EFFICACY OF TOPICAL ANAESTHESIA IN REDUCTION OF OCULOCARDIAC REFLEX DURING SQUINT SURGERY

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ABSTRACT

Objective: To determine the efficacy of Topical Anaesthesiain reduction of oculocardiac reflex incidence and severity in patients undergoing squint surgery under general anaesthesia.
Study Design: Quasi-Experimental Study.
Place and Duration of Study: Armed Forces Institute of Ophthalmology from Nov 2019 to Mar 2020.
Methodology: Two sixty-six patients (n=266) enrolled in the study, equally divided into two groups i.e. group A – Topical Anaesthetic 0.5% eye drops (n=133) and Group B–Placebo Eye Drops (n=133). Meticulous Pre anaesthesia assessment, Preoperative preparation and written consent ensured, followed by elective squint surgery under general anaesthesia with standard protocols.
Results: Two sixty-six patients were enrolled in the study with a mean age of 16.22 ± 4.75 years and there were 122 (45.9%) males and 144 (54.1%) females in the study group. At 10, 20 and 30 minutes after the start of the surgery, the heart rate was significantly lower in the placebo group B as compared to group A (73.14 ± 12.9 vs 85.14 ± 17.5, p<0.001, 73.98 ± 7.7 vs 86.51 ± 25.3, p<0.001, and 74.65 ± 7.0 vs 86.14 ± 22.7, p<0.001) respectively. Similarly, the incidence of Oculocardiac reflex was significantly lower in group A, as compared to placebo group B (20.3% vs 43.6%, p<0.001) and significantly lesser number of patients in group A required administration of atropine during the surgery as compared to group B [2 (1.5%) vs 42 (31.6%), p<0.001].
Conclusion: Instillation of Topical Anestheticin squint surgery under general anaesthesia reduce the intensity and severity of oculocardiac reflex. Therefore, alleviating requirement of anticholinergics administration.

Keywords: OCR, Squint, Topical anesthesia.

INTRODUCTION

Squint is defined as divergence of eyes, involving manipulation of six extra orbital muscles accountable for eyeball movement in the orbital cavity. Although considered childhood ailment (congenital mostly) with an approximate prevalence of 1% but adults have 4% incidence (due to diabetes, myasthenia gravis, trauma etc)[1,2].

Oculocardiac reflex (OCR) reported in the year 1908, defined as a 20% reduction in heart rate secondary to compression on globe or traction on eye muscles, notoriously medial rectus. Conspicuous with ophthalmologic surgeries, eminent in squint surgery. Variable incidence of 14- 90% seen, with increased susceptibility in the pediatric population attributable to heart rate dependence to maintain cardiac output. Stimulants are hypoxia, hypercarbia, surgical factors (nature, duration, technique) and anaesthetic regimes[3,4].

Short and long ciliary nerves transmit afferent signals to ciliary ganglion further conveyed to Gasserian ganglion via trigeminal nerve (5th Cranial nerve – afferent limb), causing severe bradycardia owing to increased parasympathetic stimulation and activation of the efferent pathway (Vagus -10th Cranial Nerve)[5] pathway illustrated in fig-1.

Predisposition to atrioventricular block, ventricular ectopics and asystole is observed. Meena *et al* reported a case of a 45-year-old female, undergoing elective squint surgery under local anaesthesia who collapsed and died due to cardiac arrest[7]. Cessation of stimulus immediately is efficacious however to address bradycardia

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intravenous atropine may be required. Atropine has notable adverse effect profile in higher doses, such as dryness of mouth, tachycardia and pupillary dilation. Pupillary dilation may block the anterior chamber angle in glaucoma patients therefore increase in intraocular tension may further provoke OCR[8].

The rationale of our study was instillation Topical Anaesthetic (TA) in patients undergoing squint surgeries under general anaesthesia perhaps alleviate OCR owing topropensity of sensory nerve endings penetration in corneal tissue, due to antagonism at voltagegated sodium channels[9,10].

METHODOLOGY

This quasi-experimental study carried out at Armed Forces Institute of Ophthalmology from November 2019 to March 2020, approval taken from ethical research committee of the institute (209/ERC/AFIO).

The sample size for this study was calculated by using WHO sample-size calculator, by considering a two-tailed hypothesis with 95% level of significance, 80% power, a portion of subjects who developed oculocardiac reflex in the exposed group to be 0.28 while the proportion of subjects who developed oculocardiac reflex in the control group to be 0.57. The minimum required sample equalled 120 (60 in each group), after 10% attrition adjustment[11].

As per study protocol, all the patients interviewed, briefed, counselled about the procedure and informed written consent taken. Before reporting to the operation theatre, a detailed pre-anaesthesia assessment was carried out in all patients with necessary laboratory evaluation parameters to adhere with our inclusion and exclusion criteria, besides, to ensure patient safety which is of utmost concern in anaesthetic management.

Non-probability convenience sampling technique was used to enrol consecutive patients undergoing elective squint surgeries under general anaesthesia from both genders with age group between 8 to 22 years and American Society of Anaesthesiologist's (ASA) status I or II and hemodynamically stable were included in the study. Non-consenting patients, BMI>30, difficult airway, respiratory diseases, history of allergy, trauma and requiring surgery of greater than two extraocular muscles were excluded. Two sixty-six patients (n=266) were enrolled in the study, equally divided into two groups i.e. group A (n=133) allocated to Topical Anaesthetic [TA (Alcaine-Proxymetacaine hydrochloride)] 0.5% eye drops and group B (n=133) allocated to normal saline (NS) placebo eye drops.

As pre-operative preparation, completion of essential documentation and an overnight fast/Nil per oral ensured. On the day of surgery,

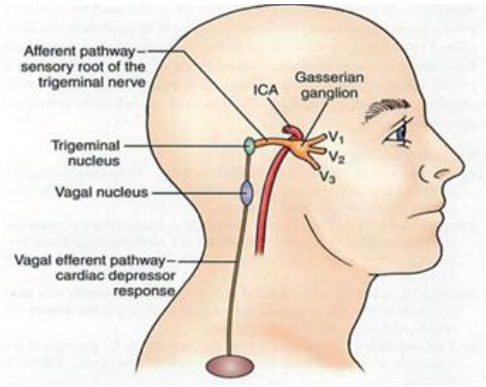

Figure-1: Oculocardiac Reflex Pathway[6].

patients brought to operation theatre and before initia-ting general anaesthesia standard monitoring such as blood pressure (non-invasive method), pulse oximeter (SpO_2), end-tidal carbon dioxide ($ETCO_2$) and electrocardiography electrodes attached.

Intravenous cannul a passed under aseptic conditions. Premedication performed with intravenous injections of nalbuphine 0.1mg/kg, paracetamol 15mg/kg, dexamethasone 0.08mg/kg and metoclopramide 0.1mg/kg. Patients were Pre oxygenated with 100% oxygen for 3 minutes. Induction performed with intravenous propofol at a dose of 2mg/kg and muscle relaxation achieved with 0.5 mg/kg of intravenous injection atracurium and depth of anaesthesia achieved by inhalational anaesthetic sevoflurane followed

by laryngoscopy and intubation by a qualified anaesthetist 03 minutes later. 3 drops of either Topical Anaesthetic (TA) or Placebo Normal Saline (NS) instilled in the eye to be operated immediately after induction of anaesthesia and before surgical incision in all four directions of patients' eye.

Inhalational anaesthetic isoflurane and injection atracurium 0.1mg/kg used for maintenance. Meticulous intraoperative monitoring was ensured, heart rate and mean arterial pressure below 20% was considered abnormal, respiratory rate and tidal volume were adjusted to achieve $ETCO_2$ between 35-40 mmHg and SpO_2 between 98%-100%.

Heart rate, systolic blood pressure, diastolic blood pressure and saturation were recorded baseline and intraoperatively after every 10 minutes from the start of surgery with automated monitor. If heart rate dropped below 20% of baseline it was considered positive oculocardiac reflex, the surgeon was requested to stop stimulus and depth of anaesthesia was increased. However even if after cessation of stimulus bradycardia did not settle, anticholinergic intravenous atropine administered as stat dose of 0.5 mg (can be given up to 3 mg), none of the subjects in our study required a second dose. At the end of surgery, reversal achieved with intravenous neostigmine + glycopyrrolate. Average surgery duration was being 30-45 minutes depending on several muscles involved.

Variables recorded were age, gender, ASA status, mean heart rate, mean systolic and diastolic blood pressure, mean oxygen saturation (SpO_2), incidence of OCR and requirement of intravenous atropine.

Data was entered and analyzed using Statistical Package for Social Sciences (IBM SPSS) version 22.0. Quantitative variables like age, heart rate, systolic & diastolic blood pressure described as mean and standard deviation while qualitative variables like gender, ASA status, and requirement of atropine administration measured in terms of frequency and percentages. Qualitative and qualitative variables compared among study groups by using independent samples t-test and chi-square test respectively. Study results further stratified based on age, gender and ASA Status. A *p*-value ≤0.05 considered statistically significant.

RESULTS

Total 266 patients were enrolled in the study, equally divided into two study groups (133 each) to either receive TA–Proxymetacaine hydrochloride 0.5% (group A) or NS - placebo eye drops (group B). There were 122 (45.9%) males and 144 (54.1%) females in the study group with a mean age of 16.22 ± 4.75 years (age range 8-22). Among group A, there were 55 (41.4%) male, 78 (58.6%) females, mean age 16.29 ± 4.1 years, while among group B there were 67 (50.4%) males, 66 (49.6%) females with a mean age of 17.17 ± 4.3. There was no significant difference between group A and

Table-I: Baseline clinical characteristics among group A and B.

Characteristics	Study Groups		*p*-value
	Group A (n=133)	Group B (n=133)	
Age in years, (Mean ± SD)	16.29 ± 4.1	17.17 ± 4.3	0.091
Gender, n (%)			
Male	55 (41.4%)	67 (50.4%)	0.140
Female	78 (58.6%)	66 (49.6%)	
ASA Status, n (%)			
I	116 (87.2%)	112 (84.2%)	0.483
II	17 (12.8%)	21 (15.8%)	
Baseline Heart Rate in bpm, (mean ± SD)	86.33 ± 24.5	85.25 ± 15.0	0.665
Systolic Blood Pressure in mmHg, (mean ± SD)	105.01 ± 13.5	105.62 ± 14.1	0.719
Diastolic Blood Pressure in mmHg, (mean ± SD)	65.84 ± 8.3	64.02 ± 9.1	0.090
SpO_2 in %, (mean ± SD)	98.50 ± 0.6	98.40 ± 0.6	0.212

B in terms of baseline clinical characteristics, as summarized in table-I.

At ten minutes after the start of the surgery, the heart rate was significantly lower in the placebo group B as compared to group A (73.14 ± 12.9 vs 85.14 ± 17.5, p<0.001) as shown in table-II. Similarly at twenty and thirty minutes after the start of the surgery, the heart rate was still significantly lower in the placebo group B as compared to group A (73.98 ± 7.7 vs 86.51 ± 25.3, p<0.001 and 74.65 ± 7.0 vs 86.14 ± 22.7, p<0.001 respectively). In terms of systolic blood pressure, there was no significant difference noted among study groups at 10, 20 and 30 minutes after the surgery started (p=0.853, p=0.971, and p=0.704 respectively, as shown in table-II. Diastolic blood pressure was significantly lower in placebo group B as compared to group A at 20 minutes after the start of the study (57.53 ± 9.3 vs 60.00 ± 8.3, p=0.023), while no significant difference was observed at 10 and 30 minutes during the surgery (p=0.207, p=0.167 respectively) as shown in table-II. Oxygen saturation level remained the same during the whole surgery procedure for both study groups.

It was observed that 27 (20.3%) patients in group A developed OCR whereas OCR was developed by 58 (43.6%) patients in group B. Therefore, the incidence of OCR was significantly lower in TA-group A, as compared to NS-group B (20.3% vs 43.6%, p<0.001) as shown in fig-2. Similarly, significantly lesser number of patients

Table-II: Comparison of Study Outcomes Among Group A and B.

Outcomes	Study Groups		*p*-value
	Group A (n=133)	Group B (n=133)	
Heart rate at 10 minutes, (mean ± SD)	85.14 ± 17.5	73.14 ± 12.9	<0.001*
Heart rate at 20 minutes, (mean ± SD)	86.51 ± 25.3	73.98 ± 7.7	<0.001*
Heart rate at 30 minutes, (mean ± SD)	86.14 ± 22.7	74.65 ± 7.0	<0.001*
Systolic Blood Pressure at 10 minutes in mmHg, (mean ± SD)	105.51 ± 12.6	1.5.80 ± 13.0	0.853
Systolic Blood Pressure at 20 minutes in mmHg, (mean ± SD)	99.73 ± 6.6	99.76 ± 6.8	0.971
Systolic Blood Pressure at 30 minutes in mmHg, (mean ± SD)	96.79 ± 7.1	97.13 ± 7.3	0.704
Diastolic Blood Pressure at 10 minutes in mmHg, (mean ± SD)	61.61 ± 12.0	59.74 ± 11.9	0.207
Diastolic Blood Pressure at 20 minutes in mmHg, (mean ± SD)	60.00 ± 8.3	57.53 ± 9.3	0.023*
Diastolic Blood Pressure at 30 minutes in mmHg, (mean ± SD)	59.92 ± 9.5	58.31 ± 9.4	0.167
SpO_2 at 10 minutesin %, (mean ± SD)	98.50 ± 0.6	98.40 ± 0.6	0.212
SpO_2 at 20 minutesin %, (mean ± SD)	98.66 ± 0.6	98.54 ± 0.6	0.121
SpO_2 at 30 minutesin %, (mean ± SD)	98.66 ± 0.6	98.5 ± 0.6	0.120

*significant p-values; p-values were calculated by Independent Samples t-test.

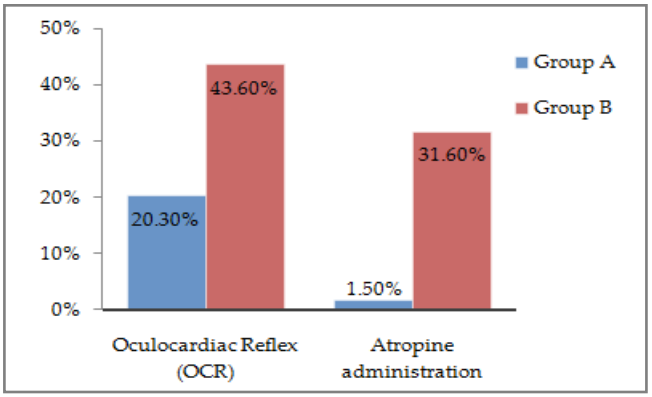

Figure-2: Comparison of occurrence of oculocardiac reflex and atropine requirement among two study groups.

in group A required administration of atropine during the surgery as compared to group B [2 (1.5%) vs 42 (31.6%), $p<0.001$] as shown in fig-2.

DISCUSSION

Data analysis of research interpreted statistically significant reduction of incidence of OCR in TA versus NS group, a common deleterious effect encountered in squint surgeries and ophthalmological procedures. Furthermore, instillation of topical anaesthetic also reduced anticholinergic (Intravenous atropine) requirement.

Numerous studies had been documented which employed local anaesthetic preemptively as a topical application or regional block to inhibit OCR in ophthalmological surgeries (LASIK, squint, retinal detachment repair, enucleation).

Varposhti *et al* compared placebo or synthetic teardrop (E) and Tetracaine eye drop (T) groups. Enumerated no significant differences between two groups related to incidence and severity of OCR in the release phase ($p>0.05$), whereas in the incision phase more obvious in group E than group T ($p=0.02$, for both). Atropine consumption was identical (p-value=0.92). Concluded TA effective only during the incision stage. On the other hand incidence of decrease in mean heart rate and atropine, consumption was less in the topical anaesthetic group compared with placebo in our study ($p<0.001$)[11].

Sajedi *et al* compared preemptive inhibition of oculocardiac reflex with 2% topical lidocaine and intravenous atropine in ophthalmological surgeries under general anaesthesia. Mean heart rate difference xylocaine group and atropine group were statistically different ($p=0.003$). However, blood pressure changes between the two groups were not significantly different as in our case no difference was seen between TA and NS group ($p=0.9$).Recommend that both topical xylocaine and intravenous atropine can be utilized for prevention of OCR a head of surgery under general anaesthesia. Furthermore, they added that intravenous atropine is preferred in high-risk surgeries and high-risk patients (cardiac patients, history of taking anti-hypertensive medications)[12].

Sinha *et al* gauged topical application of 2% lidocaine gel and 0.5% proparacaine eye drops in paediatric squint surgery. OCR recorded in lidocaine group (56.9%) and proparacaine group (63.1%) respectively. Atropine consumption in the lidocaine group was (8.6%) whereas inproparacaine group was (12.3%). Hence proved relative efficacy of Topical Anaesthetic in barring OCR. Comparable to our study results TA (1.5%) and NS (31.6%)[13].

Singh *et al* studied the effect of topical anaesthetics on oculocardiac reflex and corneal healing in rabbits (preferred rabbit because of large eye and cost). A significant reduction in heart rate was recorded after ocular manipulation (245 ± 11/min, $p<0.01$) under propofol anaesthesia as compared to the basal heart rate (278 ± 8/min). Use of topical anaesthetics proparacaine, lignocaine, bupivacaine before ocular manipulation prevented the decreased heart rate recorded after ocular manipulation under propofol anaesthesia ($p<0.01$). Mean heart rate in our study results between TA and NS group were also significant ($p<0.001$). They concluded that topical anaesthetics can significantly lower the incidence of OCR ($p<0.01$) without impairing corneal healing and TA may be recommended for inhibition of OCR without any adverse effects. We also observed a decreased proportion of OCR incidence in Trial and placebo group (20.3%) and (40.6%) respectively[14].

Talebnejad *et al* illustrated a decreased effect on mean heart rate and greater postoperative pain relief ($p<0.002$) with sub-Tenon's bupivacaine injection when compared with control (normal saline) in patients undergoing squint surgery. Intensity of OCR (mean heart rate decrease, $p<0.001$) was significantly lower in the study group. Sub-Tenon injection of bupivacaine as a local anaesthetic can significantly intercept OCR and severity of bradycardia[15].

Misurya *et al* analysed oculocardiac reflex during extraocular muscle surgery. In atropine

(0.4 -0.6 mg) premedicated group 10% patients and 20% patients in xylocaine group expressed positive OCR (p>0.60), which is not significant and combination of both provided (100%) prevention (p<0.01). Therefore local anaesthetics can be safely used with less adverse effect profile when compared with atropine[16].

Ruta *et al* Patients compared topical lidocaine with placebo. Topical administration of lidocaine reduced the incidence of the OCR (86.1% vs 37.1%) and severity of bradycardia (40% vs. 2.9%) relative to our study results [OCR (40.6% vs 20.3%)][18].

Lee *et al* investigated the effect of topical anaesthesia on the incidence of OCR by preoperative instillation of 0.5% tetracaine. The incidences of OCR in trial and control group were 33% and 71% respectively and the difference was statistically significant (p<0.025), was noted both in recession and resection. Results well versed with our research [OCR (20.3% vs 40.6%)][19].

Therefore, the peculiar aspect of our study was that instillation of local anaesthetic provides better anaesthetic considerations in squint surgeries concerning intraoperative prevention of incidence and severity of OCR without any reported adverse effects. Moreover, it reduces the requirement of intraoperative intravenous atropine administration.

Instillation of topical anaesthetic is an effortless remedy which neither involves expertise nor financial implications. On the other hand, can suppress a life-threatening complication during squint surgeries. Only limited literature and research is available on the use of topical anaesthetic in prevention of OCR, however, due to ease of administration and lack of implications, it can be routinely practised to evaluate further and additional studies can be carried out to establish an affirmative conclusion.

It is recommended to gauge benefits of this straight forward adjunct in other ophthalmological surgeries, regional blocks and procedures to evaluate its significance and gain benefit ou of it. Newer trends in anaesthesia can be adopted weighing risk-benefit ratio to pace up with evolutions in the surgical field.

CONCLUSION

Instillation of Topical Anesthesia in squint surgery under general anesthesia reduce intensity of oculocardiac reflex. Furthermore, administration requirement of anticholinergics also decreased.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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