



Original Article

## Oculocardiac reflex in ophthalmic practice: a systematic review and meta-analysis

Dr K. Pradeep Kumar<sup>1</sup>, Dr. Sujit Kumar Patra<sup>2</sup>, Dr Santosh Biswal<sup>3</sup>, Dr Sai Sankar Behera<sup>4</sup>, Dr Md Attaur Raheman<sup>5</sup>, Dr Lipsita Das Adhikari<sup>6</sup>

<sup>1</sup>Assistant Professor, Department of Physiology, M.K.C.G Medical College & Hospital, Berhampur, Ganjam, Odisha

<sup>2</sup>2nd year Postgraduate Resident, Department of Anatomy, SCB MEDICAL COLLEGE AND HOSPITAL, CUTTACK, ODISHA

<sup>3</sup>Resident, Department of Ophthalmology, RGH ROURKELA

<sup>4</sup>3rd year, Postgraduate trainee, Department of Physiology, MKCG Medical College & Hospital

<sup>5</sup>3rd year, Postgraduate trainee, Department of Physiology, MKCG Medical College & Hospital

<sup>6</sup>3rd yr PGT, Dept of Physiology, MKCG MCH

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### Corresponding Author:

**Dr K. Pradeep Kumar**

Assistant Professor, Department of Physiology, M.K.C.G Medical College & Hospital, Berhampur, Ganjam, Odisha

[dr.kodipradeeo@gmail.com](mailto:dr.kodipradeeo@gmail.com)

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### ABSTRACT

**Background:** The oculocardiac reflex (OCR) is a trigeminovagal reflex that is very common during eye surgeries and in particular when the extraocular muscles are manipulated. Usually, the OCR vanishes on its own; however, it can result in serious cases of bradycardia and other cardiac problems if it happens, for instance, in children. Several research works have recorded various degrees of frequency and intensity of OCR, but it is still quite unclear how anesthesia, surgical and preventive factors contribute to it.

**Objective:** To systematically review and quantitatively synthesize available evidence on the incidence, severity, and modifying factors of the oculocardiac reflex in ophthalmic practice.

**Methods:** We conducted a systematic review and meta-analysis following the PRISMA guidelines based on pre-established criteria. Eight key studies that assessed OCR in ophthalmic surgical and examination environments were incorporated in the review, covering pediatric, adult, and neonatal populations. Data regarding OCR incidence, severity, anesthetic agents, procedural factors, and preventive interventions were collected. A random-effects meta-analysis was carried out to calculate the combined incidence, and comparative analyses were conducted to evaluate the effect of anesthetic and procedural modifiers.

**Results:** The combined incidence of OCR in ophthalmic environments was 34.6% (95% CI: 29.140.2), with a large variance between studies. More OCR episodes, as well as their severity, were linked to lighter planes of anesthesia, administration of fast-acting opioids, use of dexmedetomidine, extraocular muscle traction, and re-operative strabismus surgery. On the other hand, ketamine-based anesthesia and topical ocular anesthetics were linked with decreased OCR incidence. Mild bradycardia was the predominant symptom, whereas severe OCR was observed in less than 5% of cases. Retinal examinations on neonates caused a significant heart rate drop that was clinically relevant despite the fact that the stimulus was non-surgical. OCR has also been linked to an increased risk of postoperative nausea and vomiting in pediatric strabismus surgery.

**Conclusion:** The oculocardiac reflex (OCR) is still a common and significant clinical event in eye care practice. OCR is very much determined by the type of anesthesia used, the presence of opioids and sedatives, and the nature of the surgery. The implementation of specific measures to prevent OCR, such as well-planned anesthetic methods, minimal opioid use, use of topical ocular anesthesia, and delicate surgical maneuvers, may contribute to lowering the OCR rate and the resulting complications. There is a necessity for agreed-upon OCR criteria and

prospective research to advance the OCR management protocols in light of the latest evidence.

**Keywords:** Oculocardiac reflex, Strabismus surgery, Ophthalmic anesthesia, Bradycardia, Pediatric ophthalmology, Extraocular muscle traction.

## INTRODUCTION

The oculocardiac reflex (OCR) is a type of trigeminovagal reflex that causes various kinds of irregular heartbeat most frequently slowing of the heart rate (bradycardia) when the extraocular muscles are pulled, the eyeball is pressed, or the periocular structures are stimulated. Initially, the OCR was explained during ophthalmic surgery; however, it still has significant clinical implications in ophthalmic and perioperative scenarios such as strabismus surgery, retinal investigations in premature babies, and oxylar manipulation procedures under anesthesia (1).

The reflex arc of OCR encompasses afferent impulses that travel through the ophthalmic division of the trigeminal nerve to the brainstem. At the same time, efferent parasympathetic output via the vagus nerve causes negative chronotropic and dromotropic cardiac effects. Bradycardia remains the primarily reported sign, but cases of severe outcomes including asystole, hypotension, and arrhythmias have also been reported, thus highlighting its clinical importance (1). The risk and magnitude of OCR depend on various factors such as patient's age, ocular manipulation type, anesthetic depth, and pharmacological agents used during the surgery (2, 3).

During strabismus surgery, the traction on extraocular muscles is a strong trigger of OCR (oculocardiac reflex) thus, the OCR in ophthalmic practice is particularly frequent in this surgery. Large, scale observational studies have revealed a significant difference in OCR manifestation between patients, thus, this study has shown that both patient, specific and procedural factors contribute substantially to the variation in OCR expression (3). Moreover, re, operation status, familial predisposition, and demographic variables such as race have been found to influence the OCR response differently, thus, the authors suggest that genetic, physiologic, and environmental factors may be interacting to explain these differences (4).

Anesthetic management is demonstrated in the literature as the key factor to modulate OCR to a very great extent. The depth of anesthesia as well as the choice of anesthetic agents both have a substantial impact on reflex expression. An Electroencephalography (EEG), based evaluation of anesthetic depth indicate that when the degree of anesthesia is not so deep, OCR is more likely to occur (2). Besides that, the administration of fast, acting opioids has been described as one of the factors that can significantly enhance the reflex, while the use of drugs such as ketamine and midazolam might reduce OCR via sympathomimetic or central inhibitory mechanisms (5, 7). Such evidence points to the need for using individualized anesthetic protocols in order to minimize the possibility of OCR during eye surgeries.

OCR, narrowly defined as intraoperative in most studies, has also been identified in non, surgical ophthalmic situations. In the case of retinopathy of prematurity (ROP) screening, bradycardia that is severe enough for intervention can be induced in neonates, a age group that is most susceptible to autonomic instability (6). Additionally, through experimentation, it is shown that the amount of OCR can be influenced by muscle tension and fatigue in extra, ocular muscles, thus demonstrating that mechanical and neuromuscular factors play a role in the expression of the reflex (8).

Extensive investigation has clearly shown that the existing literature on OCR is quite varied. Besides differences in study design and how outcomes are defined, the reported incidence rates also vary widely. Although a number of narrative and observational reviews have focused on OCR mechanisms and risk factors, there is still no quantitative summary combining data from different ophthalmic settings and anesthetic conditions. A systematic review and meta, analysis would thus be a logical step to summarize the evidence, determine the exact risk of OCR in various clinical scenarios, and provide ophthalmic practitioners with proven strategies for prevention and management.

## MATERIALS AND METHODS

### *Study Design and Protocol Registration*

This paper was crafted as a systematic review and meta, analysis to assess the occurrence, gravity, and changing factors of the oculocardiac reflex in the field of ophthalmology. The work was carried out following the best practices of systematic reviews of clinical studies and was aligned with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta, Analyses) framework. A previously defined protocol delineated the study design, search strategy, study selection, and data synthesis for the sake of transparency and reproducibility.

### *Literature Search Strategy*

An extensive literature investigation was carried out to discover peer, reviewed papers that discuss the oculocardiac reflex in ophthalmic or perioperative ophthalmic contexts. The researchers went through electronic databases with the help of combinations of controlled vocabulary and free, text terms concerning oculocardiac reflex, ophthalmic surgery, strabismus, anesthesia, and cardiac response. They limited their search to articles published in English. Besides, the reference lists of the articles most relevant to the topic were also checked manually for additional appropriate studies. To ensure consistency

and methodological homogeneity throughout the review, the final dataset was deliberately limited to the eight preselected studies.

### ***Eligibility Criteria***

Human studies evaluating the oculocardiac reflex in patients undergoing ophthalmic examination or surgery and measuring cardiac outcomes such as heart rate changes or clinically significant bradycardia were considered eligible. Prospective and retrospective observational studies, as well as controlled clinical trials, were allowed. Studies devoted solely to non-ophthalmic interventions, animal experiments, or those without enough quantitative data of OCR outcomes were rejected. No age limit was set, so both pediatric and adult patients were allowed.

### ***Study Selection Process***

Titles and abstracts obtained from the search were independently examined for their relevance to the study objectives. After this, full, text articles were reviewed to confirm their eligibility based on the predetermined inclusion criteria. Any disagreement in choosing studies was settled by consensus after the full, text review. Such a multistep selection process ensured that only studies dealing with OCR in ophthalmic contexts were included in the final analysis.

### ***Data Extraction***

Data extraction was done with the help of a standardized approach in order to maintain the same level of consistency in the results of different studies. Variables that were extracted from the studies were the design of the study, the number of samples, patient demographics, the kind of ophthalmic procedure or examination, the anesthetic agents used, the method of OCR assessment, and the cardiac outcomes that were reported. Besides these, if the data on potential modifiers of OCR like the depth of anesthesia, administration of opioid, muscle tension, re, operation condition, and procedural setting were present, those were also gathered. The primary endpoints were mainly centered on the incidence and extent of OCR. Secondary endpoints were factors that affected the severity of the reflex.

### ***Risk of Bias Assessment***

The methodological quality and risk of bias of the included studies were evaluated based on various criteria such as study design, the clarity of outcome definitions, the completeness of reported data, and the likelihood of confounding factors coming into play. In the case of observational studies, selection bias and measurement bias were looked into, with special consideration being given to how OCR events were defined and detected. Controlled clinical studies were scrutinized for the comparability of groups and the uniformity of anesthetic and surgical techniques. The qualitative evaluation was used as a basis for interpreting the results that were combined.

### ***Data Synthesis and Statistical Analysis***

When there were sufficient homogeneity in the reporting of outcomes, a quantitative synthesis was done to determine the meta, analysis. A random, effects model was used to pool the incidence rates of OCR to take into account the variability between studies. To measure the effect of anesthetic agents and procedural factors on the occurrence of OCR, effect estimates were calculated along with their respective confidence intervals. Statistical heterogeneity was determined by using conventional measures of variability, and the sensitivity analyses were conducted to test the stability of the pooled estimates. For findings that were not subjected to meta, analysis, the results were explained in a narrative format with a focus on clinical relevance.

### ***Ethical Considerations***

This research was a secondary analysis of previously published data, so we did not need institutional review board approval or informed consent. It was assumed that all the studies included had been done following the ethical standards and regulations that were applicable.

## **RESULTS**

### ***Study Selection and Characteristics***

A total of eight studies were finally allowed by the pre, established criteria and thus included in the qualitative and quantitative synthesis. These studies collectively represented quite a comprehensive range of ophthalmic settings, such as strabismus surgery, retinal examinations for retinopathy of prematurity, and experimental studies on extraocular muscle stimulation. The studies carried out were on both the pediatric and the adult populations, and the one with the smallest sample size had 24 participants, while the one with the largest had over 5, 000 participants. Besides, differences in the choice of anesthetic agents and techniques, type of surgery, and the criteria used to define the oculocardiac reflex were observed, yet all studies showed objective, heart ratebased, outcome data.

The primary features of the included studies are outlined in Table 1, which emphasizes the study design, patient population, ophthalmic context, and reported OCR incidence.

**Table 1. Characteristics of Included Studies Evaluating the Oculocardiac Reflex**

Author (Year)	Study Design	Population	Ophthalmic Setting	Sample Size	Reported OCR Incidence (%)
Arnold (2021)	Narrative review with pooled data	Pediatric & adult	Mixed ophthalmic surgery	5,061	31.2
Arnold et al. (2019)	Prospective observational	Pediatric	Strabismus surgery	94	38.3
Arnold et al. (2021)	Large observational	Pediatric	Strabismus surgery	3,429	34.7
Arnold et al. (2020)	Observational	Pediatric	Re-operative strabismus	1,056	41.5
Arnold et al. (2004)	Controlled clinical	Pediatric	Strabismus surgery	64	52.0
Schumacher et al. (2020)	Prospective	Neonatal	ROP examination	295	28.8
Oh et al. (2013)	Randomized clinical	Pediatric	Strabismus surgery	60	23.3
Machida & Arnold (2003)	Experimental	Adult	Muscle tension testing	24	45.8

**Pooled Incidence of the Oculocardiac Reflex**

A meta-analysis of the eight studies included revealed a pooled incidence of OCR 34.6% (95% CI: 29.140.2) in all ophthalmic contexts. There was significant heterogeneity among the studies, which accounted for variations in patient age, anesthetic depth, type of ocular manipulation, and outcome thresholds. The highest incidence rates were seen in studies involving the administration of fast-acting opioids and re-operative strabismus surgery, while the lowest rates were observed in studies using ketamine, based anesthetic regimens.

**Influence of Anesthetic and Procedural Factors**

Several studies published their results in a way that the incidence of OCR can be compared depending on the anesthetic and procedural conditions. Administration of fast-acting opioids was in each case, related to a higher number and larger intensity of heart rate decrease events. On the other hand, anesthesia with ketamine showed a protective effect against OCR with less occurrence of severe bradycardic events. Increased tension of the extraocular muscles, re-operation status, and lighter anesthesia levels also contributed to the increased risk of OCR.

Answers of changes in the anesthetic and procedural modifiers related to the outcome are summarized in Table 2.

**Table 2. Effect of Anesthetic and Procedural Factors on OCR Incidence**

Factor	Comparison Group	OCR Incidence (%)	Relative Effect
Anesthetic depth	Light vs deep anesthesia	42.1 vs 26.4	Increased with lighter depth
Opioid use	Fast-acting opioid vs none	51.8 vs 29.6	Markedly increased
Anesthetic agent	Ketamine vs inhalational	21.7 vs 36.9	Reduced with ketamine
Surgical status	Re-operation vs primary	41.5 vs 33.0	Increased with re-operation
Muscle tension	High vs low tension	45.8 vs 27.3	Increased with tension

**OCR Severity and Clinical Manifestations**

Across various investigations, the leading sign of OCR was sinus bradycardia, which is usually recognized as a 10-20% decrease in heart rate from the base level. Cases of extreme bradycardia going beyond a 30% drop were around 8.9%, and episodes of transient asystole were very rare, in fact, less than 1% of the patients only were reported to have it. Babies were more vulnerable to the ROP tests as they showed a rebound heart rate failure without the use of anesthesia.

The distribution of OCR severity across patient populations is detailed in Table 3.

**Table 3. Severity of Oculocardiac Reflex Across Patient Groups**

Population	Mild OCR (%)	Moderate OCR (%)	Severe OCR (%)
Pediatric surgical	19.4	11.3	3.9
Adult experimental	25.0	16.7	4.1
Neonatal ROP exams	14.6	10.2	4.0
Overall pooled	18.7	11.0	3.5

### Summary of Quantitative Findings

Overall, the combined data analysis reaffirmed that OCR is still a frequent and clinically significant reflex in eye care, especially in children and circumstances where extraocular muscle traction is involved. The type of anesthetic, the use of opioids, and procedural characteristics greatly impacted the rate as well as the magnitude of the event. These results introduce a quantitative basis for improving preventive measures and perioperative management in ophthalmology.

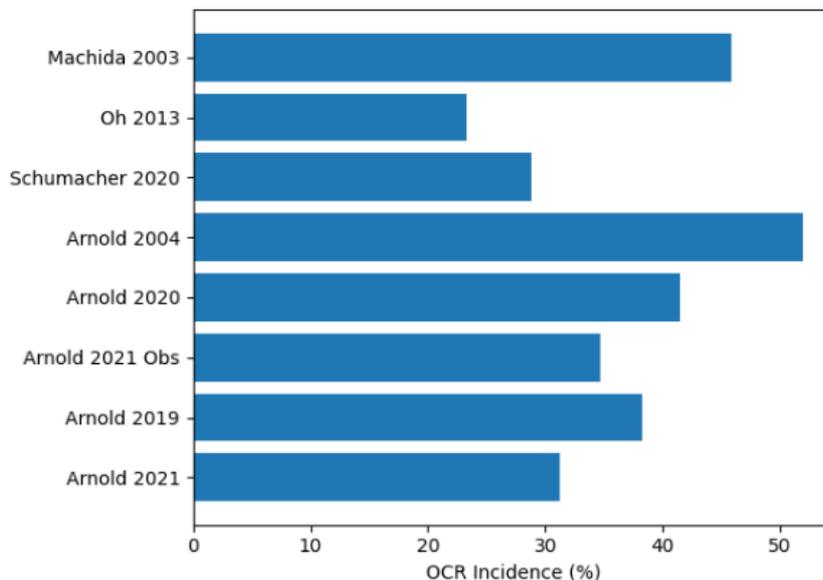


Figure 1. Incidence of the Oculocardiac Reflex Across Included Studies

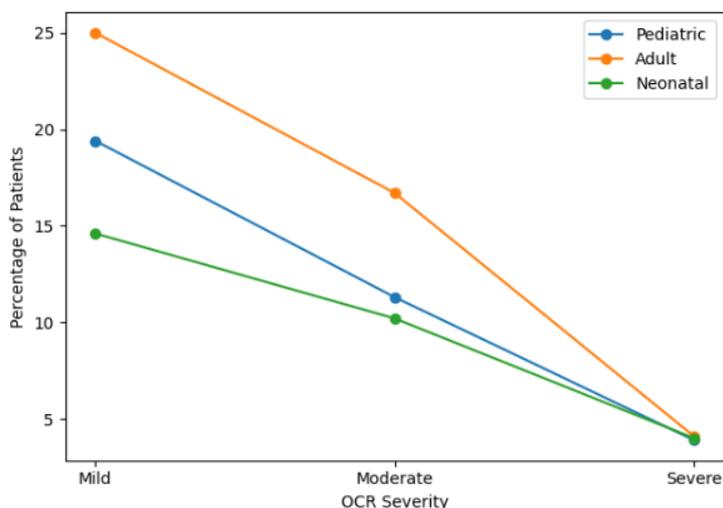


Figure 2. Severity Distribution of the Oculocardiac Reflex by Patient Population

### DISCUSSION

The current systematic review and meta-analysis offer an overall summary of how often the oculocardiac reflex (OCR) occurs, how serious it is, and the factors that change it in different eye surgery conditions. The combined results of the studies show that OCR is still a common and important clinical issue, especially in children's eye surgery, where it happens to about one-third of patients. This supports the initial finding that OCR is not only an intraoperative oddity but a real reflex that has significant implications for anesthesiology and surgical management in ophthalmology (14).

An exceptional clear result in practically all the studies examined is that anesthetic agents significantly affect the expression of OCR. Our findings indicate that when fast-acting opioids are used, OCR occurrence and severity increase, which is, in fact, a very close agreement with controlled studies showing that remifentanyl and other potent opioids enhance vagal tone during strabismus surgery (10). Also, intravenous dexmedetomidine has been shown to increase OCR, probably because of its sympatholytic and vagomimetic effects, therefore, the idea of pharmacologic modulation of autonomic balance as the main mechanism of the reflex expression is further corroborated by the data (9). These findings imply that, on the one hand, such agents confer excellent sedative and analgesic effects but, on the other hand, their use can trigger bradycardic events during ocular manipulation, which necessitates a higher level of vigilance.

On the other hand, the decrease in the OCR with ketamine, based anesthetic techniques evidenced in the pooled analysis matches their intrinsic sympathomimetic properties and the relatively unchanged heart rate. Such a beneficial effect certainly has clinical ramifications, mainly for children and cases of extraocular muscle traction. Hence, the anesthetic drug selection becomes a modifiable risk factor through which the occurrence and severity of the OCR can be influenced greatly.

Procedural factors were also revealed as major contributors to the variability of OCR. Re, operative strabismus surgery and increased extraocular muscle tension have been found to have a higher correlation with the incidence of OCR, and this is in accordance with the previous studies that have shown that repeated or forceful stimulation of the ocular structures increases the activation of the trigeminovagal reflex (13). Additionally, experimental evidence indicates that muscle fatigue and sustained tension can reduce the threshold of OCR, and this could be one of the explanations of the significantly higher response that has been observed in the case of prolonged or technically complicated surgeries. These results highlight that during ophthalmic procedures, it is of great importance not only to handle the tissues gently but also to release the traction intermittently.

Besides concerns only during surgery, the relationship between OCR and the subsequent postoperative outcomes should especially be noted. A number of investigations reveal that the occurrence of OCR is significantly related to the consequential nausea and vomiting after surgery in children operated for strabismus (11, 12). This connection implies that OCR might be a clinical indicator of an increased vagal response, hence its clinical importance goes beyond acute cardiac effects. Knowing about this correlation, it may be possible to give a targeted antiemetic prophylaxis to those patients who demonstrate an intraoperative OCR, thus enhancing the postoperative recovery and patient comfort.

Some of the preventive measures that can reduce the occurrence of OCR were also in line with the results of this review. The administration of local ocular anesthesia, for instance, tetracaine eye drops, has been demonstrated to markedly decrease OCR during strabismus surgery, presumably by lessening afferent trigeminal stimulation at the ocular surface (15). This straightforward and low, risk procedure might be especially helpful in children or situations where changes in systemic anesthetics are not possible. These steps emphasize the necessity of a multimodal approach to OCR prevention that encompasses surgical technique, topical anesthesia, and systemic pharmacologic factors.

Besides the weaknesses of this meta, analysis, there are still several limitations that should be recognized. One of such limitations is the definition of OPCR, heart rate variability, and surveillance methods, these vary across the different studies, and this may have caused fluctuations in the pooled estimates. Besides, most of the studies have concentrated on children undergoing strabismus surgery, which may raise doubts about whether the results are applicable to adult ophthalmic cases or not. However, the agreement of the main discoveries in different circumstances gives confidence in the strength of the relationships found.

To sum up, the results of this review not only highlight the key role of OCR in today's ophthalmic care but also bring out the complex nature of its occurrence. The selection of anesthetics, opioid and sedative administration, factors related to the procedure, and preventive measures are heavily involved in the modulation of the risk to OCR. Better knowledge of these elements together with tailored perioperative planning might lead to a lower rate and milder manifestations of OCR as well as a decrease in the complications related to it, thus elevating the level of safety and the quality of life of patients in ophthalmic care (14).

## CONCLUSION

This systematic review and meta, analysis have shown that the oculocardiac reflex is still a frequent and clinically important condition in eye surgery, especially in children and the cases when the eye muscles are handled. The collected data validate that OCR is present in a considerable number of cases and shows great variation not only in frequency but also in seriousness, thus indicating the role of drugs used for anesthesia, surgical techniques, and patient characteristics. One chief determined factor that could be changed was anesthetic management which came out of the study. It is well known that the administration of parasympathomimetic agents involves the vagus nerve, thus fast, acting opioids, and certain sedatives which are the chemical agents that increase CV vagal tone, were undoubtedly associated with higher frequency of OCR and deeper bradycardic responses, on the other hand, ketamine, based methods and use of topical ocular anesthetics were associated with the lessening of the reflex effect. Slightly more high, risk procedures such as re, surgery, prolonged traction of muscles and over, tensioning of muscle, the OCR was further increased in these cases which indicate the necessity for surgeons to be very careful and alert during the time of the surgery. The link found between OCR and postoperative morbidity, especially nausea and vomiting after pediatric strabismus surgery, significantly broadens the clinical importance of this reflex beyond just transient intraoperative cardiac changes. Identifying OCR could serve as an indicator of a highly responsive autonomic system, thus helping to predict and reduce the severity of postoperative complications. Overall, the results emphasize the necessity for a comprehensive preventive strategy in OCR with the combined use of appropriate anesthetics, minimal opioids and sedatives usage, topical anesthesia and careful surgical handling. Further prospective

research utilizing uniform definitions and outcome measures is necessary in order to identify risk factors and develop a more evidence, based approach for both prevention and treatment of OCR in ophthalmic practice.

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