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As new technologies and therapeutic interventions are continually being developed, Ophthalmology has become a field of rapid change, particularly in the Asia-Pacific region, where disease patterns and health care delivery differ greatly from those seen in the West. Asian Journal of Ophthalmology was established in 1998 with the aim of disseminating information relevant to Ophthalmology and glaucoma throughout Asia and to interested groups worldwide.

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Although the focus of Asian Journal of Ophthalmology mainly was on glaucoma with close ties to the South-East Asian Glaucoma Interest Group (SEAGIG) in the past, the journal now focuses on the entire spectrum of Ophthalmology. This resulted in collaboration with the Asia Pacific Ophthalmic Trauma Society (APOTS).

The Asian Journal of Ophthalmology and Kugler Publications have started to collaborate since mid 2012 on the publication of the journal. A new website has been launched (www.asjoo.com), which facilitates all aspects of the peer-review and publication process, from manuscript submission to publication.

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Asian Pacific Glaucoma Guidelines 3

The Asia Pacific Glaucoma Society (APGS) is moving ahead with preparation of the 3rd Edition of our popular Glaucoma Guidelines that are distributed and read widely across the Asia-Pacific Region. The last edition (then known as the SEAGIG Guidelines was published 6 years ago), this version was downloaded thousands of times per year since 2003. The APGG are a very important educational tool for the Asia-Pacific region and are widely used.



This latest edition of the Guidelines will be co-chaired by Profs. Aung Tin (Singapore) and Jonathan Crowston (Melbourne). Currently the Working party is researching and preparing the necessary updates. It is estimated that the e-book version will be ready in February 2015, with an official publication launch planned during the [World Glaucoma Congress 2015 \(Hong Kong June 6-9, 2015\)](#)

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Letter to the Editor: An aid for achieving the ideal laser posterior capsulotomy

Keith Ong

University of Sydney – Lecturer, Royal North Shore Hospital, Ryde Hospital, Dalcross
Adventist Hospital - Ophthalmic Surgeon, Sydney, Australia

Key words: cataract, laser capsulotomy

A 2.5- to 4-mm well-centered laser posterior capsulotomy would be ideal. A 2-mm posterior capsulotomy which is well-centered in the pupil region may be adequate. Laser posterior capsulotomies larger than 5 mm is not necessary and if not well-centered may extend over the optic of intraocular lens risking vitreous coming forward around the optic if the anterior capsulorrhexis does not cover the edge of the optic completely. Too large a posterior capsulotomy may also risk posterior migration of intraocular lens with the plate haptic intraocular lens.

It can be difficult to locate the center of the visual axis when doing YAG laser posterior capsulotomy with a dilated pupil.



Fig. 1. Approximate size of rings.

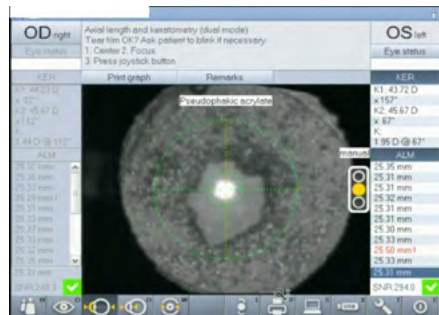


Fig. 2. Small capsulotomy which is not well centered.

The Zeiss IOL master can help with finding the center of the visual axis. When in axial length measurement mode, there is a central dot with two rings around it, a small and a large ring (Fig. 1). When the patient looks at the central light, the central spot denotes the position on the cornea which the visual axis traverses, which would correspond to center of the visual axis. The smaller ring is about 1 mm diameter and the larger ring is about 4 mm diameter (Fig. 2), and this would facilitate an estimate of the approximate capsulotomy size.

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When the eye is illuminated during the measurement phase, one can then see the edge/shadow/outline of the capsulotomy. If it is not central or big enough, we can enlarge in the direction/position required (Fig. 3).

The fundus camera can also be used, by viewing the outline of the laser posterior capsulotomy demonstrated with red reflex of the dilated pupil and assessing it with reference to the central corneal light reflex from camera flash illumination (Fig. 4).

With this aid, the risk of an eccentric or too large a capsulotomy is minimized. When the patient is examined later with the pupil in the normal state; it will be noted that the capsulotomy is usually adequate and central.

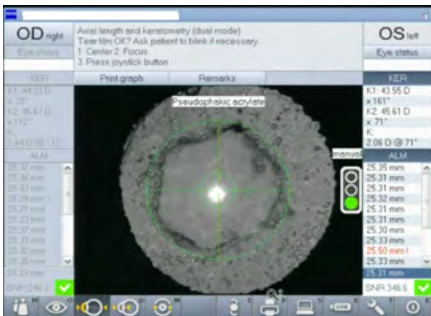


Fig. 3. Capsulotomy enlarged in appropriate direction.



Fig. 4. Fundus camera photo.

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Diagnostic value of contrast sensitivity test and conjunctival impression cytology for the detection of sub-clinical vitamin-a deficiency

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Abstract

Purpose: To determine whether or not contrast sensitivity test and conjunctival impression cytology can be used as diagnostic tools to detect sub-clinical vitamin-A deficiency; and if there is a correlation within the two diagnostic methods.

Methods: A series of diagnostic studies comprising of contrast sensitivity test, conjunctival impression examination and serum retinol concentration were performed on literate children, six to ten years old, at West Java Elementary School. All subjects underwent a basic eye examination. Sample size, receiver operator curve, negative and positive predictive values, sensitivity and specificity were calculated.

Results: A total of 109 subjects out of 154 elementary school children corresponding to the inclusion criteria were included in this study. Forty-four (41.9%) children were detected to have sub-clinical vitamin-A deficiency. The contrast sensitivity test had a sensitivity value of 45.5% and a specificity value of 50.8% with a positive predictive value of 40%. The area under the receiver operator characteristic (ROC) curve was 49.5% (95% CI 38.1%-60.9%), whereas the conjunctival impression cytology test had a sensitivity value of 90.9%, and a specificity value of 16.4% with a positive predictive value of 43.9%. The ROC area was 56.1% (95% CI 45.0% - 67.1%). Pearson's analysis showed that there is no correlation between the two diagnostic tools (p 0.538).

Conclusion: The results of this study indicated that neither the contrast sensitivity test nor the conjunctival impression cytology was found to be a favorable screening tool to detect sub-clinical vitamin-A deficiency. Moreover, there is no correlation between the two methods.

Key words: Sub-clinical vitamin-A deficiency, contrast sensitivity, impression cytology

Introduction

Vitamin-A deficiency is a state or condition resulting from a lack of vitamin-A concentration level in the body tissue, causing either sub-clinical or clinical disorders, including the eyes.¹ Vitamin-A deficiency currently remains a public health problem worldwide, especially in developing countries, such as Africa and South-East Asia, affecting predominantly the young children during their period of growth.²

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Starting as a silent threat, then later pursuing a pathological course, Vitamin-A deficiency is purported to be the cause of vision loss, especially in children, if not properly and timely managed and treated. In its early stages, it will cause difficulties in seeing in low-light settings, producing a condition known as *night blindness*. Treated inadequately, the condition will further progress to form abnormalities on the conjunctiva, and later on the cornea, generating a condition known as *xerophthalmia*, causing permanent damage in the cornea as well as loss of vision.^{2,3}

The predicament of vitamin-A deficiency is a perfect example of an iceberg phenomenon where, to date, only a few xerophthalmia cases have been established despite extensive sub-clinical vitamin-A deficiency found in the community. The ratio of sub-clinical vitamin-A deficiency to xerophthalmic patients is ten to one.³⁻⁵ Sub-clinical vitamin-A deficiency is defined as serum retinol concentration below 20 µg/dl (biochemical indicator), which serves as the gold standard, however, this measurement is an invasive, highly-skilled and costly procedure.

Early detection of sub-clinical vitamin-A deficiency is made possible by performing conjunctival impression cytology. This is an objective, less invasive, simple test performed using bio-pore membrane paper to identify the metaplastic changes of conjunctival surface epithelial found in sub-clinical vitamin-A deficiency.⁶⁻¹⁰

A contrast sensitivity test may be performed in a setting of regular lighting to detect any changes of vision quality despite normal visual acuity.^{12,13} This test is considered simple and reliable, making it a practical tool for early diagnostics.

In this study, we postulated that the contrast sensitivity test as well as the conjunctival impression cytology test prove to be an effective screening tool. The purpose of this study was to acknowledge the diagnostic value of the contrast sensitivity test and conjunctival impression cytology test in the detection of sub-clinical vitamin-A deficiency. We also aimed to compare the value of both tests as a potential tool for screening.

Methods

This diagnostic study was performed in the Elementary School of Plered Sub-district, Purwakarta, West Java, Indonesia by the School Health Unit – Community Eye Health Service in Cikampek. Thirty elementary schools were randomized and only one school was chosen. Another school was later selected, due to the insufficient number of subjects. The authors obtained prior approval for the study protocol by the Ethics Committee of the Faculty of Medicine University of Indonesia. Written informed consent was obtained from all subjects before recruitment.

Included in this study were literate subjects, six to ten years old, presenting with a visual acuity of 6/6 with maximal spectacle correction of 1.0 Dioptri and showing no abnormalities in the anterior and posterior segments, and who were willing to accept all research procedures.

All subjects underwent the contrast sensitivity examination using Pelli-Robson card with a range illumination of 60-120 cd/m².¹⁴ This was followed by a conjunctival impression cytology which was done after administration of anesthesia eye drops in both eyes. A conjunctival swab was taken with acetate cellulose paper (HA,

HA WP 04700, Millipore Corp, Bedford, MA, USA) and manipulated with an objective glass to extract the epithelial cell. The cellulose paper was then placed into a Petri dish containing fixating solution; alcohol 70%, formaldehyde 37% and acetate glacial acid (20:1:1). The fixated conjunctival samples for the impression cytology evaluation were transferred immediately after collection. The abnormal goblet cells were assessed using PAS and Papanicolaou staining. The staining procedure was conducted by a pathology expert, who was oblivious of the two previous assessment results. Density metaplasia goblet cell/mm² was calculated using Tseng criteria.¹⁰

The venous blood was drawn to quantification of serum retinol concentration using high performance liquid chromatography (HPLC) which was performed in the SEAMO-TROPMED (South East Asia Malnutrition Tropical Medicine) Laboratory, Jakarta.

Operational definition

The contrast sensitivity test is an assessment of the subject's ability to see and read letters on various gradations of contrast between characters and background under constant illumination. When the contrast sensitivity test was found to be less than 1.75 log unit, it was termed as abnormal. The ability to accurately read more than 1.75 log unit was defined as normal.

Sub-clinical vitamin-A deficiency was defined when serum retinol concentration was within the range of 0.35-0.70 µmol/l or 10-20 µg, whereas serum retinol concentration of higher than 0.70 µmol/l was defined as normal.

The interpretation of conjunctival impression cytology as grades 2, 3, 4, 5 was classified as abnormal, whereas grades 0 and 1 were considered a normal result.

Nutritional status was determined using the Growth Health Card for Elementary School Children issued by the Indonesian Ministry of Health. This chart is adopted from the Growth Reference Data for children aged between five and 19 years, World Health Organization 2007, which determines the nutritional status of elementary school children, based on gender, age and body-mass index. This chart categorizes the subjects into obese, normal and thin.

Statistical analysis

The collected data was analyzed using computerized SPSS 16 program. Sample size was calculated by expected sensitivity of both tests of 90% with an expected false value of 15%. Eighty-eight children altogether were enrolled. We calculated point estimates of predictive value, sensitivity and specificity, as well as the receiver operating curve of contrast sensitivity test and conjunctival impression cytology in detecting sub-clinical vitamin-A deficiency; this was compared to the gold standard, serum retinol concentration. Correlation between the two tests was assessed using Pearson's test.

Results

A total of 109 (70.8%) literate children out of 154 elementary school children were included in the study and underwent contrast sensitivity test, conjunctival impression cytology and blood test over a period from March to April 2009. One subject was excluded due to unsuccessful attempts to obtain venous blood. Three subjects were considered as excluded for inconclusive results of the conjunctival impression cytology; thus 105 subjects were considered favorable candidates for this study.

There were 46 (43.8%) female subjects participating in this study, the average age of subjects being eight years old. Ninety-one (86.7%) subjects were classified to have normal nutritional status. The prevalence of sub-clinical vitamin-A deficiency was found to be 41.9% (44/105), suffered equally by male and female subjects. Thirty-four (77.27%) subjects detected with decreased level of serum retinol concentration were determined as having a normal nutritional status (Table 1).

Table 1 Characteristic of subjects

	Total	Percentage (%)
Gender		
Male	59	56.2%
Female	46	43.8%
Age (years)		
6	2	1.9%
7	15	14.3%
8	44	41.9%
9	30	28.6%
10	14	13.3%
Nutritional Status		
Obese	2	1.9%
Normal	91	86.7%
Thin	12	11.4%
Sub-clinical vitamin A deficiency	44	41.9%

Contrast Sensitivity test

There were 50 (47,6%) subjects who demonstrated an abnormal ability during the contrast sensitivity test, with an average serum vitamin-A level of $0,83 \pm 0,034 \mu\text{mol/l}$ (mean \pm SD). However, the normal contrast sensitivity group showed a similar level of serum vitamin A. In order to prove whether contrast sensitivity test can be used as a diagnostic tool to detect sub-clinical vitamin-A deficiency in school children, it was necessary to conduct several statistical tests.

The sensitivity value is described as the ability of a diagnostic tool to detect a disease. Data showed that the contrast sensitivity test could only detect 45.5% of the subjects who presented with sub-clinical vitamin-A deficiency, whereas the specificity of the contrast sensitivity test to rule out subjects with sub-clinical vitamin-A deficiency is 50.8% (Table 2).

The positive predictive value (PPV) of the contrast sensitivity test was 40%, showing that there was a 40% probability of a subject indicating a positive result to actually have sub-clinical vitamin-A deficiency. Whereas the probability of not having the disease was derived from the negative predictive value (NPV), which is 56.4%.

Furthermore, receiver operator characteristic (ROC) analysis revealed that the ROC curve seems to be too close to the diagonal reference line - the area under curve 49.5% (95% CI 38.1% - 60.9%). If the cut-off point of the contrast sensitivity test is decreased into ≤ 1.57 log unit, the specificity of the test will be raised to 100%, however, its sensitivity will be down to 4.5%. These results demonstrate that the contrast sensitivity test is not an accurate tool in detecting sub-clinical vitamin-A deficiency.

Table 2 Diagnostic value of Contrast Sensitivity test

Contrast Sensitivity	Serum Retinol Level		Total
	(0.35-0.70 $\mu\text{mol/l}$)	(>0.70 $\mu\text{mol/l}$)	
Abnormal	20 (a)	30 (b)	50 (a+b)
Normal	24 (c)	31 (d)	55 (c+d)
Total	44 (a + c)	61 (b+d)	105

The sensitivity value is $a/(a+c) = 20/44 = 45.5\%$; whereas the specificity yield from $d/(b+d) = 31/61 = 50.8\%$. The PPV was derived from $a/(a+b) = 20/50 = 40\%$, whereas the NPV is $d/(c+d) = 31/55 = 56.4\%$.

Conjunctival impression cytology

Conjunctival impression cytology is a minimally invasive pathological assessment to detect any pathological changes within the conjunctival surface. There was only 1 (0.9%) subject who showed grade-2 abnormality and a total of 90 (85.7%) subjects presented with grade-4 and grade-5 abnormality of conjunctival impression cytology. Fourteen (13.3%) subjects were classified to have normal pattern (grade 1). The mean serum retinol concentration of subjects with abnormal conjunctival impression

cytology was $0.82 \pm 0.029 \mu\text{mol/l}$. Subjects with normal conjunctival impression cytology showed a mean serum retinol concentration of $0.98 \pm 0.035 \mu\text{mol/l}$. The difference of serum retinol concentration between subjects with abnormal and normal conjunctival impression cytology was statistically significant ($p: 0.036$).

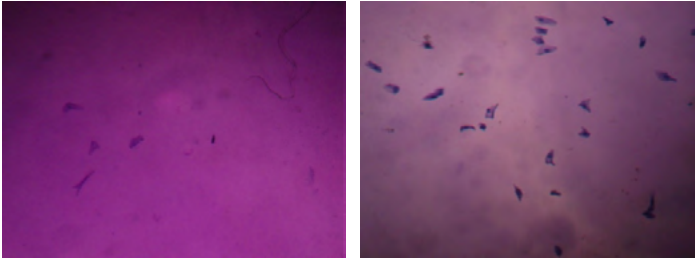


Fig. 1. Grade 4 and 5 conjunctival impression cytology abnormality, showing pycnotic nucleus and un-nucleated basophilic cells on sample no. 13 and 16.

The sensitivity value for conjunctival impression cytology was 90.9%, indicating therefore that this diagnostic tool demonstrated a 90.9% chance of detecting sub-clinical vitamin-A deficiency. The specificity value was 16.4%, which meant the probability of this test showing a negative result on a healthy subject was 16.4%. The positive predictive value (PPV) for conjunctival impression cytology was 43.9%, showing that there was 43.9% probability of a subject with a positive test result to actually have sub-clinical vitamin-A deficiency. The probability of a subject with negative result (normal conjunctival impression cytology) for not having the disease was 71.4% (negative predictive value/NPV)(Table 3).

Table 3 Diagnostic value of conjunctival impression cytology

Impression Cytology	Serum Retinol Level		Total
	(0.35-0.70 $\mu\text{mol/l}$)	(>0.70 $\mu\text{mol/l}$)	
Abnormal (> grade 2)	40 (a)	51 (b)	91 (a+b)
Normal	4 (c)	10 (d)	14 (c+d)
Total	44 (a + c)	61 (b+d)	105

The sensitivity and specificity were 90.9% and 16.4%, respectively; whereas the PPV and the NPV were 43.9%, and 71.4%, respectively.

Receiver operator characteristic (ROC) curve showed the correlation between sensitivity and specificity of conjunctival impression cytology to be a favorable diagnostic tool. The aim was to find the cut-off point of a diagnostic study. Area below ROC was 56.1% (95% CI 45.0% - 67.1%). Further analysis revealed that the most appropriate trade-off balance was 56.8% vs 52.5%, for sensitivity and specificity values, respectively, and 46.3% vs 62.7% for PPV and NPV, respectively, was achieved by using the grade-5 pathology of the conjunctival surface as the cut-off point. However, these results still indicate that conjunctival impression cytology is not sufficient enough to be used as an effective diagnostic tool.

Discussion

This study revealed that 44 (41.9%) out of 105 subjects were found to have sub-clinical vitamin-A deficiency. Surprisingly, 34 (77.27%) of them were actually grouped in the 'normal' nutritional status. This finding was in agreement with the fact that sub-clinical vitamin-A deficiency has no clinical manifestations other than the finding of serum retinol concentration is less than 20 gr/dl.^{15,16} This condition is also known as micronutrient deficiency or *hidden hunger*. People with this condition are usually unaware of the deficiency experienced by their body. These micronutrients are needed in small amounts only but are truly essential for general health, especially for the eyes.^{17,18}

Subjects aged six to ten years were selected to participate in this study, since these particular age groups are not covered by the Indonesian Ministry of Health's vitamin A supplementation program, employed in February and August annually. This program only covers pre-school children under five years old.¹⁹ This study showed that the majority of sub-clinical vitamin-A deficiency subjects are eight years old, without gender disparities. These results correspond with those of our previous studies.^{20,21}

The serum retinol concentration of 0.35-0.70 $\mu\text{mol/l}$, used as an indicator for diagnosing sub-clinical vitamin-A deficiency, does not provide an exact reflection of the total amount of body retinol stored in the liver. It represents only a borderline level between vitamin-A deficiency and normal serum level.^{22,23} A stable serum retinol level can be achieved when the liver storage level is very low.²³

High prevalence of sub-clinical vitamin-A deficiency in children in this study indicated the dietary intake situation in the area. As the nutritional status might hold a role in this finding, considering the high number of children who are undernourished in Plered sub-district, West Java.²⁴ Dietary habits of the children in this area constitute one of the factors, since this study was conducted in the mountain and plantation areas, where it is difficult for the people to find animal sources of vitamin A, such as meat, milk, fish, liver and eggs. Low social economy status might also contribute to this predicament. The level of vitamin A in the body is also influenced by respiratory tract infection, persistent diarrhea, anemia, and middle ear infection, frequent afflictions suffered by these children.^{25,26}

Detecting the manifestations of sub-clinical vitamin-A deficiency is a challenging task, considering night blindness is the early subjective symptom and more often than not unnoticed by patient. Decreased ability to see in low light intensity is caused by disturbance in the rhodopsin regeneration cycle, subsequently resulting in lower level of contrast sensitivity, which, clinically, can be assessed by contrast sensitivity test. Patients might have visual acuity of 6/6 while experiencing difficulties to see at night.²⁷

This study found that the average value of the 50 (47.6%) subjects with abnormal contrast sensitivity is 1.64 log unit, whereas the normal value is 1.75 log unit. Moreover, the mean serum retinol concentration is $0,83 \pm 0,034 \mu\text{mol/l}$ in both normal and abnormal contrast sensitivity subjects, resulting in the low sensitivity and specificity values. However, this finding was quite different from that of

Sekarsari²¹ who found the sensitivity of 100% and specificity of 80.5% based on the school children population with a mean of abnormal contrast sensitivity value of 1.52 log unit, and an average of serum retinol level of 0.63 $\mu\text{mol/l}$. Similar results were also found by Handayani.²⁸ These facts might suggest that the contrast sensitivity test appears to be successful as a diagnostic tool only in the more advanced serum retinol level depletion.

Since our finding of low sensitivity values together with the low PPV for contrast sensitivity test indicated that this test is unfavorable as a screening tool in the detection of deficiency of vitamin A, since it revealed only a 40% probability of a subject with positive test result to actually have sub-clinical vitamin-A deficiency. Several factors contribute to this result; background lighting, light reflection, distance, and personal factors pertaining to the subject. The drawback of this study was that no measurement was taken on room illumination during the test. Moreover, the contrast sensitivity test is a subjective test and might contribute to the variation of its diagnostic values found in our last studies. Fear and shyness in our subjects might also have affected the test results. Measurement bias was avoided by taking a repeated test up to two to three times.

This study showed a total of 91 subjects (86.7%) with abnormal conjunctival impression cytology, which is higher than the previous study by Rostami *et al.*²⁶ who only revealed 23.6% prevalence of abnormal conjunctival impression cytology among two to five-year-old children in Teheran. Reddy⁸ reported that 70.5% out of 246 children aged six to ten years, had serum retinol concentration which is lower than 0.7 $\mu\text{mol/l}$, whereas 85% of them were found to have an abnormal profile. The prevalence was raised to 97% in the pre-school children (one to five years old). Moreover, 65% amongst those who presented with normal conjunctival impression cytology were found to have low serum retinol concentration; which was in contrast to our finding, incorporating only 4 (28.6%) subjects.

Incongruence found in our study between conjunctival impression cytology and serum retinol concentration was most likely due to a poor cytology sample collection process, inadequate amount of serum, poor reagent quality or other unknown contributing factors.²² The disadvantage of conjunctival impression cytology as a diagnostic tool was the necessity of optimal cooperation between researcher and the subjects. Uncooperative subjects, especially the children, served to hamper sample collection process, thus affecting the end result. Conjunctival impression cytology also presented its own extent of subjectivity.²⁸

The contrast sensitivity test is a functional clinical indicator, whereas the conjunctival impression cytology is a tissue pathological indicator. Further comparability analysis using Pearson's test was not in total accordance and no correlation (p 0.538) was found between the contrast sensitivity test and the conjunctival impression cytology (Table 4). This finding may indicate that there are different kinds of vitamin-A metabolism within the two tissues.

In conclusion, the results obtained did not support our postulation that either the contrast sensitivity test or the conjunctival impression cytology can be used as a favorable diagnostic screening tool to detect sub-clinical vitamin-A deficiency.

Table 4 Comparability between conjunctival impression cytology and contrast sensitivity test.

Contrast Sensitivity	Impression Cytology		Total
	Abnormal	Normal	
Abnormal	44 (a)	6 (b)	50 (a+b)
Normal	47 (c)	8 (d)	55 (c+d)
Total	91 (a + c)	14 (b+d)	105

Pearson's analysis showed that there was no correlation (p 0.538) between the conjunctival impression cytology and the contrast sensitivity test.

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Awareness and perception of budding doctors: A focal scenario on eye donation

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Abstract

Background: Diseases affecting the cornea constitute a major cause of blindness. Corneal transplantation offers the potential for sight restoration. Due to non-availability of healthy cornea, many people continue to live in a dark world.

Objectives: To assess the awareness and perception of undergraduate medical students towards eye donation.

Methods: A cross-sectional study was conducted among undergraduate medical students of Kolkata on August 2010 using a pre-designed, pre-tested, semi-structured, self-administered questionnaire. The data were analyzed using Epi-info software package version 6.04. **Results:** Almost all (98.9%) participants knew that eyes can be donated and 70.8% were aware at the time of eye collection. However, only 43.7% respondents knew whom to approach for pledging their eyes for donation; 80.7% were either willing (76.0%) or had already pledged (4.7%) to donate their eyes. Television was the major source (78.1%) of information on eye donation. Nobility was the main motivation (87.7%) and 75.5% felt the need for helping the blind. Of these medical students, 19.3% were unaware and did not pledge eye donation due to objection by family members and dislike of the idea of separating their eyes.

Conclusion: The present study revealed that medical students were well aware of eye donation with a favorable attitude towards it and most of them were inclined to pledge for eye donation. The perceived reasons for not donating eyes need to be considered while creating awareness about eye donation in the community. Students can be actively involved as volunteers in eye donation campaigns and after proper training in counselling techniques, they can act as counsellors for eye donation activities.

Key words: Blindness, corneal transplant, eye donation, medical students

Introduction

Using the definition of blindness from International Classification of Diseases 10 (Update and Revision 2006),¹ globally the number of visually impaired is estimated to be 285 million, 39 million of whom are blind and 246 million have moderate to severe visual impairment. In the South-East Asia Region (SEAR) of the World Health Organization (WHO), apart from India, 27.9 million people are visually impaired,

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3.9 million of whom are blind and 23.9 million have low vision. In India alone, 62.6 million people are visually impaired, 8 million of whom are blind and 54.5 million have low vision.² The different causes of blindness in India are cataract (62.6%); refractive errors (19.7%); glaucoma (5.8%); corneal pathologies (0.9%).³ The prevalence of blindness is 0.6% and the prevalence of low vision is 2.0%.⁴

In West Bengal, the prevalence rate of blindness has been lowered from 1.49% to 0.63% and the goal (0.3%) is expected to be achieved by the year 2020.⁵

Diseases affecting the cornea constitute a major cause of blindness worldwide, second only to cataract in overall importance. According to WHO it is the fourth cause of blindness globally, after cataract, glaucoma and age related macular degeneration.² The global causes of corneal blindness are: trachoma, xerophthalmia and ophthalmia neonatorum, onchocerciasis, leprosy and the use of harmful traditional eye medicines.⁶ Corneal transplantation offers the potential for sight restoration to those who are blind from corneal diseases and two persons can be benefitted from a single donor. In spite of this, it is a sad fact that due to non-availability of healthy cornea many people continue to live in a dark world. The WHO reports that corneal blindness affects more than ten million people worldwide, but only 100,000 receive corneal transplants each year.^{7,8}

As many as three million people can benefit from corneal transplantation in cases where lack of awareness is the hindrance.⁹ One hundred thousand corneas are needed, but only about 10,000 are collected in India. ¹⁰ Only 30% of donated eyes are used; the rest are either discarded for not being in good shape or sent to medical colleges for educational purposes.¹¹ Until 2010, there was an upward trend in the number of corneal donations.¹² The number of corneas harvested dropped in 2010-11.¹³ If only half the deaths in India would be leading to corneal donation, the waiting list could be done with in just months.¹⁴ Eye donation fortnight is being organized in this country from 25th August to 8th September each year for last 27 years.¹⁵

Medical students are the budding physicians of the future who constitute a major potential force to increase the rate of eye donation. They have the opportunity to counsel and motivate the patients and their relatives to donate eyes. To do this, they themselves should be well aware of the need of eye donation, the success of eye transplantation and proper utilization of corneal tissue. Very few studies have been conducted on this topic among medical students in India and in West Bengal, including Kolkata.

In this context, the present study was conducted to assess the awareness and knowledge of undergraduate medical students of tertiary care hospitals towards eye donation and corneal transplantation and the willingness to donate eyes.

Materials and methods

Type of study: observational, descriptive.

Study design: cross-sectional.

Places of study: IPGMER and Midnapore Medical College, Paschim Medinipur, West Bengal.

Study population: 400 MBBS students of medical colleges. A convenient sampling technique was followed.

Study tool: pre-designed and pre-tested semi-structured self-administered questionnaire.

Outcome variables: student's knowledge and awareness regarding social and technical aspects of eye donation and corneal transplantation; their intention to donate eyes.

Explanatory variables: demographic details, perceived reasons for eye donation by donors, perceived reasons for not donating eyes and sources of information.

Study duration: included preparatory phase and designing and pre-testing of the questionnaire, data collection, analysis of data and report writing and it required one month time duration. The study was conducted in August 2012.

Data collection was done through a self-administered questionnaire. The students were approached, requested to provide data and explained on the issue of anonymity and privacy. Three hundred eighty-four students responded correctly without missing information.

Inclusion criteria: All the students who were present and gave the consent on the days of data collection.

Exclusion criteria: The students who refused to answer the questionnaire and who were unavailable at the time of data collection (three attempts).

Data management and statistical analysis: Data collection was done by way of self-administered questionnaires. Compilation in the master sheet, tabulation, analysis, interpretation was done through Epi-Info software package version 6.04. Proportion was calculated.

Ethical committee approval: The study got permission from the principals and a proposal has been sent to the ethical committee for approval. The study was carried out according to the ethical guidelines for biomedical research on human subjects (2000).

Results

Of the 400 students, 384 responded correctly in the study (response rate 96%). The respondents belonged to the age group of 19 to 21 years. Two hundred sixty-four were male (68.7%), 120 were female (31.3%).

The relevant responses on knowledge about eye donation by the 384 medical students were considered in the study. Almost all participants (98.9%) were aware of the existence and practice of eye donation and knew that eyes can be donated only after death. Ideally eyes should be collected within six hours of death and that is fairly well known to 70.8% students. Only 25% of the students knew that 70 years is the ideal donor age limit for corneal transplantation. Of the students, 54.6% were aware that after death the donor's eyes should be kept closed while waiting for the donation. The students were not very well informed about the transportation and storage of the donated eyes, with the medium of transportation known to only 34.4% students. The respondents were somewhat aware of the ocular (49.4%) and systemic contra-indications (87.5%) of eye donation (Table 1).

Table 1. Responses to the questionnaire – awareness and knowledge on eye donation (n = 384).

Characters	Number responded	Percentage
Eyes can be donated only after death	380	98.9
Ideal time for collection of donated eyes is within six hours after death	272	70.8
Person who can give consent	334	87.0
Knows institution where to be contacted for eye donation	168	43.7
Name some eye banks of Kolkata	124	32.3
Age limit of donor for corneal transplantation	96	25.0
Knows that after death donor's eye should be kept closed	210	54.6
Knows which part of eye is removed	330	86.0
Knows which part of eye is transplanted	352	91.6
Knows medium of transportation	132	34.4
Knows that eye can be stored up to 24 hours	218	56.8
Knows how storage time can be prolonged	194	50.5
Knows ocular contra-indications of cornea transplantation	190	49.4
Knows systemic contra-indications of eye transplantation	336	87.5

The study revealed that 90.6% agreed that there was shortage of eye donors in India and 80.7% were either willing (76%) or had already pledged to donate their eyes (4.7%).

Different knowledge (eye shortage, willing to donate) was seen among the participants (Table 2). Television was the major source of information on eye donation for 78.1% students (Table 3).

The specification of perceived reasons for eye donation by the donors was assessed. Noble intentions (87.7%) was the main motivation for donation and 75.5% felt the need for helping the blind (Table 4).

The specification of the 19.3% medical students who would not pledge their eyes for donation was identified with respect to the reasons for not doing so. Their

views about lack of eye donation were variable with a majority (74.7%) citing lack of awareness as the main reason (Table 5).

Table 2. More responses bordering on knowledge of eye donation/corneal transplant (n = 384).

Characters	Number responded	Percentage
Knows a person who has donated eyes	68	17.7
Knows someone who has received a donated eye	00	0
Willing to donate eyes	292	76.0
Already pledged to donate eyes	18	4.7
Willing to donate close relative's eyes	270	70.3
Knows there is an eye shortage in India	348	90.6
Awareness about selling and buying of donor eyes	60	15.6

Table 3. Source of information on eye donation (n = 384).*

Source	Number	Percentage
Television	300	78.1
Radio	32	8.3
Newspaper	272	70.8
Magazines	176	45.8
Posters	106	27.6
Friends/Neighbors	156	40.6
Relatives	106	27.7
Doctor	76	19.8
Hospitals	14	3.6
Pamphlets	90	23.4
Seminars/Lectures	04	1.0
Family members	52	13.5
Nurse	14	3.6
Health workers	94	24.5

*Multiple Responses

Table 4. Distribution of perceived reasons for donating eyes by donors (n = 310).#

Perceived Reason *	Number	Percentage
Eye donation is a noble work	272	87.7
Gives pleasure to help the blind	234	75.5
To set an example	72	23.2
To get popularity	04	1.3
A friend/relative has donated eye	64	20.6
A friend/relative has received a donated eye	00	0.0
Impressed after reading an article	96	30.9
Impressed after attending a seminar/lecture	80	25.8
Impressed after seeing a movie	42	13.5

Included students who have either pledged or are willing to donate eyes.

* Multiple Responses

Table 5. Distribution of perceived reasons for not willing to donate eyes (n = 74).*

Perceived reason	Number	Percentage
Lack of awareness	56	74.7
Objection by family members	20	27.0
Feels body ill-treated by eye donation	08	10.8
Religious restrictions	12	16.2
Unsuitability to donate eyes due to health problems	10	13.5
Dislike of separating eyes from the body	14	18.9
Signing eye donation card is like signing death certificate	06	8.1
Corneal transplant gives poor result	00	0.0

* Multiple Responses

Discussion

There are an estimated 4.6 million corneal blind people in India and 20,000 new victims join yearly. The good news is that almost 66 percent of the cases are preventable or curable if basic precautions are taken. Thus as many as 3 million people

can benefit from corneal transplantation. Yet, no more than 5000 corneal grafts are performed annually. The reason? Lack of awareness!⁹ In a *New York Times* article in 2008, the president of the International Agency for the Prevention of Blindness, Dr. Nag Rao, said that in India 100,000 corneas are needed for transplants each year, but only about 10,000 are collected each year – and fewer than 5000 transplant operations are being performed annually.¹⁰ According to the Union health ministry's own analysis, only 30% of donated eyes are used for treatment of corneal blindness. The rest are either discarded for not being in good shape, or sent to medical colleges for educational purposes.¹¹

Until 2010, there was an upward trend in the number of corneal donations.¹² Despite the growing spread of awareness campaigns, the country has registered a dip of 3.5% in the number of corneal donations in the last year, according to the latest government statistics. The number of corneas harvested dropped from 46,589 in 2009-10 to 44,926 corneas in 2010-11.¹³

In fact, in India, an average of only 38,000 corneas are donated annually, thus it will take 112 years for all corneal blind in India to get new corneas. If only half the deaths in India led to corneal donation, the waiting list could be wiped out in just months.¹⁴ It was found that of the total number who pledged to donate their eyes, less than 1% was actually donated finally, according to Union Health ministry officials (August 26, 2011).¹¹ 'Eye donation fortnight' is organized from 25th August to 8th September every year to promote eye donation. Gujarat, Tamilnadu, Maharashtra, Delhi, Chandigarh, Andhra Pradesh, Kerala and Karnataka are at the forefront of this activity.¹⁵ Targets for 11th five year Plan (Indian plan system for development activities) is to collect 260,000 donated eyes (after death) for transplantation in persons with corneal blindness.¹⁶ West Bengal collected 2152 eyes in 2010 according to Union Health Ministry Officials.¹¹

As early as 1905, doctors had discovered that corneal blindness could be cured by carrying out a corneal transplant. In most countries, especially in the developing ones, the numbers of corneas available do not meet the demand. In order to increase the potential for eye donation it may be imperative to promote awareness among potential donors and healthcare workers.²⁷ Post-graduation medical students might serve as terminal care doctors of suitable eye donors; they would have a great opportunity to motivate patients or relatives to donate eyes.²³

Data from the present study suggest that the level of awareness on eye donation/corneal transplant among these students were high, as 98.9% students were aware that eyes can be donated only after death which was corroborative with the findings of some other studies in Delhi,¹⁷ Bangalore,¹⁸ Ahmedabad,¹⁹ Brahmapur,²⁰ Karnataka,²¹ and Nagpur.²² However, the rate was somewhat lower (79.6%) in another study among final year medical students of Delhi by Dhaliwal U,²³ 86% among University students of Malaysia,²⁴ 81% among secondary level students of North Kolkata²⁵ and only 27.5% among medical students of Nigeria.²⁷ Information by mass media could be related to the high level of awareness in these study participants.

When the study population were asked about the time of collection of cornea, a correct answer was given by 70.8 % of students of this study, which was almost

similar to the Delhi study (63.35%) on medical students²³ and the Karnataka study (61%) on college students including medical students.²¹ The corresponding figures were only 41.1% in Delhi,¹⁷ 32.8% in Bangalore,¹⁸ 40.0% in Nagpur,²² 32.1% in North Kolkata²⁵ and 37% in Kolkata.²⁶ Lack of knowledge of this aspect on the part of doctors would result in unnecessary wastage of potential donor tissue. But it was encouraging that the Brahmapur study,²⁰ the Ahmedabad study¹⁹ and the Nigeria study²⁷ revealed that 90% of the medical students were aware of the ideal time of removing donated eyes (after death). In this study, 43.7% respondents knew about the appropriate place of contact for an eye donation; which was higher than the Delhi study (27.2%),¹⁷ the Bangalore study (32.9%),¹⁸ and the Nagpur study (29.3%)²²; but lower than the study by Nekar, et al. (74.1%),²¹ Dhaliwal (61.2%),²³ Jena, et al. (83.6%)²⁰ and Sarkar et al. (66%).²⁶

In the present study, 90.6% of the medical students agreed that there is a shortage of eye donors in India and 76.0% students were willing to donate their eyes, whereas 4.7% had already pledged for eye donation. This represents a total of 80.7%; corresponding with some other studies on medical and nursing students.¹⁷⁻²² This was a very encouraging feature which could motivate unwilling and undecided individuals by showing the merits of eye donation.

Nobility was the prime reason (87.7%) followed by pleasure to help the blind (75.5%) felt by the willing donors of this study, a result that was almost similar to some other studies.^{17,18,21,22}

The reasons for lack of eye donation were variable as perceived by the unwilling respondents. Of this study population, 74.4% told that lack of awareness was the main reason for people not to donate eyes. Similar results were obtained from other studies.¹⁷⁻²² Other reasons included objection by family members, body ill-treated by eye donation, religious restrictions, health problems, dislike of separating eyes from the body, etc. Other studies revealed similar reasons.^{17-19,21,22,27}

If these students were well-informed about eye donation and corneal transplant, they could be expected to influence eye donation rates. Television was the most important source of information on eye donation (78.3%) revealed from the present study. According to other studies also, television was the major source of information.^{17,18,20,21,24-26}

Using mass media to increase the awareness regarding corneal blindness and eye donation to treat it is not enough. There is a great need to educate students, as they are an important part of our society. If they are educated about the preventive and curative aspects of corneal blindness, they can spread the message among their friends and family members, thus acting as important motivators. It is also essential to dispel their misconception regarding eye donation.

Conclusion

The present study revealed that medical students were well aware of eye donation (98.9%) with a favorable attitude towards it and most of them were inclined to pledge (80.9%) for eye donation. The majority had correct knowledge of time of collection of eye (70.7%) and 32.5% knew about the correct place of contact for eye

donation. The perceived reasons for not donating eyes need to be considered while creating awareness about eye donation in the community.

Medical students can be actively involved as volunteers in eye donation campaigns and after proper training in counselling techniques, they can act as counsellors for eye donation activities.

In undergraduate courses, more emphasis should be given to eye donation and eye banking so that they will play a pivotal role in the eye donation movement in our country; the Hospital Corneal Retrieval Program (HCRP) will be successful by active involvement of medical students.

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Epidemiology of ocular trauma hospital presentations in Sydney, Australia: insights for management and prevention

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Abstract

Aim: To facilitate care delivery and injury prevention by investigating the nature and outcomes of ocular trauma presentations to a tertiary care center serving an estimated 1.3 million people.

Patients and methods: This is an observational case series, retrospectively analyzed, of all patients that presented to the tertiary care center for management of ocular trauma between 01/01/2006-31/12/2006. Data collected included: patient's clinical findings, major diagnoses, initial and final visual acuity, whether the injury was work related, whether protective eyewear was worn, and whether the patient required surgery or admission to hospital. A final BCVA < 6/12 was defined as significant visual deficit.

Eligible patients were identified prospectively by researchers. Patients underwent standardized clinical assessment. De-identified clinical data was entered into a Microsoft Access database retrospectively and analyzed by separate, blinded researchers. Descriptive statistical analysis was then performed in Microsoft Excel. Analysis based on an ordinal regression model and risk factor analysis was performed in SAS.

Results: There were 214 cases of ocular trauma in 197 individuals (17 bilateral injuries). Patients were mostly male (83%) with average age 35. The majority of cases were closed globe injuries (92.1%) with no significant final visual deficit (88.3%). Open globe injuries (7.9%) were more likely to have visual deficit (i.e., 47% with final BCVA < 6/12) ($p < 0.01$). In total, 13.1% required surgery and 12.1% required admission to hospital. Eye protection was worn in 7.9% of all cases, and 19.1% of work related cases. Nearly one quarter of cases (22.4%) were work related. Open globe injuries were more likely to occur at work. Open globe injuries at work were caused by a metal projectile in 85.7% of cases. Thirty percent of workers suffered a burn, with final BCVA < 6/12 in 10% of burns.

Conclusions: While the vast majority of ocular trauma is superficial with low morbidity, trauma persists as a significant cause of visual impairment. Most vision impairing injuries occur at work, where metal projectiles and burns are common, preventable causes of significant vision loss, which could be targeted in prevention efforts.

Key words: Ocular, trauma, epidemiology

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Introduction

Eye injury is a significant cause of morbidity and economic burden to the community.¹ A 1995 study by Fong conservatively estimated the annual cost in Australia at \$155 million.² Twenty percent of the population were found to have suffered eye injury in their lifetime according to McCarty *et al.*,³ slightly higher than a lifetime prevalence of ocular injury in the United States of 14.4%-19.8%.^{4,5} Annual incidence of eye injury has been estimated at 11.4 per 1000 of population.^{2,6} The incidence of hospitalized eye injuries was found to be 15.3 per 100,000.⁷

The purpose of this study is to investigate the etiology, clinical features, and resulting visual impairment related to ocular trauma in South West Sydney, in order to inform delivery of care and injury prevention efforts. Region specific studies of ocular trauma are important since socioeconomic and demographic variables are significantly correlated with injury frequency and severity.^{6,7} Additionally, the study region is significant due to its size, covering a catchment area of 1.35 million people, or 6.5% of the Australian population.^{8,9}

Patients and methods

The study is an observational case series of all patients presenting to Liverpool Hospital, including those directly referred to the Liverpool Ophthalmology Department clinic, with ocular trauma during 2006. Participants were referred into the study by treating clinicians in the Emergency Department and Ophthalmology Clinic, and the Emergency triage database was periodically reviewed to identify potentially missed cases. All patients presenting to the care of tertiary hospital ophthalmology department in this manner between 01/01/2006 and 31/12/2006 were considered to meet the inclusion criteria of the study. The exclusion criteria were absence of ocular trauma during the study period, or death prior to ophthalmic assessment, for example due to multi-system trauma.

Patients underwent standardized assessment of ocular trauma, as per the training guidelines of the Royal Australian and New Zealand College of Ophthalmology (RANZCO). This comprised of history taking and an examination including external examination, orbital and full ocular examination for all patients, with subsequent further examination and investigations, including imaging, tailored to clinical findings and suspicion, in keeping with RANZCO training guidelines. Management was also appropriate to diagnosis as per RANZCO training guidelines.

All ocular examination findings were recorded, including initial best corrected visual acuity (BCVA), and final BCVA. For the purposes of statistical analysis, a final BCVA < 6/12 was defined as a significant deficit in BCVA. Other variables recorded were: patient demographics, diagnosis, open globe injury etiology, whether the injury was work related, whether protective eyewear was worn, and finally whether the patient required surgery or admission to hospital (under the care of an ophthalmologist).

De-identified clinical data was entered into a Microsoft Access database retrospectively and analyzed, by separate, blinded researchers. The ocular trauma was

categorized according to Kuhn's classification of ocular trauma into either open globe or closed globe injuries, with further sub-classification by clinical diagnosis (10). Descriptive statistical analysis was then performed in Microsoft Excel. Analysis based on an ordinal regression model and risk factor analysis was performed in SAS (version 9.2).

This study was conducted with the approval of the Human Research Ethics Committee, Liverpool Hospital. The study was conducted as per the tenets of the Helsinki Declaration.

Results

General overview

One hundred ninety-seven individuals presented to Liverpool Hospital with ocular trauma to 214 eyes (17 bilateral injuries). For the purposes of this study, each eye injured was considered a single 'case', with bilateral eye injury counted as two cases.

Age and sex

The average patient age was 35.4 (\pm 17.1) years. Patients were predominantly male (83%). The average patient age was lower in females (32.9 years) than males (35.8 years).

Nature of Injuries

The majority of injuries were closed globe (197 eyes or 92.1%). The relative frequency of ocular examination findings are listed in Table 1. Occasionally, a single eye had multiple clinical findings. Thus, in total there were 250 clinical findings in 214 injured eyes in 197 patients. Table 1 lists the number of eyes with each clinical finding, as well as the proportion of all 250 findings this represented.

Orbital trauma was the most common finding, recorded in a fifth of all cases. The vast majority of these were orbital wall fractures (47 of 50 orbit trauma cases). Lacerations, to the conjunctiva, cornea or sclera comprised 17% of findings. Iris trauma (12%) was relatively common. Retinal trauma was observed in 10.0%, and lenticular trauma in 4.4%. Vitreous hemorrhages were rarer, observed in 2.8%. Optic nerve trauma and uveal trauma each comprised of 1.6% of cases respectively.

Surgery and hospitalization

Of all cases, 13.1% required surgery, and 12.1% required admission to hospital.

Eye protection

Seventeen (7.9%) patients reported wearing eye protection at the time of trauma. Of those injured at work, eight (19.1%) wore eye protection.

Visual outcomes

Table 2 lists final best corrected visual acuity (BCVA) findings in three categories: (1) all eyes; (2) closed globe eyes; and (3) open globe eyes. Analyzing all eyes, 84.1% had no significant deficit in BCVA at final examination (defined as final BCVA \geq 6/12).

Table 1. Ocular examination finding frequency is listed by number of cases with each clinical finding. There were 250 findings in 214 eyes. Percentages reflect the proportion of total findings found in each category.

Findings	Number of cases (%)
<i>Orbit trauma</i>	50 (20.0)
- orbital wall fractures	47 (18.8)
- other orbital trauma	3 (1.2)
<i>Lacerations</i>	43 (17.2)
- corneal laceration	16 (6.4)
- scleral laceration	14 (5.6)
- conjunctival laceration	13 (5.2)
<i>Hyphema</i>	39 (15.6)
<i>Iris trauma</i>	30 (12.0)
- traumatic mydriasis	17 (6.8)
- iris prolapse	6 (2.4)
- sphincter tear	3 (1.2)
- other iris trauma	4 (1.6)
<i>Retinal trauma</i>	25 (10.0)
- commotio retinae	13 (5.2)
- retinal hemorrhage	4 (1.6)
- retinal detachment	2 (0.8)
- other retinal trauma	6 (2.4)
<i>Lid trauma</i>	20 (8.0)
<i>Raised intra ocular pressure</i>	16 (6.4)
<i>Lens trauma</i>	11 (4.4)
<i>Vitreous haemorrhage</i>	7 (2.8)
<i>Uvea trauma</i>	4 (1.6)
- uveal prolapse	3(1.2)
- choroidal rupture	1(0.4)
<i>Optic nerve trauma</i>	4 (1.6)

Table 2. Final best corrected visual acuity (VA) of: all 214 eyes; 197 closed globe eyes; and 17 open globe eyes. Percentages, in parenthesis, describe the proportion of each group with a particular visual outcome. For the difference in final VA between closed globe and open globe cases, p-value < 0.001.

Visual Outcomes: Final VA	All Injured Eyes (%)	Closed Globe Eyes (%)	Open Globe Eyes (%)
VA ≥6/12	180 (84.1)	174 (88.3)	6 (35.3)
VA <6/12	8 (3.7)	7 (3.5)	1 (5.9)
VA < 6/60	5 (2.3)	2 (1.0)	3 (17.6)
NPL*	7 (3.3)	3 (1.5)	4 (23.5)
Incomplete data	14 (6.5)	11 (5.6)	3 (17.6)

* NPL = no perception of light

Closed globe injuries

There were 197 eyes (92.1%) with closed globe injuries with an average patient age of 35.7 (\pm 17.1) years, and male preponderance (87.8%).

There were 224 closed globe diagnoses in 197 eyes, as detailed in Table 3, according to Kuhn's diagnostic categories of closed globe injuries. The most common findings were contusion (34.3%), superficial foreign body (31.3%), and burns (17.4%).

Table 3: Closed globe ocular diagnosis frequency is listed by number of eyes with each clinical finding. There were 224 findings in 197 eyes. Percentages, in parenthesis, reflect the proportion of total diagnoses found in each category. Lamellar laceration includes corneal abrasion and conjunctival abrasion.

Findings	Number of eyes (% of total findings)
Contusion	77 (34.3)
Superficial Foreign Body	70 (31.3)
Burns	39 (17.4)
Lamellar laceration	38 (17.0)
- Corneal abrasion	36 (16.1)
- Conjunctival abrasion	2 (0.9)

There were 39 eyes with burns in 28 individuals. Most burns were alkali (61.5%), then acid (15.3%), ultraviolet (12.8%), and thermal (10.2%).

Visual outcomes for the closed globe group are shown in column three of Table 2. Most eyes (88.3%) had no significant deficit of visual acuity. However, twelve (6%) did have significant deficit, including three (1.5%) with no perception of light (NPL) secondary to traumatic optic neuropathy.

Table 4 summarizes visual outcomes for the various diagnostic categories of

closed globe injury. Corneal abrasions and foreign bodies while common were rarely associated with visual deficit. Burns, however, were high morbidity with a significant visual deficit in 10.2% of cases.

Table 4: Final best corrected visual acuity (VA) for various categories of closed globe eye injuries. Numbers of eyes in each category are listed. Percentages, in parenthesis, reflect the proportion of injured eyes in each diagnostic category that have a given visual outcome.

Visual Outcomes (Final VA)	Contusions	Foreign body	Burn	Lamellar laceration	Corneal abrasion	Conjunctival abrasion
VA ≥ 6/12	65 (84.4)	66 (94.3)	34 (87.2)	35 (92.1)	34 (94.4)	0
VA <6/12	2 (2.6)	2 (2.9)	2 (5.1)	3 (7.9)	1 (2.8)	2 (100)
VA < 6/60	1 (1.3)	1 (1.4)	2 (5.1)	0	0	0
NPL	3 (3.9)	0	0	0	0	0
Incomplete data	6 (7.8)	1 (1.4)	1 (2.6)	0	1 (2.8)	0

Open globe injuries

There were a total of seventeen patients with open globe injuries representing 7.9% of the total number of injured eyes. Penetrating globe injuries were observed in nine eyes (52.9%) of which three also had an associated intraocular foreign body. There were five ruptured globes (29.4%), and three full thickness lacerations (17.7%).

The majority (80%) of open globe injuries were in males (14 eyes). Four patients (23.5%) were age 18 or below.

No patient wearing eye protection suffered an open globe injury, and while the findings were suggestive of an association with eye protection use and a reduced risk of open globe injury ($p = 0.30$), the sample size was not large enough to demonstrate statistical significance.

Amongst open globe cases, injury by a metal projectile was involved in seven of seventeen injuries (41.1%), making it the most common mechanism. Six of these seven cases were work-related. The next most common mechanism was assault, with three cases (18%). The other causes were varied including one motor vehicle accident (6%), and one explosion.

In Table 2, column four summarizes the visual outcomes for the open globe cases. As expected, visual outcomes were worse for the open globe cases than the closed globe cases (p value < 0.001). Six eyes (35.3%) had final BCVA ≥ 6/12, the remaining eight eyes (47%) had final BCVA < 6/12 including four eyes (23.5%) with NPL.

Table 5 shows final BCVA for the various types of open globe injuries. The five ruptured globes (29.4% of the open globe eyes) all had poor visual outcomes, four with NPL and one with final BCVA of < 6/60. All three eyes with full thickness laceration had final BCVA \geq 6/12.

Table 5: Final best corrected visual acuity (VA) for various diagnostic categories of open globe eye injuries. Numbers of eyes in each category are listed along with the percentage, in parenthesis, of total open globe cases that they represent.

Visual Outcomes (Final VA)	Penetrating globe injury	Ruptured globe injury	Perforating globe injury
VA \geq 6/12	3 (17.0)	0	3 (17.3)
VA <6/12	1 (5.9)	0	0
VA < 6/60	2 (11.8)	1 (5.9)	0
NPL	0	4 (23.5)	0
Incomplete data	3 (17.6)	0	0

Work-related injuries

There were forty-nine work-related (WR) eye injuries, which represented 22.4% of all ocular trauma cases. This included two females and four bilateral injuries.

Forty-two (85.7%) of the work-related injuries were closed globe. These were mainly superficial injuries. Superficial foreign body (SFB) was the most common finding, observed in twenty-three cases (46.9%). Burns were the next most common with thirteen cases (30%). Ten of the burns were alkali (77%) and three (23%) were ultraviolet. Work related alkali burns constituted 50% of total presentations with alkali burns. There were also eight contusions (16.3%), and five lamellar lacerations (10.2%).

There were seven open globe work-related injuries (41.4% of all open globe injuries). Five (71.4%) were penetrating eye injuries and two ruptured globes (28.5%). All but one of the work-related open globe cases involved a metal projectile. In no case of open globe injury eye protection had been worn.

Risk factor analysis suggests open globe injuries are more commonly work-related, albeit not quite reaching statistical significance (p value < 0.06). Eight of the work-related cases (19.1%) wore eye protection, and all of these had good visual outcomes (final BCVA \geq 6/12).

In 92.3% of work-related closed globe cases there was no significant deficit of final BCVA. The final visual outcomes for open globe work related cases reflected the recognized poor visual prognosis associated with open globe injuries, with two thirds of the patients suffering significant visual deficit, and nearly one third of patients with NPL.

Discussion

This study provides insights into ocular trauma in Australia. It contributes information about frequency of different types of injury and their associated visual outcomes, injury etiology, use of eye protection and features of work place injury. These insights are useful clinically, logistically, and for injury prevention.

Regional ocular trauma studies are important due to the lack of a national ocular trauma database, and significant local variations in ocular trauma epidemiology.¹¹ This study was performed in South-West Sydney, Australia, a region that warrants attention due to its size, and high risk demographic features. The 2006 population of South-West Sydney was approximately 1,350,000 (8), or 6.5% of the Australian population.⁹ The area is serviced by the South-Western Sydney Local Health District and Liverpool Hospital is the district's only tertiary ophthalmology referral center. The catchment region includes five of the ten most disadvantaged local government areas of Sydney.¹² Employment in the region includes industrial, manufacturing and service sectors. These work types and socioeconomic disadvantage are associated with higher risk of ocular trauma.^{13,14}

This study's demographics findings are similar to other studies of its kind, both in Australia and abroad. Males constituted 83% of the cohort; in a similar range to previous studies (70-85%). This is traditionally attributed to higher risk taking and occupational exposure.^{13,15} Average age of patients in the low thirties is also consistent with previous studies.⁶ Children are well known to have high rates of ocular trauma. Previous studies have found that children account for 20 to 50% of all ocular injury.¹⁶⁻¹⁸ In this study, 23% of the open globe injuries occurred in children.

The study demonstrates that ocular trauma commonly presents to tertiary hospital emergency departments whether the injury is low (84.1%) or high morbidity (15.9%). This is partly due to the pain associated with even superficial injury. Ophthalmologists are rarely the first to see an ocular trauma due to the referral system. Thus, GPs, ED staff and optometrists play an important role in emergency management of cases, which can be critical to visual outcomes. They also play an essential role in appropriately triaging which patients need to see an ophthalmologist urgently. Thus, it is vital that generalists are well-trained in ocular trauma emergency management including identification of urgent referrals.

The ratio of open globe to closed injuries was comparable with other studies in developed countries. Open globe injuries comprised 7.9% of cases, compared to 5% in a recent Singaporean study.¹⁵

This study demonstrates the heavy burden of disease associated with open globe injury. The visual outcomes were worse for the open globe cases than the closed globe cases (p value < 0.001). Roughly a quarter of the open globe cases had NPL.

In this study, 22.4% of cases were work-related injuries. This is less than reported by McCarty in 1999, which was the most recent study of this kind. That study found 60% to be work related, but included a rural population.³ Another rural study found that eye injuries accounted for 12% of all injuries to the regional hospital and one third of these were work-related.¹⁹ While the discrepancies may represent

demographic differences in the study populations, recall bias, or differences in reporting eye work-related injury, it is possible that this finding represents a true decrease in the proportion of work-related injuries. To some extent, a reduction should be anticipated. The prevalence of worker eye injury has been on a steady decline in the western world, due to eye protection and safety standards, and a shift of many high-risk manufacturing jobs to the developing world.¹⁵

In this study, workers were more likely to sustain an open globe injury than those not injured at work, albeit with a p value < 0.06 . Open globe injuries are associated with the poorest visual outcomes and therefore the greatest morbidity and associated costs.

It has been estimated in the ocular trauma literature that 90% of ocular trauma is preventable.¹⁷ The prevention of eye injury amongst workers and in the general community is influenced by awareness of risk, and subsequent steps to prevent injury. One important protective measure is the use of protective eyewear. In Australia, eye protection use is governed by various standards and pieces of legislation, both at the state and national level, and is primarily focused on encouragement of eye protection use in the workplace. In Sydney, the main government bodies affecting use of eye protection by workers are Work Cover NSW and Safe Work Australia. Important legislation at the state level includes the New South Wales Occupational Health and Safety Act of 2000 and New South Wales Occupational Health and Safety Regulation of 2001. Section 8 of the Act specifies that employers must provide safe working conditions, and section 15 of the Regulations specifies that employers must provide adequate personal protective equipment, including eye protection, should a modifiable risk to employees exist. It advises that personal protective equipment should meet standards specified by Standards Australia. Key standards that apply to eye protection include AS1067, 1336, 1337, 1338, 2211, and 2397. Government bodies also provide worker education. For example, WorkCover NSW offers educational workshops for businesses, which include discussion of eye protection. An employee who does not wear available eye protection provided can be reported to WorkCover NSW for failure to cooperate, as can an employer who fails to appropriately provide eye protection.

The findings in this study suggest that people working with metal may be a worthwhile target for injury prevention campaigns. Of workers who suffered an open globe injury, 85.7% were hit by some form of metal projectile. None of these patients wore eye protection. Thompson *et al.* also found in their study in rural NSW that penetrating eye injuries were most commonly caused by metal projectiles, including fencing wire.⁶ The study by McCarty *et al.* found that overall 30.7% of cases were caused by metal.³

The findings in this study suggest that people working with alkalis are also worthwhile targets for injury prevention efforts. Burns were a leading cause of vision loss amongst workers. Burns comprised 30% of work-related injuries, and nearly 80% of those were alkaline. Burns patients had significant visual deficit in at least 10.2% of closed globe cases. It is possible that alkali burns are becoming more common. Of all cases in this study, 11.2% suffered alkali burns, compared to 4.7%

of the study population in McCarty's 1999 study.³ However, McCarty's study was a self-reported population-based cross-sectional study, with associated risk of recall bias. Regardless, the risk of an alkali burn, from the likes of cleaning products and cement, could be effectively reduced through more prominent warning labels and consumer education to encourage use of eye protection.

In this study, eye protection was worn in 7.9% of cases in this study, and 19.1% of work-related cases, compared to 3.2 % of non-work-related cases. This study found 7.9% of the total trauma cases wore eye protection, less than the 13% reported in McCarty's 1999 study.³ Since 1999, extensive ocular trauma prevention strategies have been implemented, including the aforementioned legislation (*e.g.*, *New South Wales Occupational Health and Safety Act of 2000*) and work safety standards by Work Safe NSW and Safe Work Australia. This study is not designed to assess prevalence or effectiveness of eye protection. It primarily identifies patients who did not wear eye protection, or for whom eye protection failed, at least partially. However, future research into the effectiveness of these regulations would be valuable.

A strength of this study is that the data was collected prospectively from a single catchment area within a finite time and is therefore likely to be representative of true community presentation patterns to tertiary care.

A possible weakness of the study is that some patients may not have been captured in the database. It is possible, for example, that some minor cases of ocular trauma seen in the emergency department were not registered in the study. While this study contributes to the epidemiology knowledge base, individual studies at individual centers are prone to bias. Also, data is incomplete, with respect to final BCVA in 6.5% of eyes.

This study provides useful clinical and public health insights into ocular trauma injury patterns in metropolitan Australia by contributing information about injury relative frequency, causation, visual outcomes, burden of disease, use of eye protection and features of work place injury. There is a significant loss of vision related to open globe injury from metal projectiles and closed globe injuries from burns, especially alkali burns. Given the morbidity and relative frequency of these injuries, they are worthy of consideration for targeted prevention efforts.

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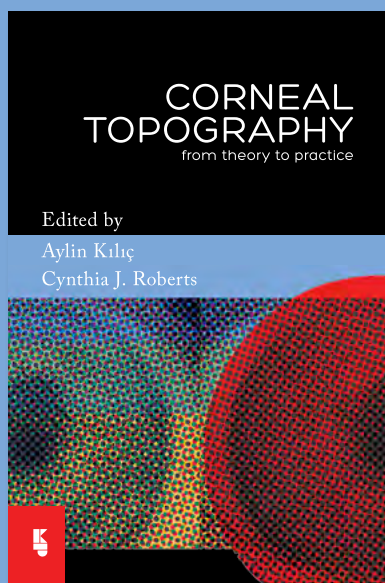
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A case series of bilateral electric cataract in high-voltage electrical injury

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Key words: *Electric cataract, lagophthalmos, chorioretinal lesion, subcapsular vacuoles, high-voltage electric current*

Introduction

A 39 year-old female presented with progressive diminution of vision in the right eye for six months after sustaining an injury from a high-voltage electric current to the right side of her forehead, face, around the right eye and to the scalp. On examination with the slit lamp, the right eye showed a mature cataract and anterior subcapsular opacities, with early lental opacity in left eye. She suffered from lagophthalmos and slight conjunctival congestion in the right eye. Vision in the right eye was only perception of light and in the left eye accurate projection of rays and 6/24. From the history, the type of injury (wound of entry and exit), and slit-lamp examination confirmed a case of bilateral electric cataract. We performed manual small-incision cataract surgery with posterior chamber intraocular lens implantation in right eye and in the left eye, using local anesthesia. Postoperative visual acuity was only 3/20 in the right eye and 6/6 in the left eye. In this case we have seen three circumscribed retinal lesions in the right eye; the left eye it was normal. This has been documented.

The second case was a 20-year-old male, who was admitted to our center with bilateral electric cataract. He was treated the same way as the first case. He regained normal BCVA after cataract surgery with posterior chamber intraocular lens implantation.

Case report

Case 1 is a 39-year-old female who presented to our outpatient department with painless, progressive dimness of vision in her right eye that started six months previously, and inability to close the right eye properly. She had suffered from a high-voltage electric injury about six months before, while she was doing her morning work in her own home. She had been unconscious for about 15 minutes and was admitted to a nearby private hospital in Tamluk, West Bengal, where she was given primary treatment.

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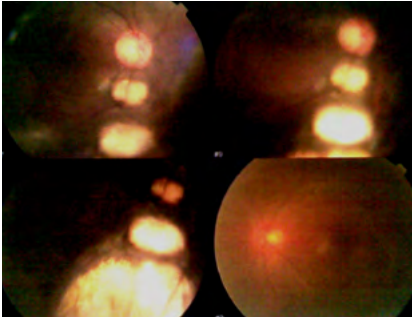


Fig. 1. Lagophthalmos (first case).

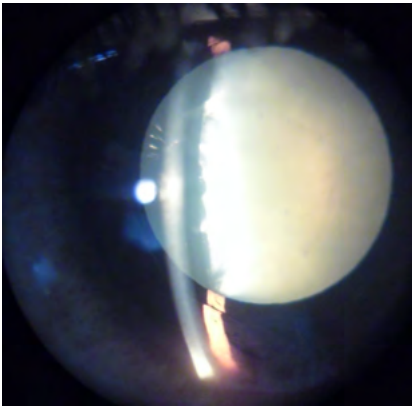


Fig. 2. Anterior subcapsular opacities.

On examination at our center there was lagophthalmos (Fig. 1) in the right eye due to severe scar tissue formation in the upper and lower lid. There was scar tissue on the forehead and the right side of her face and areas of alopecia and scarring on her scalp. Slit lamp examination showed a milky white lens (Fig. 2) with anterior subcapsular opacities. Conjunctiva was slightly congested in the right eye. Cornea, sclera, iris and anterior chamber were normal in both eyes. Ocular movement was full in both eyes. Visual acuity was only perception of light with accurate projection of rays in the right eye and 20/20 in the left eye. Upon examination with a direct ophthalmoscope, the dilated fundus of the left eye was within the normal limit and the dilated fundus of the right eye was obscured by lens opacity. Intraocular pressure was 14.0 mmHg in both eyes, measured by applanation tonometry.

After admission of the patient, we did all routine examinations. We then performed a correction of the lagophthalmos (Fig. 3) with the assistance from a plastic surgeon. After two weeks, we performed small-incision cataract surgery and posterior chamber intraocular lens implantation in the right eye under peribulbar anesthesia.



Fig. 3. Lagophthalmos after plastic reconstruction.

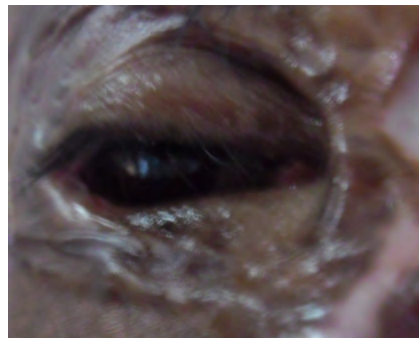


Fig. 4. Three circumscribed lesions in the retina of the right eye (first case).

Surgery was successful and the patient's vision improved only to 3/20 from PL postoperatively after two weeks. Before the electric injury, there was no evidence of diminished vision in both eyes. Thorough fundus examination by direct and indirect ophthalmoscope (+20D and +90D) revealed presence of three circumscribed chorioretinal lesions (Fig. 4) in the retina, starting from just below the fovea. We did fundus photography for documentation. The patient was referred to a retinologist for further evaluation and management of the case. After two months, the patient developed cataract in the left eye which was operated by the same method and vision was 20/20 postoperatively with normal fundus findings.

Case 2 was a 20-year-old male patient who presented to our hospital with progressive dimness of vision in both eyes, but worse in the right eye than in the left eye. The patients had suffered electric injury on the right side of the scalp four months previously. Upon examination, vision was F.C 2 ft in the right eye and 6/18 in the left eye. Slit lamp examination revealed anterior subcapsular vacuoles in both eyes. Fundus detail in right eye was not well seen and in left eye it was within normal limits. Other ocular findings are within normal limits. There was area of alopecia on the scalp of about 2 x 3 inches which indicated the wound of entry (Fig. 5) and scar marks in both feet indicating the exit wounds (Fig. 6). Patient underwent small-incision cataract surgery with posterior chamber intraocular lens implantation in the right eye and two months later in the left eye. The patient regained 6/6 BCVA in both eyes.



Fig. 5. Wound of entry. Alopecia with cataract.



Fig. 6. Exit wounds.

Discussion

The progressively increasing dependence on electricity, unsafe wiring and hooking has resulted in a rise in injuries due to contact with electrical current.¹ The earliest record of cataract development from lightning shock was made by Saint Yves in 1722.² According to statistical data, 0.8-1% of all accidental deaths are caused by an electrical injury.³ Cataractogenesis following electrical trauma has been reported to occur with a latency period varying from immediately after injury to a few years after injury.⁴ The exact pathogenesis of the effect of electric current on the proteins

of the crystalline lens and the process of lenticular opacification is unclear.⁵ Hess⁶ and Croci⁷ proposed extensive epithelial damage as the cause of the lenticular opacities. Kiribuchi⁸ postulated that cataract was the result of uveitis and circulatory changes. Decreased permeability of the lens capsule, a direct coagulative effect on the proteins of the lens cells, powerful contraction of the ciliary muscle causing a concussion type of cataract due to mechanical damage, nutritional disturbances of the lens due to iritis and impaired circulation, or ultraviolet and infrared irradiation could be causative factors in electric cataract.

In our first case we found three circumscribed skip retinal lesions. These lesions are produced by electrical current when it passes through any structure of the body. There are some reports in various journals regarding the skip lesion:

- Gregory⁹ *et al.* showed that 'damage to the internal structures of the body may be spotty, with areas of normal-appearing tissue adjacent to burned tissue and with damage to structures at sites distant from the apparent contact points. Electrothermal heating is the main cause of muscle damage and is almost exclusively seen in high voltage accidents with prolonged (seconds) contact and current flow. The histologic change seen in muscle injury that results from direct contact with an electrical source is coagulation necrosis with shortening of the sarcomere. Muscle damage can be spotty, so areas of viable and nonviable muscle are often found in the same muscle group.'
- Marry¹⁰ *et al.* showed preretinal fibrosis and chorioretinal atrophy surrounding the optic nerve and two smaller regions superonasal and inferotemporal lesion of one of their patients. Results of optical coherence tomography (OCT) correlated with fundus examination findings, showing retinal thinning and retinal pigment epithelium/choriocapillary irregularity in the area adjacent to the optic nerve.
- Jin¹¹ *et al.* reported a case of retinal lesion due to electric injury which showed axial symmetrical meridional atrophies around the optic disk in both eyes in the patient's fundus fluorescein angiography and indocyanine green angiography image.
- Al Rabiah¹² *et al.* showed after histopathological examination that the retinal lesion contained relatively intact retinal neuropile although the retinal and choroidal circulations were severely compromised. Electroretinographic tests and pseudo-random binary stimulus visually evoked responses were useful in predicting the visual outcome.

In conclusion, high-voltage electrical injury usually causes unilateral cataract because current passes through a straight line connecting wound of contact and wound of exit and the affected eye but it can cause bilateral cataract earliest site is ipsilateral to the site of impact. Outcomes after surgery are very good if not associated with other ocular lesion like optic atrophy, retinal lesion, uveitis etc.

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A novel method to convert bicanalicular intubation into monocanalicular intubation in endoscopic dacryocystorhinostomy

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Abstract: *Endonasal endoscopic dacryocystorhinostomy (EN-DCR) is an effective treatment for acquired nasolacrimal duct obstruction. Although the exact role of silicone intubation remains controversial, it is routinely performed to increase the success rate of the procedure. Occasionally, difficulty may be encountered during silicone tube intubation commonly when one end of the bicanalicular stent has been successfully passed into the nasal cavity but the other end fails. In which case either this has to be converted to a monocanalicular stent or leave without stenting. We hereby report a novel method to tackle this situation by converting a bicanalicular stent into a monocanalicular stent using simple knotting steps. From our experience with three patients, the end-results were safe and well-tolerated. This modified lacrimal intubation stent may also be used when the standard Monoka monocanalicular stent is not available.*

Key words: *Bicanalicular intubation, endoscopic dacryocystorhinostomy*

Introduction

Endonasal endoscopic dacryocystorhinostomy (EN-DCR) is a popular surgical procedure for acquired nasolacrimal duct obstruction. The most common reason for failure in EN-DCR is re-stenosis of the rhinostomy site,¹ up to 83% of failed DCR was secondary to obliterative scarring at the ostium in Sprekelsen's cohort.² Various adjunctive measures have been introduced to overcome this problem, including intubation with silicone tubes, use of anti-metabolites like mitomycin-C. However, the exact role of lacrimal intubation has recently been challenged as some authors suggested that the placement of silicone tubes increases the risk of osteotomy closure by causing granulomatous reaction.^{3,4} Till date, there are only limited published data comparing EN-DCR with and without intubation^{5,6} and the necessity for stenting remains controversial. Many surgeons still prefer intubation especially in cases where the mucosal flaps are not well apposed or in revision DCR¹.

Lacrimal intubation during EN-DCR may not always be smooth and successful. Possible causes of difficult intubation include a proximal upper or lower canalicular stenosis which is under-diagnosed before the operation or formation of false-tract during forceful silicone tube insertion. When one end of the bicanalicular stent

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is successfully passed into the nasal cavity but the other end fails to negotiate through, the conventional solution is to remove the half- inserted bicanalicular stent, and either to leave without stenting or to re-insert a new monocanalicular stent through the patent pathway. We hereby report a novel method to tackle this situation by manually transforming a bicanalicular stent into a monocanalicular stent using simple knotting steps.

Procedure

We report three patients with acquired NLDO who underwent primary EN-DCR. Initial steps for the DCR were performed in a standard fashion and were uneventful. Since no canalicular obstruction was noted in pre-operative probing, bicanalicular lacrimal intubation was planned for all three cases. In each of these cases, one end (referred to as 'distal end') of the bicanalicular silicone stent (BD Visitec™ Lacrimal Intubation Set, BD Ophthalmic Systems, UK) was successfully intubated reaching the nasal cavity. However, the other end (referred as 'proximal end') failed to negotiate through the other canaliculus despite repeated attempts. This was postulated to be due to tissue edema secondary to trauma from initial attempts to probe through the canaliculi. Instead of pulling out the 'distal end' that was already in the nasal cavity, we took the following steps: (1) Use the 'proximal end' of the silicone tube to tie two simple knots, one next to the other (Fig. 1); (2) Use a straight iris scissors to cut away the excessive tube, leaving a free end of about 1-1.5 mm; (3) Pull the 'distal end' in the nasal cavity until the knots reach the punctum and act as a 'collarette'; (4) Rotate the tube in a way that the cut end of the tube is not touching the globe; (5) cut the 'distal end' to the appropriate length and secure with a metal clip. The nose was packed as usual and the surgery completed.

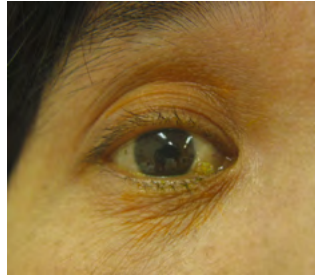
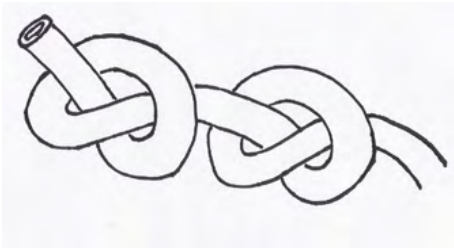


Fig. 1. Tying two simple knots with the silicone tubing.

Fig. 2. The 'simple knots' act as a 'collarette'. There was no ocular surface abrasion or inflammation.

Post-operatively, all patients experienced minimal to no discomfort. There was no evidence of conjunctival and corneal abrasion or inflammation, or movement of the knots with ocular movement on slit-lamp biomicroscopy on follow-up visits at Week 1 (Fig. 2) and Week 4. As the knots rest well on the punctum with minimal movement, no trapped mucus or debris in the knots was observed. All the modified stents stayed *in situ* until the planned removal at Week 4. No spontaneous extrusion or migration was observed. All three dacryocystorhinostomies remained patent up to the follow-up at six months.

Discussion

It is generally accepted that lacrimal intubation increases surgical success in EN-DCR,¹ especially in cases where the mucosal flaps cannot be well apposed during the procedure and in revision cases. However, there are some instances when bicanalicular intubation may not be possible. The above-mentioned manual transformation of bicanalicular stent to monocalicular stents offers a number of benefits. Firstly, one does not need to remove the silicone tube that is already passed into the nasal cavity and reinsert a new monocalicular stent, as two possible problems can be associated with the removal-reinsertion procedure: (1) Repeated trauma to the DCR pathway, leading to scarring and subsequent stenosis of the osteotomy site; (2) Re-insertion may be difficult or impossible. By reducing excessive manipulation, we avoid jeopardizing the chance of success of the EN-DCR. Secondly, the maneuver of tying a simple knot is quick and easy to learn. This manual transformation significantly saves the surgeon's time as compared to removal-reinsertion procedure. Finally, this manual transformation also saves the cost of a new monocalicular stent.

In our experience with the three patients in this series, these modified monocalicular stents were safe and well-tolerated. Since the silicone tubes were soft and the cut edges were relatively smooth, they did not cause significant irritation or trauma to the ocular surface. There was minimal movement of the knots on ocular movement, as there was a substantial segment of silicone tubing in the canaliculi and osteotomy to create enough friction to stabilize the tubing. Although the size of the double knots was bigger compared to the collarette of the commercially available Monoka monocalicular stent, our patients did not complain of any significant discomfort. In fact, this relative big-sized 'collarette' carries a lower risk of being buried and intracanalicular migration. Its large size also facilitates subsequent removal. Finally, this technique may also be used to produce monocalicular stent substituting standard Monoka device when the latter is not available, *e.g.*, in emergency room for repair of lacrimal laceration, or in smaller ophthalmic units, where stock is not available due to low utilization rate or cost concern.

Summary

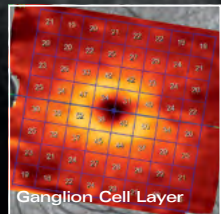
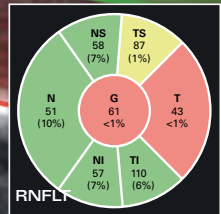
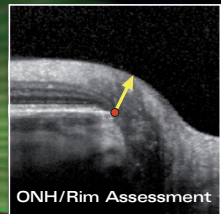
We report a novel method to convert a bicanalicular stent into a monocalicular stent in EN-DCR. From our experience, the end-product is safe and well-tolerated by patients.

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