival injection, hyperemia, intensive papillary reaction, and rhinitis within 30 min of instillation.<sup>2</sup> Both the patients immediately showed dramatic improvement after cessation of the topical medication and administration of anti-allergic therapy.

In the OT, allergic reaction to local anesthetic agents used in ophthalmic surgeries is rare. Literature review shows only four documented cases with allergic reaction to lignocaine. The first patient developed a reaction after sub-conjunctival anesthesia, the second and third patient developed after peribulbar anesthetic injection, and the fourth one developed after local infiltration for blepharoplasty.<sup>3-6</sup> The first three cases developed reaction several hours after the administration of anaesthetic, but the fourth case developed reaction immediately after the injection. The signs and symptoms were mostly localized in and around eye with proptosis, swelling of the upper and lower eye lid, conjunctival redness and extraocular movement restriction. In most of the cases with early detection and prompt treatment with IV antihistamines and steroids symptoms resolved completely. Deshmukh et al reported optic atrophy, a potentially blinding adverse drug reaction to peribulbar lignocaine anaesthesia.<sup>5</sup>

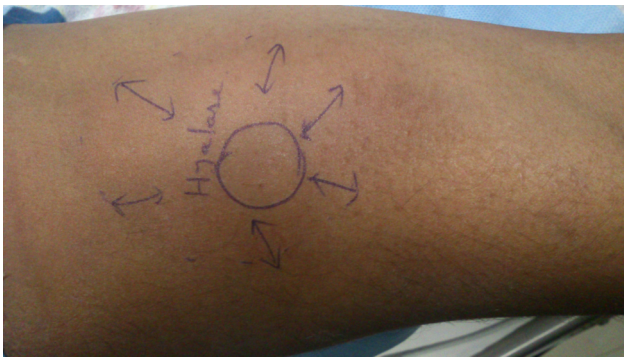
Additives in local anesthetic solutions such as antioxidants or preservatives (metabisulphite or parabens) and other adjuvants used especially injection hyaluronidase may also be responsible for adverse reactions. Peribulbar and subtenon use of hyaluronidase injection have been reported to cause both vision and life threatening reactions.<sup>7,8</sup> Ocular signs and symptoms include periorbital edema and erythema (unilateral or bilateral), conjunctival chemosis, proptosis, restriction of eye movements (ranging from mild to total ophthalmoplegia), puffiness of face/ear lobe, Figure 1.



**Figure 1. Contralateral periorbital swelling.**

The cornea and anterior chamber remain clear although loss of vision occurred in some cases as a result of compression of the optic nerve or increase in IOP. Systemic reactions include nausea, vomiting, sweating, generalized rash, itching, tachycardia, dyspnea, angioedema of the larynx, swallowing difficulties, incontinence and anaphylactic shock. Most of the patients had undergone an earlier procedure that included hyaluronidase use, which suggests that these reactions may be a result of sensitization to the animal-derived product. It can be either due to Type I IgE mediated reaction or delayed Type IV cell mediated reaction.

The differential diagnosis includes retrobulbar haemorrhage and orbital cellulitis. Complete normal blood count with absence of fever, pain etc, history of positive exposure to hyaluronidase, positive intradermal test, serum IgE antibodies level specific to hyaluronidase, CT scan to look for any increased orbital fat haziness and /or enlargement of extraocular muscles are some of the investigations that can be done to confirm the diagnosis, Figure 2.



**Figure 2. Positive intradermal skin test to Injection hyaluronidase.**

Treatment for anaphylaxis includes epinephrine 0.3-0.5mg intramuscular, preferably in the mid-outer thigh, maintenance of airway, IV H1 antihistamine (chlorpheniramine 25-50 mg), IV steroids (Dexamethasone 8mg) and IV fluids.

To prevent such type of adverse reactions, we, at our institution, have started adopting preoperative intradermal skin test with 0.3ml of lignocaine HCL and Hyaluronidase mixture. Intradermal skin test is done for patients with history of allergy to food, insect bite, medications, bronchial asthma, allergic rhinitis, allergic skin disorders etc.

Previous authors have also reported that postoperative periorbital inflammation following use of excessive dose of hyaluronidase (50-250 IU/ml).<sup>9,10</sup>

This type of augmented (Type A) adverse drug reaction can be prevented by using hyaluronidase within the permissible limit of 15 IU/ml.<sup>10</sup>

### **The burden of ADR**

It is clear that ADR adversely affect patient's quality of life and can also cause patients to lose confidence in the healthcare system. There is a significant impact through increase costs of patient care and the potential to lengthen hospital stay. ADR may also mimic disease, resulting in unnecessary investigations and delays in treatment. At times, ADR are serious enough to result in readmission to hospital or even referral to higher care center. It is well recognized that ADRs place a significant burden on the health service. Studies performed in an attempt to quantify this have shown adverse drug reactions account for 1 in 16 hospital admissions.<sup>11</sup>

### **Prevention of ADR**

Once an ADR is suspected or diagnosed; it is important to report it as an incident to the hospital safety/drug committee so that trends can be monitored. The goal of evaluating ADRs is to increase patient safety by preventing harm. Each patient harmed by an ADR should be treated and evaluated as an individual case. Reporting leads to increased awareness and detection of ADRs and can prevent their occurrence in both inpatient and outpatient settings, which in turn can help to prevent hospital admissions or readmissions.

Following reporting of an ADR, a thorough evaluation should be done by a committee comprising of multidisciplinary team members. Begin by evaluating the nature of the event. A complete review of the patient's medical history, medication lists followed, classification of the severity of the reaction must be done.

After the reaction is evaluated, the cause of the reaction should be established, if possible. Simple tools such as the Naranjo ADR probability tool can be used to assist in determining causality.<sup>12</sup> By answering 10 questions about the ADR and assigning a numeric score to each answer, the ADR probability classification can be determined, see Table 1.<sup>12</sup>

**Table 1. Naranjo ADR Probability Scale.**

Question	Yes	No	Do Not Know	Score
1. Are there previous conclusive reports on this reaction?	+1	0	0	
2. Did the adverse event appear after the suspected drug was administered?	+2	-1	0	
3. Did the adverse reaction improve when the drug was discontinued or a specific antagonist was administered?	+1	0	0	
4. Did the adverse event appear when the drug was re-administered?	+2	-1	0	
5. Are there alternative causes (other than the drug) that, on their own, could have caused the reaction?	-1	+2	0	
6. Did the reaction reappear when a placebo was given?	-1	+1	0	
7. Was the drug detected in the blood (or other fluids) in concentrations known to be toxic?	+1	0	0	
8. Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	+1	0	0	
9. Did the patient have similar reaction to the same or similar drugs in any previous exposure?	+1	0	0	
10. Was the adverse event confirmed by any objective evidence?	+1	0	0	

**Total Score: 9 – Highly Probable; 5–8 – Probable; 1-4 Possible; 0 - Doubtful**

One should make sure the ADR is not caused by a medication error. This could influence whether a treatment is continued or discontinued. If the reaction can be attributed to a drug, a suggestion is to update the patient's allergy profile with the name of the drug and a brief description of the reaction.

Regular educational programs must be carried out. This can help remind health care professionals or the stakeholders involved about the importance of identifying and reporting ADRs. Another way of alerting health care practitioners is through publishing as case reports in the medical literature.



## Conclusion

ADR will never completely be eliminated, even with the most sophisticated pharmacovigilance systems in place. The duty of the health care practitioner is to minimize the occurrence of ADRs by working to prevent them. Prevention is made possible through knowledge gained by the reporting of ADRs and in published primary literature. Sharing this information with colleagues and patients will create an awareness of ADR potential and can save lives. By including an ADR on the differential when a patient present with new or worsening symptoms, the process of identifying, classifying, and determining the causality of a potential ADR can begin immediately, and future harm may be prevented.

## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

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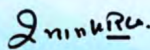
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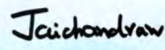
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## Gift of Sight

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Dear Sir/Madam,

I turn one year old today and I'm so excited to share my experiences so far with all of you. I was born on a beautiful Monday morning and was overjoyed to be in mother's arms finally! "She is going to be an influencer on social media for sure!" beamed my proud father as he clicked a million pictures "look how beautiful she is!" he said. Damn right he was!

Little did I know that my life was going to change forever. Out of the blue, I was yanked away to this strange room with other tiny humans like me called the ICU. Oh! How I yearned to be with my mother again but more importantly, the room got dimmer and dimmer as the day passed.

The doctors informed my mother that I had a white spot in my eye and I needed a corneal transplantation to restore vision in my affected eye.

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### Article History

Received: 14<sup>th</sup> September 2021

Revision: 20<sup>th</sup> October 2021

Accepted: 24<sup>th</sup> November 2021

Published: 17<sup>th</sup> January 2022

I could sense the anxiety creep through my mother as she heard the news. I cooed in her arms to try and comfort her but my effort went in vain. "Isn't transplantation a major surgery with poor outcomes doctor?" she asked the doctor with glasses as she rocked me back and forth. The doctor gave her an all knowing smile; he probably had been asked this question multiple times before. "Corneal grafting is the most successful of all tissue transplants" he said. Corneal grafting? what's this now? I wondered. I was told my entire eye needed to be transplanted. I frowned. "We were told she would need an eye transplant doctor. What is this corneal grafting?" my father quizzed. Daddy reads my mind so well sometimes I thought. "Of course she needs an eye transplant, but not the whole eye. Only the outer portion of the eyeball called the cornea is transplanted in these surgeries" he explained. "Being a transparent tissue, the cornea acts like a glass window through which we see the entire world and since it is devoid of blood vessels, it is an ideal tissue for transplantation" he added. "We can safely transplant it without matching the donors as it is the case in other transplants" he explained.

WOW! Isn't that simple! I tried to send a telepathic message to my father sitting across the room.

**How to cite this article:** Pushpha Susan Isaac, Sugaranjini G. Gift of Sight. Indian J Ophthal Anaesth 2022;2(1): 46-8

Ok daddy, Let's go buy me some corneas. "That's fantastic doctor! No matter the cost, we are willing to pay the donor for the cornea" my father quipped. I smiled thinking my telepathy worked. "Absolutely not" said the doctor in haste. "Eye donations are done free of cost. Only a person who has pledged his eyes or relatives of a deceased person can give consent for eye donation. One can neither buy nor sell donated eyes. It is the most noble form of charity." All of us were awestruck.

"May God bless the one who donated their eye so that my granddaughter can see" said my grandmother. She muttered a silent prayer for the unknown person and asked, "So you must be getting a lot of eye donations every day, right doctor?". "Unfortunately that is not the case ma'am" the doctor sighed. "Most people are superstitious. It is hard to convince them otherwise" he replied. "How can this be?" exclaimed my grandmother, who was the most spiritual amongst us all. "No religion can be against such an honourable deed" she guaranteed. "Well said ma'am. It is the mindset of the people that needs to change." remarked the kind looking nurse in white uniform. We all nodded in agreement

"Can a living person donate their eyes doctor?" asked my elder brother. My heart swelled with love for him at that instant. "Only the deceased can, little boy" replied the tall junior doctor with a smile. My brother tried to hide his disappointment. "But you can pledge your eyes, buddy" encouraged the other red haired doctor with a smile. "There is no age limit for eye donation" she said, patting him.

My family processed all this with a sense of hope growing within. "Is the eye collection a complicated process doctor? Does it delay the cremation proceedings of the deceased? Is that why people shy away from pledging their eyes?" inquired my curious grandfather. This is a valid question, I thought. "That is not the case either. The entire procedure of retrieving the eyes takes less than 20 minutes and does not delay the cremation process. We have trained personnel and doctors who finish the process with absolutely no waste for the family to clear." The doctor replied. "Also, the eyes are collected only if the relatives of the deceased give their consent" the doctor further added. "All that we ask of the relatives is to inform us within 6 to 8 hours after the demise and to switch off the fans or cover the eyes of the deceased with a moist cloth to prevent the cornea from drying. It's fairly simple. In fact, we never refuse an eye donation unless the donor had died from or had been diagnosed with AIDS, Hepatitis, rabies, septicemia, Covid or some prion associated diseases. Even if the eyes cannot be used for transplantation, they can be used for medical education and research" he explained.

"Will the face of the donor have holes in them after you remove the eyes doctor?" asked my little brother sheepishly. The doctors and nurses laughed in unison. "Of course not, my boy, we place an artificial eye in its place. You wouldn't know the difference even if we told you" said the doctor with a wink. The smile was back on my brother's face now.

An eye donation counsellor then handed the eye pledge form to all my family members. My grandparents scurried through it.



"But we have had a cataract surgery doctor. Does that mean we cannot donate our eyes?" They asked in worry. Nobody can do for little children what grandparents do. "This is a common misconception" the doctor clarified. "Even people with eye diseases can donate their eyes. Even I wear glasses but that has not curtailed me from pledging my eyes" he pointed out.

Ah! There are so many aspects of this eye donation, I marvelled. What a beautiful way to leave this world, I thought as I slowly drifted to sleep. I hummed my favourite rhyme as I yawned.

Humpty Dumpty sat on a wall.

Humpty Dumpty had a great fall

All the king's horses and all the king's men

Couldn't put Humpty together again

So Humpty Dumpty left his eyes behind.

So children like me wouldn't be blind

All the king's horses and all the king's men

Lauded Humpty for being so kind.

We were then sent to meet the anaesthetist. She was hands down my most favourite person in that hospital. She wrapped me in her arms like I was her own while I tried to pull the pink beads dangling from her spectacles all the while. "Such a cutie" she gushed pinching my cheeks. "Say hello to your new friend" she said as she brought me close to my new bestie, Baby Z, also with a white patch in her eye. We were scheduled for corneal transplantation on the same day. Isn't it amazing that a single donor changed both our lives by just donating their two eyes?

### **Financial support and sponsorship**

Nil.

### **Conflicts of interest**

There are no conflicts of interest.



# *2nd National Conference of Indian Ophthalmic Anaesthesiologists Conference*

*Aravind Eye Hospital, Madurai*



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