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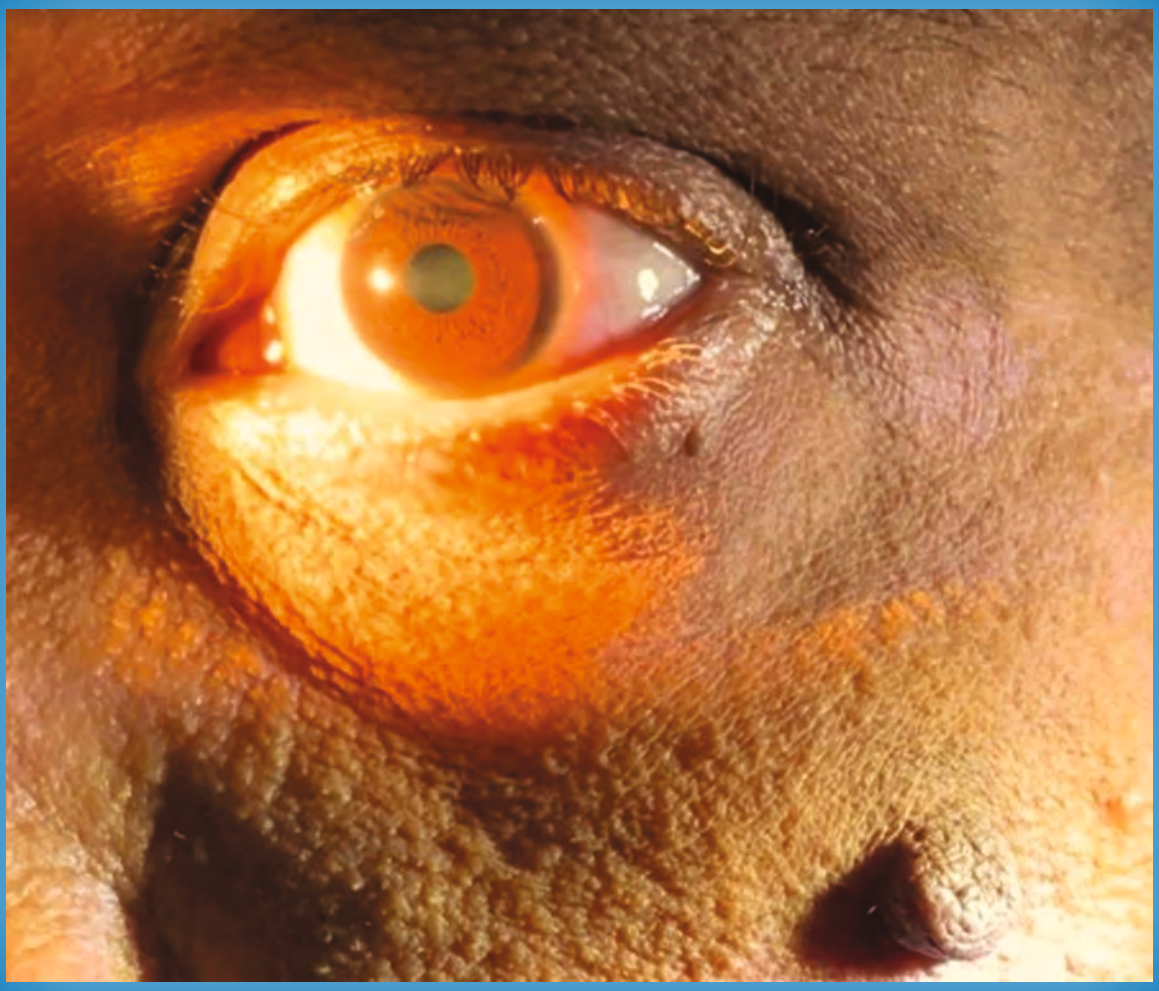

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Evidence-Based Medicine in Medical Practice

"The integration of best research evidence with clinical experience and patient values."

–David Sackett.

Definition

Evidence-based medicine (EBM) is the assiduous, unambiguous, well-judged, and practical use of modern, ethical value-based clinical research best evidence to make conclusions in delivering cost-effective and better health care to individual patients.

EBM gives a clinician a new way of understanding and integrating the best clinical research, clinical expertise, and patient preferences to optimize clinical decision-making. Systematic reviews and meta-analyses are important milestones in applying EBM for better medical practice.

What is true today in science may not be true tomorrow. The exponential growth of basic research and changing trends in patient value-added treatment patterns have put the clinician in academic isolation and to keep abreast of the knowledge needed to meet this scientific explosion and information overload of published literature.[1] EBM approach suggests reading and focusing only on specific clinical/patient problems to improve the clinician's knowledge. It enhances the use of available relevant literature in reducing the gap between good clinical research and clinical practice. It identifies and promotes those practice preferences that improve quality care and also eliminates harmful and ineffective treatment modalities.

EBM is a lifelong learning and application of the best clinical research evidence arrived through systematic reviews of medical literature to the individual patient on a specific clinical scenario by the medical practitioners.[2] In a limited time, clinicians can be highly selective and focus on knowing the latest trends in the various advancements in optimizing clinical care.

What is the Evidence in Evidence-based Medicine?

It is the most relevant and effective intervention or treatment in patient care based on the findings from patient-centered clinical research.

A hierarchical system of classifying levels of evidence depending on the probability of bias is the cornerstone of EBM. The grading system has placed randomized controlled trials (RCTs) at the highest level because they are designed to have low selection bias and fewer systematic errors. As opposed, case series and expert opinions are graded as lowest.[3] However, higher the quality of evidence closer to the truth, though not a study design, taking the totality of the evidence, systematic reviews summarize the best available evidence in all types of study designs including cohort studies, case–control studies, and even case reports and hence in the hierarchy of evidence, systematic reviews are kept on the top. To overcome the shortcomings of the hierarchical pyramidal grading system, the "GRADE = Grading of Recommendations Assessment, Development, and Evaluation, system[4]" has been introduced, which resulted in great improvement in the quality of systematic reviews.

For developing clinical practice guidelines and designing new research studies, systematic reviews are essential in standardization of the health care. EBM gives trustworthy clinical practice guidelines to the clinician, at the point-of-care delivery. These guidelines decrease inappropriate and wasteful procedures in clinical care and research.[5]

Clinical expertise, so-called the art of medicine – medical education, clinical skills, and clinical experience, should be considered a complementary source of knowledge which supports the effective use of available literature and facilitates the collective clinical decision of patient care.[6] However, it is essential in framing the clinical question, collecting the evidence, appraising, integrating, and considering its ethical applicability to the patient. Choosing evidence from a peer-reviewed article mitigates the chances of misjudgment.[6]

For individual patients with rare diseases, personalized research protocols are designed to improve care, by integrating, the best clinical research, and medical care and incorporating individual patients' preferences. This led to individual point-of-care trials designed in lines of N-of-1 studies.[7] It is useful in determining optimal therapy, in patients with rare diseases, with comorbidities who do not meet the RCT criteria, or patients with unusual side effects or idiosyncratic treatment responses.[8]

Evidence-based medicine Steps in Clinical Practice

Ask, acquire, appraise, apply, and assess are the important steps of EBM.[9,10] Asking well-built specific problem-oriented relevant answerable questions about the clinical case is the key to acquiring the best clinical research evidence from the medical literature databases (PubMed, Google Scholar, Trip Medical Database, etc.,). PICO (patient, intervention, comparison, and outcome)[9] model as a search strategy tool for creating the apt research question with which literature search improves the quality and comprehensiveness of the results and decreases errors. The clinician should possess the skills in exploring databases such as PubMed, Google Scholar, Embase,

and Cochrane Library. He should be conversant with the use of keywords, Mesh terms,[11] Boolean operators,[12] and validation filters in acquiring appropriate evidence from the databases.

Critical appraisal assesses the trustworthiness of the article and its relevance to the research question in a given situation. It evaluates the appropriateness of inclusion criteria, searching strategy, supporting data, and level of publication bias. JBI critical appraisal tools are the ones that are developed to aid in this process.[13,14]

Advantages of Evidence-based Medicine in the Medical Practice

By adopting EBM, one can minimize errors, reduce cost of treatment, and optimize the quality of patient care. It ensures the physician to daily access to the relevant literature advances in medicine and keeps him abreast with the present scientific progress. Thus, EBM indirectly influences the professional conduct of the physician more efficiently. This process maximizes the benefits of scientific research for patient care.

There is a paradigm shift from expertise-based medicine to EBM. Let us strengthen the EBM movement through JOCR.

Historical Perspective

David Sackett is considered to be the father of EBM. The word EBM was coined by Gordon H Guyatt in 1991.[15]

Professor Archibald Cochrane (1909–1988) a British clinical epidemiologist insisted on systematic, up-to-date reviews of all relevant RCTs of health care, which has led to the founding of Cochrane Collaboration (1993)-http://www.cochrane.org. He could convince the medical world that EBM is a good tool for evaluating the research evidence for better medical care.[16]

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Statistical Significance versus Clinical Significance

Introduction

Medical research can be analyzed under two primary domains: clinical significance and statistical significance. Both ideas have different functions, but they are essential to comprehending study results and their practical implications. The primary distinction between clinical and statistical significance is that clinical significance takes into consideration the improvement in quality of life where as statistical significance refers to the claim that a result from data generated by testing or experimentation is likely to be attributed to a specific cause. At times, research may show statistical significance but may not be clinically significant and vice versa. There are many factors that affect statistical and clinical significance; hence, it becomes important to understand these before taking statistical or clinical significance into consideration.

Understanding Statistical Significance

Every clinical research starts with a hypothesis, that is, the researcher must have some idea about what they want to scrutinize or conclude from the research. There can be multiple outcomes to research; hence, it becomes difficult to come to a single conclusion. Hence, formulating a null hypothesis and disproving it by calculating a statistically significant *P* value helps us to come to single conclusion.[1]

To have a better understanding about statistical significance, we need to first learn about *P* value, so here is a brief discussion about the evolution of *P* value.

Arbuthnot observed that the number of males born in London were more than the number of females (1629–1710). He stated that if the birth rates of males and females were equal, then the probability of observing more male newborns for 82 consecutive years would be 0.582.[2]

Later, breakthrough discovery was made by Fisher's Ronald Aylmer. According to Fisher, any finding that is likely to occur by random variation no more than 1 in 20 times is considered significant. Neyman J and Pearson ES subsequently argued that Fisher's definition was incomplete. They proposed that statistical significance could only be determined by analyzing the chance of incorrectly considering a study finding was significant (type I error) or incorrectly considering a study finding was insignificant (type II error). Their definition of statistical significance is also incomplete because the error rates are considered separately, not together. A better definition of statistical significance is the positive predictive value of *P* value, which is equal to the power divided by the sum of power and *P* value. This definition is complete and more relevant than Fisher's or Neyman–Pearson's definitions because it considers both concepts of statistical significance.[3]

There are three ways to determine statistical significance

a. *P* value method
b. Critical value method/level of significance
c. Confidence interval method.

The goal of any study is to understand the underlying mechanism that gives rise to the observed data using the parameters. To understand the mechanism for observed data, one must perform a hypothesis test to examine how close the estimated parameters maybe. This process usually involves hypothesis testing, wherein you compare your observed data against a null hypothesis.

Steps to Calculate Statistical Significance

Define the hypothesis

- Null hypothesis (H_0): This is the assumption that there is no effect or no difference between the two study groups. For example, "There is no difference in the mean blood pressure between two groups"
- Alternative hypothesis (H_1 or Ha): This is the hypothesis you want to test, which suggests that there is an effect or a difference between the two study groups. For example, "There is a difference in the mean blood pressure between two groups".

Choose the significance level (α)

The significance level is the threshold for deciding whether the observed data are sufficiently unlikely under the null hypothesis.

- Most common level is $\alpha = 0.05$, especially in scientific and consumer research
- And in medical research $\alpha = 0.01$ (where quality matters more)
- Political polling $\alpha = 0.1$.

Collect data and calculate the test statistics

Obtain data relevant to your hypothesis and conduct a statistical analysis by computing key summary metrics, including the mean, proportion, and variance.

The significance level (α) is the threshold at which you reject the null hypothesis. It is usually set at 0.05, which corresponds to a 5% risk of concluding that an effect exists when there is none (Type I error).

Select the appropriate statistical test

- *t*-test: For comparing the means of two groups
- Chi-square test: For categorical data
- ANOVA: For comparing the means of three or more groups
- *z*-test: For large samples, comparing means or proportions.

Determine the *P* value

P value indicates the probability of obtaining a test statistic as extreme as the one observed, assuming the null hypothesis is true.

- If $P < 0.01$ very strong evidence to support H_1
- If $P = 0.01–0.05$ strong evidence to support H_1
- If $P > 0.01$ weak evidence to support H_1.

Compare *P* value to the significance level

- If *P* value is less than or equal to α\alpha α, you reject the null hypothesis, indicating that your results are statistically significant
- If *P* value is greater than α\alphaα, you fail to reject the null hypothesis, indicating that your results are not statistically significant.

Interpret the results

If *P* value is less than or equal to α\alpha α, you reject the null hypothesis, indicating that your results are statistically significant.

If *P* value is greater than α\alphaα, you fail to reject the null hypothesis, indicating that your results are not statistically significant.

Factors Affecting *P* Value

- Sample size – Depends vastly on the sample size, larger the sample size more likely a study will find a significant relationship if one exists. The overall variability is decreased, and the measure becomes more precise for a population as whole[4]
- Magnitude of difference between groups – If there is a large magnitude of difference between groups, it becomes easier to detect.[4]

To Summarize

Uses

- The *P* value does not establish probabilities of hypotheses. Rather, it is a tool for deciding whether to reject the null hypothesis[5]
- The interpretation of the *P* value needs to be contextual, accounting for the experimental design, model specification, sample size, significance level, desired power, and the scientific question.

Misuses

- According to the American Statistical Association, there is widespread agreement that *P* values are often misused and misinterpreted[6]
- Generalizing specific threshold level of 0.05
- p-hacking (e.g., conducting several statistical tests and only reporting those that pass the threshold)
- Increasing the sample size may yield a more significant but not necessarily a meaningful *P* value.

Clinical Significance

Clinical significance is a concept that transcends the boundaries of statistical analysis, addressing the real-world relevance of study outcomes in healthcare settings. While statistical significance is concerned with whether a result is likely to be due to chance, clinical significance focuses on the practical importance of the results – how they can be applied to improve patient care, influence clinical decisions, and ultimately enhance health outcomes. Clinical significance is evaluated based on the magnitude of the effect and its relevance to patient care. It is concerned with whether a treatment effect, even if statistically significant, is large enough to be considered beneficial in a clinical context. Clinical significance helps bridge the gap between research and patient care by ensuring that medical decisions are based on results that are not only statistically sound but also relevant and meaningful in real-world settings.

For example:

1. Visual function beyond visual acuity: Some treatments might not show improvement in traditional metrics like visual acuity but can have clinically significant improvement in qualitative metrics such as brightness and contrast sensitivity
2. Economic considerations of loading dose versus pro re nata protocols in antivascular endothelial growth factor (VEGF) therapy: The loading dose regimen may deliver superior short-term anatomical outcomes, but its economic impact must be carefully considered, especially in populations with limited financial resources. Balancing the clinical benefits of early, intensive treatment with the economic feasibility of long-term care is critical to ensuring equitable access to effective therapies
3. Choroidal neovascularization in age-related macular degeneration: In patients with wet age-related macular degeneration, a slight improvement in vision after anti-VEGF treatment (for instance, an improvement of just five letters on the visual acuity chart) may not reach statistical significance but can be clinically meaningful for the patient's quality of life, especially in preserving functional vision and ability to perform daily tasks
4. Preventing disease progression: In cases of active tractional retinal detachment, early vitrectomy may not always produce statistically significant improvements in final visual acuity compared to deferred surgery. However, clinically, it could halt disease progression, preventing severe vision loss or complications, which is crucial for long-term patient outcomes
5. Vitrectomy in cases of subfoveal perfluorocarbon liquid: In cases of subfoveal perfluorocarbon liquid (PFCL) retention, vitrectomy has demonstrated statistically insignificant anatomical outcomes on optical coherence tomography in most studies. However, patients who underwent surgical removal of PFCL reported subjective improvements in visual quality, specifically in terms of enhanced brightness, color saturation, and decrease of central scotoma. These findings suggest that despite limited anatomical changes, the procedure may offer clinically meaningful benefits in visual perception for affected individuals.

There are a variety of ways to calculate clinical significance. Five common methods are the

- Jacobson-Truax method
- Gulliksen-Lord-Novick method
- Edwards-Nunnally method
- Hageman-Arrindell method
- Hierarchical linear modeling method.[5]

Jacobson-Truax is a common method[7] of calculating clinical significance. It involves calculating a Reliability Change Index (RCI).[8] The RCI equals the difference between a participant's pretest and posttest scores, divided by the standard error of the difference. Cutoff scores are established for placing participants into one of four categories: recovered, improved, unchanged, or deteriorated, depending on the directionality of the RCI and whether the cutoff score was met.

The Gulliksen-Lord-Novick method is like Jacobson-Truax, except that it considers regression to the mean. This is done by subtracting the pretest and posttest scores from a population mean and dividing by the standard deviation of the population.[9]

Importance of Clinical Significance

1. Improved patient care: Decisions based on clinically significant findings are more likely to lead to better patient outcomes
2. Informed decision-making: Clinicians can make more informed treatment decisions by considering the clinical significance of study findings
3. Resource allocation: Resources in health care are limited, and focusing on interventions that have clinical significance ensures that they are used effectively to improve health outcomes.

Limitations of clinical significance

While clinical significance is a valuable concept, it is not without its limitations. The assessment of clinical significance can be subjective and context dependent. What is clinically significant in one population or setting may not be in another. In addition, clinical significance does not always account for the variability in patient responses to treatment or the potential for side effects. Therefore, it is important for researchers and clinicians to use a combination of statistical and clinical significance, along with clinical judgment, to make well-rounded decisions.

Conclusion

Both statistical and clinical significance are crucial in the interpretation of research findings, but they serve different purposes. Statistical significance informs us about the likelihood that an observed effect is not due to chance, while clinical significance tells us whether the effect is meaningful in a practical context. The proper interpretation of research outcomes requires an understanding of both concepts and their interplay. Researchers and clinicians must consider both statistical and clinical significance to make informed decisions that ultimately benefit patient care and public health.

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Review Article

Case Control Study

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Abstract

Observational studies constitute an important category of the research study designs. A case–control study, one of the subtypes of observational study, is widely used to find answers for various research questions. It shows a more accurate link between the cause and effect, gives reliable results quickly with less work and is cost-effective. As the study is also easily understandable, this can be done even by a novice researcher/epidemiologist. It is often the first choice for research during disease outbreaks or when studying rare diseases. However, case-control studies are more prone to biases. To ensure more reliable results, it is essential to have a clear hypothesis, carefully select case and control groups and conduct thorough follow-ups.

Keywords: Case–control study, observational study, research study design

Introduction to Case–Control Studies: A Research Study Design

Research study designs refer to the overall plan or strategy that researchers use to conduct a study and gather data. The choice of study design depends on the research question, the nature of the study, and the available resources [Figure 1].

Each study design has its own merits and demerits. The type of study which is used to answer a particular question depends on the nature of the question, the variables used, the goal of the research, the availability of resources, and many other factors. The study design has to be chosen very appropriately, as the validity of the study depends on the type of study design chosen.

There are a few terms to be understood clearly when classifying a study design, which are described in the following sections.

Variable

A variable is any characteristic or factor that can change or vary among individuals or over time. Examples include age, gender, height, weight, occupation, habits, and comorbidities.

Exposure

Exposure refers to the risk factor whose effect is being studied.[1] The outcome of the study is being decided and correlated based on the exposure. Study designs such as case–control studies determine the strength of association between the outcome and exposure. Examples include the prevalence of Eales disease in patients with tuberculosis compared to patients without tuberculosis.

Intervention

In this study, if the researcher actively introduced a treatment or procedure to some or all participants instead of allowing the study to proceed naturally, it is considered an interventional approach. It is usually seen in experimental studies, for example, to see the effect of a drug, for evaluating a patient postoperatively.

If a drug has been started even before the study has begun, it will be considered "exposure" and not as "intervention." If the drug is administered after the study has begun and is done for study, it is said to be an intervention.

Descriptive Studies (Nonanalytical Studies)

In this study design, the data are described based on one or a few characteristics of the individuals in the group. For example, dietary habits in pregnant women.

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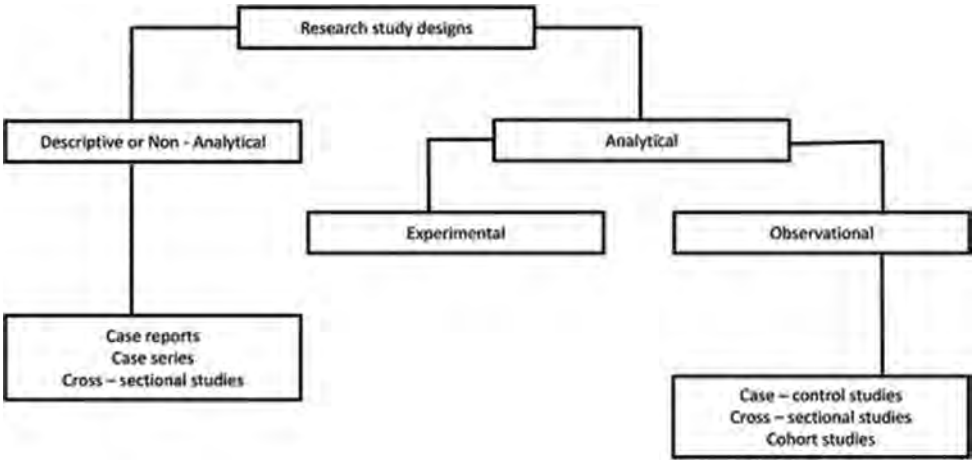

Figure 1: Classification of research study designs[1]

Analytical Studies

Here, a hypothesis is made initially and then a causal relationship is established between the exposure/intervention and the outcome. For example, incidence of primary open-angle glaucoma in patients with diabetes mellitus.

Directionality of Study Designs

Concerning the direction of inquiry, it can be forward direction or backward direction. In this study, if the researcher begins by identifying the exposure and then observes whether the outcome occurs at a later time, it is known as a forward-directed or prospective study. This study design is time-consuming and the researcher will be unaware of the accurate outcome of the study. This study is also known as a prospective study. For example, incidence of lung cancer in smokers and nonsmokers.

If the direction of enquiry is in backward direction study which is also called as retrospective study, in this the researcher begins by checking if the outcome (like a disease) is already present. Then looks back to see if there was any prior exposure in past. Case-control study is a common type of retrospective study. For example, a group consisting of patients suffering from lung cancer and another group who do not have lung cancer are selected and both groups are retrospectively enquired regarding their smoking habits. In this way, an association is formed whether or not smoking leads to lung cancer.

Case–Control Study

A type of observational study design is generally done to identify the factors/exposures leading to the outcome and the strength of association between the exposure and the outcome.[2]

How Is a Case–Control Study Done?

Initially, the researcher hypothesizes that an exposure/risk factor is causing the disease.

The researcher first selects a group that has the disease/the outcome of interest – the case group. Then another group is selected who does not have the disease/the outcome of interest – the control group, but the two groups have the same variables of age, gender, etc., After the two groups are selected, the researcher retrospectively checks if the exposure/risk factor is present more in the case group. If the exposure/risk factor is present more in the case group, the researcher concludes that the hypothesis is true and the exposure does lead to outcome/disease.

Hence, the study gives us information that the exposure leads to the outcome, but to find out how strongly the exposure is related to the outcome, we need to calculate odds ratio (OR).

Method of calculating odds ratio

Primarily, a table of outcome against exposure is constructed [Figures 2 and 3]:

- If OR > 1, this implies a positive association
- If OR < 1, this implies a negative association
- If OR = 1, this implies no association.

OR and relative risk (RR) are not the same. OR tells about the strength of association, whereas RR is a measure of the probability of the disease/outcome of interest in the exposed vs. nonexposed groups.

Example

In a retrospective case–control study done in New York by Koizumi *et al.*,[3] the duration of the study was 1 year, i.e. from July 1, 2005 to July 31, 2006.

Method for selection of cases and controls

The cases and controls with their details were procured through a review of medical and billing records.

Both the case and control groups consisted of 144 patients each. The case group consisted of patients with central retinal vein occlusion (CRVO). The control group consisted of patients with other pathologies such as rhegmatogenous retinal detachments, epiretinal membrane, macular hole/cyst, pathologic myopia, central serous retinopathy, retinoschisis, retinitis pigmentosa,

lattice retinal detachment vitreous floaters, and dislocated lens. Age, gender, and race were matched. The mean age was found to be 69.6 years (±13.6 years). Gender in both the groups was distributed equally with male-to-female ratio of 87:57.

Factors determined

Through univariate analysis, factors such as hypertension, diabetes mellitus, glaucoma, atrial fibrillation, aspirin use, warfarin use, angiotensin-converting enzyme inhibitor use, and estrogen use in postmenopausal women were tested.

Conclusion

They found the same risk factors which were previously identified for CRVO by other studies, but interestingly, other two factors which were identified in this study were the use of aspirin and warfarin [Table 1].

Advantages of Case–Control Studies

There are many advantages of a case–control study. A few of them are as follows:

	CASES	CONTROL
EXPOSED	a	b
UNEXPOSED	c	d

Figure 2: 2 × 2 table in which "a" Indicates the number of cases who had exposure to the event/drug/intervention. "b" Indicates the number of controls who were exposed. "c" Indicates the number of cases who were not exposed. "d" Indicates the number of controls who were not exposed.

$$\text{Odds of exposure in cases} = \frac{\text{Number of cases with exposure}}{\text{Number of cases without exposure}}$$

$$\text{Odds of exposure in controls} = \frac{\text{Number of controls with exposure}}{\text{Number of controls without exposure}}$$

$$\text{ODDS RATIO} = \frac{\text{Odds of exposure in cases}}{\text{Odds of exposure in controls}} = \frac{a/c}{b/d} = \frac{a*d}{b*c}$$

Figure 3: The formula for calculating odds ratio in cases and controls separately

1. As it is a retrospective study, it does not take much time for the researchers to test their hypothesis. It even does not require multiple follow-ups as in the prospective study
2. Very useful in studying even rare diseases. If a disease occurs very infrequently, one would have to follow a large group of people for a long period to collect enough incident cases to study. In such cases, case–control studies come to the rescue. For example, if a disease developed in 1 in 1000 people per year (0.001/year), in ten years, one would expect about 10 cases of a disease to exist in a group of 1000 people. If the disease is much rarer, say 1 in 10,000,000 per year (0.0000001/year), this would require either having to follow 10,000,000 people for 10 years or 1000 people for 1000 years to accrue ten total cases. As it may be impractical to follow 1,000,000 for 10 years or to wait 1000 years for recruitment, so a case–control study allows for a more feasible approach
3. The case–control study design makes it possible to look at multiple risk factors at once
   Example: In a study done by Harding *et al*.,[4] the effect of diabetes, gender of the patient, and glaucoma on cataracts were tested. The study selected a total of 1940 subjects, 723 cases and 1217 controls, between the ages of 50 and 79 years with a response rate of 97% for cases and 94% for controls.
   Result: Diabetes was shown to be a powerful and highly significant risk factor for cataracts with a Relative risk of 5.04. More than 11% of cataracts in Oxfordshire were due to diabetes. The RR did not increase significantly with age within the range of 50–79 years, but was higher in females than in males. Diabetes remained a powerful risk factor when other identified risk factors had been controlled for. The RR appeared to be greater in women than in men, but this difference was not statistically significant. There was no significant change in risk with age. Glaucoma is a powerful and independent risk factor for cataracts in both sexes and may be responsible for 5% of all cataracts in our area

Table 1: The Odds ratio (OR) was calculated between the case and the control groups to assess the association. Odds ration (OR) for all the characteristics is greater than 1 indicating a positive association, except for the characteristic "Oestrogen use in menopausal women" which is lesser than 1 indicating a negative association

Characteristics	Central retinal vein occlusion group n - 144	Control group n - 144	Odds ratio (95% Confidence interval)
Hypertension	90	59	2.40
Diabetes	23	12	2.09
Glaucoma	44	13	4.43
Atrial fibrillation	18	8	2.47
Aspirin use	69	39	2.48
Warfarin use	24	10	2.68
Clopidogrel use	10	5	2.08
Any anticoagulant use	91	51	3.13
Angiotensin converting enzyme inhibitor use	46	29	1.86
Oestrogen use (Post-menopausal women)	2(54)	9(53)	0.19

4. It is very useful even in case of disease outbreaks to find out potential risk factors in a short duration of time
5. The researcher also has the freedom to choose the size of the groups. To increase the power of the study, he can also increase the size of the case group compared to the control group.

Limitations of case–control study

1. Recall bias: This is the most common and most cited limitation of case–control study. In this bias, the individuals with the disease/outcome will report the history of exposure more easily than the individuals without the disease/outcome. For example, individuals with allergic conjunctivitis often remember and say they visited a garden or were around flowers, which could indicate they were exposed to pollen or dust. But people without the condition may not mention visiting a garden. So, recall bias may lead to concluding there is an association between the disease and the exposure, which in reality is not true
2. Confounding bias: There are always confounding variables present in any study. Failing to identify them leads to confounding bias. Confounding variables are those which are linked both to the exposure and the outcome but are not accounted for as one of the factors. For example, alcohol increases the risk of myocardial infarction. The confounding bias here is smoking, as most alcoholics even smoke
3. Selecting the case and control groups. All of the characteristics should match in both groups

For example, to search for occupational risk factors, Lynge *et al.*[5] conducted a case–control study in nine European countries of cancers of the melanoma of the eye, small intestine, male gallbladder, thymus, bone, male breast, melanoma of the eye, and mycosis fungoides. They recruited 3374 population (61% interviewed) and 1284 colon cancer controls (86% interviewed).

In the process of selection of controls, selective recruitment was noted for the patients with colon cancer.

Importance of Case–Control Study in Clinical Studies

Case–control studies are very useful in finding out the risk factors of rare diseases or in case of outbreaks.

The researcher initially hypothesizes all the possible risk factors involved in the causation of the disease. Then they look for which factors are actually present and check how they are linked to the disease. After finding the possible risk factors, he creates even more questions to test. He chooses other studies such as randomized control studies and cohort studies to answer all his questions and also to strengthen the evidence of the study.

Hence, case–control studies are useful in various ways from the effects of environmental exposure to the effectiveness of a surgery. It also asks for a multidisciplinary involvement of nurses, pharmacists, and doctors as selecting the case and control groups means making sure all their characteristics are closely matched. Any mistakes in matching can lead to invalid outcomes.

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Conflicts of interest

There are no conflicts of interest.

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Review Article

Comprehensive Review of Anatomy and Features of Oculomotor Nerve Palsy

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Abstract

The oculomotor nerve, with its intricate nucleus complex, plays a pivotal role in controlling eye movements and pupil size. Understanding the anatomy and localization of lesions within this complex is critical for accurate diagnosis and effective management. Third-nerve palsy can manifest in multiple ways, including nuclear lesions, fascicular syndromes, and involvement of different anatomical portions such as the subarachnoid space, cavernous sinus, and orbital region. Etiologies vary with common causes being ischemia, aneurysms, and neoplasms, while rarer conditions such as recurrent painful ophthalmoplegic neuropathy and congenital palsy present their own unique challenges. This review article explains comprehensively about the topographical location of third-nerve palsy and the varies clinical manifestations noted with the comment on aberrant degeneration.

Keywords: Aberrant degeneration, basilar, cavernous sinus, fascicular, nuclear, oculomotor nerve, orbital

Introduction

Oculomotor nerve palsy can have a varied presentation and can be because of multiple etiologies starting from metabolic causes to complex neurological conditions. Understanding the anatomy and specific clinical features is of paramount importance in diagnosing as well as managing the patient effectively. Determining whether a third-nerve palsy is isolated or if other cranial nerves are affected, along with assessing the presence of additional neurological symptoms such as ataxia, tremor, and gait disturbances is of paramount importance.[1]

Most third-nerve palsy is typically attributed to microischemia of the nerve, primarily caused by occlusion or hypoperfusion of vasa vasorum, leading to isolated occurrences. In contrast, when third-nerve palsy results from different factors than microischemia, other neurological signs and symptoms are more likely to be present.

In this review, we will explore the various causes of third-nerve palsy based on the anatomical location of the lesion.

Overview of anatomy

The oculomotor nucleus complex is situated within the midbrain, ventral to the periaqueductal gray matter. It extends rostrally toward the posterior commissure and caudally toward the trochlear nucleus. This complex comprises multiple subnuclei responsible for innervating various extraocular muscles, including the levator palpebrae superioris, superior rectus, medial rectus, inferior rectus, inferior oblique muscles, and the Edinger–Westphal nuclei which control the pupillary sphincter and ciliary muscles through parasympathetic fibers [Figure 1].[2]

The oculomotor nerve's nuclear complex is located in the midbrain, precisely at the level of the superior colliculus and ventral to the Sylvian aqueduct. This complex comprises various paired and unpaired subnuclei.

- One of these is the levator subnucleus, which is an unpaired structure situated along the caudal midline. The primary function of the levator subnucleus is to innervate both levator muscles. Consequently, when lesions are localized within this specific area, they will result in the development of bilateral ptosis

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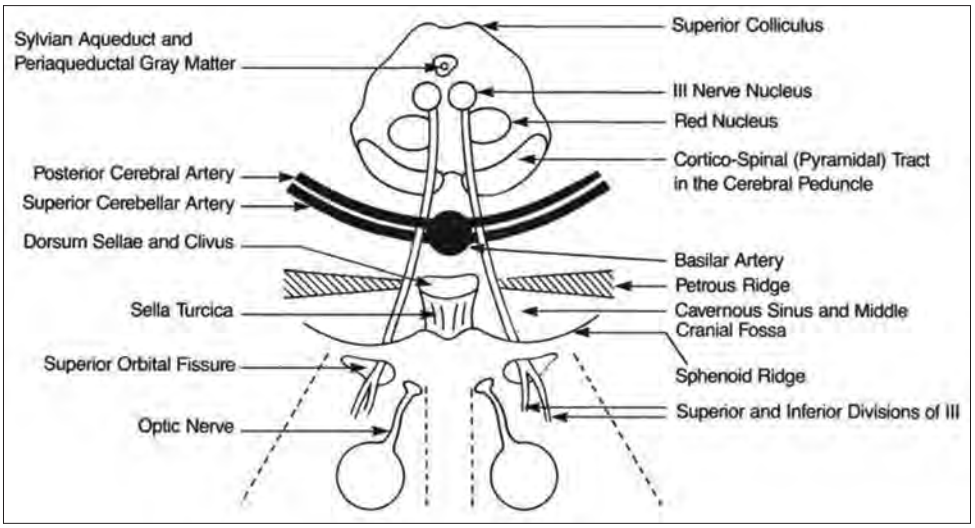

Figure 1: Anatomical representation of the third-nerve course with landmarks being described

- The superior rectus subnuclei exist in pairs, each responsible for innervating the respective contralateral superior rectus muscle. Consequently, in cases of nuclear third-nerve palsy, the impact is selective, sparing the ipsilateral superior rectus while affecting the contralateral one
- On the other hand, the subnuclei governing the medial rectus, inferior rectus, and inferior oblique muscles also come in pairs and serve their corresponding ipsilateral muscles. Instances of lesions isolated within the nuclear complex are relatively infrequent. The most common culprits behind such lesions are vascular diseases, primary tumors, and metastases
- Involvement of the paired medial rectus subnuclei can lead to a condition known as wall-eyed bilateral internuclear ophthalmoplegia.[3] This condition is characterized by exotropia, defective convergence, and adduction. It is worth noting that lesions affecting the entire nucleus often coincide with the involvement of the adjacent and caudal fourth nerve nucleus.

Nuclear third-nerve palsies can manifest as bilateral ptosis or isolated bilateral superior rectus palsies if the lesion affects the medial subnucleus only. However, isolated medial rectus palsy cannot be attributed to a nuclear lesion, as multiple subnuclei contribute to its innervation.

The Edinger–Westphal nucleus is a small but vital structure situated in the midbrain, specifically within the oculomotor complex. Its primary function lies in regulating certain autonomic functions of the eye, particularly those related to pupillary constriction and the accommodation reflex.

This nucleus serves as the origin for parasympathetic preganglionic neurons, which travel through the oculomotor nerve (cranial nerve III) to synapse in the ciliary ganglion. Upon reaching the ciliary ganglion, these preganglionic fibers make synaptic connections with postganglionic neurons.

From the ciliary ganglion, postganglionic fibers extend to innervate several eye structures, including the iris sphincter muscle. The iris sphincter muscle encircles the pupil and controls its size by contracting or relaxing. When stimulated by the parasympathetic fibers originating from the Edinger–Westphal nucleus, the iris sphincter muscle contracts, leading to pupillary constriction.

This constriction of the pupil serves several functions. Primarily, it reduces the amount of light entering the eye, which is particularly useful in bright environments to prevent overwhelming the retina with excessive light intensity. In addition, constriction of the pupil enhances visual acuity by increasing the depth of field and sharpening focus, a process known as the accommodation reflex.

Fascicular Syndromes

The fascicles of the third-nerve traverse the midbrain from dorsal to ventral directions, passing through areas such as the red nucleus, corticospinal tracts, and near the cerebellar peduncle. Lesions involving these locations can result in distinct clinical syndromes.

- Benedikt syndrome affects the fasciculus as it passes through the red nucleus, resulting in an ipsilateral third nerve palsy and contralateral extrapyramidal signs such as hemitremor[4]
- Weber syndrome involves the fasciculus as it traverses the cerebral peduncle, leading to an ipsilateral third-nerve palsy and contralateral hemiparesis[5]
- Nothnagel syndrome encompasses the fasciculus and the superior cerebellar peduncle, and it presents with an ipsilateral third-nerve palsy and cerebellar ataxia[6]
- Claude syndrome is a combination of Benedikt and Nothnagel syndromes, resulting in a unique clinical presentation.[7]

Ischemia is the primary cause of fascicular third-nerve palsy, followed by hemorrhagic and demyelinating lesions, while

neoplasms and inflammatory conditions are less common causes.[8]

Subarachnoid Portion

The subarachnoid space is the most common anatomical location for third-nerve injury. This segment is vulnerable to compression, often due to an aneurysm arising from the junction of the internal carotid and posterior communicating arteries. Despite advancements in neuroimaging and neurosurgery, missing an unruptured cerebral aneurysm causing a compressive third-nerve palsy can have fatal consequences.[9]

Rare causes of third-nerve palsy in the subarachnoid space include compression by the dolichoectatic basilar artery, schwannomas of the third nerve, infections in the central nervous system, and compression by neoplasms. Head injuries leading to the formation of extradural or subdural hematomas can create a condition known as a tentorial pressure cone. This cone exerts downward pressure on the temporal lobe, subsequently compressing the third nerve as it traverses over the edge of the tentorium. Initially, this compression results in an irritated constricted pupil (miosis), followed by pupil dilation (mydriasis), and ultimately culminating in a complete third-nerve palsy.

Cavernous Portion

After traversing the subarachnoid space, the third-nerve pierces the dura and enters the cavernous sinus, where it is situated in the lateral dural folds above the fourth nerve and lateral to the intracavernous portion of the internal carotid artery.

The cavernous sinus's unique neurovascular anatomy can lead to other cranial nerve involvements in addition to third-nerve palsy. Various neoplasms, infections, metastatic lesions, pituitary tumors, aneurysms, dural cavernous fistulas, and dural sinus thrombosis can affect the third nerve in this region.[10] Inflammatory conditions such as granulomatous disorders and idiopathic inflammatory syndrome (Tolosa–Hunt syndrome) are also potential causes of third-nerve palsy in the cavernous sinus. Both superior and inferior division palsies can be seen in traumatic or vascular causes.

Orbital Portion

As the third-nerve exits the cavernous sinus, it divides into superior and inferior divisions, each responsible for innervating specific extraocular muscles. The superior division supplies the superior rectus and levator palpebrae superioris and the inferior division supplies the medial rectus, inferior rectus, and inferior oblique. Understanding this split can aid in localizing the lesion when dealing with a palsy that only involves muscles innervated by a specific division.

Various other conditions can lead to third-nerve palsy which may not fit into the anatomical description mentioned above.

Disorders of Neuromuscular Junction

Ocular myasthenia gravis can sometimes mimic third-nerve palsy but does not involve the pupil, affecting acetylcholine receptors on striated muscles only.[11]

Third Nerve Palsy Associated with Guillain–Barre Syndrome

Guillain–Barre syndrome can be associated with multiple cranial neuropathies, including isolated third-nerve palsy. This typically results from peripheral nerve demyelination and often includes ataxia and areflexia.[12]

Congenital Third Nerve Palsy

In children, nearly half of the cases of third-nerve palsy are congenital and are presumed to result from embryologic insults, intrauterine damage, or birth trauma. Segmental internal carotid artery agenesis has been proposed as a cause.[13]

Rare Causes of Third Nerve Palsy

Several fewer common causes of third-nerve palsy include giant cell arteritis, perineural spread of tumors, recurrent painful ophthalmoplegic neuropathy, cyclic oculomotor paresis with spasms, and dissection of the intracavernous internal carotid artery.[14]

Pupils in third nerve palsy

Pupillomotor fibers, responsible for controlling the pupil's size, are situated in the upper and inner portion of the third nerve as it extends from the brainstem to the cavernous sinus. These fibers receive their blood supply from the pial blood vessels, while the primary central portion of the nerve is nourished by the vasa nervorum.

- Compressive lesions, such as aneurysms, trauma, and uncal herniation, typically impact the pupil by putting pressure on the pial blood vessels and the superficial pupillary fibers
- Metabolic etiologies, as observed in conditions such as hypertension and diabetes, generally do not affect the pupil. This is because medical lesions are associated with microangiopathy that primarily affects the vasa nervorum, leading to ischemia in the primary nerve trunk while leaving the superficial pupillary fibers intact.

These principles, while generally reliable, are not without exceptions. Pupillary involvement can be present in certain cases of microangiopathic palsies, and the absence of pupillary involvement does not always rule out the presence of an aneurysm or other compressive lesions. Pupillary changes may manifest a few days after the onset of double vision as an aneurysm enlarges. In rare instances, pupillary involvement might be the sole indication of a third-nerve palsy, as seen in cases of basal meningitis or uncal herniation. Like other aspects of third-nerve palsy, pupillary involvement can range

from complete to partial, and even mild pupillary signs can carry clinical significance.[15]

Classical clinical features

Partial involvement results in less severe forms of ophthalmoplegia. It is essential to conduct a thorough examination of the other cranial nerves and the peripheral nervous system.[16]

The following clinical signs and symptoms may be observed:

- Profound ptosis caused by weakness in the levator muscle, potentially leading to a lack of spontaneous reporting of double vision [Figure 2]
- In the primary gaze position, there is outward deviation and downward movement (referred to as "down and out"). This results from the unopposed action of the lateral rectus and superior oblique muscles. In addition, the unaffected superior oblique muscle induces intorsion of the eye when at rest, which becomes more pronounced during attempted downward gaze [Figure 3]
- Normal abduction because the lateral rectus muscle remains unaffected
- Limited adduction due to weakness in the medial rectus muscle
- Limited upward movement due to weakness in the superior rectus and inferior oblique muscles
- Restricted downward movement results from weakness in the inferior rectus muscle
- In addition, there are manifestations of parasympathetic palsy, including a dilated pupil and impaired accommodation.

Figure 2: Clinical photograph of the patient showing right eye complete ptosis due to third-nerve palsy

Aberrant regeneration of third nerve palsy

Aberrant regeneration is a phenomenon that can occur after acute traumatic and compressive third nerve palsies, but it is not typically seen in vascular lesions. This is because traumatic and compressive injuries can damage the endoneural nerve sheaths, allowing for abnormal regrowth of nerve fibers. In cases of aberrant regeneration, unusual eye movement patterns may be observed, such as the elevation of the upper eyelid when attempting to look downward (known as the pseudo-Graefe or pseudo-von Graefe phenomenon). This occurs because regenerated axons can misdirect and connect to the wrong extraocular muscles, resulting in these abnormal eye movements.[17]

Isolated third cranial nerve palsy which is pupil-sparing in patients with comorbidities may not warrant the detailed evaluation, however, certain factors, especially pupil involvement, associated neurological features, young age, posttraumatic, and multiple cranial nerve palsy, must need detailed evaluation including neuroangiographic imaging techniques.

Management of third-nerve palsy is a multi-disciplinary approach and it varies as per the etiologies. In brief, pupil involving third-nerve palsy, associated with other neurological signs, multiple cranial nerve palsy, young patients, and clinicians suspected warning signs need computed tomography or magnetic resonance imaging angiography and prompt referral to neurosurgery is recommended. If the etiology is suspected to be metabolic as in diabetes where pupil involvement is not there, the patient can be advised systemic control and masterly inactivity for the nerve palsy of up to 6 months. Surgical correction for squint and ptosis can be planned if nonresolving for 6 months.

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Conflicts of interest

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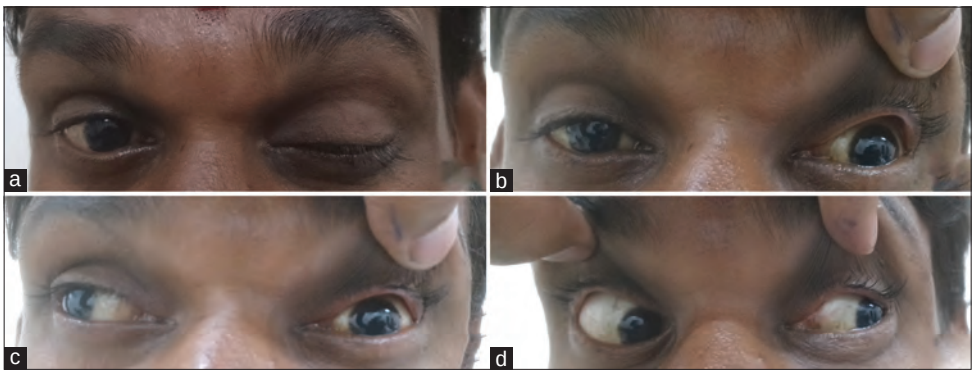

Figure 3: Clinical photographs of patient showing ptosis and down/outward deviated eyeball in primary gaze (a and b), right gaze (c) and left gaze (d) showing limitation of muscle action related to third cranial nerve

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Review Article

Intraoperative Floppy Iris Syndrome - Review Article

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Abstract

Since its initial description by Chang and Campbell in 2005, the understanding and management of intraoperative floppy iris syndrome (IFIS) have evolved significantly. This review aims to examine the changing landscape of IFIS with respect to its pathophysiology, risk factors, preoperative evaluation, and both preventive and intraoperative management strategies. Special emphasis is placed on recent insights and practical approaches that enhance surgical safety and outcomes in patients at risk of IFIS.

Keywords: Alpha adrenergic blockers, intraoperative floppy iris syndrome, pupil expanders

Introduction

Cataract surgery has evolved over time to become one of the most successful surgical procedures. Phacoemulsification is the preferred technique; however, certain conditions – such as small pupils, hard cataracts, and poor zonular support – continue to pose challenges for surgeons. Among these, small pupil size is particularly common and can lead to suboptimal outcomes, especially for less experienced surgeons.

One important cause of small pupil size during surgery is intraoperative floppy iris syndrome (IFIS), first described by Chang and Campbell in 2005.[1] IFIS is classically characterized by a poorly dilated pupil, progressive intraoperative miosis, marked iris billowing, and frequent iris prolapse through surgical incisions. Initially thought to occur exclusively in males taking alpha-adrenergic receptor blockers for benign prostatic hyperplasia (BPH), further research over the past 15 years has revealed a broader spectrum of etiologies.

The evolving healthcare landscape, coupled with the introduction of new systemic medications, has led to the identification of numerous additional factors contributing to IFIS. This review analyzes the current understanding and management strategies for IFIS, based on a comprehensive literature search using PubMed through December 2024.

Epidemiology

The reported prevalence of IFIS varies. In 2005, Chang and Campbell reported an incidence of 2%.[1] Subsequent studies have shown higher rates, up to 12.6%,[2] likely due to increased prescribing of associated medications and improved clinical awareness among surgeons.[3]

Pathophysiology

The iris is innervated by the autonomic nervous system, which regulates pupil size involuntarily through sympathetic and parasympathetic pathways:

1. The sympathetic pathway is responsible for pupillary dilation through innervation of the dilator pupillae muscle[4]
2. The parasympathetic pathway mediates pupil constriction, or miosis.[5]

The predominant receptor subtype involved in sympathetic dilation is the alpha-1 adrenergic receptor (α_1), particularly the α_1A subtype, which is abundant in the iris dilator muscle.

- Distribution of α-adrenergic receptors
  - α_1A: Predominant in the iris dilator muscle and urinary bladder
  - α_1B: Involved in vascular smooth muscle regulation; primarily affects blood pressure
  - α_1D: Found in the bladder and sacral spinal cord.[6]
- Pharmacologic modulation

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- Agonists (e.g., phenylephrine) stimulate α_1 receptors, causing mydriasis[7]
- Antagonists (e.g., prazosin, tamsulosin) block these receptors, leading to reduced pupillary dilation and contributing to IFIS.[5]

The use of alpha-adrenergic antagonists, especially selective α_1A blockers, is strongly implicated in the development of IFIS. Their clinical applications are summarized in Table 1.

Current understanding of intraoperative floppy iris syndrome risk factors and preventive strategies

With the evolving landscape of systemic disease management, alpha-blockers have become a routine part of therapy. Importantly, IFIS is no longer considered exclusive to the medical treatment of BPH. A wide range of other commonly used medications have also been implicated in its pathogenesis. Beyond the direct effects of alpha-blockers, drugs influencing the sympathetic nervous system may also contribute to the development of IFIS.

Our current understanding of the disease process has expanded, and several risk factors have been identified that show a strong association with the occurrence of IFIS.

Risk Factors

Age

A linear correlation has been observed between advancing age and the incidence of IFIS.[8] While the exact mechanism remains unclear, it is hypothesized that the age-related decline in norepinephrine release and activity may play a role.[9] In addition, age-related changes in vascular permeability may lead to iris muscle flaccidity, predisposing to IFIS.[10]

Table 1: Classification of alpha blockers

Nonselective α-blockers (block both α_1 and α_2)		
Drug	**Clinical use**	**Notes**
Phentolamine	Hypertensive emergencies (e.g., pheochromocytoma), extravasation of vasopressors	Short-acting, reversible
Phenoxybenzamine	Long-term management of pheochromocytoma	Irreversible blocker, long duration
Selective α_1-blockers		
Drug	**Clinical use**	**Notes**
Prazosin	HTN, PTSD-associated nightmares, Raynaud's disease	First-dose hypotension risk
Terazosin	HTN, BPH	Longer acting than prazosin
Doxazosin	HTN, BPH	Once-daily dosing
Tamsulosin	BPH	Selective for α_1A subtype (prostate, bladder neck, iris)
Alfuzosin, silodosin	BPH	Similar to tamsulosin; minimal cardiovascular effects

HTN: Hypertension, PTSD: Posttraumatic stress disorder, BPH: Benign prostatic hypertrohy

Gender

Although originally reported predominantly in males, subsequent studies have documented IFIS in female patients as well. Women are increasingly prescribed α_1-adrenergic receptor antagonists for urinary outlet obstruction and detrusor underactivity. Other medications implicated in IFIS, such as benzodiazepines, angiotensin receptor blockers, and antipsychotics, are also commonly used in women.[11]

Systemic comorbidities

A higher incidence of IFIS has been observed among patients with comorbid conditions such as hypertension, diabetes mellitus, and urinary tract disorders. However, the current literature does not conclusively establish a direct causal relationship.[12]

Management

Preoperative evaluation, surgical planning, and prevention

Although IFIS is a well-documented phenomenon, predicting its occurrence remains challenging. A thorough preoperative evaluation – including assessment of risk factors, medication history, and pupil dynamics – can enhance predictive accuracy.

Initial reports suggested that discontinuing the offending medication might reduce IFIS risk,[1] but subsequent studies have shown that drug cessation does not reliably prevent IFIS.[12]

Pupil diameter

Preoperative pupil size is an important predictor. A dilated pupil diameter <7 mm has been shown to predict IFIS with 73% sensitivity and 95% specificity.[13] In addition, a dilated pupil-to-corneal diameter ratio <0.6 has been identified as a useful predictor.[14]

Surgical planning

Given the potential for increased complications, informed consent should specifically address the heightened risk. It is advisable to assign these cases to more experienced surgeons.[15] Surgical modifications – such as using a more anterior incision site and constructing elongated corneal incisions – may reduce the risk of IFIS, especially when the preoperative pupil size is ≥4.5 mm.[16]

Adjustments to phacoemulsification parameters, including low-flow settings, can help control iris billowing and mitigate the severity of IFIS.[11] Other helpful strategies include gentle hydrodissection, minimizing instrument movement, and maintaining irrigation flow above the iris plane.[17,18]

Prophylactic Measures

Currently, there is no universally effective pharmacological prophylaxis for IFIS. Nevertheless, several strategies have shown promise in reducing its incidence:

- Preoperative topical nonsteroidal anti-inflammatory drugs (e.g., ketorolac) help maintain mydriasis
- Topical atropine, used alone or in combination with intracameral epinephrine, can lower the risk in high-risk patients[15]
- A recent study demonstrated that atropine sulfate 1%, administered 40 and 20 min prior to surgery, significantly reduced IFIS incidence, especially its milder forms.[19,20]
- In high-risk patients (dilated pupil <5 mm), the combined use of epinephrine and ketorolacsignificantly reduced the need for iris fixation rings – from 50% in the control group (epinephrine alone) to 0% in the study group ($P = 0.0034$). Furthermore, mean surgical time was significantly shorter in the study group ($P = 0.0068$).[21]

Intraoperative Strategies

Maintaining adequate and sustained pupil dilation is critical for the safe and effective completion of phacoemulsification. In cases where intraoperative visualization is compromised due to poor dilation, mechanical pupil dilation tools, such as pupil expanders and iris hooks, can significantly improve outcomes.[22] In patients with suspected IFIS, traumatic maneuvers – such as aggressive pupil stretching or multiple small sphincterotomies – should be avoided, as they may exacerbate iris billowing and increase the risk of complications.[1]

For high-risk cases, it is often advisable to employ mechanical dilating devices from the outset of the surgery to prevent iris damage and capsular complications. While both iris retractors and pupil expanders have demonstrated efficacy in managing IFIS, each has distinct advantages and limitations.

Iris Hooks

Iris hooks offer a cost-effective and accessible solution for managing IFIS, with a relatively short learning curve. However, their use in IFIS requires technical modifications:

- Hooks should not excessively retract the iris toward the cornea or incision site, as this can increase the risk of iris prolapse and other complications
- Incisions for hook placement should be constructed at the iris plane, just wide enough to accommodate the hook and minimize iris extrusion
- Strategic placement is crucial. A diamond-shaped configuration, with one hook positioned directly inferior to the phacoemulsification incision, can create sufficient subincisional space and help maintain pupil dilation throughout the procedure[23]
- In surgeries involving anterior clear corneal incisions, placing a hook directly beneath the main wound provides added iris support and reduces the risk of prolapse or trauma.

While iris hooks are effective, they can distort the pupillary margin and potentially compromise iris integrity. Even with careful technique, there is a risk of upward traction on the iris, which may predispose it to wound prolapse or entrapment at the hook insertion sites.

Pupil Expanders

Pupil expanders offer several advantages in the management of IFIS:

- Most designs require only a single insertion point, typically through the main surgical port
- These devices provide stable mechanical support, maintaining the iris at the pupillary plane, which reduces the risk of iris prolapse and iatrogenic trauma
- Consistent pupillary expansion supports better intraoperative visualization, reducing the incidence of postoperative pupil distortion, inflammation, and photophobia[24,25]
- Devices with four-point or six-point fixation are available and should be selected based on surgeon preference and intraoperative conditions
- In IFIS cases, bulkier expanders with wider diameters are preferred, as they counteract iris flaccidity more effectively and prevent progressive miosis.

While slightly more technique sensitive, most surgeons can become proficient in deploying pupil expanders with minimal additional training, making them a practical option in IFIS management.

Combined Strategies and Iris Prolapse Management

Despite the benefits of mechanical dilation devices, iris prolapse remains a common intraoperative challenge in IFIS. Prolapse may lead to wound instability, iris trauma, or even postoperative complications such as endophthalmitis.[26]

Management techniques include

- Reducing intraocular pressure and gently repositioning the prolapsed iris into the anterior chamber with a blunt instrument, a technique commonly referred to as "milking"[27]
- Equalizing pressure across the iris plane by releasing aqueous humor or balanced salt solution from the posterior chamber to reduce anterior displacement
- The use of high-viscosity ophthalmic viscoelastic devices anterior to the iris to create a mechanical barrier and minimize iris billowing[28]
- Near the completion of surgery, particularly after intraocular lens implantation, intracameral miotic agents (e.g., acetylcholine or carbachol) can induce miosis, facilitating iris repositioning[29]
- If wound integrity is compromised or iris stability is unachievable, suturing the main incisionshould be performed promptly to preserve anterior chamber depth and prevent postoperative complications.

Conclusion

IFIS has transitioned from a rarely recognized intraoperative complication to a well-characterized surgical challenge with established risk factors and targeted management strategies. The growing prevalence of IFIS – driven by increased use of α_1-adrenergic antagonists, an aging global population, and its occurrence in both sexes – emphasizes the importance of preoperative risk assessment and intraoperative preparedness.

Although a definitive prophylactic solution remains elusive, significant advances in surgical techniques and mechanical devices have improved intraoperative control and patient outcomes. Collaborative care between ophthalmologists and other medical specialists is crucial – particularly in educating prescribers and patients about the ocular risks associated with systemic medications. A multidisciplinary approach is essential to reducing the incidence of IFIS and optimizing safety in modern cataract surgery.

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Conflicts of interest

There are no conflicts of interest.

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Original Article

A Cross-sectional Analysis of Visual Field Defects in Newly Diagnosed Glaucoma Patients at a Tertiary Care Center

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Abstract

Introduction: Glaucoma is a leading cause of global blindness and often remains undetected until significant vision loss has occurred. In India, it contributes to 23.5% of blindness, with socioeconomic factors influencing the severity of the disease at presentation. **Objective:** The objective of this study was to assess visual field defects in newly diagnosed glaucoma patients and explore the clinical and social factors influencing disease severity. **Materials and Methods:** This cross-sectional study involved 50 glaucoma patients at a tertiary care center in Central India (December 2022–September 2023). Visual acuity, intraocular pressure, anterior chamber angle, optic disc status, and socioeconomic status (SES) were evaluated. Data were analyzed using Fisher's exact test ($P < 0.001$). **Results:** In our study, 52% of participants were male, with a mean age of 59.65 years. (1) Forty percent of eyes had moderate visual field defects, and 24% had severe defects. (2) Severe defects were more frequent in patients from lower SES groups, whereas higher SES patients tended to have milder defects. **Conclusion:** Glaucoma severity correlates with SES. Disadvantaged groups are more likely to present with advanced disease due to delayed care. Public health efforts should prioritize early detection, particularly in lower SES communities.

Keywords: Glaucoma, gonioscopy, Kuppuswamy classification, newly diagnosed glaucoma, socioeconomic status, visual field defects

Introduction

Glaucoma accounts for approximately 8% of global blindness cases, affecting over 3 million individuals worldwide with glaucoma-induced visual loss.[1] Despite its prevalence, the disease often remains undiagnosed until significant vision loss has occurred, as it typically presents with no symptoms in the early stages.

Glaucoma is a major public health issue in India, contributing to the highest regional share of global blindness at 23.5%. Approximately 11.9 million people in India are affected by glaucoma.[2]

Only a few studies to date have examined the relationship between socioeconomic status (SES) and the severity or presentation of glaucoma.

Aim and objectives

Aim

The aim of this study was to analyze the visual field status in newly diagnosed glaucoma patients.

Objectives

- To study the location and pattern of visual field defects in newly diagnosed glaucoma patients
- To correlate clinical factors (chief complaints and visual acuity at presentation) with the extent of visual field loss
- To identify social risk factors (occupation, education, and SES) contributing to the late presentation of primary glaucoma in newly diagnosed patients.

Materials and Methods

Study design and duration

A total of 50 patients recently diagnosed with glaucoma who reported to the ophthalmology department of a tertiary care

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center in Central India were included in this cross-sectional study. The study was conducted for 9 months, from December 2022 to September 2023.

Study center

Department of Ophthalmology, Tertiary Care Center, Central India.

Sample size

Fifty subjects participated in the study.

Inclusion criteria

All newly diagnosed glaucoma patients reporting to the ophthalmology outpatient department at the tertiary care center who provided informed consent.

Exclusion criteria

- Patients diagnosed with any other retinal disease, tumors, or optic neuritis causing visual field loss
- Patients on medication are known to affect the visual field.

Data collection procedure

- Clinical history and SES
  - Clinical history: Each patient provided a detailed history, including personal and family history of glaucoma, systemic illnesses such as diabetes or hypertension, any history of ocular trauma or surgery, and current medications
  - SES: Occupation, education, and income were recorded. The modified Kuppuswamy Scale was used to determine SES.
- Visual acuity assessment: Visual acuity was tested using the Snellen chart and the tumbling E chart. For patients who could not understand the E chart, light perception and finger counting were used
- Anterior chamber angle assessment: During the slit-lamp examination, the angle was evaluated using van Herick grading
- Gonioscopy: Gonioscopy was performed to determine the type of glaucoma (open-angle or angle-closure). A slit-lamp and Goldmann three-mirror lens were used. Schaffer's gonioscopic grading system was employed
- Optic disc evaluation: The optic disc was examined using slit-lamp biomicroscopy with a +78D lens to detect glaucomatous changes
- Intraocular pressure (IOP) measurement: IOP was measured using the Goldmann Applanation Tonometer, considered the gold standard. Central corneal thickness was measured through pachymetry, and corrected IOP values were used
- Visual field testing: Visual field testing was conducted using the Humphrey Automated Perimeter to map visual fields and detect areas of vision loss.
  - Criteria for classifying mild, moderate, and severe field defects are listed in Table 1.

Results

Sex distribution

Out of the 50 participants, 52% were male and 48% were female.

Age distribution

The mean age of the patients was 59.65 ± 1.5 years. The highest proportion of patients was in the 55–64 years age group.

Chief complaints

Among the 100 eyes evaluated, the most common complaints at presentation were eye pain (33 eyes, 33%) and blurring of vision (33 eyes, 33%) [Figures 1 and 2].

Visual acuity (Snellen's chart)

Most patients had visual acuity between 6/12 and 5/60 in both eyes.

- Right eye (RE): Fifty-four percent of patients had acuity between 6/12 and 5/60 [Table 2]
- Left eye (LE): Sixty-four percent had acuity in the same range [Table 3].

Gonioscopic findings

Using the Goldmann three-mirror goniolens and Schaffer's grading method:

- Grade 4 angles were observed in 54% of patients

Table 1: Criteria to decide mild, moderate, severe visual field defects

Parameters	Criteria for glaucomatous field defects		
	Early defects	Moderate defects	Severe defects
MD (dB)	<−6	−6–−12	>−12
CPSD	Depressed to *P* <5%	Depressed to *P* <5%	Depressed to *P* <5%
Pattern deviation plot			
Point depressed below *P*<5%	<18 (25%)	<37 (50%)	>37 (>50%)
Point depressed below *P*<1%	<10	<20	>20
GHT	Outside normal limits	Outside normal limits	Outside normal limits
Sensitivity in central 5°	No point <15 dB	One hemifield may have point with sensitivity <15 dB No point has 0 dB	Both hemifield have points with sensitivity <15 dB Any point has 0 dB

MD: Mean deviation, GHT: Glaucoma hemifield test, CPSD: Corrected pattern standard deviation

- Grade 3 angles were observed in 22% [Figures 3 and 4].

Severity of glaucomatous visual field defects

- RE: Forty-two percent had moderate defects, 32% mild, and 26% severe [Table 4]
- LE: Forty percent moderate, 38% mild, and 22% severe [Table 5]
- In total, out of 100 eyes, 40% presented with moderate defects, while 24% had severe defects at the time of diagnosis [Figures 5 and 6].

Socioeconomic distribution (modified Kuppuswamy scale)

- The majority of patients belonged to the upper lower class (42%), followed by the lower middle class (17%) [Figure 7].

Statistical analysis

Data were analyzed using IBM SPSS Statistics software (IBM corp., Armonk, NY, USA). Fisher's exact test was applied, with significance set at $P < 0.001$.

Correlation between socioeconomic status and severity of visual field defects

- Regardless of SES, most patients presented with moderate field defects
- Mild defects were predominantly found in the lower middle and upper middle classes
- Moderate defects were common in the lower and upper lower classes
- Severe defects were observed primarily in patients from the lower and upper lower classes [Tables 6 and 7].

Discussion

- A correlation was found between lower SES and severe visual field defects in newly diagnosed glaucoma patients
- Few studies conducted in the last 20 years have shown more severe visual field defects associated with lower socioeconomic conditions at presentation
- Oh *et al*. made the discovery that the prevalence of glaucoma was highest among persons with the lowest income levels, which indicates that there is a negative

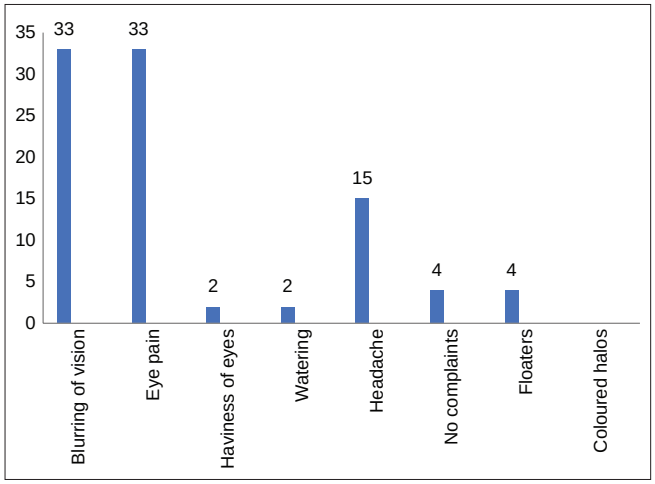

Figure 1: Frequency of complaints

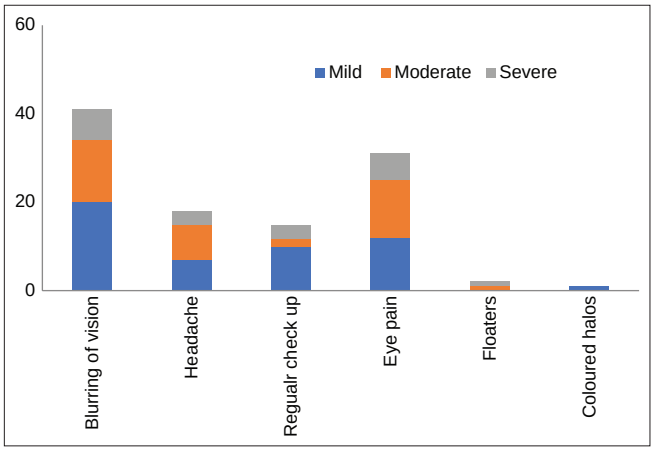

Figure 2: Chief complaints observed in various severity of glaucoma at presentation

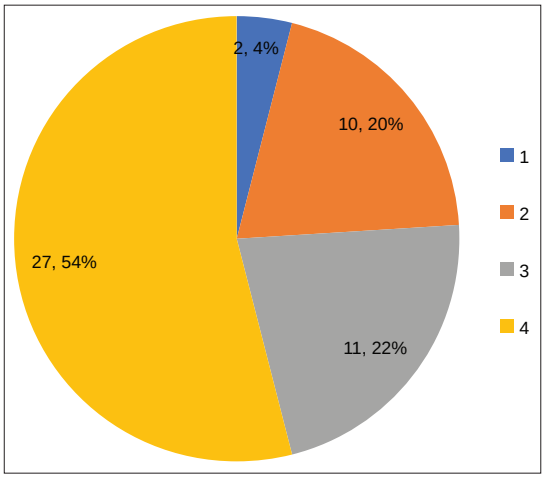

Figure 3: Gonioscopic findings of right eye. RE: Right eye

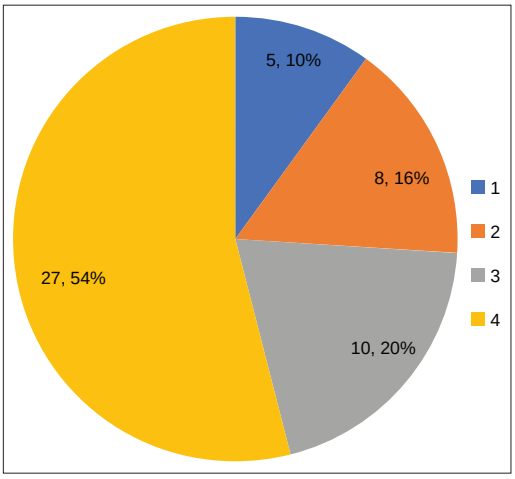

Figure 4: Gonioscopic findings of left eye. LE: Left eye

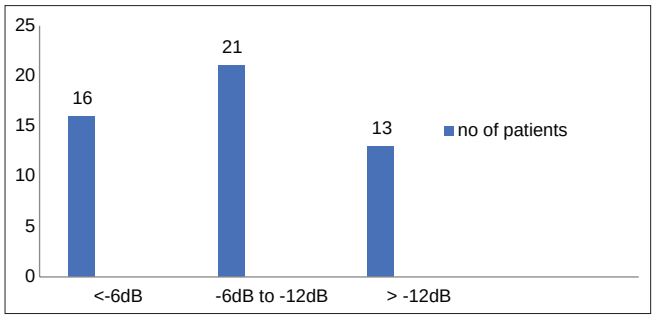

Figure 5: Values of mean deviation in right eye. RE: Right eye, MD: Mean deviation

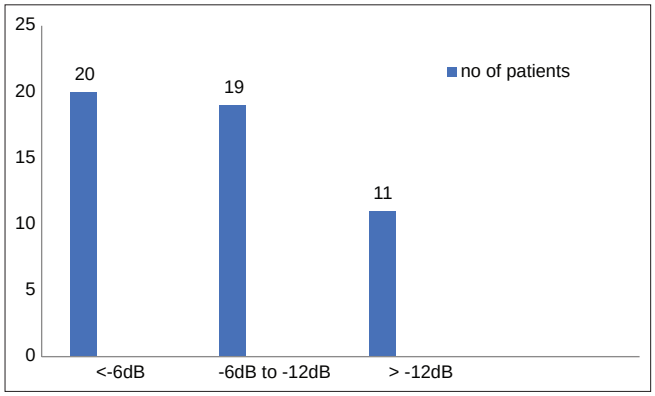

Figure 6: Values of mean deviation in left eye. LE: Left eye, MD: Mean deviation

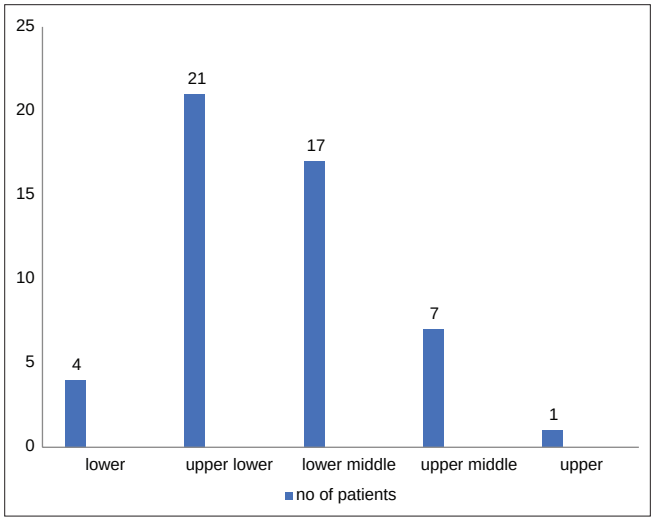

Figure 7: Socioeconomic distribution

association between income and the prevalence of glaucoma[3]

- In a similar vein, research conducted by Sung *et al*. and Ramdas *et al*. demonstrated that a higher level of education and income is connected with a reduced likelihood of developing glaucoma[4]
- Furthermore, Fraser *et al*. and Bunce *et al*. conducted case–control research that showed individuals with primary open-angle glaucoma were more likely to have a lower socioeconomic position in terms of car ownership and home ownership[5]
- Zhang *et al*. conducted cross-sectional research in the United States, which showed that individuals with lower SES have a reduced frequency of seeing eye care providers. This results in greater impairments in angle-closure glaucoma due to the decreased frequency of visits[6]
- Furthermore, Seo *et al*. and Kim *et al*. conducted the Korea National Health and Nutrition Examination Survey, which revealed that only nine percent of glaucoma patients were aware of their condition. This indicates a low level of awareness of glaucoma in the Korean population, particularly among those with lower SES[7]
- Fraser and associates compared 110 patients suffering from advanced glaucoma with 110 patients with mild to moderate glaucomatous damage in the United Kingdom. The authors reported a strong association between socioeconomic deprivation and late presentation of the disease[8]

Table 2: Visual acuity of right eye

Visual acuity of RE	Number of patients (%)
6/6–6/12	13 (26)
6/12–5/60	27 (54)
5/60–PL positive	10 (20)

RE: Right eye, PL: Perception of light

Table 3: Visual acuity of left eye

Visual acuity of LE	Number of patients (%)
6/6–6/12	8 (16)
6/12–5/60	32 (64)
5/60-PL positive	8 (16)
No PL	2 (4)

Maximum patient were found to be of visual acuity in between 6/12–5/60. (Table no 2 and 3). LE: Left eye, PL: Perception of light

Table 4: Severity of glaucomatous field defects in right eye

Severity of glaucomatous field defects RE	Number of patients (%)
Mild	16 (32)
Moderate	21 (42)
Severe	13 (26)

RE: Right eye

Table 5: Severity of glaucomatous field defects in left eye

Severity of glaucomatous field defects LE	Number of patients (%)
Mild	20 (40)
Moderate	19 (38)
Severe	11 (22)

Out of total 100 eyes most commonly presented group was moderate defect that is 40 eyes, 24 eyes were found with the severe defect at the time of presentation. LE: Left eye

Table 6: Correlation between socioeconomic status and severity of visual field defects in right eye

Severity of glaucomatous field defects RE	Lower, *n* (%)	Upper lower, *n* (%)	Lower middle, *n* (%)	Upper middle, *n* (%)	Upper, *n* (%)	Total
Mild	0	5 (10)	9 (18)	7 (14)	0	21
Moderate	3 (6)	9 (18)	4 (8)	0	0	16
Severe	1 (2)	7 (14)	4 (8)	0	1 (2)	13
Total	4	21	17	7	1	50

RE: Right eye

Table 7: Correlation between socioeconomic status and severity of visual field defects in left eye

Severity of glaucomatous field defects LE	Lower, *n* (%)	Upper lower, *n* (%)	Lower middle, *n* (%)	Upper middle, *n* (%)	Upper, *n* (%)	Total, *n* (%)
Mild	1 (2)	4 (8)	7 (14)	7 (14)	0	19 (38)
Moderate	0	12 (24)	8 (16)	0	0	20 (40)
Severe	1 (2)	7 (14)	4 (8)	0	1 (2)	13 (26)
Total	2 (4)	23 (46)	19 (38)	7 (14)	1 (2)	50 (100)

Mild defects mainly found in lower middle and upper middle class most of moderate defects found in lower and upper lower class no moderate defcts in upper middle and upper class. Severe defects found in lower and upper lower class. LE: Left eye

- Ng and associates evaluated the effect of socioeconomic deprivation on the severity of glaucoma at presentation in 122 new cases of glaucoma in the UK[9]
- Several mechanisms have been proposed to explain the effect of SES on health, including endocrine responses, exposure to carcinogens and pathogens, health-related attitudes and resources, and psychological and environmental influences.[10] Some of these are especially relevant for glaucoma, namely an endocrine response with increased intrinsic cortisone levels due to stress,[5,11,12] and patients' attitudes regarding the nature of the disease.

Conclusion

- This cross-sectional study aimed to analyze the visual field status in newly diagnosed glaucoma patients at a tertiary healthcare center, focusing on the location and pattern of visual field defects, correlating clinical factors with the extent of visual field loss, and identifying social risk factors for late presentation of primary glaucoma
- According to the findings of the study, SES is responsible for a considerable portion of the severity of visual field abnormalities that are present at the time when glaucoma is diagnosed. Patients who came from families with lower SES revealed more advanced visual field abnormalities and more severe visual impairment, which suggests that delayed diagnosis and treatment are common in these communities. It was also found that patients from lower SES groups had a higher prevalence of elevated IOP, which was another factor contributing to the advanced stage of illness at presentation
- One of the findings of our study was that the majority of patients, regardless of their socioeconomic situation, had moderate field abnormalities. This underscores the segment of society that requires the most awareness about glaucoma.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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Case Report

Extraocular and Facial Rose Gardener's Disease: Uncommon Demographics

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Abstract

Rose gardener's disease is caused by the saprophytic dimorphic fungus, typically in lymphocutaneous form involving the subcutaneous tissue. It is one of the most common mycoses affecting different regions of the world, especially people of low socioeconomic status, and it is rare in South India. Involvement of the eye and face is even more occasional, with periorbital tissue being the susceptible part. We report a young boy who presented with multiple nodules involving the right upper and lower eyelid and right nasojugal fold for 30 days with mild pain, unresponsive to conventional broad-spectrum antibiotics, and infective workup turned negative for common infections. Histopathology examination and cultures showed Sporothrix schenckii and then managed with oral itraconazole regimen with complete cure of the disease. Sporotrichosis is a common subcutaneous disease in certain demographic regions like Brazil, but is very rare in demographics like South India and so treating doctors should be aware of this disease for prompt and easy diagnosis.

Keywords: Demographics, itraconazole, nodules, rose gardener's disease, Sporothrix schenckii

Introduction

Dimorphic fungus infections are the common cause of subcutaneous mycosis, and sporotrichosis is endemic in certain demographic regions and the Indian subcontinent. This saprophytic fungus is typically found in soil, and the transmission mode is often by means of traumatic implantation, rarely via an inhalational route. Cats have also been the source of transmission to humans by bites and scratches, and the commonly involved site is finger or toes. Involvement of the face and eye is very rare; however, few reports of periocular tissue and conjunctival involvement have been reported in studies done in endemic regions.[1] Few cases of lymphocutaneous sporotrichosis have been reported in the Indian subcontinent, and most cases were not direct diagnosis due to common mimickers, especially tuberculosis. We report a young boy with facial skin nodules who was not responding to antibiotics, and most routine investigation modalities turned negative were turned up to be a case of rose gardener's disease on histopathology examination of the lesion. The patient responded well to itraconazole treatment, and skin lesions disappeared over 1 month.

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Case Report

A 10-year-old boy presented with complaints of nodular lesions on the right side of his face involving the right upper and lower eyelid and near nasojugal fold which was gradually progressing in size with mild pain for 1 month. The patient had no other systemic complaints such as fever or any other swelling in the body. The child belongs to a low socioeconomic group and had itchy lesions in both the fingers, which were diagnosed to be scabies, and completed a course of treatment. On examination, Snellen's visual acuity of child was 6/6 in both the eyes, a nodule of size 1 cm × 1 cm below the right upper and lower eyelid, and a nodule of 2 cm × 1.5 cm along the right nasojugal fold noted with ipsilateral submandibular nontender lymphadenopathy [Figure 1]. For the facial skin lesion, initially, topical steroid and antibiotics ointment was used for local application with no improvement. The child was started

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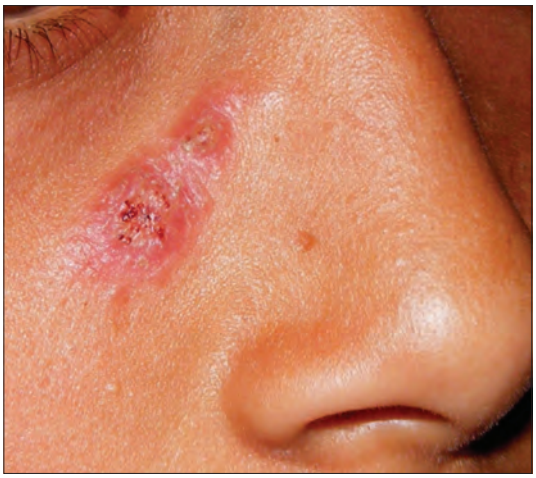

Figure 1: Photograph of the patient's face showing the presence of erythematous nodule noted below the right lower eyelid

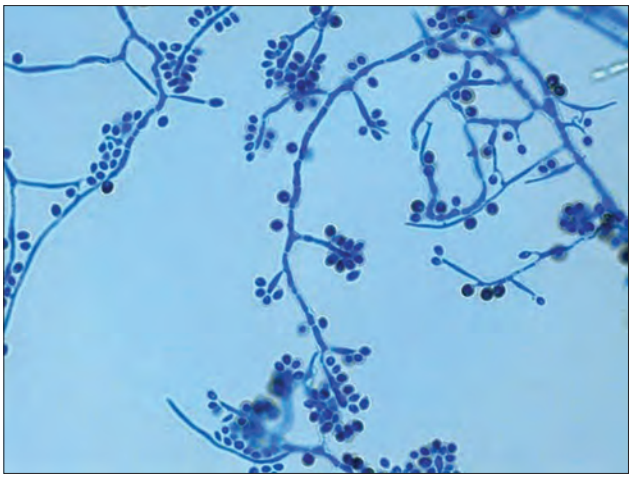

Figure 2: Microscopic picture of the patient sample from SDA showing flower-like branching molds with conidia suggestive of Sporothrix schenckii. SDA: Sabouraud's Dextrose Agar

on oral amoxicillin with clavulanic acid antibiotics for 5 days, which was also in vain. On follow-up, slit-lamp examination of the child showed congestion of the right upper and lower palpebral conjunctiva with follicular response and enlargement of skin nodules. History revealed presence of multiple cats in neighborhood with which child used to play and a cat died recently before her symptoms onset. The skin biopsy was performed and evaluated for subcutaneous mycosis as well. The culture turned positive in Sabouraud's dextrose agar with flower-like branching molds with conidia at 24 degree Celsius likely to be Sporothrix schenckii [Figure 2]. X-ray of the chest posteroanterior view showed no abnormalities. Diagnosis of rose gardener's disease involving the face has been made, and the child was started on oral itraconazole at a dose of 200 mg daily for 3 months. The child has been followed up regularly, and skin lesions gradually reduced and eventually turned into small scars with no further recurrence on follow-up for 1 year.

Discussion

Dimorphic fungi Sporothrix typically causes subcutaneous mycosis characterized by skin nodules. This fungal infection is more common in low socioeconomic populations in Africa and not so common in the Indian subcontinent. Ocular involvement of Sporothrix is rare and granulomatous conjunctivitis with irregular surface abnormality and nodules mimicking hordeolum and stye have been reported.[2] Various other ocular involvements in the form of scleritis, keratitis, MALT lymphoma, and granulomatous uveitis have also been rarely reported.[3,4] A cutaneous lesion due to Sporothrix typically occurs at the site of inoculation and is often either on fingers or toes, presenting with skin nodules and localized lymphadenopathy. Disseminated infection with pulmonary involvement can occur from skin lesions, and radiographical imaging helps know the severity of the disease, and bronchoalveolar lavage or sputum culture will be diagnostic. In our case, we believe that the source is from the feline based on the environmental condition, and self-inoculation/scratch from the cat is the possible mode that resulted in multiple nodules. The diagnosis of this condition, especially in nonendemic regions like South India, requires very high clinical suspicion and careful history. Culture is the gold standard modality, and polymerase chain reaction also will be helpful, but availability is an issue.[5] Histopathological analysis typically shows granulomatous inflammation but is often inconclusive without culture. The patient requires treatment with itraconazole 200–400 mg per day for a period of 3–6 months; especially, immunocompromised patient requires a longer duration. In slowly responding cases, hyperthermia and saturated solution of potassium iodide oral administration may be considered. Fluconazole also can be used if itraconazole is not available.[6] In our report, the patient has complete recovery from the illness with the resolution of all skin nodules after receiving itraconazole for 3 months. Sporotrichosis is a preventable disease, and the chance of getting the infection is greatly reduced by wearing gloves and long sleeves when touching plant matter that can cause minor cuts, and if accidental cuts occur, the site has to be thoroughly washed in running water.

Conclusion

Cutaneous mycotic infections such as rose gardener's disease are very rare in the Indian population, and a high index of suspicion with detailed history and culture will help identify the pathology. To our best knowledge, facial sporotrichosis in the South Indian population is very rare, and prompt diagnosis requires a high index of suspicion.

Consent for publication

Written informed consent was obtained from the father of the child for publication of the case details including the photographs taken.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the parents have given

their consent for images and other clinical information to be reported in the journal. The parents understand that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

Acknowledgment

The authors like to acknowledge the parents of the child for their cooperation.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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Case Report

Podophyllin Keratopathy – Refractive Change

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Abstract

Objective: A case report of "Podophyllin keratopathy and its impact on corneal refractive change" due to accidental corneal touch of PODOWART solution from a cutaneous wart-like lesion over the left cheek. **Design:** This study involves case report and interventional. **Methods:** The authors present a 50-year-old male with acute podophyllum keratopathy that developed over 36 h of accidental corneal touch of topical podophyllum (Podowart). It responded well with topical steroids and anticollagenase drugs. The case followed up with a series of corneal topography and refractive error evaluations. Various changes in the topography and refractive changes were discussed. **Results:** refractive change and mild corneal haze. **Conclusions:** Early intervention can prevent severe damage to the cornea and refractive change, after accidental touch of podophyllin. Podowart should not be used for periocular cutaneous lesions.

Keywords: Podophyllin, podophyllin keratopathy, podowart, refractive change

Introduction

The most important external surface of the cornea is at risk of accidental exposure to extraneous toxic materials, such as custard apple seed paste, podophyllin skin paint, Calotropis plant juice, acids, and alkalis.[1] The topographic corneal profile was documented and analyzed in this case report of a podophyllin keratopathy.

Case Report

A 50-year-old male wearing myopic glasses (OD − 3.0 sph/-0.5cyl 48//OS − 4.0 sph, best corrected visual acuity [BCVA] 6/6 in both eyes) presented to the clinic with a history of mild pain, watering, photophobia, and redness in the left eye for the past 36 h. While he was sleeping with a folded elbow under the head, after applying Podowart (topical podophyllin resin 20%, marketed by Manarini India Pvt. Ltd.), solution to a 4.00 mm × 4.00 mm size pedunculated sebaceous cyst-like lesion over the left cheek [Figure 1], accidentally left cheek rolled over the left eye and a small droplet of solution touched the left cornea.

At the time of presentation, fluorescein staining revealed a small pinhead size chemical burn over the central cornea [Figure 2]. There were signs of mild keratoconjunctivitis and mild haze over the central cornea. There are no signs of anterior uveitis.

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The case was diagnosed as toxic chemical keratoconjunctivitis. After first aid, local steroids (Loteprednol 0,5% eye drops QID -Sun Pharmaceutical Industries Ltd.) and lubricating

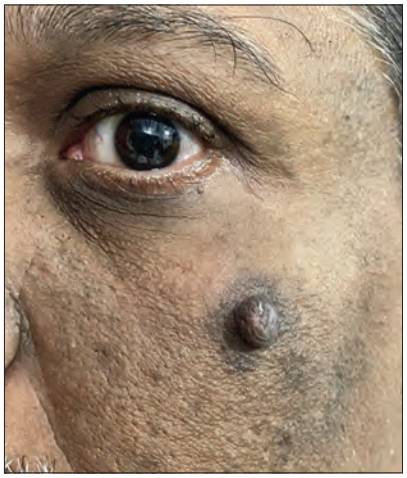

Figure 1: Sebaceous cyst-like lesion over left cheek

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eye drops along with systemic tetracycline (Doxt-SL 100 mg – Dr. Reddy's Laboratories Ltd., contains a combination of doxycycline and lactobacillus) twice a day for 3 weeks and Vitamin A and D 1 BD capsules were given for 3 weeks. The redness and other inflammatory signs came down and developed a diffuse haze [Figure 3] in the second week after the accident. The patient started complaining that he is not able to see well in his left eye with his old spectacle glasses. Upon doing corneal topography, it showed uniform flattening of the central 3 mm zone correlating with change in the refraction of the eye (oculus sinister [OS]). From then onwards, the case was followed up for 3 months with refraction and corneal topography in each visit, change in the refraction [Table 1], and pachymetry and corneal K readings [Tables 2 and 3] are documented.

There was a gradual decrease in the refractive power in the left eye [Table 1].

During the follow-up of 3 months, there is no change in the corneal K readings in the right eye [Table 2].

However, the changes in the corneal K readings in the left eye are noted [Table 3].

The refractive power in the left eye has gradually decreased during the first 6 weeks and the central 3 mm zone on the corneal topography getting flatter and flatter [Figure 4a-c]. With BCVA improved to 6/9.

Spectacle power in the left eye has gradually changed from −4.0° D sph to −0.25°/−0.5 80° (6/18) over 2–3 weeks with

Table 1: Refractive change in both eyes

Date	OD refractive error - spherical/ cylinder	Visual acuity	OS refractive error - sph/cyl	Visual acuity
October 7, 2024	−3.5/−0.5 50°	6/6 parts	−4.0	6/6p
October 17, 2024	−3.5/−0.5 50°	6/6 parts	−1.25/−0.75 10°	6/18
October 25, 2024	−3.5/−0.5 50°	6/6 parts	−0.25/−0.5 80°	6/12
November 5, 2024	−3.5/−0.5 50°	6/6 parts	−0.25/−0.5 70°	6/9
November 18, 2024	−3.5/−0.5 50°	6/6 parts	−0.25/−0.75 85°	6/9
December 4, 2024	−3.5/−0.5 50°	6/6 parts	−1.5/−0.5 70°	6/9
December 20, 2024	−3.5/−0.5 50°	6/6 parts	−1.25/−0.5 85°	6/9
January 10, 2025	−3.5/−0.5 50°	6/6 parts	−1.75d sph	6/9

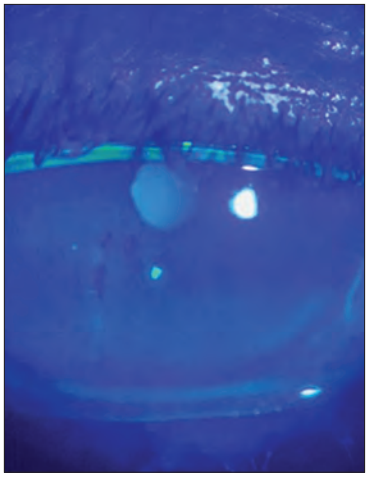

Figure 2: Small pinhead size of fluorescein staining of the left cornea

Table 2: OD keratometry readings change during follow-up

Duration after exposure - OD	Simulated keratometry - average	Anterior 3 mm- average	Anterior 5 mm - average	Anterior 7 mm - average	Thickness (µm)
3rd week - OD	47.18	47.22	47.16	46.91	501
5th week - OD	47.23	47.26	47.21	46.99	501
7th week- OD	46.65	46.63	46.61	46.42	503
9th week - OD	47.10	47.07	47.06	46.82	503
11th week - OD	47.05	47.22	47.09	46.84	504
16th week - OD	47.12	46.96	47.03	46.85	505

Table 3: OS keratometry readings change during follow-up

Duration after exposure - OS	Simulated keratometry - average	Anterior 3 mm - average	Anterior 5 mm - average	Anterior 7 mm - average	Thickness (µm)
3rd week - OS	45.30	44.13	45.07	45.52	367
5th week - OS	45.66	44.58	45.45	45.83	406
7th week - OS	45.78	45.04	45.64	45.94	426
9th week - OS	46.51	46.08	46.42	46.46	450
11th week - OS	46.53	46.09	46.44	46.5	457
16th week - OS	46.69	46.22	46.58	46.61	459

a corneal thickness of 367 μm [Figure 4a]. From the 8th week onwards refractive power increased to − 1.25°/−0.5 85° (6/9) corresponding period the corneal thickness increased to 450 μm indicating recovery of stromal thickness. In the 16th week, refractive power increased to − 1.75 (6/9), and the corneal thickness increased to 459 μm indicating further recovery of stromal thickness [Figure 4d]. Refractive power in the left eye is more or less stabilized by 4th month. Central corneal haze in left eye resolved into a faint haze.

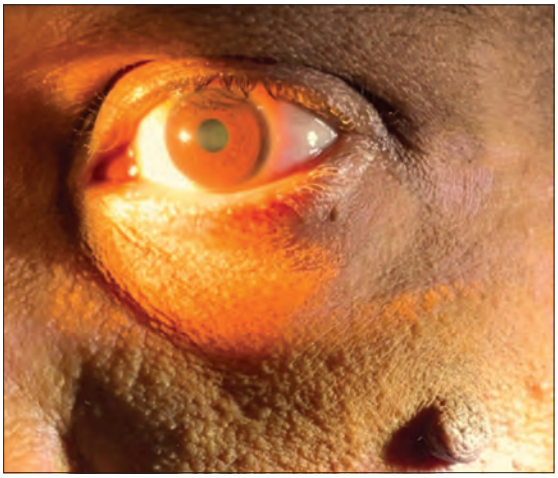

Figure 3: Corneal haze in the 1st week in the left eye

Discussion

Podophyllin is a resin mixture, cytotoxic material, obtained from the dried rhizome and roots of *Podophyllum peltatum* (North America) and *Podophyllum emodi* (India). Topical podophyllin has been used for the treatment of many different conditions in the human body, including condyloma, verruca, molluscum contagiosum, seborrheic keratosis, solar keratosis, and basal cell carcinoma.[2]

In India, it is commercially available as a PODOWART paint solution. It contains podophyllum resin (20% w/v), benzoin (10% w/v), aloe vera (2% w/v), ethanol, methanol and isopropyl alcohol.[3]

Corneal insult from the podophyllin resin application for the skin warts around the eye has been reported by

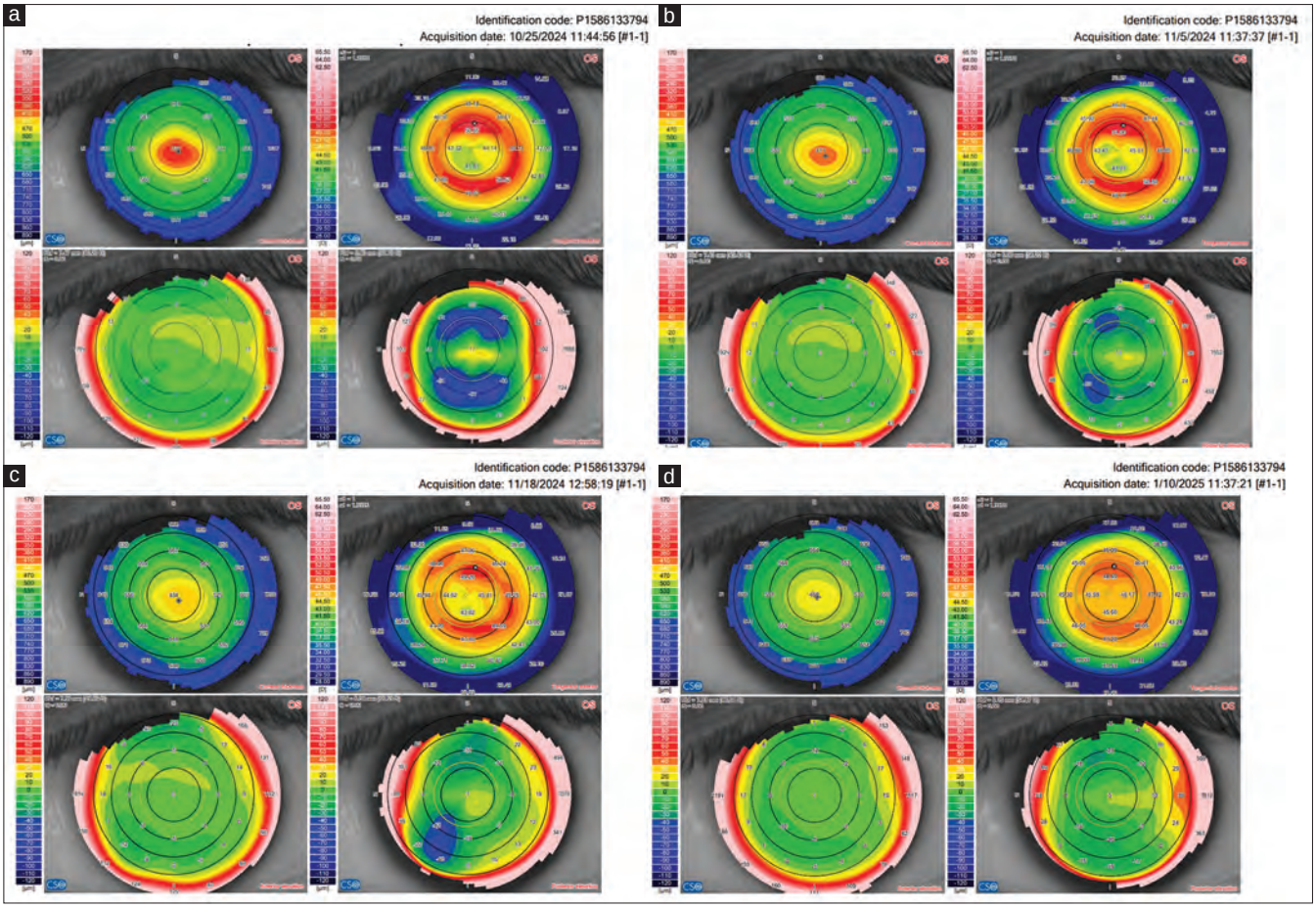

Figure 4: (a) OS Corneal topography on 3rd week after the exposure to PODOWART the central corneal 3mm zone thinnest patchy 367 μm, refractive power changed to − 0.25/−0.570 D. (b) OS 5th week after the accident the central corneal 3mm zone thinnest pachy 406 μm, refractive power changed to − 0.25/−0.5 700 D. (c) OS 7th week after the accident the central corneal 3mm zone thinnest pachy 426 μm refractive power changed to − 0.25/−0.75 850 D. (d) OS 16th week after the accident the central corneal 3mm zone thinnest pachy 459mÂμ refractive power changed to − 1.75 d shp

Rosner.[4] Topical podophyllin has the potential to cause toxic conjunctivitis, keratopathy, and uveitis.[5]

The accidental touch of podophyllin resin caused an acute inflammatory reaction and necrosis over the affected area. It produced thinning of the cornea (364 μm) due to stromal loss at the end of 3rd week, which in turn results in loss of anterior tangential curvature in the 3 mm zone. Necrosis of stromal tissue leads to stromal haze in the initial stages. From the 5th week onwards, corneal thickness begins to increase gradually to 459 μm in 16th week, which may be due to stromal remodeling and epithelial wound healing.

In photorefractive keratectomy (PRK), the excimer laser acts on the anterior corneal stroma, producing a stromal remodeling, and, consequently, inducing a change in corneal refraction. Similar to post-PRK reepithelialization and stromal remodeling of the corneal stroma,[6] chemical injury from PODOWART paint has produced corneal topography and refractive changes in the cornea.

Although in the modern literature, toxic kerato conjunctivitis secondary to exposure to podophyllin is reported, corneal refraction and corneal topography changes are neither documented nor reported to the best of my knowledge.

The case report highlights the treatment given to a patient who presented with podophyllin keratopathy and subsequent changes in his corneal topography and refractive error.

Conclusions

Early intervention can prevent severe damage to the cornea and refractive change, after accidental touch of podophyllum. Podowart should not be used for periocular cutaneous lesions.

Acknowledgment

I thank Dr. C V Gopalraju for giving good suggestions in interpreting the corneal topography changes.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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Case Report

Unilateral Antero-nasal Transposition for Primary Inferior Oblique Over Action with Esotropia in an Adult

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Abstract

Inferior oblique over action (IOOA) is a common ocular motility disorder causing elevation of the affected eye in adduction. It can be primary with unknown etiology or secondary to superior oblique palsy. The evolution of surgical procedures done to weaken the muscle began with tenotomy, myectomy, recession, disinsertion and now to anteriorization of inferior oblique muscle. In recent times, emphasis has shifted from bilateral to unilateral muscle surgeries, yet with optimal outcome. In this case report, Antero-nasal transposition of inferior oblique is one such procedure explored to treat hypertropia as high as 30 PD due to primary IOOA.

Keywords: Anatero-nasal transposition, large hypertropia, single procedure

Introduction

Inferior oblique muscle overaction (IOOA) manifests as overelevation of the eye in adduction and is frequently associated with horizontal deviations. Seventy percent of patients with esotropia and 30% of the patients with exotropia have IOOA. IOOA can be primary or secondary. Primary IOOA is usually bilateral with unclear etiology, but secondary IOOA is unilateral, caused by ipsilateral superior oblique (SO) palsy or contralateral superior rectus palsy.

Surgical weakening of the inferior oblique (IO) muscle can be either unilateral or bilateral, for functional or esthetic reasons. Various weakening procedures for the IO muscle are tenotomy, myotomy, recession, extirpation-denervation, hang – back recession, nasal transposition, muscle fixation, anterior transposition (AT), and graded AT. The best surgical procedure for weakening of the IO muscle has not yet been confirmed.

This case report highlights the judicious use of unilateral antero-nasal transposition (ANT) as the weakening procedure of IO muscle along with medial rectus recession for horizontal deviation as a single procedure with an optimal outcome.

Case Report

A 30-year-old male came with complaints of squinting of the right eye since childhood and history of using glasses for the last 6 years. On examination, his best-corrected visual acuity was 20/40 in the right eye with −1.50D sphere and −1.25D cylinder at 180 axis. The left eye vision was 20/20 with −0.75D sphere, −2.25D cylinder at 180 axis.

Sensory and motor evaluation of the squint was performed meticulously. Extraocular movements showed IO over action of Grade 3+ in the right eye and grade 1+ in the left eye, respectively [Figure 1]. A prism bar cover test showed 10PD of esotropia and 30PD of right hypertropia in the primary position. Negative for Bielschowsky test rules out SO palsy. Asymmetric IOOA in both eyes led to hypertropia in the right eye. Fundus examination showed extorsion of 18° in the right eye and 14° in the left eye measured by disc-foveal method [Figures 2 and 3].

As large hypertropia is noticed in the nondominant eye with amblyopia, a unilateral IO weakening procedure with medial rectus weakening was planned. To minimize the need for re-surgery or bilateral surgeries, ANT was performed.

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Procedure of choice

A conjunctival fornix incision was made at 10.00 mm infero-temporal to limbus to visualize the IO muscle. An exaggerated traction test for IO was negative. After hooking the muscle, a 6-0 double-edged Vicryl suture was used to secure the muscle and was disinserted as close to the insertion as possible. After meticulous dissection of the surrounding tissue, the direction of the IO muscle fibers is rotated and sutured nasal to the nasal border and 2.0 mm behind the insertion point of the inferior rectus muscle. IO was reattached to the sclera without spreading at the insertion site, changing the line of insertion perpendicular to the inferior rectus (IR) axis.

A new limbal conjunctival incision was taken and medial rectus was recessed by 4.00 mm in the same sitting. Conjunctiva was closed by continuous purse string sutures with 8-0 Vicryl for fornix incision and intermittent sutures for limbal incision.

Postoperatively, the patient achieved orthophoria, IOOA collapsed significantly with residual 10PD hypertropia in the right eye [Figure 4]. Right lower lid fullness was observed during the immediate postoperative period. At 1-month follow-up, only 6PD of vertical deviation was noted in the right eye with full movements in all directions.

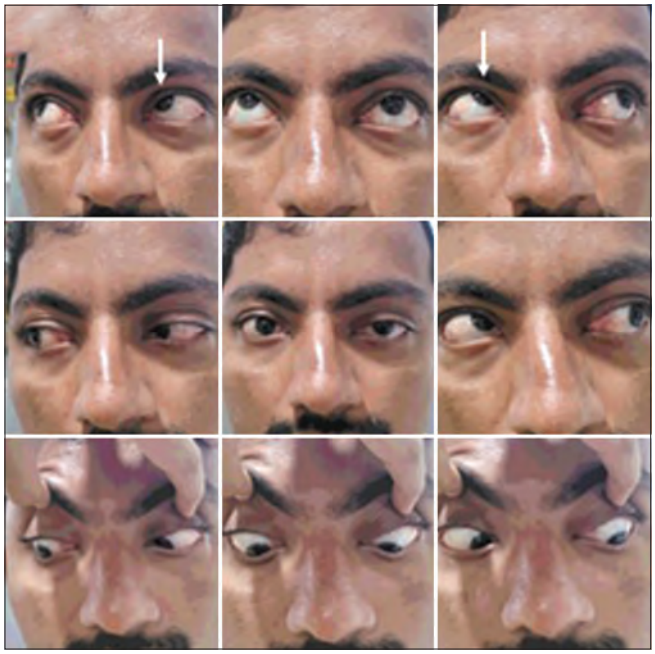

Figure 1: A composite 9-gaze photograph with white arrow showing overelevation in adduction

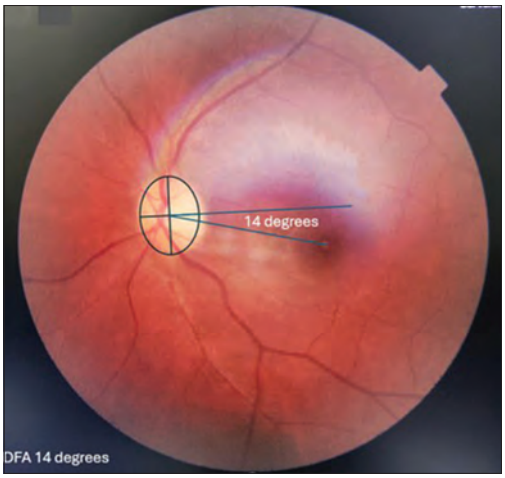

Figure 3: Fundus photograph of the right eye measuring 14° of torsion by disc-foveal angle method

Discussion

IO overaction is a common ocular motility disorder

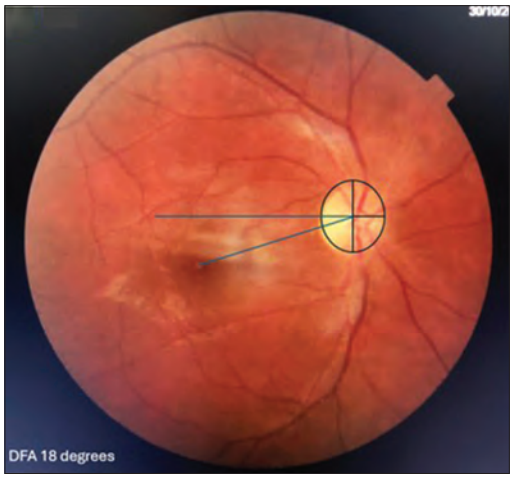

Figure 2: Fundus photograph of the right eye measuring 18° of torsion by disc-foveal angle method

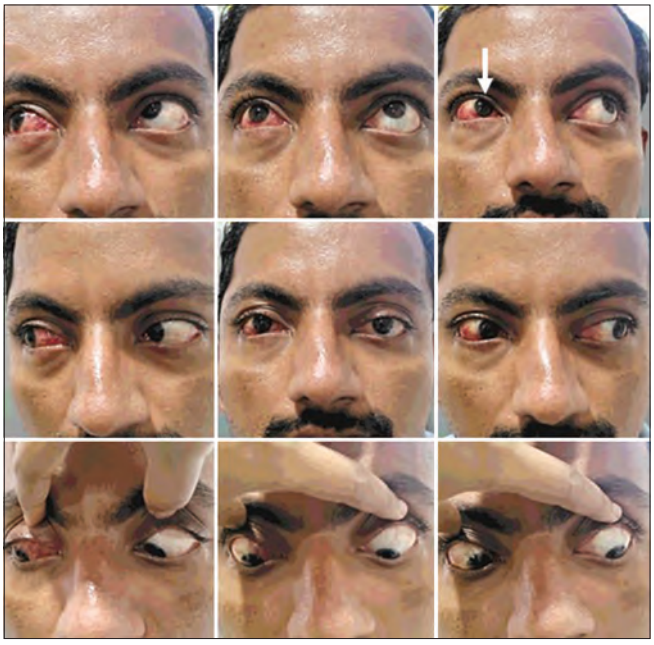

Figure 4: A composite 9-gaze photograph showing orthophoria in primary gaze and collapse of Inferior oblique over action in the right eye at 1 week postoperative

characterized by elevation of the affected eye during adduction, usually seen in association with horizontal strabismus.

It can be primary or secondary based on the cause resulting in the asymmetric vertical deviation in the eyes.[1-3] Primary IOOA is reported in 70% of patients with esotropia and 30% of patients with exotropia.[1,3] Secondary IOOA is unilateral and usually due to SO muscle palsy.[1,2,4] Clinically, primary IOOA presents as overelevation in the adducted eye, small hypertropia in primary gaze, slight head tilt, and negative Bielschowsky test.[1,2]

To eliminate symptoms or correct the misalignment of the eye, surgical intervention is the current treatment modality for IOOA. Several procedures evolved over time to treat primary or secondary IOOA. These include tenotomy, myectomy, recession, Z myotomy, denervation-extirpation, and anteriorization of IO. Myectomy, recession, and AT of IO muscle are the most commonly adapted procedures.[1-5]

Recession of the IO muscle is the most performed procedures in patients with mild IOOA. Myectomy is performed mainly in patients with higher grade IOOA.[1-5] Nankin and Elliot performed anteriorization of IO in moderate-to-severe cases of IOOA.[6] Sanjari *et al*. studied 122 eyes, retrospectively, and compared the results of disinsertion, myectomy, and AT in these cases and concluded that all three procedures were equally effective at long-term follow-up.[3]

Rajavi *et al*. compared myectomy with recession and found that recession was effective in reducing the overaction of the muscle. In this study, the IO muscle was sutured to the globe at 4 mm posterior and 2 mm temporal to the inferior rectus insertion.[7] Bothun and Summers studied the outcomes of unilateral AT of IO muscle in manifest dissociated vertical deviation. They concluded that the procedure was effective in patients with strong contralateral fixation preference.[8]

ANT is a relatively newer and less explored technique that was initially done in patients with weak SO muscle. This technique converts the IO from extorter and elevator to intorter and depressor, thus collapsing the hypertropia.[9] M F Farid studied the technique implemented in cases of DVD with IOOA and found significant correction of hypertropia compared to AT.[10]

In this case report, unilateral ANT was done for +3 IOOA along with medial rectus recession. None of the complications such as IO under action, consecutive A pattern, and hypotropia which were observed in other procedures were noted in this case.

Limitations of this procedure are difficulty in redirecting the IO muscle below the inferior rectus which needs meticulous and careful dissection of the surrounding tissue resulting in longer surgical time than the standard procedure. Temporary fullness in the lower lid during the immediate postoperative period can be worrisome to the patients, which disappears slowly.

Conclusion

ANT is a novel procedure providing the optimal outcome in a single surgery for primary IOOA of higher grade and hypertropia as high as 30PD.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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Case Report

Ocular Toxicity of *Calotropis Gigantea* (Jilledu) – Case Scenarios

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Abstract

Purpose: The purpose of the study was to study the ocular toxicity of *Calotropis gigantea*. **Material and Methods:** This is a prospective case series study done on the patients presenting with Calotropis-induced ocular toxicity in the last 1 month of our outpatient department (OPD). **Results:** Calotropis produces copious amounts of latex, which has been shown to possess several pharmacological properties. Its local application produces an intense inflammatory response. In these two cases of Calotropis-induced keratitis reported here, the clinical picture showed corneal edema with superficial punctate keratopathy with little evidence of intraocular inflammation in one case and intense corneal edema with the Descemet's folds in the other. The inflammation was reversed by the topical application of steroid drops. **Conclusion:** The latex of C. gigantea causes significant ocular morbidity which may be preventable by simple health education, elaborative history taking and vigilant clinical examination. These cases teach us the importance of extracting history from the leads of a patient's profession and/or myths being followed in the rural areas till today. Diagnosing the signs of failure of the endothelial pump may prevent further progression leading to intense endothelial damage, and early aggressive steroidal treatment, if started well in time, saves further damage.

Keywords: *Calotropis gigantea*, corneal edema, Jilledu, keratitis, latex, milkweed

Introduction

Calotropis gigantea (L.) Dryand (giant milkweed; family Asclepiadaceae) [Figure 1] has been traditionally used in the treatment of bronchitis, asthma, leprosy, eczema, and elephantiasis. This review emphasizes the ethnopharmacology, chemical constituents, and pharmacology of C. gigantean.[1] The available information on *C. gigantea* was collected through the electronic search of major scientific databases in the last 1 month. A literature revealed that cardenolides, flavonoids, terpenoids, glycosides, steroids, and nonprotein amino acids constitute major groups of chemical constituents in *C. gigantea*. The plant has been evaluated for varied pharmacological activities and reported to exhibit analgesic, antimicrobial, antioxidant, antipyretic, anti-inflammatory, insecticidal, cytotoxic, hepatoprotective, pregnancy interceptive, procoagulant, and wound-healing activities. Further, thorough scrutiny of the literature revealed a startling fact that clinical reports are not available on any disease caused by the plant, instead in 2009 Basak SK[2] reported in 29 eyes depicting its use as a part of tradition and religious use of the plant sap as an offering to Hindu deity (Lord Shiva) during the festival. The pharmacological work carried out on the plant for validation of its traditional claims is not convincing, as crude extracts used in the experimental studies have not been characterized. The plant could provide therapeutically active constituents, which may be developed as clinically potential drugs.

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Case Reports

Case 1

A 70-year-old patient came with the complaints of diminution in vision in his right eye (RE) over the last 2 days. There was no significant history of trauma. On examination, uncorrected visual acuity (UCVA) in the right eye (RE) was finger counting at 3 m and the left eye (LE) was 6/12; the RE anterior segment revealed intense inflammation with conjunctival congestion, corneal edema with the descemet membrane folds [Figure 2], anterior chamber depth was deep but details were

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not clearly seen due to corneal edema with pseudophakia, and the periocular skin was normal while the LE had early nuclear sclerosis Grade 1. The fundus glow in the RE was present but the disc details were hazily seen and LE had a normal cup–disc ratio of 0.3:1 with foveal reflex present. There was no history of any viral illness or any history of upper respiratory infections or any episode of fever in the remote past. The priest attire of the patient unfolded the mystery, as he gave a positive history of Calotropis (Jilledu) milk sap being instilled in his eye (RE), as a part of a religious myth for improving the vision. The patient noticed a diminution of vision in the RE when he incidentally closed his better eye (LE). The treatment was then started on topical steroids six times per day with eye ointment of sodium chloride 6% three times per day in his RE. The patient responded well to the treatment with 1-week follow-up; the Descemet's folds got cleared [Figure 3] and the vision improved to UCVA 6/12 with pinhole 6/9.

Case 2

A young 8-year-old girl came to our emergency outpatient department (OPD) when she complained of diminution of vision in her RE following Calotropis milk sap instillation by her parents for the myth of having beautiful eyes. On examination, UCVA in the RE was 6/18 and in the LE was 6/6; the anterior segment revealed conjunctival congestion with superficial punctate keratitis with mild stromal edema with no periocular skin lesions, but the Descemet's involvement was not seen; the fellow eye (LE) was normal. This was a mild RE toxicity caused by Calotropis, and the patient was started on low potency topical steroids four times per day in a tapering dose with lubricants six times per day with weekly follow-up. The patient responded well and her vision gained back to 6/6 after 2 weeks of treatment.

Discussion

C. gigantea L. (synonym giant milkweed; family Asclepiadaceae): the plant is commonly known as Milkweed, Akand, Bowstring Hemp, Akado, Ark, Arka, Erukku, Lal akra, Akondo, Moto-aak, Verukku, and Jilledu belonging to the family Asclepiadaceae.[1] The plant is distributed throughout India, mostly on Andaman Island up to 900 m altitude in hills. The plant is also abundant in Cambodia, Indonesia, Malaysia, Philippines, Thailand, Sri Lanka, India, and China. The plant is a large shrub or small tree, about 4 m in height. The stems are erect and milky. The leaves are broadly elliptical to oblong–obovate in shape but subsessile. The sepal lobes are broadly egg-shaped, clustered in flowers that are either white or lavender in color. The flower consists of five pointed petals and a small crown which holds the stamens. The fruit is a follicle, and when dry, the seed gets dispersed in the air by wind. It grows especially in the region of sandy soil and dry, uncultivated land. The root, root bark, leaves, and flowers are basically used in the traditional system of medicine.

Accidental exposure to the latex has been reported to cause inflammation of the skin and eyes.[3,4] Ocular injury from this plant can be mechanical, or more commonly, toxic, due to the exposure to its latex.[5] Studies suggest that this response was caused by the presence of histamine in the latex itself, as well as the release of mast cell histamine by the latex.[6] Both histamine and prostaglandins are the key mediators in an inflammatory response. Another possible mechanism is direct endothelial pump failure because of the toxic effects of the latex as is seen in one of our cases.

Figure 1: The calotropis-flowering plant

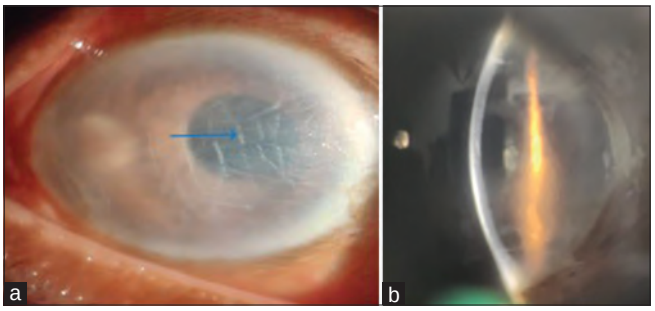

Figure 2: (a) The endothelial pump failure depicting corneal edema with the Descemet membrane Folds. (b) Slit section of the endothelial toxicity

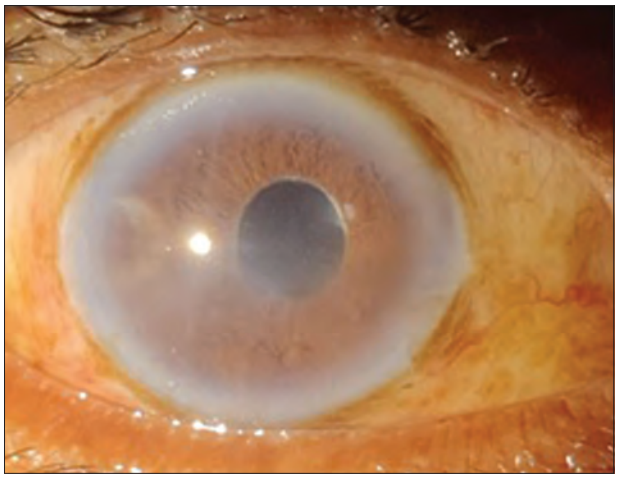

Figure 3: 7-day posttreatment resolution of the Descemet membrane folds and corneal edema

Conclusion

The diagnosis that starts the moment the patient enters our OPD is as important as we were taught in the medical school. These cases teach us the importance of history taking from the leads of a patient's profession and/or myths being followed in the rural areas till today. Diagnosing the signs of the endothelial pump insult may prevent further progression leading to intense endothelial damage/failure, and early aggressive steroidal treatment if started well in time, saves the visual health of the patient.

Take-home message

In epitome, such a case scenario should make all the residents / trainees and the first line care providers at the peripheries aware about such findings. In addition, this case reveals the importance of history taking, knowing the regional beliefs, practices and the clinical examination, which will always hold an utmost important place in providing the best of the eye care services to make a conclusive diagnosis.

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2. The author acknowledges the immense motivational support from the better half Mrs. Dr. JKS Gujral, to continue the passion of writing.

Declaration of patient consent

The patients have given their consent for images and other clinical information to be reported in the journal. The patients understand that their name and initials will not be published and due efforts will be made to conceal the identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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Case Report

Role of Neodymium Yttrium Aluminum Garnet Capsulotomy in Anterior Capsular Phimosis-A Case Report

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Abstract

Capsule contraction syndrome is an exaggerated reduction in anterior capsulectomy and capsular bag diameter after cataract surgery. It is particularly common in patients with pseudoexfoliation and in eyes with a history of uveitis, myotonic dystrophy, and retinitis pigmentosa. Its effects, which include extreme reduction in the capsulectomy opening, malposition of the opening, reduction in equatorial capsular diameter, and displacement of the intraocular lens (IOL), seem more exaggerated in small capsulorhexis openings. We report a case operated for cataract elsewhere who had developed capsular phimosis and was successfully treated with Neodymium doped Yttrium Aluminum Garnet Capsulotomy. In this, the laser radial anterior capsulotomies were done which relieved the contraction forces within the bag and thereby improving the vision of the patient. Examination revealed a best-corrected visual acuity (BCVA) of finger counting at 4 m with 3 mm phimosis. Slit-lamp examination revealed a quiet anterior chamber without any cells-flare nor any posterior synechiae, but the IOL seemed tilted due to contraction forces and the fellow eye examination had pseudoexfoliation with both eyes normal fundus study. A four-petal Nd:YAG Capsultomy with four laser shots of 0.5 mJ was done with no surgical intervention, and proved a useful management protocol with the patient improving to BCVA 6/18 in less severe cases of phimosis. A prophylactic preventive measure is to do radial nicks after IOL implantation and/or a capsular tension ring (CTR) can also place in the fellow eye if phimosis is noted in the first eye and it is our institute policy to put a CTR in retinitis pigmentosa cases to prevent contraction of the bag and phimosis which is indeed a take-home message.

Keywords: Capsular contraction syndrome, capsular phimosis, neodymium-doped yttrium aluminum garnet laser capsulotomy

Introduction

Continuous curvilinear capsulorhexis is a common technique used for cataract surgery to provide an opening for phacoemulsification and the introduction of an intraocular lens (IOL) through the capsulorhexis opening and into the capsular bag.[1] Shrinkage and whitening of the anterior capsule opening – capsular contraction syndrome (CCS) – is a well-distinct known complication after continuous curvilinear capsulorhexis. It has been described as an exaggerated fibrotic response that can lead to a reduction in the size of the anterior capsulotomy and capsular bag diameter following capsulorhexis.[2]

Case Report

A 65 year old male presented with insidious onset, gradually progressive, painless diminution of vision in the left eye from the past 1 year. He was operated for cataract about 8 years ago elsewhere. Examination revealed best-corrected visual acuity of finger counting at 4 m in the left eye and 6/12 in his right eye with grade two nuclear sclerosis. A slit-lamp examination revealed a quiet anterior chamber without any cells-flare nor any posterior synechiae, and the right examination had cataract with PXF with both eyes normal fundus study.

The anterior capsular phimosis was 3 mm [Figures 1 and 2] for which the patient was planned for four-petal neodymium-doped yttrium aluminum garnet (Nd:YAG) capsulotomy under topical anesthesia [Figure 3]. We planned a successive increasing power starting from 0.1 mJ till we were able to

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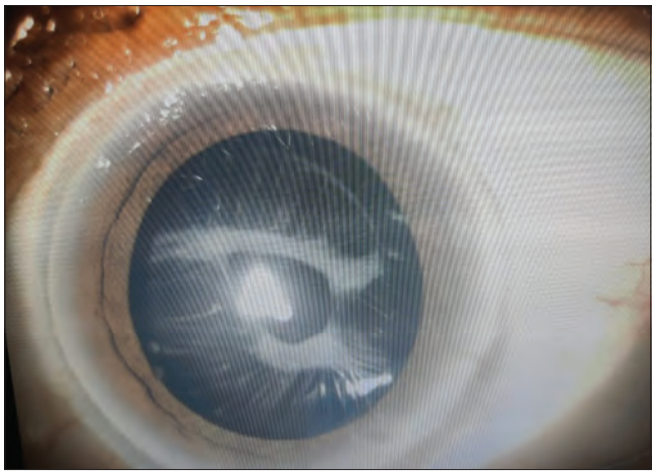

Figure 1: Shows anterior capsular phimosis

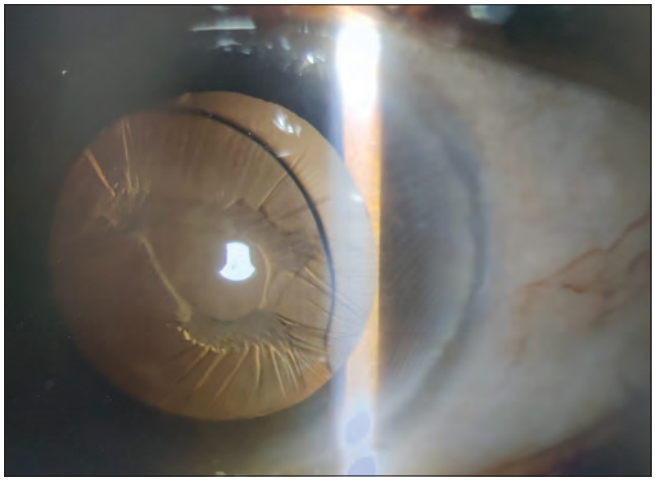

Figure 2: Shows anterior capsular phimosis in retroillumination

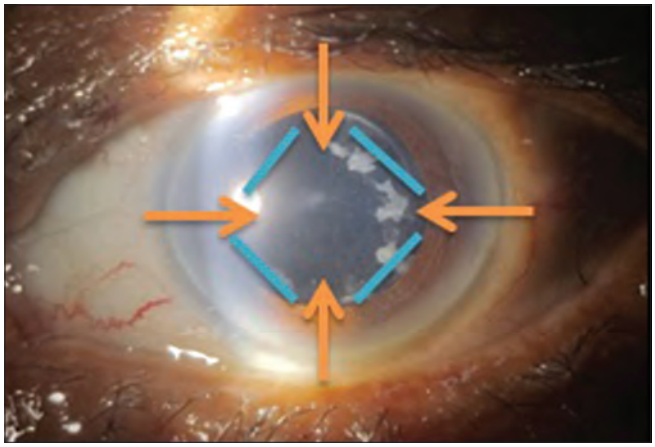

Figure 3: Shows Nd:YAG Laser Capsulotomy

achieve success at 0.5 mJ as it was a fibrosed capsule; four shots of 0.5 mJ were enough to bombard the capsule, which by secondary contraction opened up the phimosis to a diameter of approximately 5 mm. The maneuver is to defocus the laser anteriorly to focus at the fibrosed capsule and to avoid hitting the IOL at the same time. This seems a safe OPD procedure that can be conducted and gives immediate good results with the patient improving to best-corrected visual acuity of 6/18. The reason behind the possible poor vision in this case could have been because of the contracture of the anterior capsule, resulting in the contraction forces leading to tilt in the IOL and, thereby, a change in refractive power, as is also suggested by the study in the year 1993[2] which improved once these contraction forces were relieved.

On the contrary, had the IOL been decentered significantly in a phimosed anterior capsule, it may have even resulted in a decision to take the patient for revision of fibrosed capsulorhexis or IOL explantation with or without secondary IOL implantation. The rationale behind this approach is whenever there is a significant contraction of the margins leading to folding of the IOL haptics and/or decentration as was done in the case scenario by Wong *et al*.[3] In cases of pseudoexfoliation, prophylactic radial nicks could be made after IOL implantation to anterior capsule margins to prevent contraction.[3]

In our experience, four-petal Nd:YAG laser capsulotomy is a preferred choice in case of capsular phimosis, followed by postoperative topical nonsteroidal anti-inflammatory drugs three times per day bromfenac 0.09% for 3 weeks would suffice the treatment with a dilated fundus examination at 1-month follow-up visit which completes the full regimen.

Discussion

Capsular phimosis is usually seen in patients with a history of pseudoexfoliation, diabetic retinopathy, myotonic dystrophy, retinitis pigmentosa, uveitis, Marfan's syndrome, high myopia or other factors associated with weakened zonules.[4,5] Capsular phimosis is associated with size of capsulorhexis, retained lens epithelial cells (LECs), and IOL position. The most frequent method of treatment is Nd:YAG laser anterior capsulotomy.[6]

Anterior capsule contraction syndrome is thought to result from metaplastic LECs, which undergo differentiation into myofibroblasts, causing constriction and obstruction of the visual axis.[7] A report analyzed the capsular phimosis membrane, which showed the composition of fibrous tissue interspersed with cells that resembled fibrocytes with elongated nuclei representing metaplasia of LECs.[8]

"Capsular Bag Phimosis" or CCS is not an uncommon entity. Al-Kharashi and Al-Obailan,[9] Wong *et al*.[3] and Narnaware and Bawankule[10] have reported similar cases in the literature, but the slit-lamp examination images reported by them demonstrated anterior capsular phimosis resulting from scarring and contraction of the capsulorhexis diameter.

CCS was initially reported in eyes with pseudoexfoliation,[2,11] uveitis,[2,8] myotonic dystrophy.[2,12] Then, subsequently reported in eyes with retinitis pigmentosa[11] and diabetic retinopathy.[13]

Intraoperatively, excessive manipulation leading to zonular dehiscence and resultant capsular tension ring insertion might maintain the integrity and shape of the capsular bag and protect against the development of CCS. Surgical risk factors, such as small capsulorhexis size and insufficient aspiration of residual LECs, as well as IOL design and material, play important roles in the pathogenesis of CCS.

As per literature, a step-by-step approach in such cases should be done if documented progressive shrinkage of anterior capsule opening in CCS can be managed with early Nd:YAG radial anterior capsulotomy to interrupt the contraction forces,[2] surgically by vitrector (vitrectorhexis)[14] and/or anterior repeat capsulorhexis[8] or y diathermy.[15]

Decision-making for the treatment of anterior capsule phimosis depends on the severity and progression of the contraction. In less severe cases, Nd:YAG laser anterior capsulotomy is preferred. Patients treated with Nd:YAG laser anterior capsulotomy had stable or improved vision, a capsular opening greater than the opening before treatment, and had no recurrence thereof.[16] Laser treatment has been shown to prevent the progression of the contraction using 3 or more nicks around the capsular annulus.[17] In severe or Nd:YAG laser-resistant cases, surgery with microscissors or vitrectorhexis to cut the fibrotic membrane is considered.[14,18] Moreover in case the patient's vision is good with normal fundus examination, no refractive surprise or any intra-ocular lens decentration despite a phimosed anterior capsule, we can observe such cases indeed.

Conclusion

Capsular bag phimosis is not an uncommon complication seen routinely as a complication of capsulorhexis and can be easily managed with Nd:YAG laser capsulotomy. This case helps us to make a decision based on case severity from laser capsulotomy in less severe cases to surgical intervention in cases of complete occlusion of phimosis or microexcision/revision of rhexis in decentered IOL/folded haptic which will need surgical intervention and cases with preserved good vision can still be observed *per se*.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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