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President's Message

It is a matter of pleasure and great satisfaction that 1st issue of e-Journal of Indian Journal of Ophthalmic Anaesthesia (IJOA) is being brought out.

Ophthalmic Anaesthesia Forum of Indian Society of Anaesthesiologists (OFISA) was formed on 27th December 2009 at the Annual conference of Indian Society of Anaesthesiologists (ISA).

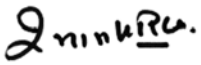
In addition to conducting sessions on ophthalmic anaesthesia at Annual Conferences of ISA, OFISA had been conducting CMEs and Conferences involving Ophthalmic Anaesthesiologists, ophthalmic surgeons, optometrists and others involved in ophthalmic surgery.

With the expanding knowledge and scope of ophthalmic anaesthesia, it was felt that an independent Association of Indian Ophthalmic Anaesthesiologists (AIOA) should be formed. Thus AIOA was formed a registered on 18th June 2020.

Success of eye surgery depends upon coordinated work and efforts of ophthalmic anaesthesiologists, ophthalmic surgeons, assisting nursing staff, operation room technicians, optometrists and other supporting staff. Keeping this in view, membership of AIOA has been kept open for all those involved in ophthalmic surgery in whatever capacity. I congratulate Dr Renu Sinha, Editor, IJOA for bringing out this 1st issue of Journal in such a short time after inception of AIOA.

I want place on record untiring efforts of our Secretary, Dr. Jaichandran V V for launching AIOA and issuing IJOA to all its members. I also congratulate and thank all the contributing authors for this issue.

I wish AIOA and IJOA all the success in future.



Dr. S. C. Parakh

President, AIOA

Hyderabad.

From the Editor's Desk

Dear Friends,

The year 2021 brings a fresh belief that the whole world will now become free of corona pandemic and we all will be back to our normal life style by the later part of this year as we used to have earlier. This year also marks a new beginning in the field of ophthalmic anaesthesia. We now have an independent society dedicated to ophthalmic anaesthesia which has been named as Association of Indian Ophthalmic Anaesthesiologists (AIOA). It was registered on 18th June 2020; thanks to the sincere efforts of Dr Jaichandran V V who is the Secretary of this society and the support of Dr Parakh S C, the President of the society.

It gives me immense pleasure to present to you the first issue of the e-journal of this society which has been named as Indian Journal of Ophthalmic Anaesthesia (IJOA). The journal includes original articles, review article, case reports, letters to editor and brief correspondence relevant to ophthalmic anaesthesia and ophthalmic surgery. It will bring the ophthalmologists and the ophthalmic anaesthesiologists on the same platform so that we arrive at a consensus and uniform understanding on various issues.

I thank Dr Jaichandran and Dr Parakh for giving me the opportunity to work for the journal as the Editor. I request the ophthalmic anaesthesiologists and ophthalmologists to become a part of this society and contribute to the academic contents of this journal. I thank the authors for contributing to the journal and would also like to request the readers to provide their feedback so that we can work on those and make improvements.

I wish you all a very happy, healthy and prosperous new year.

Dr Renu Sinha

Editor

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Indian Journal of Ophthalmic Anaesthesia

The Official Journal of Association of Indian Ophthalmic Anaesthesiologists

Original Article

Magnesium versus dexmedetomidine as adjuvant to local anaesthetic in peribulbar block for vitreoretinal surgery.

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ABSTRACT

Background: Peribulbar anaesthesia (PBA) is widely used in ophthalmic anaesthesia and is a suitable technique for vitreoretinal (VR) surgery. VR surgery requires dense analgesia and good akinesia. Longer acting local anaesthetic agents and adjuvants have been used to prolong the duration of anaesthesia, hasten onset of akinesia, reduce LA toxicity and offer greater patient satisfaction. The aim of our study was to find out the efficacy of adding magnesium or dexmedetomidine to 0.5% ropivacaine or 0.5% levobupivacaine in PBA for VR surgery.

Material and methods: One hundred and twenty adult patients undergoing VR surgery were randomized into the four groups. The composition of the drug used for peribulbar anaesthesia in the 4 groups were Group RM (8 ml of 0.5% Ropivacaine + Hyaluronidase 150 IU+ Magnesium sulphate 0.5 mg), Group RD (8 ml of 0.5% Ropivacaine+ Hyaluronidase 150 IU+ 25µg Dexmedetomidine), Group LM (8 ml of 0.5% levobupivacaine + Hyaluronidase 150 IU+ Magnesium sulphate 0.5 mg) and Group LD (8 ml of 0.5% levobupivacaine + Hyaluronidase 150 IU+ 25 µg dexmedetomidine).

Results: The groups were comparable in terms of patient demographics, duration of surgery, onset of surgical anaesthesia and need for supplementation of block. Patients in Group RD (478±298 min) had prolonged post-operative pain relief when compared to RM (280±135 min). The time to first request for analgesia was 449±289 min in group LD and 405±285 min in group LM.

Conclusion: Addition of dexmedetomidine to 0.5% ropivacaine significantly improved the post-operative analgesia in VR surgery. 0.5% ropivacaine with dexmedetomidine is a good combination for peribulbar block in VR surgery. No hemodynamic disturbance occurred with dexmedetomidine 25µg or Magnesium 0.5 mg in peribulbar block.

Key Words: Peribulbar anaesthesia, dexmedetomidine, magnesium, ropivacaine, levobupivacaine, vitreoretinal

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Introduction

Regional anaesthesia with a peribulbar technique is the preferred anaesthetic modality in patients undergoing vitreoretinal (VR) surgery. This is attributed to the better analgesia, early rehabilitation and increased safety in the presence of systemic comorbid illnesses that co-exist in 47.5% to 70% of patients undergoing VR surgery.[1,2]

The left isomers of bupivacaine, namely ropivacaine and levobupivacaine are preferred due to their long duration of action and reduced systemic toxicity in the event of overdose or accidental intravascular injection.[3]

Multimodal perineural anaesthesia using local anaesthetic (LA) with a synergistic adjuvant has been practised to reduce the cumulative dose of LA, augment block success and provide superior post-operative pain relief. These have also helped to reduce turnover time in a busy ophthalmic operating room. An assortment of opioid and nonopioid adjuncts are available, of which the $\alpha 2$ agonists- clonidine and dexmedetomidine, are a popular class. In one meta-analysis, dexmedetomidine as part of intrathecal or brachial plexus block prolonged duration of action without causing any significant hemodynamic instability.[4] Dexmedetomidine has been used in peribulbar anaesthesia (PBA) to hasten onset of akinesia and prolong duration of analgesia in cataract surgery. It also reduces intra-ocular pressure.[5]

Dexmedetomidine has been postulated to have a central and peripheral site of action.

Magnesium (Mg) is a physiological calcium channel blocker and non-competitive antagonist of N-methyl-D-aspartate (NMDA) receptors. Its site of action is presumed to be on the peripheral nerve where it inhibits calcium influx and blocks the release of excitatory neurotransmitter. Mg has been shown to potentiate LA action and have an opioid sparing effect.[6]

In this study, we aimed to study the efficacy of adding dexmedetomidine or Mg to 0.5% ropivacaine or 0.5% levobupivacaine in PBA for VR surgery. The primary outcome of the study was the time to onset of globe akinesia. The secondary outcome was the requirement of supplementation of peribulbar block prior to or during the surgery and post-operative analgesic requirement.

Materials and methods

This prospective double blinded randomized controlled study was conducted after approval of the institutional ethics committee. One hundred and twenty ASA I-III adult patients aged greater than 18 years, undergoing VR surgery under peribulbar block were included in the study after obtaining a written informed consent. Patients with a history of hypersensitivity to the study drugs, significant cardiovascular disease, impaired mental status, refusal to use local anaesthestic technique and pregnant women were excluded from the study.

All patients underwent routine pre-operative evaluation for VR surgery. Details of the anaesthetic technique and study protocol were explained to the patients at the preoperative visit. No topical anaesthetic or sedative medications were used before or during the block. Details regarding the side, surgery and whether it was a redo procedure were noted.

In the operating room, an intravenous cannula was secured and standard monitors including ECG, pulse oximeter and non-invasive blood pressure were applied. The patients were randomized using a computer generated random number table into one of the four groups. The composition of the study drug used for peribulbar anaesthesia in each of the 4 groups was Group RM (8 ml of 0.5% Ropivacaine + Hyaluronidase 150 IU+ Magnesium sulphate 0.5 mg), Group RD (8 ml of 0.5% Ropivacaine+ Hyaluronidase 150 IU+ 25µg Dexmedetomidine), Group LM (8 ml of 0.5% levobupivacaine + Hyaluronidase 150 IU+ Magnesium sulphate 0.5 mg) and Group LD (8 ml of 0.5% levobupivacaine + Hyaluronidase 150 IU+ 25 µg dexmedetomidine). The total volume was 8.5 ml in all groups.

The peribulbar block was administered by an anaesthesiologist with adequate experience in ophthalmic regional anaesthesia. All healthcare personnel including the anaesthesiologist and surgeon involved in direct patient care were blinded to the study drug.

Peribulbar block was administered using a 24G, 25mm needle using a transcutaneous two injections technique. The first injection was in the inferotemporal quadrant, as far lateral as possible where 4.5ml of the drug administered after negative aspiration. Gentle compression was applied on the eyeball using the middle three fingers. The second injection was given 2mm medial and inferior to the supraorbital notch where the remaining 4 ml of drug was deposited. If the eyeball was firm or tense after the first injection, gentle pressure was applied until the eyeball was soft before the second injection. After the second injection the eye was examined every 30 second for onset of corneal anaesthesia and akinesia. Corneal anaesthesia was assessed by checking the corneal reflex in response to instillation of physiological solution of saline. Onset of motor block was assessed by grading the movement of the eyeball in the four directions- superior, inferior, lateral and medial using a score of 0, 1 or 2. [0= no movement, 1= mild movement, 2= full movement]. A total score ≤1 was considered adequate for surgery. Onset of lid akinesia was assessed by testing the ability of the patient to open, and close the eye and graded as 0 = Complete akinesia, 1 = Partial movement in either or both eyelid margins, 2 = Normal movement in either or both eyelid margins. A lid akinesia score of zero was considered acceptable. The time to onset of sensory and motor block and lid akinesia was noted.

A supplementary block was given in the inferotemporal quadrant with 3 ml of 2% xylocaine if satisfactory anaesthesia or akinesia was not achieved by ten minutes. The supplementation was repeated if the anaesthesia was incomplete after another 5 minutes.

Intra-operative details including the hemodynamic variables (heart rate, blood pressure, SpO2), Richmond agitation sedation scale (RASS) were noted every 15 min for one hour and every 30 minutes thereafter till completion of the surgery. The duration of surgery was noted. Any need for intra-operative analgesia or akinesia was achieved by administering a Sub Tenon's block with 3 ml of 2% xylocaine. The patient was excluded from the study if more than two supplementary injections were needed after the initial peribulbar block. The patient was encouraged to communicate verbally for pain during the surgery. At the end of surgery, the surgeon's satisfaction score was obtained using a grading for the efficacy of anaesthesia. 1 = poor (inadequate for surgery) 2 = acceptable (block is incomplete but the surgeon could proceed) 3 = perfect (effective block). The patient satisfaction is recorded as 1 = Complete dissatisfaction, 2 = some dissatisfaction, 3 = Complete satisfaction. The requirement of intra-operative sedation is also noted. All patients were given an eye patch that was opened only the next morning. The pain relief was scored using a verbal numerical rating scale (NRS) of 0-10 with 0 representing "no pain" and 10 representing "worst pain".

The pain score was recorded at 1h, 2h, 6h and 24 h post op. A pain score ≥4 was treated with tablet paracetamol 650mg. This tablet was repeated not earlier than 6 hours and not more than three tablets in 24h. Pain not responding to paracetamol was treated with intravenous injection of tramadol 50mg. The time to first request for analgesia and total analgesic requirement in 24 hours was noted. The end point of the study was at 24 hours.

Statistics

The sample size was calculated assuming a type I error of 0.05. It was estimated that a sample size of 20 patients in each study group would be required to achieve a power of 80% to detect an effect size (d) of 0.4 in the primary outcome of interest. The statistical software R version 4.0.2 (R core team, 2020) was used for the analysis of the data and the graphs were drawn on Microsoft Excel. Results on continuous measurements are presented as mean ± SD, if parametric and in median (interquartile range), if the distribution is non-Gaussian. Results on categorical measurements are presented in number (%). Chi-square/ Fisher Exact test was used to find the significance of study parameters on categorical scale, non-parametric setting and for qualitative data analysis. Analysis of variance (ANOVA) was used to find the significance of normally distributed continuous data between the three groups. Continuous data with non-parametric distribution was analysed using Kruskal Wallis test. A p value <0.05 was considered significant.

Results

Thirty patients were enrolled in each group. All 120 patients were included in the analysis. There was no statistical difference between the 4 groups with regards to the patient demographics or surgical details. (Table 1)

Table 1: Patient demographic and surgical details

		LD (n=30)	LM(n=30)	RD(n=30)	RM(n=30)	P value
Age (years) (Mean±SD)		**58.1±13.3**	**57.8±9.79**	**58±12.9**	**59.2±7.36**	**0.93**
Gender (M/F)		15/15	25/5	19/11	23/7	0.03*
Weight (kg) (Mean±SD)		62.2±12.8	67.9±9.6	64.6±9.78	65.7±13.4	0.29
ASA grade (I/II/III)		4/21/5	1/24/5	5/17/8	1/27/2	0.13
Resurgery (Y/N)		1/29	4/26	1/29	3/27	0.6
Right eye/Left eye		15/15	13/17	10/20	17/13	0.25
Surgery	**Vitrectomy + oil / gas insertion**	12	13	10	15	0.72
	Cataract+ vitrectomy	16	14	16	14	
	Buckling procedures (including sclera buckle ±vitrectomy ± cataract)	2	3	4	1	
Duration of surgery (min) (Mean±SD)		91.5±35.3	78.5±38.2	84.3±27.5	73.5±30.2	0.19

***- p<0.05, significant LM vs LD**

The characteristics of the peribulbar block in terms of time to onset of anaesthesia and post-operative analgesia are given in Table 2.

Table 2: Onset of anaesthesia and time to first request for analgesia

	LD (n=30)	LM(n=30)	RD(n=30)	RM(n=30)	p value
Onset of corneal anaesthesia (sec)	58±106.6	54.5±117.3	31±28.9	65±154.6	0.29
Onset of globe akinesia (sec)	376±312.4	276.2±298.4	234±248.4	225±291.3	0.21
Onset of lid akinesia (sec)	219.5±280.6	178.9±228.1	144.3±191.1	180±236.7	0.68
Time to first request for analgesia (min)	449±289	405±285	478±298*	280±135*	0.04*

*** : p<0.05, significant RM vs RD, values are in Mean±SD**

There was no difference between the four groups with regards to onset of corneal anaesthesia (p=0.29), globe akinesia (p=0.20) and lid akinesia (p=0.68). No statistical difference existed in the proportion of patients not requesting for any pain relief in the first 24 hours after surgery (p=0.18). Among those requesting for analgesia, the time to first request for analgesia was shortest in RM (280±135 min) and longest in RD (478±298 min) group (p=0.04). The groups were comparable in the need for block supplementation (pre-operative or intra-operative) with 40%, 43.3%, 16.7% and 23.3% of patients in group LD, LM, RD and RM respectively, needing an additional LA injection (p=0.07) (Fig 1). The proportion of patients in these four groups requesting for post-operative analgesia was 63.3%, 53.3%, 80% and 66.7% respectively (p=0.18) (Fig 2).

Fig 1: Need for supplementation of peribulbar anaesthesia

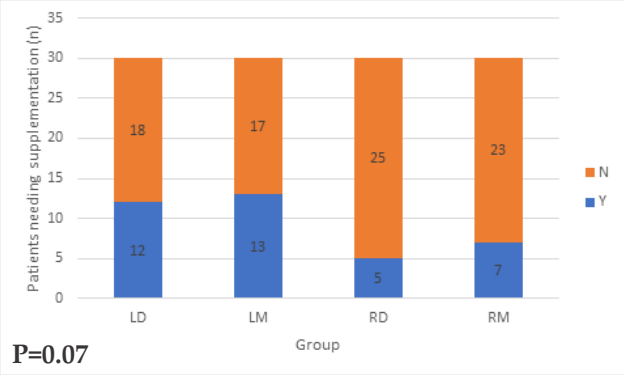
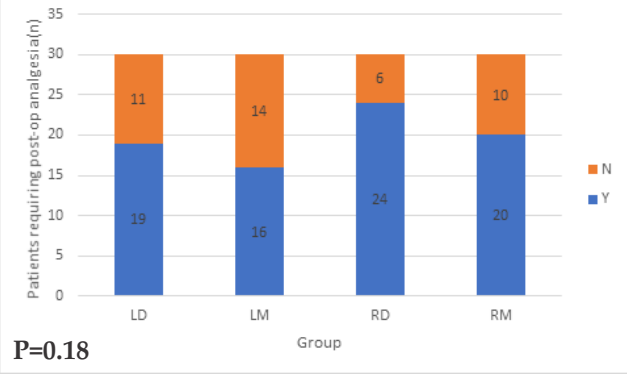


Fig 2: Requirement of post-operative analgesia



The requirement of intra-operative sedation(p=0.86), pain score at 1h, 2h, 6h and 24h was similar across the four groups. The patient as well as surgeon satisfaction scores were similar across the four groups (p=0.60 and p=0.11 respectively) (Table 3).

Table 3: Sedation requirement, pain and satisfaction scores

	LD(n=30)	LM(n=30)	RD(n=30)	RM(n=30)	P value
Need for intra-operative sedation n(%)	7(23.3)	10(33.3)	9(30)	9(30)	0.86
Median NRS at 1h/2h/6h/24h	0/1.5/3/2	0/1/3/2	0/1/4/2	0/2/3/1.5	>0.05
Surgeon satisfaction score(median) 1/2/3	0/3/27	2/5/23	0/7/23	0/2/28	0.11
Patient satisfaction score(median) 1/2/3	0/7/23	1/8/21	0/5/25	0/5/25	0.60

1=poor, 2=acceptable, 3=good: NRS= Numerical rating score

On analysing the hemodynamic parameters, patients in the RD group had significantly lower heart rate than LM at 15 and 60 minutes and mean arterial pressure at 30 and 45 minutes was significantly lower in the LD group compared to RM. No intervention was needed. There was no significant alteration in other parameters like SpO2, respiratory rate and RASS score.

Discussion

Several nonopioid additives have been used in PBA to hasten the onset of action, reduce the need for supplementation, enhance analgesic profile and improve surgeon satisfaction.[7] The uniqueness of this study is that it analyses four groups including various combinations of two long acting LA and two adjuvants in patients undergoing VR surgery.

In a meta- analysis, Li et al found no significant difference in onset time, duration of motor block and patient overall satisfaction between ropivacaine and levobupivacaine in peripheral nerve block though patients receiving levobupivacaine had significantly less request for post-operative rescue analgesia.[8] 0.75% Ropivacaine and 0.5% levobupivacaine compared by other authors in PBA who have shown that 0.5% levobupivacaine has better anaesthetic property than 0.75% ropivacaine in terms of block onset and offset times.[9,10]

In our study, no difference was found between the four groups in the onset time. Although the ropivacaine containing groups (RM, RD) required fewer supplementary injection and took lesser time to achieve globe akinesia but this was not statistically significant. Ghali et al observed that block failure and need for supplementation was greater with 0.5% ropivacaine (25%) than 0.5% levobupivacaine(8.3%) after single injection peribulbar block.[9] This is in contrast to our findings where 0.5% ropivacaine had lower failure rate.

A meta-analysis by Abdallah et al showed that dexmedetomidine in peripheral nerve blocks significantly prolonged motor block and time to first analgesic request but not onset time.[4] Hafez et al opined that 25µg is the most appropriate dose of dexmedetomidine for PBA.[11] The addition of dexmedetomidine has been associated with reduced need for additional LA injection but no such benefit was observed in our study. Similar to our study, Gujral et al found no added benefit in speeding block onset with dexmedetomidine but they observed greater surgeon satisfaction, probably due to co-operative sedation with 20µg dexmedetomidine in VR surgery.[12]

When added to a mixture of 0.5% bupivacaine and 2% lidocaine in PBA for phacoemulsification, Mg has been shown to accelerate onset of akinesia and delay first request for pain relief.[13] Sinha et al observed that adding Mg to PBA improved block onset time without any side effect.[14] Adding 100 mg Mg was not more useful than 50 mg.[15] It has been found to be inferior to fentanyl and rocuronium in establishing condition suitable for cataract surgery in terms of better akinesia and speed of onset.[16,17]

El-Hamid compared Mg with clonidine in PBA and observed that the use of Mg resulted in faster onset while clonidine provided longer pain relief post-operatively.[18]

In PBA, dexmedetomidine and Mg have been compared previously. Mohamed and Genidy found no difference between the groups receiving dexmedetomidine or Mg as an additive in peribulbar block though both enhanced the quality of anaesthesia in terms of speed of onset, patient satisfaction and need for second injection as compared to a mixture of 2% lignocaine and 0.5% bupivacaine.[19] Previous studies have compared dexmedetomidine and Mg with plain LA in PBA in cataract surgery and found significant difference between the control and study groups but did not publish post hoc tests to identify inter-group differences.[20,21] Shoukry et al found that Mg is superior to dexmedetomidine in establishing a block rapidly while dexmedetomidine provided longer post-operative analgesia in VR surgery. They concluded that Mg was a more economical additive with qualities comparable with dexmedetomidine.[22]

Ocular anaesthesia is achieved by blockade of saltatory conduction of the sensory and motor nerves traversing the intraconal area. Extraconal blocks have a longer latency period in view of the greater diffusion barrier for the LA before it reaches its site of action. Winder et al visualised LA in the muscle cone when B scan was done 10 minutes after administration of the peribulbar block.[23] The rapidity of perineural anaesthesia onset is a function of LA used including its lipophilicity, degree of ionisation and pKa.[24] Drugs like hyaluronidase and ocular compression serve to improve diffusion across the muscle cone.[25]

In our study, difference in the time to onset of globe akinesia was not statistically significant in all the groups. The onset time of PBA is a function of the type of LA. RD and RM group with 0.5% ropivacaine showed quicker onset but it didn't provide significant advantage in our study. Dexmedetomidine provided prolonged post-operative analgesia as compared to Mg. No hemodynamic disturbance occurred with dexmedetomidine 25µg or Mg 50 mg in PBA.

Limitation

This study lacks a true control group with only LA. A study including such a group would better explain the rightful effect of adjuvant on LA.

Conclusion

0.5% ropivacaine had a higher success rate for PBA with lesser rate of supplementation needed in comparison to 0.5% levobupivacaine. Addition of dexmedetomidine significantly improves the post-operative analgesia in VR surgery. 0.5% ropivacaine with dexmedetomidine is a good combination for peribulbar block in VR surgery.

Presentation:

Presented at the World Congress of Ophthalmic Anaesthesia, Jakarta, Indonesia in Feb 2020

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All authors have no financial interest to disclose

Conflict of Interest:

There are no conflict of interest.

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Original Article

Comparative Evaluation of Efficacy and Safety of Dexmedetomidine in patients with and without Beta blockers for Vitreo-retinal surgery

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ABSTRACT

Background: Dexmedetomidine is an alpha-2 adrenoceptor agonist that has sedative and analgesic effects with no respiratory depression. There was a need to verify the safety and efficacy of intravenous Dexmedetomidine in patients on therapeutic doses of beta blockers posted for vitreo-retinal surgeries under peribulbar block.

Material and methods: A prospective, comparative cohort study with 35 patients on beta blockers in Group B and 35 patients without beta blockers in Group N, over one year was included in the study. All patients received Dexmedetomidine 0.25µg/Kg loading dose over 10 min followed by maintenance dose of 0.25µg/Kg/hr, titrated to attain 3-4 Ramsay sedation score.. Following fifteen minutes of Dexmedetomidine IV infusion, peribulbar anaesthesia was administered. The vital parameters monitored were heart rate, blood pressure (BP) (systolic, diastolic, mean), respiratory rate, nasal end-tidal carbon di-oxide, SpO_2 and level of sedation.

Results: There was no statistically significant fall in the heart rate or BP in patients on beta blockers (Group B) compared to patients without beta blockers (Group N). No respiratory depression was observed.

Conclusion: Dexmedetomidine is a safe and efficacious sedative in the patients on beta blockers when loading dose (0.25µg/Kg over 10mins) and maintenance dose (0.25µg/Kg/hr) is titrated through close monitoring of vital parameters.

Key Words: Dexmedetomidine, peribulbar block, intravenous Sedation, beta blocker, vitreo-retinal surgeries.

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Introduction

In ophthalmic surgical procedures, regional anaesthesia is preferred over general anaesthesia owing to quicker patient rehabilitation and better analgesia provided post operatively. But, injection of local anaesthesia and lying down still for prolonged period of time can cause pain, discomfort and phobic attack. Sedatives with stable haemodynamics can alleviate these problems. Alpha-2 adrenergic agonists have both sedative and analgesic properties. It augments the local anaesthetic effects by altering trans membrane potential and ion conductance at locus ceruleus in the brainstem. Also, it produces stable haemodynamics and decreased oxygen demand due to enhanced sympatho-adrenal stability.

Dexmedetomidine ($C_{13}H_{16}N_2$) is an highly selective alpha-2 adreno-receptor agonist with sedative, analgesic and anxiolytic properties with minimal respiratory depression.[1,2] α-1 to α-2 ratio of 1:1600 makes it as a highly selective α-2 agonist compared to clonidine, thus reducing the unwanted side effects involving α-1 receptors. Dexmedetomidine-induced biomimetic sleep states benefit patients by eliminating drug-induced neurocognitive dysfunction that result from unintended drug action in sensory, memory encoding, and cognitive processing circuits. Early (Dexmedetomidine-induced) and late (Dexmedetomidine-associated) N2, N3 sleep stages are biomimetic.[3]

It is increasingly being used as a sedative for monitored anaesthesia care (MAC) due to its analgesic properties,"conscious sedation," and lack of respiratory depression.[4] It also provides better patient satisfaction, less opioid requirements, and less respiratory depression than placebo rescued with midazolam and fentanyl.[5] Peribulbar block (PBB) with Dexmedetomidine provide conscious sedation, decreases pain during performance of block,[6] lowers intraocular pressure,[7] prevents hypertensive response to anxiety, improves patient's comfort[8] and thus provide potentially better operating conditions for the surgeon. The usual dose for procedural sedation is 1 μg/ kg, followed by an infusion of 0.2 μg/kg/hr. Its onset of action is less than 5 minutes and the peak effect occurs within 15 minutes. As the pharmacologic effects can be reversed by the α2-AR antagonist Atipamezole, Dexmedetomidine provides hypnotic sedation that can be reversed readily.[4]

Intraoperative bradycardia and hypotension are major concerns with the above recommended dose. But, when it is infused at a reduced loading dose of 0.25μg/Kg over 10min followed by titrated maintenance dose it provides stable hemodynamics. Avoiding narcotic analgesics reduces post-operative nausea and vomiting which is an additional benefit.[9] In the adult studies, Dexmedetomidine yielded significantly lower pain score levels compared to the other sedatives (31.25%) and significantly more patient satisfaction (68.2%).[10]

The purpose of this study was to evaluate efficacy and safety of intravenous Dexmedetomidine in patients with or without beta blockers undergoing vitreo-retinal surgeries under regional anaesthesia. Noninvasive measures of respiratory status with sufficient accuracy and reliability are preferred. Pulse oximetry is a valuable indicator of oxygenation but cannot substitute capnography as an indicator of ventilation, given oxygenation and ventilation are distinctly different physiological processes and thus require separate but complementary monitoring methods.[11] The primary aim of the study was to compare the haemodynamic parameters, respiratory parameters and the level of sedation. The secondary aim was to evaluate the role of nasal capnography ($EtCO_2$) during procedural sedation for vitreo-retinal surgeries.

Material and methods

This observational cohort study was started after approved by institutional ethics committee [IEC NO:2017/10 Dt: 15.05.2017] and clinical trial registry [CTRI/2018/08/015387]. Written informed consent was obtained from all the patients. Sample size was based on the average number of patients on beta blockers per year posted for vitreo-retinal surgeries under intravenous sedation and PBB in the last three years. Total 70 patients posted for elective vitreo-retinal surgery under intravenous sedation and PBB, over one year were included.

Patients were divided into two groups (n=35), Group B, on beta-blockers and Group N, not on beta-blockers.

Patients aged between 40 to 75 years, belonging to ASA grade 1 to 3 were included. Patients aged more than 75 years, having basal heart rate less than 50 beats per minute, severe left ventricular dysfunction (Ejection fraction <35%), hypovolemia with systolic blood pressure <90mm Hg, heart blocks, chronic renal failure and hepatic impairment, bleeding or coagulation abnormalities, psychiatric diseases and having history of allergy to the local anaesthetic or dexmedetomidine were excluded from the study.

Pre anaesthetic check-up was done and fasting of 3-4 hours was ensured. Baseline vitals (heart rate, systolic, diastolic, mean blood pressure (BP), respiratory rate) were noted and all patients received oral Alprazolam 0.25mg-0.50mg as anxiolytic premedication and oral Pantoprazole 40mg with Domperidone 30mg. Patient was shifted to operation theatre, and monitors were connected. Intravenous access was secured and maintenance fluid was started. Vitals parameters (heart rate, systolic BP, diastolic BP, mean BP, respiratory rate, SpO_2, nasal $EtCO_2$ at zero minute was noted before starting Dexmedetomidine IV sedation.

Dexmedetomidine concentration 5µg/ml (dilution 100µg in 20 ml normal saline) loaded in a 20ml syringe and delivered through a syringe pump.

All patients received loading does of Dexmedetomidine 0.25µg/Kg over 10 min followed by maintenance dose of 0.25µg/Kg/hr, titrated to attain 3-4 Ramsay sedation score.8 Supplemental oxygen 3-4 liters per min via nasal cannula was given to all patients, till the end of the surgery. Following 15 mins of infusion, PBB with 8ml of local anesthetic (4 ml of 0.5% bupivacaine plus 4ml of 2% lignocaine and hyaluronidase 15 IU/ml) was given.

Patients were evaluated for motor akinesia from grade 0-2, zero [free movement], one [partial movement and 2 [no movement]. This was done for each of four recti, levator superioris and orbicularis oculi muscles. The maximum score 12, indicated total akinesia. An eye with a score less than 8 received a repeat injection with the same local anesthetic mixture (not exceeding maximum safe dose) and recorded. Vital parameters were noted every 5 minutes for the first 15 minutes and then every 15 minutes till the end of the surgery. The bed side monitoring of vital parameters continued every 30 minutes for 2 hours in the post- operative ward.

Critical values of vital parameters are shown in Table 1.

Table 1: Critical values of vital parameters

CRITICAL VALUES								
	HR (bpm)	**Blood Pressure (mmHg)**			**RR**	**$EtCO_2$**	**SpO_2**	**LOS**
		Systolic	**Diastolic**	**Mean**				
High	>100	>180	>100	>140	>30	>40	NA	>4
Low	<50	<90	<60	<60	<10	<15	<90	NA

HR – Heart rate; bpm – beats per minute

Adverse effects like bradycardia, hypotension, respiratory depression, deeper level of sedation (level >/=5) were noted and treated. Bradycardia was considered as heart rate <50bpm and managed with IV Atropine 10 mcg/Kg or IV glycopyrrolate 0.2mg in IHD patients. Hypotension was defined as SBP <80mmHg or fall of >30% from baseline and treated with foot end elevation followed by bolus IV fluid 200-300ml, if no response then IV ephedrine 6mg considered. Respiratory depression was managed with no intervention for RR>10 / min and SpO_2 > 92%. Patient was awakened and nasal oxygen increased to 4litres / min if RR was < 10 / min and /or SpO_2 <90. In persistent respiratory depression, then plan was to stop Dexmedetomidine infusion. With deeper levels of sedation (level >/=5) maintenance dose was titrated and stopped when necessary. Dexmedetomidine infusion was stopped 10min prior to the end of the surgery (as informed by the surgeon). Post-operative pain was noted and treated with oral analgesics.

Statistical Analysis

The data was entered in Microsoft Excel and statistical analysis using Z-test. Graphs were constructed for 95% confidence interval for all parameters from baseline to 150mins. The results are considered statistically significant whenever p value is <=0.05.

Results

The data of 70 patients were collected, tabulated and analyzed. Demographic data were comparable between the groups (Table 2). The difference in heart rate between the two groups at various time intervals throughout the surgery was comparable but not statistical significance (p = 0.38). There was no statistically significant fall in the heart rate or mean BP in Group B compared to Group N, (Figure 1). P value of 0.50 at 10 mins after completing loading dose was observed. Systolic and Mean BP was comparable in both the groups, (Figure 2). At 45 mins after starting Dexmedetomidine IV infusion in Group N, diastolic BP was significantly decreased (p value=0.04), but no active intervention was required, (Figure 3). There was no statistically significant difference in respiratory rate, SpO_2 and $EtCO_2$ in both the groups.

After the loading dose of Dexmedetomidine IV infusion over 10mins, the level of sedation at 15mins was observed as Level 2 and level 4 at 60mins in both the groups, (Figure 4). There was no statistically difference in both the groups. P value was 0.5 at all-time intervals throughout the procedure.

Table 2: Demographic profile of the patients in both the Groups

Parameters		Group B (n=35)	Group N (n=35)	t-value	p value
Age (years) (mean± SD)		60.97 ± 10.15	54.57 ± 17.04	1.909	0.031
Weight (Kg) (mean±SD)		73.01 ± 12.90	66.14 ± 12.27	2.281	0.013
Gender: Male/ Female		20/15	22/13	-	-
ASA Status	ASA 1	0	2	1.456	0.073
	ASA 2	4	18	2.021	0.022
	ASA 3	31	15	4.597	P < 0.001
Mean duration of surgery (min) (mean ± SD)		105 ± 24.87	102 ± 33.11	0.469	0.320 (one-tailed) and 0.640 (two-tailed)

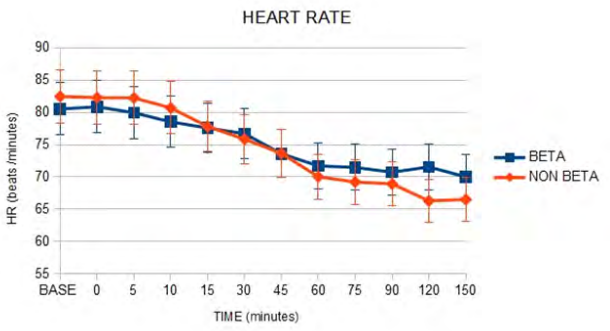

Figure 1: Heart Rate variations among the two groups at different time points

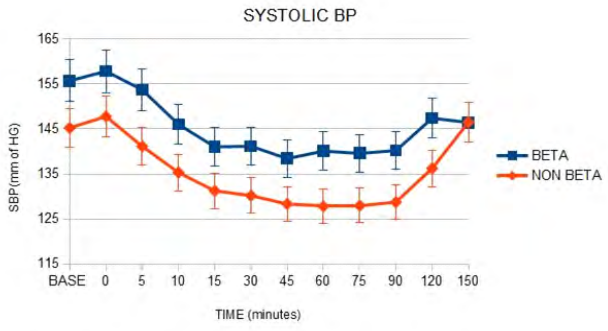

Figure 2: Systolic Blood Pressure (SBP) variations among the two groups at different time points

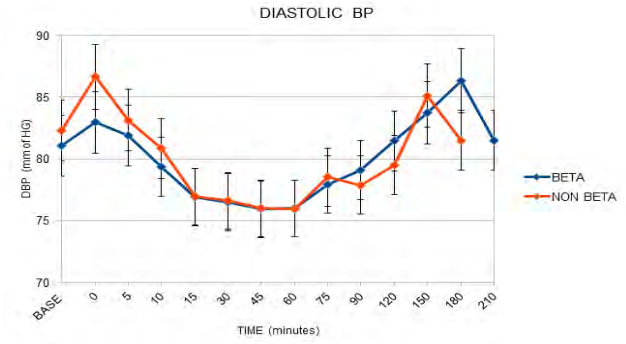

Figure 3: Diastolic Blood Pressure (DBP) variations among the two groups at different time points

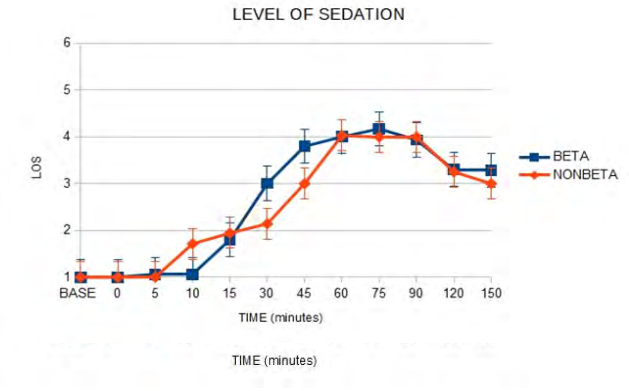

Figure 4: Level Of Sedation (LOS) variations among the two groups at different time points

Discussion

Dexmedetomidine is a highly selective alpha-2 agonist that provides anxiolysis and controlled sedation without respiratory depression. It has organ protective effects against ischemic and hypoxic injury, including cardio-protection, neuro-protection and reno-protection.[12] It produces dose dependent sedation with no respiratory depression and only modest haemodynamic effects.[13] It also has sympatholytic and anti-nociceptive effects that allow hemodynamic stability during surgical stimulation. Intravenous Dexmedetomidine exhibits linear pharmacokinetics with a rapid distribution half-life of approximately 6 minutes and a terminal elimination half-life of approximately 2 hours. It gives protection against apoptosis in retinal Ischemia/reperfusion injury in rats.[14] During pars plana vitrectomy under local anaesthesia, if need arises for cryopexy, scleral buckle or intense laser retinopexy, then sedation with Dexmedetomidine can help with good intra-operative and immediate post-operative hemodynamic control with possibility of supplemental rescue analgesia.[15]

It produces a biphasic response of the blood pressure i.e. transient hypertension (α2B - Adrenergic Receptors) followed by hypotension (α2A- Adrenergic Receptors). Bradycardia action of Dexmedetomidine is

due to the vago-mimetic action and decreased tachycardia (block of cardio acceleratory nerve). Effect of Dexmedetomidine on peripheral vasculature is vasodilation (Sympatholytic mediated) and vasoconstriction (smooth muscle cell receptor mediated). Most frequent adverse effects reported in the literature are bradycardia and hypotension mainly with loading dose of 1 μg/ kg. This can be avoided by omitting the loading dose or limiting the loading dose to 0.4 μg/ kg.[16]

Other side effects reported to occur are sinus pause/arrest, orthostatic hypotension, dry mouth. Intranasal Dexmedetomidine in elderly subjects has sedative effect, but causes a high incidence of profound and sustained hypotension irrespective of β-blocker use.[17]

Dexmedetomidine at loading dose of 0.25mcg/kg over 10 mins is a comparable, safe and effective primary sedative alternative to traditional midazolam-fentanyl combination for vitreoretinal surgery under peribulbar anaesthesia. It can be a preferred mode of sedation for better control of intraoperative hypertension. In our study there was no significant fall in the heart rate in both the groups. Atropine was not required in any patient in both the groups. There were no significant changes in the systolic blood pressure in both the groups. There was no significant fall in diastolic blood pressure in both the groups except in three patients at 45 mins in the Group B, but these three patients did not require any drug intervention and recovered by stopping the Dexmedetomidine infusion. There was no specific confounder in these three patients.

Dexmedetomidine sedation during retinal surgery improved both patient's and surgeon satisfaction without respiratory complication.[18] It is a safe and effective agent for sedation in critically ill patients.[19] In our study there was no significant change in the respiratory rate, nasal $EtCO_2$ and SpO_2 along with stable the level of sedation (Ramsay sedation score between 2-4) in both the groups.

Conclusion

Dexmedetomidine is a safe and efficacious sedative in patients on beta blockers in low doses (loading dose of 0.25μg/Kg over 10mins and maintenance dose of 0.25μg/Kg/hr) with close monitoring of vital parameters.

Financial disclosure

All authors have no financial interests to disclose.

Conflicts of Interest

There are no conflicts of interest.

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Review Article

Oculocardiac Reflex: Know-How?

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ABSTRACT

This review article presents an overview of the current literature concerning the Oculocardiac reflex (OCR). It's a reflex in which bradycardia or arrhythmia occurs due to stretching of the extraocular muscle or increase in the eye ball pressure. It is mostly encountered during squint surgery. Mechanism, cardiac effects and the various predisposing factors leading to OCR are described. The interesting association of OCR with postoperative nausea and vomiting (PONV) is also described. Last but not the least, chapter also presents a detailed guide to preventing and managing this phenomenon.

Key Words: Oculocardiac reflex, bradycardia, strabismus, vagus, extraocular muscles (EOM), autonomic nervous system (ANS)

History

The Oculocardiac reflex (OCR) is a physiological response of the heart to physical stimulation of the eye or the ocular adnexa, characterized by bradycardia or arrythmias, which sometimes leads to cardiac arrest. It was in 1908, both Bernard Aschner and Guiseppe Dagnini, independently reported cardiac slowing after pressure on the eyeball.[1,2]

Aschner demonstrated by animal investigations that the afferent impulse is carried via the ophthalmic division of the trigeminal nerve to the vagal centres, from where the impulses are relayed to heart via the vagus nerve.

The importance of OCR was brought to light when Sorenson and Gilmore in 1956 reported that traction on the medial rectus muscle caused cardiac arrest in a patient.[3] Following this fatal cardiac arrest as a response to the OCR been reported by Walton (1957), Kirsh and others (1957) Mallinson and Coombes (1960), and Smith, Douglas and Petruscak (1972).[4-7] Alexander reported 90% incidence of positive OCR in children under 15 years of age using the criteria of 10% change in the heart rate as a positive OCR.[8] This reflex is especially sensitive in neonates and children, as their vagal tone in higher.[9]

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However, it is also reported in adults. The overall incidence of OCR, both reflex bradycardia and dysrhythmias is higher with general anesthesia compared with regional anesthesia.[10]

Positive OCR is defined as dysrhythmia or bradycardia of 10% or more below relative baseline heart rate resulting from traction of an extraocular muscle.[11] Vrabec et al[12] and Eustis et al[13] defined it as a 10% decrease, while Karhunen et al[14] defined it as a 20% decrease in baseline heart rate. Other reports defined it as at least a decrease of heat rate 10 beats per minute at any time during surgery and persisting for more than 15 seconds as study criteria and OCR as slowing of heart rate by more than 20% or arrhythmia during traction irrespective of heart rate.[15]

Braun and his colleagues divided the haemodynamic response of OCR into two phases. The first phase is cholinergic, causes bradycardia and the second phase of the reflex, adrengeric, is described as counter-regulation (CR). The counter-regulatory process maintains the heart rate during traction at the extraocular muscles after the bradycardic reflex has been initiated.[16]

Mechanism

The trigeminocardiac reflex (TCR), previously known as the OCR or Aschner phenomenon, is a relatively well-known reflex that may arise through manipulation of the trigeminal nerve, via its pathway from the cranial base to its nerve endings on the mouth, jaws, and face.

The reflex is mediated by nerve connections between the trigeminal cranial nerve and the vagus nerve of the parasympathetic nervous system. The afferent tracts are derived mainly from the ophthalmic division of the trigeminal nerve. These afferents synapse with the visceral motor nucleus of the vagus nerve, located in the reticular formation of the brain stem. The efferent tract is carried by the vagus nerve from the cardiovascular center of the medulla to the heart, of which increased stimulation leads to decreased output of the sinoatrial node (figure 1).

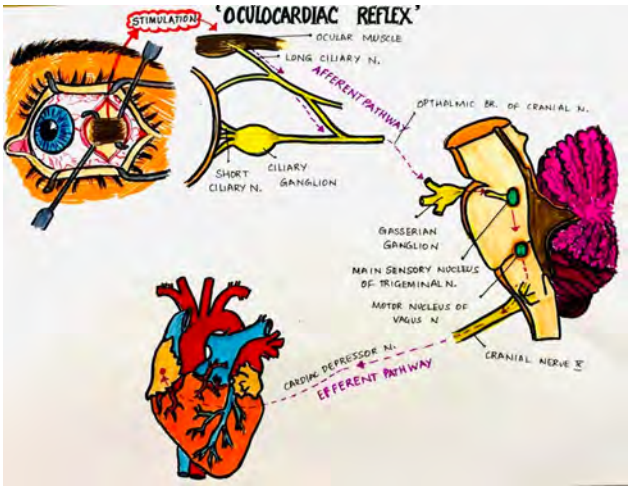

Figure 1. Afferent and efferent pathways of oculocardiac reflex

This reflex sets in due to stretching of the extraocular muscle or increase in the eye ball pressure. In clinical practice, OCR is most often encountered during squint surgery in paediatric age group. It can also occur in repair of detached retina,[10] especially during tagging of extraocular muscles, enucleation of eye,[17] intraorbital injection of local anaesthetics, following digital pressure to the eye, pinching of the conjunctiva with a forceps and post-operative ocular pressure due to bandage.[18]

The reflex is also evoked by contact lens,[19] repair of nasal fracture under general anaesthesia,[20] and by stimulation of eye lids (blepharocardiac reflex),[21] face and oral cavity.

Predisposing factors

The various factors that can increase the risk of OCR reviewed by Scott Lang and van der Val are hypercarbia, hypoxaemia, hypoventilation, acidosis, light anaesthesia, young age due to higher resting vagal tone, pharmacological agents such as potent narcotics (sufentanil, alfentanil), β blockers and calcium channel blockers, and the nature of the provoking stimulus—namely, strength of stimulus, and duration.[22] Though retrobulbar anaesthetic infiltration is a method of prophylaxis to prevent OCR (figure 1), yet still before the block has taken full effect, the reflex may be induced by stimulus of needle disturbance, retrobulbar bleeding, or even the anaesthetic solution (2.5 ml) which probably has effects on intraorbital pressure within a short time. Ocular compression following regional block was found to be the most common triggering event in precipitating the OCR.[23]

Cardiac effects

OCR may manifest as bradycardia, bigeminy, ectopic beats, junctional (nodal) rhythm with disappearance, inversion or shift of the P wave on the ECG, AV block and cardiac arrest.[7,24] Initial baseline heart rate has no influence on the incidence of OCR: tachycardia is therefore not protective.

Ohashi found that occurrence of reflex bradycardia was a graded phenomenon as a function of the tension applied to the extraocular muscles. In addition to the depth of the bradycardia, the period of time to reach the minimum heart rate also became shortened as the tension increased.[25]

Thus, Ohashi suggested that the depth and occurrence of bradycardia in the OCR were closely related to the strength of tension, and that the responses of extraocular muscles to stretch were quantitatively transmitted to the heart and then suppressed the heart rate. He also showed that there were differences of depth and threshold of the reflex as well as the incidence among the medial rectus, the inferior oblique, and the lateral rectus muscle. Stretch on the medial rectus and the inferior oblique evoked the reflex in all the patients tested, whereas, in the lateral rectus, the reflex could be induced only in about 50% of patients. The discrepancy in heart rate sensitivity between surgical extraocular muscle tension and ocular compression might be due to different sensory receptors and brain stem processing for the trigeminal mediated OCR.

Vagal escape

There is a tendency for the patient to adapt to the vagal tone with the traction of the extraocular muscle with the heart rate returning to the pre-traction rate.[26] The OCR normally fatigues with repetitive stimuli and thus lesser decrease in heart rate is observed when the second muscle is stimulated compared to first muscle traction.[27,28]

This was pointed out by Platen (1958).[27]

Association between OCR and Postoperative nausea and vomiting (PONV) in strabismus surgery

PONV is particularly common after strabismus surgery in children. In addition to the distress caused to child and parent, it is also the most frequent cause for unplanned admission after day-case surgery. Although many factors may influence the occurrence of PONV, its particular propensity for occurring after strabismus surgery has led to the theory that an oculo-emetic reflex is responsible.

This has been described as a reflex resetting of the vomiting centre in the medulla following stimulation of the ophthalmic division of the trigeminal nerve during extraocular muscle manipulation.[28] Allen et al found that there was a significant association between a positive intraoperative OCR and PONV. Children with a positive OCR were 2.6 times more likely to vomit than those without the reflex.

It is clearly desirable to reduce the incidence of both the OCR and PONV, and possible methods for prophylaxis include pharmacological inhibition of either the afferent or efferent pathways of the reflex arc. Although prophylactic anti-cholinergic agents such as atropine/glycopyrrolate prevent the bradycardia produced by the OCR there are conflicting reports as to whether they lower the incidence of post-operative emesis.

This may imply that the effect of the OCR on the vomiting center in the medulla may not be reliant purely on cholinergic pathways but on other neurotransmitters.

Local anaesthetic infiltration of the orbit has been shown to inhibit the OCR, by blocking the afferent limb of the reflex. Thus Allen et al, were trying to detect whether sub-tenon's infiltration before muscle traction can reduce the subsequent emesis in the postoperative period.[28]

Prevention of OCR

To avoid any untoward effect of OCR it is recommended to monitor ECG, pulse oximetry, encourage surgeon to be gentle and ensure adequate depth of anaesthesia during surgery.

A quick traction on extraocular muscle provoked a reflex in 87% of instances, whereas progressive traction did so in only 51% of instances. Thus, to reduce the incidence of OCR occurring during strabismus surgery, minimal and gentle manipulation of the extraocular muscles must always be employed by the surgeons.[29]

The regional eye block (peribulbar or retrobulbar) can block the afferent limb of the reflex, while intravenous injection of an anti-muscarinic acetylcholine (ACh) antagonist, such as atropine or glycopyrrolate can block or attenuate the efferent limb of the reflex.

Topical lignocaine applied to eye muscles also significantly attenuates the OCR.[30]

Grover and his colleagues have shown that local anaesthesia produces less bradycardia

and ectopic arrhythmia and is better than general anaesthesia for surgeries in which traction of extraocular muscle is required.[10]

Incidence of OCR was found to be lesser with induction of general anaesthesia with ketamine IV compared with induction using Pentothal sodium / propofol IV.[24] Ketamine by increasing the sympathetic tone, counteract the vagal stimulation during the first phase of the OCR.

Treatment

If bradycardia does occur, removal of the inciting stimulus is immediately indicated, and is essential for successful termination of OCR. The surgeon operating on the eye should be asked to cease their activity and release the applied pressure or traction on the eyeball. This often results in the restoration of normal sinus rhythm of the heart. If not, the use of atropine or glycopyrrolate will likely successfully treat the patient and permit continuation of the surgical procedure. If bradycardia persists or is worrisome, the patient may be given atropine (10 to 20 mcg/kg, IV) or glycopyrrolate (10 mcg/kg, IV). The initial effects of atropine should be evident within 20 seconds, and the maximal response is observed after 80 seconds.[16]

Conclusion

Prevention of OCR requires awareness of the anatomical structures involved, good understanding between the surgeon and anaesthesiologists, and knowledge of the pre-disposing factors known to favor or evoke these reflexes.

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Conflict of Interest:

Nil

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Case Report

Retinal Detachment Surgery in the presence of Haemophilia under regional anaesthesia

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ABSTRACT

Objective: Patients with hereditary bleeding disorders rarely present with intraocular complications. Conducting posterior segment surgery in a haemophiliac, where achieving a perfect haemostasis is in jeopardy and in turn, poses a challenge to predict the outcome of surgery. Awareness of retinal surgical management of such conditions can improve surgical decisions.

Case description: An 55 year old gentleman, known case of haemophilia and who has recovered from COVID infection recently was posted for retinal detachment surgery in his left eye (LE). At the age of seven, he was diagnosed to have haemophilia with multiple joint haemarthroses and arthropathy. His present co-morbid conditions include Type 2 diabetes and hypertension. As per the protocol drawn by the Haematologist, on the day of surgery, 2,250 IU of the recombinant factor VIII [Eloctate] was administered slowly over fifteen minutes. Thirty minutes later, patient was shifted to operation theatre. Under episcleral block, 25 G vitrectomy was conducted on a phakic myopic eye with inferior retinal detachment and peripheral tear. Retinotomy was performed to remove the band and drain all the fluid. Surgery was completed after tamponading with silicon oil. His post operative recovery of the eye condition was found to be satisfactory.

Conclusion: Bleeding disorders present a dilemma in the surgical management of retinal detachment in a high myopic with a known case of hemophilia and recent Covid exposure. Close follow up with Haematologist to conduct the retinal surgery under the cover of reconstituted recombinant Factor VIII went a long way in achieving the desired results.

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Introduction

Haemophilia is the most common and serious X-linked inherited coagulation factor deficiency. Multiple subtypes of haemophilia exist, 85% of which are of the factor VIII deficiency or haemophilia A type. Clinically, however, haemophilia are all virtually identical and manifest in the same way, and is due to the similarity in their patho-physiologies, affecting the same coagulation pathway of the human body, albeit at different points for each type.[1] A deficiency of a factor in a certain step identifies the type of haemophilia or manifesting as prolonged bleeding into the joints and muscle. Other bleeds, which include ocular bleeding and trauma, comprise only 5% of reported cases of initial presentation of haemophilia. Ocular haemorrhage can be from both traumatic and non-traumatic causes. Diagnosis and management of haemophilia in consultation with the haematologist is more vital in these patients who are to undergo ocular surgery.[2]

In 2014, a meta-analysis[3] found that orbital haemorrhage was attributed to inherent bleeding disorders in only 19% of reported cases in literature over the past 30 years. Of these 24 cases, only 0.8% of the total was due to haemophilia, showing the rarity of non-traumatic ocular bleeding as a presentation of haemophilia. Traumatic orbital haemorrhage is more common. However, bleeding from ocular trauma as the only initial manifestation of an underlying haemophilia condition is rare.[4]

Haemophiliac patients usually present with other forms of prior bleeding episodes. Paying attention to disproportionate decrease in the visual acuity to the amount/manner of trauma should therefore alert the attending ophthalmologist to the presence of a more serious underlying condition. In haemophiliac patients, continuous traumatic orbital bleeding causing proptosis of the globe could actually develop into total peribulbar haemorrhage within 24 hours.[5]

Case Description

A 55 year old business man presented with complaint of diminution of vision in the left eye (LE) due to retinal detachment for 6 months. He had postponed the immediate surgical intervention due to fear of the prevailing Covid pandemic. Subsequently, he had Covid infection and was hospitalised for treatment. His left eye is myopic since childhood; and he was treated for haemophilic multiple joint hemarthroses, arthropathy from the age of 14 years. This resulted in painful and restricted right elbow, left hip and knee joints.

His present co-morbid conditions include type 2 diabetes and hypertension. His surgical history included left knee and hip replacement ten years back. Three years back, he underwent laparotomy to drain left psoas hematoma for peritoneal bleed. Following laparotomy, he developed urinary infection, renal failure, type 1 septicaemia and blood transfusion induced Hepatitis C.

He gave no history of ocular trauma or surgery Family history confirms that his 50 years old cousin is also a haemophiliac. He presented for retinal detachment surgery with treatment protocol for haemophilia before surgery and with arrangements to report back to his haematologist at a Medical centre after surgery for further care and follow-up. His preoperative eye examination revealed: high myopia in both eyes and LE also had sub-total rhegmatogenous retinal detachment with macula off and proliferative vitreo-retinopathy (PVR).

On admission, a detailed informed consent was obtained for vitrectomy to address the detachment in the LE under episcleral block. He was counselled about the indication for the proposed surgery to save his vision; and the unforeseen prognosis in presence of his bleeding disorder.

As per the protocol drawn by the Haematologist, on the day of surgery 2,250 IU reconstituted recombinant factor VIII [Eloctate] was administered slowly over 15 minutes. Thirty minutes later, the patient was shifted to operation theatre. Episcleral block was administered with 4 ml of 2% Lignocaine with 1 in 200,000 adrenaline, 200 IU of hyaluronidase and 4 ml of 0.75% Ropivacaine. 25 G vitrectomy was conducted on a phakic myopic eye with inferior retinal detachment and peripheral tear. Retinotomy was performed to remove the band and drain all the fluid. Surgery was completed after tamponading with silicon oil.

The anaesthesia concerns included the possibility of retrobulbar hemorrhage with serious consequences following needle or cannula based regional anaesthesia block. He was discharged and sent back to his haematologist at the Medical Institute. At the Institute, he received an additional dose of recombinant factor VIII before discharge. The post operative course was found to be uneventful expect for high intraocular pressure on day seven, which was managed medically.

Discussion

Robert A Rubenstein et al[6] reported ocular complications in 123 patients with hemophilia. In one of these patients severe spontaneous retrobulbar hemorrhage resulted in loss of vision in the affected eye. Prolonged bleeding followed extraocular muscle surgery, enucleation, chalazion surgery, and cataract extraction was observed in other patients. In addition, 20 patients with haemophilia had sub-conjunctival haemorrhage or other haemorrhages in the eye.

Jijina F et al[7] published their experience of eye surgery in five patients with haemophilia of varying severity aged between 8 and 75 years. The surgery included intraocular lens implantation, trabaculectomy and vitrectomy. They reported successful outcome with haemostasis with moderate dose of clotting factor concentrate along with oral epsilon aminocaproic acid and IV desmopressin wherever feasible.

They also treated a patient with 32% of factor VIII presenting with hyphaema following ocular surgery conducted without knowing the underlying hemophilic condition. They conclude that satisfactory eye surgery is possible in presence of haemophilia with recombinant factor VIII therapy.

Luis Miquel Aquino and Felice Katrina Ranche[5] reported an eight year old Filipino boy presenting with traumatic hyphaema with corneal staining following a blunt trauma in the right eye. Sub-retinal hemorrhage was seen on ultrasound. The patient underwent anterior chamber washout with temporary keratoprosthesis and pars plana vitrectomy with silicon oil tamponade. Nineteen days later, he presented with recurrence of hyphema with a new onset of proptosis and retrobulbar hemorrhage. A bleeding disorder was suspected at this point. Further probing revealed a family history of prolonged bleeding time in an X-linked genetic inheritance pattern spanning three generations. Laboratory testing revealed factor VIII deficiency, diagnostic of haemophilia A. No further surgery was done.

Our 55 years old wheelchair bound haemophilic patient presented with complaint of diminution of vision in the LE for six months due to retinal detachment and also had type 2 diabetes and controlled hypertension. He was treated for multiple joint haemarthroses from the age of 14 and had undergone left knee and hip replacement and laparotomy for left psoas hematoma. Meanwhile he had Hepatitis C, urinary infection, renal failure and type 1 septicaemia. Recently he suffered Covid infection. He gave no history of ocular trauma or surgery. He presented for RD surgery with haemophilia treatment protocol from his referring haematologist. After surgery, he was admitted at medical institute for further care and follow-up.

Patient received recombinant factor VIII 30 minutes before shifting to OT. Our patient did not have petechial lesion or haemorrhagic discoloration at the IV cannulation site indicating presence of near normal clotting process. 25 G Micro-Incision Vitrectomy Surgery (MIVS) was conducted on a phakic myopic eye with inferior retinal detachment with peripheral tear under episcleral block. We planned to modified ocular surgery in this patient with haemophilia like regular circumferential scleral buckling procedure as part of retinal surgery was not considered since it involved extensive dissection and handling of structures in presence of haemophilia; routine pneumatic retinopexy with air or heavy gas tamponading was not considered since the patient had to remain in face down position for a long period of time. We performed retinotomy to remove the band and drain all the fluid. Surgery was completed after tamponading with silicon oil. After surgery, he received an additional dose of recombinant factor VIII before discharge.

His post operative course was found to be satisfactory, except for high intraocular pressure on day seven, which could be managed medically.

Conclusion

Bleeding disorders like haemophilia present a dilemma in the surgical management of retinal detachment in a high myopic. Our patient presented with a history of recent Covid infection with implication of cytokine storm and haemorrhages in the lungs. Close liaison with haematologist and following a well drawn protocol to conduct the retinal surgery under the cover of recombinant Factor VIII goes a long way in achieving the desired results.

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Brief Communication

Nitrous oxide and the Eye

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Fewer anaesthetists seem to be using nitrous oxide (N_2O) off late, presumably due to a combination of factors such as reported side effects, concern for environment and availability of newer agents.[1] However, a recent review concluded that it is not yet time to abandon it completely due to emerging evidence for newer applications as also better understanding of its benefits and risks.[2] Concerns about its use in ophthalmic anaesthesia mostly stem from fear of causing adverse effects due to postoperative nausea and vomiting (PONV) and intraocular pressure (IOP) issues. This brief report will look at the relevant evidence and attempt to make recommendations.

There are three main scenarios where N_2O is of relevance to the eye in discussions relating to general anaesthesia (GA):

- Ophthalmic procedures not involving insertion of intraocular gas (IOG)
- Ophthalmic procedures involving IOG
- Non-ophthalmic procedures in the first three months following an eye procedure.

1) Ophthalmic procedures not involving IOG: These procedures can involve any part of the eye including lens, cornea, extra-ocular muscles, as also for glaucoma, dacryocystorhinostomy, oculoplastic etc. Majority of these are done under local anaesthesia but certain groups of patients need GA. N_2O itself does not seem to affect the IOP much. IOP increased by a maximum of 2.4 mmHg from baseline in healthy volunteers when N_2O was administered.[3] Of interest, nitric oxide plays an important role in lowering / regulating IOP and is the subject of recent research.[4] Due to its low solubility, N_2O contributes to the 'second gas effect' leading to faster induction and improved arterial oxygenation compared to a combination of oxygen and air.[2] This is useful for inhalational induction of anaesthesia especially in children where rapid induction is desirable. N_2O has 'MAC-sparing properties' which allows lower concentration of volatile agents, improved haemodynamic properties and decreased risk of respiratory depression.[5]

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As a high proportion of patients undergoing ophthalmic surgery have systemic co-morbidities, this property is very useful. N_2O allows faster emergence from anaesthesia due to its short context-sensitive elimination half-life and reverse 'second gas effect' when inhaled volatile agent is stopped.[2] PONV is not an issue if the duration of exposure is less than 75 minutes and when pharmacological prophylaxis is used.[6]

Nevertheless, it may be prudent to avoid N_2O for certain procedures known to be associated with increased incidence of PONV such as strabismus repair. N_2O is a greenhouse gas and can contribute to ozone depletion. Although medical use of N_2O is estimated to represent < 1% of global N_2O pollution, routine use of low flow anaesthesia will further reduce this.[7] Due to its multiple advantages, for the majority of procedures not involving IOG, N_2O can be safely used for general anaesthesia.

2) Ophthalmic procedures involving IOG: IOG is used as a tamponade agent in vitreo-retinal surgery such as retinal detachment and macular hole repair. Following intravitreal administration, gas surface tension holds the retina against the choroid allowing retinal pigment epithelial pump to remove sub-retinal fluid and aid healing of the retinal breaks. IOG is also being used in endothelial keratoplasties (lamellar corneal grafts) either during the initial procedure or for "re-bubbling" dislocated grafts. The gases used in all of the above context include sulphur hexafluoride (Sf6), perfluoroethane (C2F6) or perfluoropropane (C3F8). They differ in their physical properties including expansibility, concentration and time taken to get reabsorbed. Any injected gas needs to stay in the eye for at least twelve days to aid effective healing.[8] Air alone is not used anymore as it tends to get reabsorbed by about a week and does not last long enough. An IOG bubble injected during surgery typically consists of a mixture of air and one of the other gases.

Mostafa et al found that when nitrous oxide is used in the setting of an air bubble in eye, the IOP rose steadily over the first few minutes to a peak level which was 18-20 mm Hg above the baseline.[9]

Thereafter no further rises occurred, but gas bubbles were noted to be escaping from the sclerostomy sites. Towards the end of surgical procedure, the IOP was frequently observed to return towards the baseline level. They considered that per-operative rise in IOP secondary to N_2O movement (when air is used as IOG) are not of significance in vitrectomy because of the venting effect of the sclerostomies. However, they recommended that N_2O be discontinued prior to air injection due to potential for globe hypotony at the end of procedure. Indeed, it has been shown in an animal study that the cornea tends to become concave due to rapid efflux of N_2O.[10]

N_2O is 117 times more soluble than SF6. When SF6 is injected into the vitreous cavity, the more soluble N_2O present in the

surrounding blood and tissues diffuses into the bubble faster than SF6 diffuses out.[11] Almost threefold increase in volume of the injected SF6 bubble has been estimated when 70 per cent N_2O is administered, with only minor increases if N2O is discontinued prior to injection.[12] If N_2O is added following SF6 intravitreal injection, the IOP increases significantly.[13] However, in a later study, Briggs et al observed that at 24 hours, there was no difference in size of gas bubble (C3F8) with or without N_2O.[14] The postoperative IOP at 20 minutes was raised in 50% of patients in non-N_2O group and 44% of patients in N_2O group. It was postulated that uncontrolled leakage from the sclerostomies was the most likely reason. It is to be noted that those days, 20 G needles were used for sclerostomies compared to 25 or even 27 G needles today. Hence, the leakage is likely to be much lower. Manufacturer information warns that the use of N_2O must be stopped at least ten minutes prior to gas injection.

With the advent of remifentanil, there is not a huge justification of continuing to use N_2O in vitreo-retinal surgery. In patients with limited systemic reserve requiring general anaesthesia for vitreo-retinal procedures, a local anaesthetic block prior to surgical incision will allow smaller doses of general anaesthesia agents and minimise adverse haemodynamic effects.[15] In procedures involving IOG, it would be best to avoid N_2O.

3) Non-ophthalmic procedures following a recent eye procedure: IOG vary in their degree of expansion and time taken to disappear from the eye is directly proportional to this. For example, SF6 remains in the eye for two weeks whereas C3F8 can be present for two months. Gas expansion may cause increased IOP in four circumstances: high altitude, influx of N_2O, excessive concentration of IOG, and decreased aqueous drainage through the trabecular meshwork.[16] If N_2O is inhaled (either for analgesia, anaesthesia or use as a recreational drug), influx into this gas bubble (similar to closed air spaces) can cause acute increase in IOP with potential for blindness due to retinal ischaemia.[17]

Study in cats showed that when SF6 is the IOG, the bubble volume increases 300% with N_2O and 50% with air. Hence, even when N_2O is avoided, there is some increase in the IOG volume.[18] In the presence of SF6, IOP could rise by 100% during N_2O anaesthesia within 24 min.[19] A more than threefold volume increase may be seen over 1 hour of N_2O use, which is sufficient to occlude the central retinal artery blood flow.[20]

Duration of administration of N_2O as also the size of IOG bubble at the time are important determinants of degree of damage.

If a patient had SF6 12 days ago, the size of the residual bubble would be small leading to reduced magnitude of increase in IOP by N_2O. The longest reported duration between a retinal procedure with IOG and subsequent

visual loss from N_2O anaesthesia is 41 days.[21] Irreversible damage to retina can happen after 100 minutes of ischaemia.[22] It is recommended that N_2O be avoided for 3 months in patients who had IOG. This blanket rule is necessary as it may be difficult to know the exact gas patient had in the eye and the benefits of avoiding N_2O outweigh the risks.

Preoperative assessment must include details about any recent procedure involving the eye. Patients may not necessarily feel that the eye procedure done a few weeks ago is relevant. Hence the nature and timing of past surgical procedures must be specifically questioned. Certain episodes of IOG instillation are done in outpatient setting in some centres which the patients may not deem as a 'surgical procedure'. The risk increases significantly when patient is unable to give a history due to decreased consciousness or lack of mental capacity. If there is doubt, N_2O must be avoided. To aid safety, patients are now being issued with wristbands with relevant advice. The Royal College of Ophthalmologists issued a safety alert in Dec 2018.[23]

There is a theoretical risk of harm (raised IOP or hypoxic iris) in anterior chamber gas bubbles during keratoplasty in the same circumstances such as flying, high altitude or N_2O use. It is currently unclear at present whether this represents a significant risk but patients are being warned against flying postoperatively. If N_2O is inadvertently given to a patient with IOG and is recognized intraoperatively, immediate steps should be taken.[24] N_2O should be ceased immediately and 100% oxygen should be administered. Oxygen has been shown to lead to faster reversal of bubble expansion than air alone. Ophthalmology consultation should be sought. If ophthalmologist is not available, and the eye feels hard to palpation after 5 minutes of stopping N_2O (using other eye for comparison), then consideration of pars plana paracentesis should be given to vent excess gas from the eye. The principle is similar to needle thoracostomy for relieving tension pneumothorax except that the needle can be removed once the globe is decompressed. There is no risk of continued influx of N_2O if it has been stopped.

Using a short (1/2 inch) needle (26 – 30 G), pierce the sclera of the eye 4 - 5 mm from the limbus (junction between clear cornea and white sclera, see Figure 1.

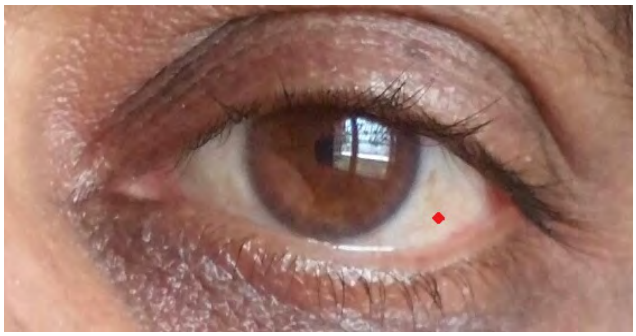

Figure 1. The red dot represents the area for needle puncture for the pars plana paracentesis.

The needle should be directed perpendicularly toward the centre of the eye. A few seconds is typically enough to reduce IOP to safe pressures and removal of a precise amount is not essential. The sclera is only 1 mm thick and hence the needle need not be inserted too deep to enter the globe.

It is essential to be away from limbus to prevent damage to the aqueous draining mechanisms and lens. However, being too far away from the limbus carries the risk of inadvertent retinal damage. Vitreoretinal surgeons insert needles for procedures and usually use a calliper to measure the distance. Due to potential for damage, it is recommended that this procedure is preferably done by an ophthalmologist (or someone who has done intravitreal injections before). It will take more than half an hour for sufficient N_2O to diffuse into IOG bubble. Hence, just because N_2O has been given for half an hour is not an automatic indication for pars plana paracentesis. There must be evidence of raised IOP.

In summary, N_2O is a useful adjunctive general anaesthetic agent for use in most eye procedures not involving insertion / presence of gas bubble. The only exception could be strabismus surgery where the potential risk of PONV is higher. For procedures involving gas bubble, it is best avoided and other agents such as remifentanil should be considered. In patients who have undergone a procedure in the eye within the last three months, the potential for presence of gas bubble must be considered. Wider availability and routine use of 'alert wristbands' should help in eliminating the risk of avoidable blindness due to use of N_2O. When N_2O is used, low flow anaesthesia should be used where possible.

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Wish you all very Happy New Year 2021!

Dr Renu Sinha
Editor, Indian Journal of Ophthalmic Anaesthesia, IJOA

Brief Communication

Aerosol Containment Box for General Anaesthesia under Spontaneous Ventilation

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Examination of eyes in children nearly always requires general anaesthesia (GA). Spontaneous ventilation via face mask can be suffice for simple eye examinations while insertion of laryngeal mask airway(LMA) allows ophthalmologists, easier access towards eyes for completion of short procedures under microscope, fundoscopy, measurement of intraocular pressure, retinoblastoma follow up etc. At our institute, it is carried out using an inhalational technique with facemask connected to Jackson's Rees circuit attached to a reservoir bag with pressure adjusting valve connected to the tail end.

In the COVID pandemic time, we attach a heat and moisture exchange filter (HMEF) between the LMA and circuit and a bacterial / viral filter between the circuit and the bag. Filters in mechanical breathing systems are designed to capture pathogens and particles that range from 0.1 μm to larger than 10 μm. A SARS-CoV-2 virion is between 0.06 to 0.14 μm in diameter. [1]Respiratory transmissions of pathogens occur via carrier particles, classified as either a droplet or an aerosol. Respiratory droplets are particles sized larger than 5 to 10 μm in diameter [2,3] and aerosols are particles sized smaller than 5μm.[4] Filters capture particles larger than 1.0 μm via inertial impact and interception, and particles ranging from 0.1 to 1.0 μm via diffusion.[5] However, the combined effects of interception, inertia and diffusion have the least ability to efficiently capture particles sized 0.3 μm, well within the range of aerosols.[5] No data exists examining the efficacy of breathing circuit filters in preventing SARS-CoV-2 transmission to patients or healthcare workers.[5] Such an evaluation would require using live virus, and has yet to be concluded.[5] Moreover, the microbial penetration value (MPVs) for the viruses were much greater than for the bacteria. Since the droplet sizes are the same, both the bacterial and viral droplets impact on the filter media, but that the viruses, released from the droplet after contact with moisture accumulated on the filter, can be driven onwards by the flow of gas, whereas

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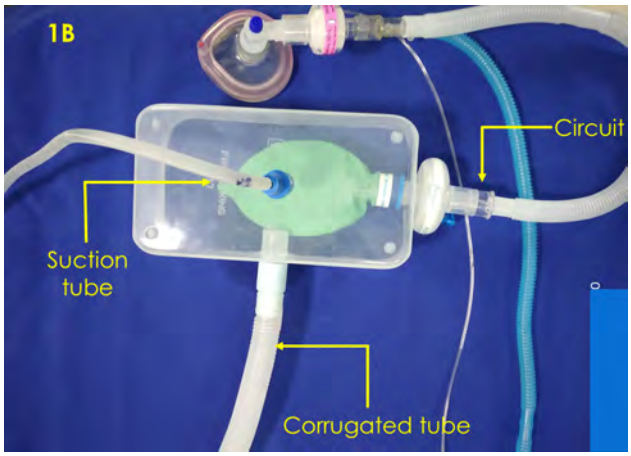
the bacteria remain attached to the filter media. Thus, in spite of the usage of above filters in the circuit, there is possibility of operation theatre (OT) contamination during spontaneous ventilation under GA. To prevent OT contamination when the child is under spontaneous ventilation, indigenous aerosol containment box was developed at our Institution, see Figure 1A.

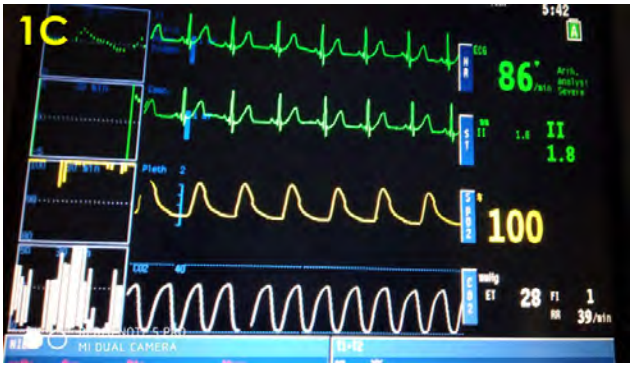
Figure 1A Aerosol containment box used in spontaneous ventilation

A transparent plastic box of dimension 8.5 x4.5x4.5 meter was taken and three holes were made; one hole at the front side, second one at the side, the third hole at the top of the box. Anaesthesia circuit was passed through the hole at the front side of the box, a corrugated tube connected to the return air duct was passed through the hole at the side of the box and a suction tube attached to suction machine, was passed through the hole at the top of the box, see Figure 1B.



1B The tubing connections given to the box

The suction bottle was filled with 1% hypochlorite solution. During inhalational technique, the box was kept over the reservoir bag. Anaesthetic contaminated gases exiting from the reservoir bag through the pressure adjusting valve is vented through the corrugated tubing to the return air duct. Routine monitoring of heart rate, etCO2 and pulse oximetry was done as shown in Fig.1C.



1C Monitoring being used during the procedure

At the end of the procedure, to ensure more complete and effective suctioning of the contaminated air, suction machine is switched on. Following the procedure and after each case the box is cleaned with 1% Virkon solution and at the end of the day the box is cleaned with 1% Sodium hypochlorite solution.

The box is easier and cheaper to make. As children with retinoblastoma requires repeat GA examination of eyes quite often, it is not practical to subject them to Reverse Transcriptase Polymerase Chain Reaction(RT-PCR) test for COVID-19 often. Hence, at our Institution we do not take RTPCR for examination of eyes alone under GA. In such scenario, and also in cases of false negative RTPCR report, this aerosol box for spontaneous ventilation gives an extra protection against virus transmission to health care workers from any asymptomatic children.

Also, this box prevents OT theatre contamination with anaesthetic gases during spontaneous ventilation. Since the box is transparent, movement of the reservoir bag can be observed easily throughout the procedure. One of the limitation encountered in using such box is that, in case of any episode of apnea or breath holding, the box needs to be removed for assisting ventilation.

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Brief Communication

Systemic Chemotherapy in Retinoblastoma: Anaesthetic Implications

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Retinoblastoma is one of the most common primary paediatricintraocular malignancy arising from embryonic neural retina. It accounts to 3% of cancers among children less than 15 years. Annual incidence of retinoblastoma across the globe is 15,000 to 20,000 live births. Retinoblastoma gene RB1 is a tumour suppressor gene located on the long arm (q) of chromosome 13 (13q14.). A retinoblastoma forms when both copies of the RB1 gene are affected by a gene alteration (mutation). Inheritance is either hereditary or sporadic. Sporadic is prevalent and accounts to 60% while heritable accounts to 40%. It neither has gender nor laterality predilection. The nternational Classification for Intraocular Retinoblastoma is based on the extent of the cancer and on the chances that the eye can be saved using current treatment options.

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This staging system is widely accepted and currently in use. Intraocular retinoblastomas are divided into 5 groups labelled from A to E.

Retinoblastoma is both chemo and radio-sensitive. The treatment of the retinoblastoma has evolved from primarily enucleation to highly selective methods of chemotherapy administration. Chemotherapy was introduced in the 1950s and has become an integral component in management of RB. At one time, chemotherapy was used mainly to manage metastatic retinoblastoma, but later used for non-metastatic retinoblastoma. Now, four main routes of administration of chemotherapy are present, and these are: intravenous chemotherapy (IVC), intra-arterial chemotherapy (IAC), intra-vitreal chemotherapy (IVitC) and periocular chemotherapy (POC).

The likely complications and systemic toxicities of IVC are important to be looked at carefully before any anaesthetic procedures.

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Intravenous chemotherapy for retinoblastoma (IVC)

In 1953 Carl Kupfer reported the successful use of intravenous nitrogen mustard along with irradiation to treat a child with recurrent retinoblastoma thereby starting the era of chemotherapeutic treatment for retinoblastoma.[1] In the early 1990s use of systemic chemotherapy was popularized and strongly advocated. The use of external beam radiation was restricted in favour of chemotherapy due to the considerable risk of secondary tumours in patients receiving radiotherapy. IVC is used in patients with intraocular disease only with or at high risk of extraocular disease. When the disease is limited to the eyes, IVC aims at shrinking the size of the tumour to expedite cure and lessen the damage induced by consolidating local therapies to follow, especially when the tumour involves sensitive retinal areas such as the macula. This has been termed chemo-reduction and it had been shown to achieve adequate tumour control and eliminated the need for enucleation or external beam radiation (EBR) in more than 75% of patients in a large series.[2]

IVC is used also as an adjuvant therapy after enucleation in patients with extraocular disease (metastasis) as well as patients with intraocular disease associated with high-risk histopathological features (e.g., optic nerve invasion beyond the lamina cribrosa and choroid invasion >3 mm) demonstrated on histopathological examination of the enucleated eye.[3]

It is speculated that patients with high-risk features might presumably have micro-metastasis and administering systemic chemoprophylaxis helps in improving their prognosis. Evidence in the literature supports the use of prophylactic IVC in high-risk patients and it is safe and effective in decreasing the risk of metastasis.[4]

Systemic chemotherapy as neo-adjuvant

Indications

I) To facilitate ocular salvage by achieving chemo reduction making the tumour more amiable to local therapy.

ii) To reduce the need for external beam radiation with a view to limiting the late effects.

iii) When upfront enucleation may not be immediately acceptable to the families.

Systemic chemotherapy as Adjuvant chemotherapy

Indications

High Risk Features on pathology where **6 cycles of Standard dose** adjuvant chemotherapy are indicated:

i) Anterior segment invasion

ii) Ciliary body infiltration

iii) Any choroidal invasion (invasion 3 mm in basal diameter or thickness)

iv) Retro-laminar optic nerve invasion

v) Combination of optic nerve infiltration till pre-laminar/laminar along with one more high risk feature.

High Risk Features on pathology where **high-dose** adjuvant chemotherapy **12 cycles** are indicated :

i) Full thickness scleral extension
ii) Extrascleralextension
iii) Optic nerve invasion at line of transaction

Indications for standard dose chemotherapy

1. Intraocular retinoblastoma Group A to E
2. Histo-pathological high risk factors following enucleation (massive choroidal invasion, anterior segment invasion and retro-laminar optic nerve invasion not involving transected margin)

Indications for high dose chemotherapy

1. Extraocular retinoblastoma (orbital extension or optic nerve involvement on imaging)
2. Histo-pathological high-risk factors (Full thickness scleral invasion, Extra scleral extension, optic nerve involvement till transection)

Metastatic disease

Patients with CNS involvement usually have a very poor prognosis with low survival rate. The usual approach consists of platinum-based IVC with agents having good CNS penetration along with focal CNS treatments such as radiotherapy. Distant metastasis usually occurs to the bone and promising results using cisplatin based regimens and consolidation with high dose chemotherapy and autologous hematopoietic progenitor cell rescue is reported in a small group of patients.[5]

Salvage therapy

In children who failed first line of treatment, systemic therapy with cyclophosphamide and topotecan was reported to be effective in globe preservation.[6]Topotecan combined with vincristine and carboplatin with aggressive focal therapies have been found to be effective regimen in advanced retinoblastoma and resulted in globe salvage with vision.[7]

Chemotherapeutic protocol

The most commonly employed IVC therapy is the VEC protocol: Vincristine, Etoposide, Carboplatin in standard doses based on the body weight. Higher doses may be used in patients with more advanced disease (bilateral group D or E).[8]The Standard and high dose VEC regimens followed is shown in Table 1 and Table 2 respectively. In high risk pathology cases, VEC is used alone or alternating with cyclophosphamide and doxorubicin.The goals of RB treatment are firstly patient survival, then protection of the eye and finally visual function

Table 1. Standard dose VEC regimen

Drugs	< 3 years		>3 years	
	Dose	Duration	Dose	Duration
Vincristine	0.05 mg/kg/day	1 day	1.5mg/m2/day	1 day
Carboplatin	18.6mg/kg/day r	1 day	560mg/m2/day	1 day
Etoposide	5 mg/kg/day	2 days	150 mg/m2/day	2 days

Table 2. High dose VEC regimen

Drugs	Dosage	Duration
Vincristine	0.025 mg/kg/day	1 day
Etoposide	12mg/kg/day	2 days
Carboplatin	28mg/kg/day	1 day

Side effects of chemotherapy

Vincristine – Headache, mental depression, dizziness, convulsions, anemia, leukopenia, thrombocytopenia and hepatic impairment (hepatic veno-occlusive disease –VOD, hepatitis)

Etoposide–nausea, vomiting, diarrhea, hypotension(if injected rapidly), thrombocytopenia, leukopenia.

Carboplatin – dizziness, confusion, tinnitus, ototoxic, hepato and renal toxic, cytopenia, electrolyte imbalance

Nadir (Point in time between chemotherapy cycles in which low blood counts will be detected) will be seen in the second week of chemotherapy and usually resolves in the third week. Doxorubicin cardio-toxicity can be acute, occurring during and within 2–3 days of its administration. The incidence of acute cardio-toxicity is approximately 11%.[9,10] The manifestations are usually chest pain due to myopericarditis and/or palpitations due to sinus tachycardia, paroxysmal non-sustained supraventricular tachycardia and premature atrial and ventricular beats. The mechanisms for these acute changes are not clear but may be due to doxorubicin-induced myocardial oedema, which is reversible.[9,11]

Acute left-ventricular (LV) failure is a rare manifestation of acute cardio-toxicity, but it is also reversible with appropriate treatments.

Pre anesthetic Implications

Complete blood count must be checked prior to any anesthetic procedures.

Liver function tests, renal function parameter (urea, serum creatinine) and serum electrolytes test to be performed prior to initiation of every cycle of chemotherapy.

Children receiving doxorubicin should have echocardiogram done after every 2 cycles.

It is also important to remember during pre-anaesthetic evaluation that orbital disease could have CNS involvement during the course of treatment. Hence, if there is a subtle sign of raised intra cranial tension, it should be evaluated with imaging.

Conclusion

Pre-anaesthectic evaluation for all retinoblastoma children post chemotherapy should include evaluation for cytopenia, liver and renal function, electrolyte level and if anthracyclines are received then cardiac evaluation must be done.

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Conflicts of interest

There are no conflicts of interest.

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Brief Communication

Retained Visual Sensations in Ophthalmic Surgery

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Retained visual sensation are visual perception or experiences encountered by the patient in the operated eye during surgical procedure. The regional techniques such as retrobulbar, peribulbar and subtenon's block involve administration of a considerable volume of local anaesthetic in restricted compartment of the orbit. The effects of regional techniques of anaesthesia on optic nerve function ranges from no perception of light to impaired visual activity, changes in visual evoked potential (VEP) or relative afferent pupillary defect. The proposed mechanisms for the effect are transient conduction blockade of the optic nerve, relative ischemia due to compression from anaesthetic volume, saturation of photoreceptor elements and retinal pigment epithelium, blur by post injection digital pressure and posterior globe indentation by anaesthetic volume causing hyperopia.

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Retained visual sensations can occur during cataract, glaucoma, vitreous and lasik surgeries. These include perception of light, change in light brightness, flashes of light, one or more colors, movements, instruments, surgeon's finger or hands. The visual images are unique and are a combination of images of objects close to the eye but outside the eye (fingers, instruments) and entoptic phenomena produced by structures and objects on the corneal surface and in the eye. Dynamic factors like moving fluids and bubbles on the corneal surface and the eye as well and the moving instruments in the eye add to the changing kaleidoscope of colors and shapes.

During cataract surgery under topical anesthesia the ever changing shape and opacity of the lens as it is being emulsified, aspirated and extracted, as well as changes in the refractive state of the eye from phakic to aphakic and finally pseudophakic influence the focusing light rays on retina. Patient undergoing phacoemulsification under topical anaesthesia' perceive light, colors and changes in light brightness[1] when compared to those under regional analgesia. Glaucoma patients undergoing trabeculectomy, phaco/trab and valve devices implant can

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also see images similar to those experience during cataract extraction. About 41 to 43% of patients undergoing glaucoma surgery[2] see surgical instruments and surgeon's hands compared to 7 to 26% of patients undergoing phacoemulsification; this is because the instruments in anterior chamber are not clearly seen as instruments are outside the eye (extra ocular). In phacoemulsification there is disruption and removal of crystalline lens, the optical elements are disturbed which does not occur in glaucoma. Glaucoma surgery doses not disturb optical elements of eye and so refractive status remains unchanged allowing better perception. Retained visual sensation are less common during vitreous surgery[3] and could be attributed to greater volume of anaesthetic agents and presence of severe preexisting retinal pathology. Patient who report intraoperative sensation of light, colors, moving objects have better postoperative visual acuity and it is correlated with macular function.

During lasik[4] whether using microkeratome or femtosecond, patients may see flashes, colors, surgeon's hand or fingers during surgery. The deformation of cornea in excimer laser and lifting of the lasik corneal flap create visual images. In microkeratome during vacuum suction and corneal flap fashioning is done a high percentage of patients lose light perception compared to femtosecond lasik.

Retained visual sensations during ophthalmic surgeries can also be unpleasant and some patients find them frightening. The visual sensations can make the patients uncooperative and stimulate a sympathetic response in patients leading to tachycardia and increase in blood pressure. This in-turn can lead to undesirable effects in elderly and in patients who have associated systemic (cardiac) comorbidities. Also, these frightening experience can decrease patient's satisfaction too.

Preoperative counseling[5], verbal and picture illustrations was found to reduce the negative impact caused by the retained visual sensations. But, previous survey has confirmed that although many ophthalmologists are aware of this phenomenon, they do not counsel their patients.[6] Judicious use of sedation reduces awareness to environment. Intravenous sedation with midazolam 0.015 mg/kg was found to reduce the ability to see and recall intraoperative visual images /sensations in patients undergoing phacoemulsification cataract surgery under topical anaesthesia.[7] Patients sedated with midazolam experience less disturbances to the light emanating from the microscope.[7] These in-turn can improve overall patient's satisfaction too.

Conflicts of interest

There are no conflicts of interest

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Muthusamy Sub-Tenon's Cannula: An Untold Story

Dear Sir / Madam,

Sub-Tenon's block was first described by Turnbull in 1884[1] and later by Swan in 1956.2 During that period retrobulbar anaesthesia was the preferred technique of local anesthesia for ocular surgery. The report of the joint working party on anaesthesia in ophthalmic surgery by the Royal College of Ophthalmologist (March 1993)[3] has shown that life-threatening complications occurred in 1:750 anaesthetics administered and serious complications occurred in 1:360 cases following retrobulbar anaesthesia. So, again in early 1990's, Sub-Tenon's anaesthesia was revisited by many workers including Hansen[4] and Stevens.[5] During that time, I designed a modified Sub-Tenon's cannula for the placement of anaesthetic solution into the Sub-Tenon's space. In this letter, I would like to share with the readers, two interesting inciting events which led to the birth of my cannula, Muthusamy Sub-Tenon's cannula,[6] Figure 1.

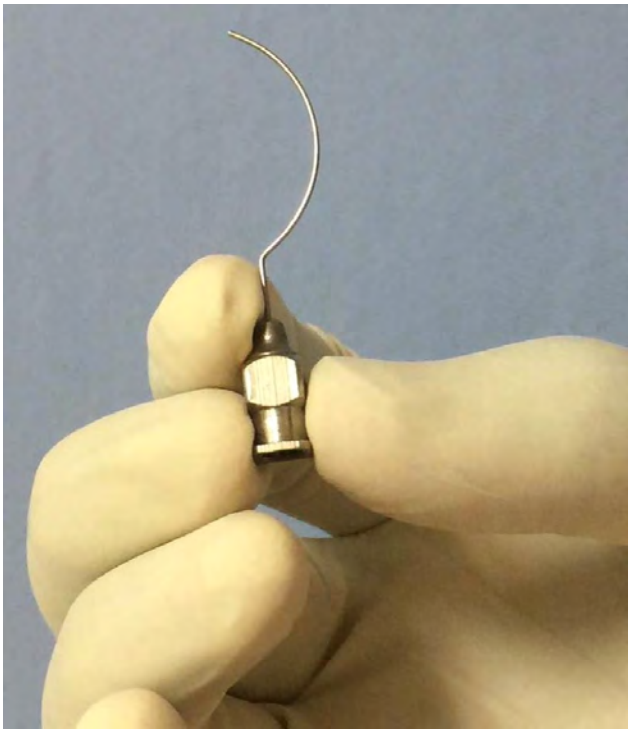

Figure 1. Muthusamy Sub-Tenon cannula

One fine day, I was examining my close friend, who was having bilateral cataract. He had a vision better than 6/18 in one eye and a vision of counting fingers in the other eye. He requested me to operate the eye with the poorer vision that was bothering him.

His son who was studying medicine in Manchester was back home for his holiday and was eager to watch the operation.

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Normally, I encourage patient's relatives/friends to be in the operation theater during surgery, if they are insisting to see operation because it is very reassuring to the patient. The onlookers always go back enthralled at the skill needed to perform a cataract surgery and they become a mouth piece whenever they come across a patient with cataract.

So during surgery, I was explaining every step of the surgery to his Son and he was very much impressed. After I finished the surgery, I told to his Son, "In cataract surgery, there is only a very narrow line between perfection and disaster. As you have seen, this surgery was perfect".

The eye was padded for the night. Next day morning, in the presence of his Son, I removed eye pad of my friend and instructed him to read the Snellen's chart. I was shocked to hear his words, "Muthu, I can't see anything". I assured him, "Don't worry. Relax a little while and you will be able to see". When I asked him to read again he, very worriedly said, "Muthu, I can't see anything". I quickly took a bright torch and shined the light into the eye and asked him, "Can you see the light, he said a soft "No". I knew exactly what had happen. The retrobulbar injection has damaged the central retinal artery and caused central retinal artery occlusion. Damage to the central retinal artery is extremely scary and is a drastic complication. Although I was devastated, I maintained my professional cool.

I knew for sure the retro bulbar injection needle has injured the central retinal artery and the vision was irrecoverable. The only consolation to me was that his Son had witnessed the whole surgery.

During that time, ophthalmologists all over the world were looking for a better and safer alternative. There were already a few Sub-Tenon's cannulas available but each one of them had some limitations. I did hours of research and read the history of ophthalmic surgery from the time of the first cataract surgery done by Sushruta: the father of Indian surgery and ophthalmology in the 6th Century BC to the advent of pre-bulbar anaesthesia.

I spent many grueling hours and finally I designed and developed a Sub-Tenon's cannula on my own. I sent them to all leading ophthalmology institutions in the world and received letters of appreciation from many corners.

The second inciting event which helped me to produce the cannula in larger number was a letter from Professor David Guyton, Professor of Pediatric Ophthalmology, The Johns Hopkins Institute. He praised my cannula saying the curve and the length is perfect and congratulated my effort. I felt enthused and exhilarated. So I wrote a letter thanking him and volunteered to send him a few of my cannula to try and assess. To my dismay, he replied that what he sent was an "ANECTODAL PRAISE". I knew exactly what it meant.

I was the student with the most powerful vocabulary in my class! It meant, "praise and inspirational words not based on facts or careful study, unreliable, unscientific, entrust worthy". I did not expect a letter of this sort from a man of his standing and caliber. I wrote a reply letter. I read and re-read that letter about 6 times to make sure he cannot find fault with the views that I expressed. I felt that he will ignore it. But, to my surprise, I received again a letter from him, in which he apologized for his faux pas, and constructively suggested that my cannula was excellent but it was crude and he also wrote that if I can get it manufactured to perfection, he would use and promote it. Then I immediately got it manufactured and sent it to him. He supported it. The rest was history…… birth of Muthusamy's Sub-Tenon cannula.

By the way, David Guyton is the son of the author who wrote the famous book Guyton Textbook of Medical Physiology. You might have all read it.

In the next issue, I will be writing to you all about how the cannula got popularized and manufactured[7] without my knowledge, how I came to know about it later and I will also be describing the cannula in detail.

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Conflicts of interest

There are no conflicts of interest.

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