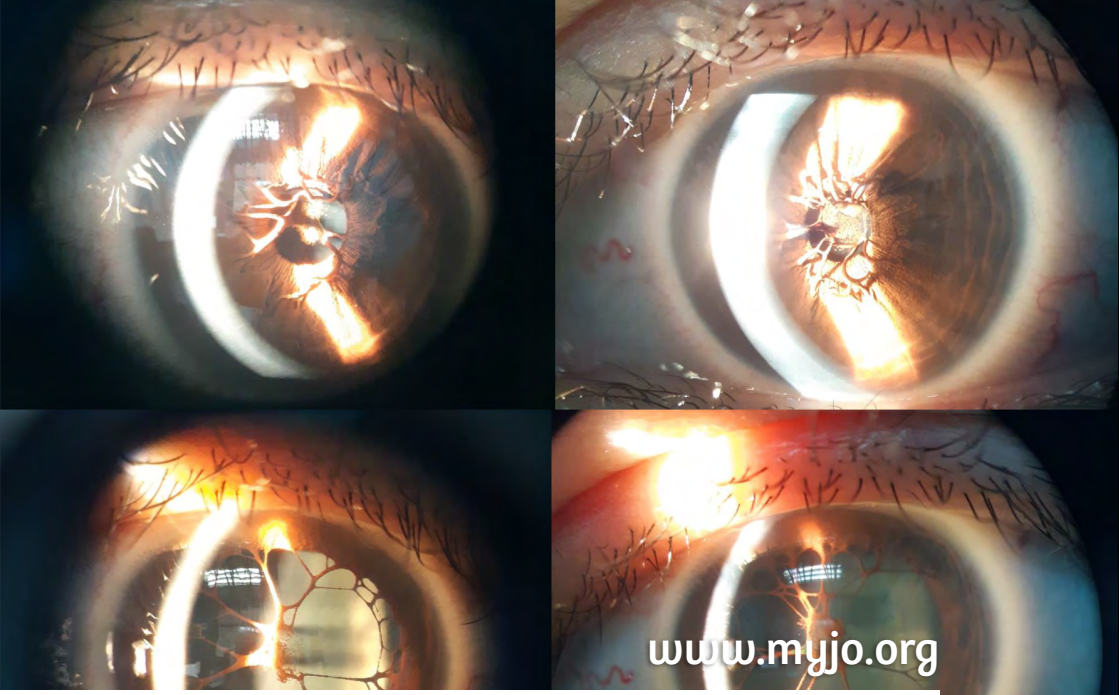

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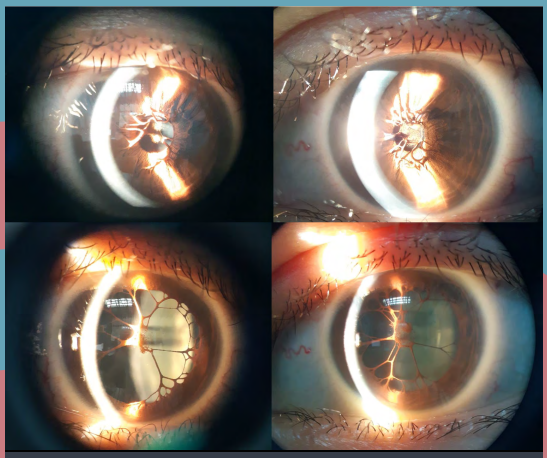

ABOUT THE COVER IMAGE

Bilateral persistent pupillary membranes (pre- and post-dilatation) in a patient with concurrent juvenile open angle glaucoma. The images were obtained by Associate Professor Dr Amir Samsudin from the Department of Ophthalmology, Universiti Malaya Medical Centre, Kuala Lumpur, Malaysia.

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Visual impairment in developing countries

Othmaliza **Othman**[1], Amir **Samsudin**[2]

[1]*Department of Ophthalmology, Faculty of Medicine, Hospital Cancellor Tuanku Muhriz. Universiti Kebangsaan Malaysia Medical Centre, Kuala Lumpur, Malaysia;*

[2]*Universiti Malaya Eye Research Centre (UMERC), Department of Ophthalmology, Faculty of Medicine, Universiti Malaya, Kuala Lumpur, Malaysia*

We are now entering the endemic phase of COVID-19, a worldwide medical scourge which brought upon tremendous effects in our lives, and especially to the children and the elderly... the vulnerable ones. For children in particular, the impact of these effects has been tremendous. The consequences have been the acceleration of myopia[1] and the threat of digital eye strain,[2] which make up an emerging public health problem globally.

In this issue, we have articles that report cross-sectional, prevalence data on visual impairment and refractive errors from tertiary referral centres in Malaysia as well as Nigeria. In the study by Teoh *et al.*, the causes of visual impairment in children under 7 years of age were collated and examined. The authors reached an opinion that more than half of the cases had preventable or treatable causes, thus highlighting the importance of early screening and intervention programmes to prevent childhood visual impairment. They also suggested raising awareness and developing clinical guidelines into the national health program. The study by Otulana *et al.* reminds us that a significant proportion of visual deficit in developing countries is still contributed by relatively simple and correctable causes such as refractive errors. The authors stress that when left uncorrected, these problems may lead to disadvantages in education and employment opportunities, while also reducing quality of life.

These studies are important for healthcare planning and policy-making as they help us understand the kind and magnitude of problems that are common in the community, identify priorities, and strategize in terms of appropriate funding and distribution of health measures to combat the issues. They also inform the assessment of interventions or prevention measures, since they provide data on the baseline risk for a given disease in a patient group or population which influences effect measures.[3] We hope that these articles will help generate more interest and subsequent reports on population-based ophthalmological conditions and their related impact.

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Prevalence and causes of visual impairment in children aged seven years and below in a tertiary eye care centre in Malaysia

Teoh Ru Jian Jonathan[1], Nor Akmal **Bahari**[1], Juhaida **Zahri**[2], Jamalia **Rahmat**[1]

[1]*Department of Ophthalmology, Hospital Kuala Lumpur, Kuala Lumpur, Malaysia;* [2]*Malaysian Optical Council, Ministry of Health, Putrajaya, Malaysia*

Abstract

Purpose: To determine the prevalence and causes of visual impairment among children aged 7 years and below in a tertiary eye care centre in Kuala Lumpur, Malaysia.
Study design: Cross-sectional retrospective study.
Methods: Medical records of all children aged 7 years and below who attended the paediatric ophthalmology clinic in a tertiary eye care centre in 2020 were reviewed.
Results: In 2020, 2,460 children were seen in the clinic, of whom 549 (22.3%) presented with visual impairment. At the time of presentation, 73.2% of the visually impaired children were diagnosed with blindness; of these children, 62.8% were under 1 year old. The percentage of treatable causes of visual impairment was 38.4%, while 31.1% of them were preventable. The most common causes of visual impairment were cerebral visual impairment (24.2%), congenital cataract (16.6%), and retinoblastoma (6.2%).
Conclusion: More than half of the causes of childhood visual impairment were preventable or treatable. The majority of children were under 1 year old. Cerebral visual impairment was the main cause of visual impairment. This study highlights the importance of early screening and intervention programs to prevent childhood visual impairment.

Keywords: Malaysia, paediatric visual impairment, prevalence

Correspondence: Nor Akmal Bahari, MBBS, MS Ophthal, Department of Ophthalmology, Hospital Kuala Lumpur, Kuala Lumpur 50586, Malaysia.
E-mail address: norakmalbahari@gmail.com

Prevalens dan punca-punca gangguan penglihatan dalam kalangan kanak-kanak berumur tujuh tahun dan ke bawah di sebuah pusat penjagaan mata tertiari di Malaysia

Abstrak

Objektif: Menentukan prevalens dan punca-punca gangguan penglihatan dalam kalangan kanak-kanak berumur tujuh tahun dan ke bawah di sebuah pusat penjagaan mata tertiari di Malaysia.
Reka bentuk kajian: Kajian keratan rentas secara retrospektif
Metodologi: Rekod perubatan semua kanak-kanak yang mengunjungi klink mata kanak-kanak di sebuah pusat penjagaan mata tertiari dalam tahun 2020 dikenalpasti dan data klinikal dikaji.
Keputusan: Sebanyak 2,460 kanak-kanak telah mendapat rawatan dalam tahun 2020, di mana 549 (22.3%) kanak-kanak didapati mempunyai gangguan penglihatan. 73.2% dari kanak-kanak tersebut didapati telah dikategorikan sebagai mengalami kebutaan. 62.8% kanak-kanak dengan gangguan penglihatan adalah berumur di bawah satu tahun. 38.4% dari punca gangguan penglihatan merupakan punca yang boleh dirawat, manakala 31.1% adalah yang dapat dielakkan. Punca-punca yang paling lazim ialah gangguan penglihatan serebral (24.2%), katarak kongenital (16.6%), dan retinoblastoma (6.2%).
Kesimpulan: Lebih daripada separuh punca gangguan penglihatan kanak-kanak dapat dirawati atau dielakkan. Kebanyakan gangguan penglihatan berlaku ke atas kanak-kanak yang berumur kurang daripada satu tahun. Gangguan penglihatan serebrum adalah punca utama gangguan penglihatan. Kajian ini menekankan kepentingan pemeriksaan dan program intervensi awal untuk mencegah gangguan penglihatan dalam kalangan kanak-kanak.

Kata kunci: gangguan penglihatan, *:* kanak-kanak, Malaysia, prevalens

Introduction

Visual impairment in childhood is a serious issue that needs to be addressed worldwide. It was estimated that 1.4 million children in the world are blind, and most of these children are living in Asia and Africa.[1] Studies found that an estimated 283,151 children in South East Asia were blind in 2020, of whom 27.3% were due to lesions of the whole eye, *i.e.*, microphthalmos, anophthalmos, or disorganized

eyes.[2] Other main causes include corneal conditions (*i.e.*, scarring, staphylomas, and phthisis from ulceration), lens abnormalities (*i.e.*, cataract and complications of surgery), and retinal conditions (*i.e.*, retinopathy of prematurity and retinal dystrophies).[2]

Visual impairment in childhood has a significant impact on a child's development, academic opportunities, employment, and social life.[3] It is also associated with a considerable lifelong burden of disability and cost on the nation's economy.[4] Previous studies have found that the majority of visual impairment in childhood is either preventable or treatable.[1,5] Preventable causes of visual impairment include measles infection, vitamin A deficiency, ophthalmia neonatorum, congenital rubella syndrome, and the use of harmful traditional eye medications, whereas treatable causes of visual impairment in childhood include glaucoma, retinopathy of prematurity, cataract, and selected cases of corneal scarring.[1]

There were a few studies conducted in Malaysia that estimated the prevalence and causes of visual impairment in childhood. The study with the largest sample size was conducted in Gombak District, a suburban area near Kuala Lumpur, involving 4,634 children aged 7 to 15 years old. It was found that 17.1% of the children had visual impairment and 2% of these children were blind.[6] Another study involving 100 indigenous children found that 40.9% of them had visual impairment,[7] while two studies conducted on preschool children aged 4 to 6 years estimated that the prevalence of visual impairment was 12.5% (n = 1,287)[8] and 5% (n = 400),[9] respectively. A study including 1,398 children below 4 years of age from two public tertiary referral hospitals in Selangor, Malaysia, found that 17.38% of the children were visually impaired.[10] In all the above studies, refractive error was the main cause of visual impairment.[6-10]

In Malaysia, there are five tertiary referral centres for paediatric ophthalmology service. To date, there is no data available on the prevalence of visual impairment from paediatric ophthalmology clinics in Malaysia. Therefore, this study was undertaken to determine the prevalence of visual impairment and its causes among children who attended the paediatric ophthalmology clinic of a tertiary eye care centre in Kuala Lumpur. This centre is located in the urban area of Kuala Lumpur, the capital city of Malaysia. By identifying the avoidable causes, relevant strategies could be implemented in the community and in the primary, secondary, and/or tertiary levels of health system, which may reduce the national health care burden.

Methods

This was a retrospective cross-sectional study. The target population was children aged 7 years and below who attended the paediatric ophthalmology clinic in the eye care centre. The majority of the attending patients in the paediatric oph-

thalmology clinic in this tertiary eye care centre was referred from downstream public healthcare providers and from the private sector. A referral from health care practitioners is required for registration at the clinic, hence the number of walk-in patients is very small. This study was conducted in accordance with the Declaration of Helsinki; consent and prior ethical approval was obtained from the Medical Research and Ethics Committee of the Malaysian Ministry of Health (NMRR ID NMRR-21-1768-60877).

The inclusion criteria of this study were all children aged 7 years and below who attended the paediatric ophthalmology clinic from January 2020 to December 2020, with best-corrected visual acuity worse than 6/18 in the better eye. Exclusion criteria were patients aged 8 years and above, and children aged 7 years and below without visual impairment.

The medical records of all eligible children were assessed to extract the necessary data. Data collected included the patients' demographical data (age, gender, and ethnicity), best-corrected visual acuity, and causes of visual impairment. The definitions of visual impairment used were based on the World Health Organization (WHO) classification: mild or no visual impairment is defined as visual acuity equal to or better than 6/18; moderate visual impairment is defined as visual acuity worse than 6/18 and equal to or better than 6/60; severe visual impairment is defined as visual acuity worse than 6/60 and equal to or better than 3/60; and blindness is defined as visual acuity worse than 3/60.[11]

The ocular diagnosis was extracted from the medical records. When there were two or more causes for visual impairment, the major cause that contributed to the visual impairment was selected. For instance, if both cataract and retinal abnormality coexisted, and removal of cataract did not restore the vision, the cause of visual impairment was considered to be retinal abnormality. The diagnosis was classified according to the WHO's anatomical classification and aetiological classification.[12] The anatomical classification of causes of visual impairment includes retina, cornea, whole globe, lens, optic nerve, glaucoma, uvea, and other causes.[12] The aetiological classification includes unknown, hereditary, childhood, perinatal, and intrauterine causes.[12] No identifiable information was extracted from the medical records.

All statistical analyses were performed using the Statistical Package for Social Science (SPSS) version 20.0 (SPSS Inc., Chicago, IL, USA). Descriptive data analysis was expressed as percentages.

Results

The medical records of 2,460 patients were reviewed during the study period. There were 549 (22.3%) patients who were visually impaired. The prevalence of visual impairment in the sample population was 2.2 per thousand: 73.2% of them presented with blindness at the time of diagnosis, 25.1% had moderate visual impairment, and 1.6% had severe visual impairment.

The majority of the visually impaired children were of Malay ethnicity (70.1%), followed by Chinese ethnicity (15.9%), Indian ethnicity (11.1%), aborigines (1.5%), and foreigners (1.5%). More than half of the visually impaired children were males (64.3%). The majority of the children who had visual impairment were under 1 year old (n = 345, 62.8%) at the time of diagnosis. As age increased, the incidence of visual impairment decreased (Fig. 1).

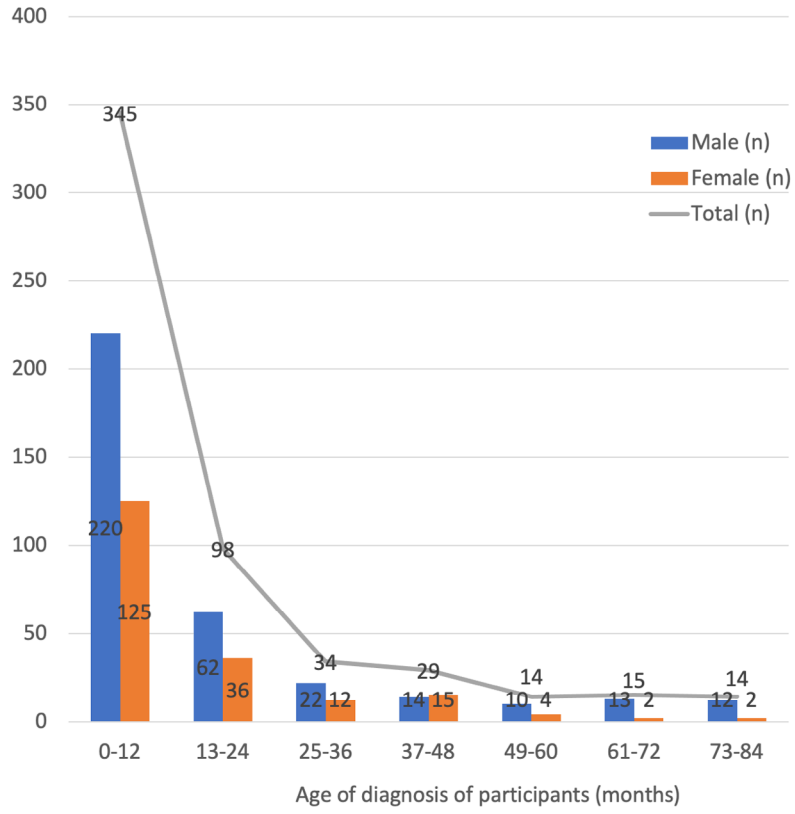

Fig. 1. Age of diagnosis and gender distribution of participants.

The primary causes of visual impairment are presented in Table 1. Most of these children had a normal eye globe (28.0%), followed by retinal causes (25.5%), and lens causes (18.9%). Using the WHO aetiological classification, 74.9% of the causes were unknown and 13.5% were childhood causes (Table 2). Of the causes, 38.4% were treatable, whereas 31.1% were preventable. Among the visually impaired children, 24.2% of them had cerebral visual impairment, 16.6% of them had congenital cataract, and 6.2% had retinoblastoma (Table 3).

Table 1. Anatomical causes of visual impairment in children

Anatomical causes	**Cases (%)**
Normal eye globe	154 (28.0)
Retina	140 (25.5)
Lens	104 (18.9)
Cornea	52 (9.5)
Glaucoma	33 (6.0)
Others	25 (4.6)
Optic nerve	23 (4.2)
Whole globe	18 (3.3)
Total	549 (100)

Table 2. Aetiological causes of visual impairment in children

Etiological causes	**Cases (%)**
Unknown	411 (74.9)
Childhood	74 (13.5)
Perinatal	27 (4.9)
Intrauterine	26 (4.7)
Hereditary	11 (2.0)
Total	**549 (100)**

Table 3. Anatomical causes of visual impairment in children

Type of visual impairment	Cases (%)
Cerebral visual impairment	133 (24.2)
Congenital cataract	91 (16.6)
Retinoblastoma	34 (6.2)
Corneal opacity with associated syndrome (anterior segment dysgenesis, Peter's anomaly, Goldenhar syndrome)	33 (6.0)
Retinal detachment	32 (5.8)
Retinopathy of prematurity (ROP)	25 (4.6)
Secondary glaucoma	20 (3.6)
Refractive error	14 (2.6)
Corneal opacity due to trauma, sclerocornea	14 (2.6)
Coats disease	13 (2.4)
Congenital glaucoma	13 (2.4)
Others	113 (20.6)

Discussion

From our study, the prevalence of childhood visual impairment aged 7 years old and below was 22.3%. This value is higher than most of the previous Malaysian studies, which are district-based and school-based. This may be due to the inclusion criteria of our study, which targeted a different sample population and age group.

As the subjects in our study were children who were referred to a specialized paediatric ophthalmology clinic from downstream healthcare institutions, the less complex or less severe cases may have been already dealt with by the primary health care providers and general ophthalmologists. This might have resulted in a discordance of prevalence of visual impairment compared to previous population studies, which were district-based (17.1%)[6] and school-based (12.5% and 5%).[8,9] The greater prevalence of childhood visual impairment in our study may also be attributed to the wider range of age, as we included children from birth to 7 years old, compared to from birth to 4 years old in a previous study conducted in two tertiary referral hospitals.[10]

Our study demonstrated a higher proportion of blindness (73.2%) at onset of diagnosis, compared to a previous study, in which most patients (49.0%) had moderate visual impairment at the time of diagnosis.[10] This might be attributed to the nature of our study site, which is the largest specialized national paediatric ophthalmology referral centre in the country; therefore, the study site might have received referrals of more complex cases with higher severity of visual impairment.

A change in the trend of main causes of visual impairment among children was noticed in this study. In our study, cerebral visual impairment (24.2%) overtook refractive errors as the main cause of childhood visual impairment, followed by congenital cataract (14.8%) and retinoblastoma (6.2%). Cerebral visual impairment is a condition in which there is damage to the retrochiasmatic pathway with normal or near-normal eye health.[13] It is often a diagnosis of exclusion, where the visual impairment could not be attributed to abnormalities in the anterior visual pathway. The above finding corresponds to a 2017 review on the epidemiology of blindness in children worldwide, which found that the most common cause of childhood blindness in middle-income and high-income countries was cerebral visual impairment.[14] Countries which have moved up from lower to middle socioeconomic strata also demonstrated a shift in the cause of visual impairment attributed to cerebral visual impairment and retinopathy of prematurity.[14] In the BCVIS2 study, the main cause of childhood visual impairment was also cerebral visual impairment (48%).[15] A recent study conducted in a tertiary eye care centre in south India also demonstrated similar results, of which cerebral visual impairment was the major cause of profound visual impairment in children below 3 years old (33%), followed by congenital cataract (13.1%), and retinopathy of prematurity (12.6%).[16]

Compared to previous Malaysian studies, the causes of childhood visual impairment were mainly refractive error and retinopathy of prematurity.[8-10,17] The low number of cases of refractive error in this study might be attributed to the nature of the study site being a national paediatric ophthalmology referral centre; hence, cases of refractive error may have been already dealt with by downstream healthcare practitioners. In this study, retinopathy of prematurity contributed to 4.6% of the causes of childhood visual impairment, which is lower when compared to previous local studies.[10,17] The reduction in the prevalence of retinopathy of prematurity might be explained by the increased efficacy of retinopathy of prematurity surveillance by ophthalmologists in the neonatal units.[18] More studies are needed to better understand the epidemiology of visual impairment of children in Malaysia.

Retinal causes were the second major cause of visual impairment in childhood (25.5%) in our study. In addition to retinoblastoma and retinopathy of prematurity, other retinal diseases include retinal detachment (5.8%), Coats disease (2.4%), persistent foetal vasculature (2.0%), familial exudative vitreoretinopathy (1.1%), macular scar (1.1%), retinal dystrophy (1.1%), vitreoretinal fibroplasia (0.4%), and Leber's congenital amaurosis (0.4%). Most of the retinal conditions are either idiopathic or hereditary, and often lead to severe visual impairment or blindness. A study on the health-related quality of life of children with hereditary retinal disorders found that children with retinal disorders reported a lower quality of life than those with congenital cataracts, likely attributed to the nature of it being untreatable *versus* cataract being a treatable condition.[19] It also demonstrated that retinal disorders led to an adverse impact on the quality of life of the entire family.[19]

These children usually require low vision aids and special assistance in schools, including front row seats, magnified fonts, and better lighting conditions.

Our study also found that the majority (62.8%) of the sample population was below 1 year of age when diagnosed with visual impairment. This corresponds to previous Malaysian studies that found that most children who are diagnosed with visual impairment are under 1 year of age (45.7%[10] and 48%,[17] respectively). Our study also demonstrated similar results to a recent study conducted in 89 hospitals and community centres across the United Kingdom, which found that the incidence of visual impairment in the first year of life was 5.19 per 10,000 children, and more than half (51%) of the children were diagnosed with visual impairment in their first year of life.[15] In our study, most of the cases of visual impairment below 1 year old were related to congenital disorders, such as congenital cataract (16.6%), corneal opacities with associated syndrome (6%), and congenital glaucoma (2.4%). Most of these cases were detected during newborn screening programs in health clinics, presenting as leukocoria, corneal opacity, and buphthalmos. Of the 91 cases of congenital cataract, ten were associated with intrauterine infection. Congenital cataract is a reversible ocular condition, which if detected and treated early, may improve the child's visual prognosis. This indicates the importance of integrating effective screening programs for visual impairment among children in their first year of life.

Among our sample population, 74.9% of the aetiologies of visual impairment were not attributed to any known cause, whereas 13.5% was attributed to childhood aetiology, including trauma, drug-induced, and infection. This corresponds to a previous nationwide Malaysian study in schools for the blind, which found that most of the causes of childhood blindness were unknown.[17] In our study, 38.4% of causes of visual impairment in childhood were treatable, whereas 31.1% of them were preventable. The treatable causes in this study include congenital cataract, corneal diseases, glaucoma, and retinopathy of prematurity, while preventable causes include trauma, drug allergy, and infection. A global epidemiological study on causes of childhood blindness demonstrated that the most common avoidable causes were retinopathy of prematurity, cataract, and corneal opacity,[14] which correlated with the findings of our study. These findings emphasize the importance of primary prevention, such as public health awareness, health parenting classes, and immunization. Secondary prevention is also crucial for early detection and intervention to reduce the lifelong burden of disability of visually impaired children.

Limitations

The results of this study should be interpreted with caution as the sample population is not representative of the entire population. Hospital-based surveys are not representative of the true prevalence of ocular diseases in the community. Asymptom-

atic patients might not present to health care institutions. However, this data can still provide valuable information on the causes of childhood visual impairment and blindness in the country, as the study site is a largest tertiary referral centre for paediatric ophthalmology service nationwide.

Conclusion

More than half of childhood visual impairment can either be prevented or treated. Cerebral visual impairment is the main cause of childhood visual impairment. This reflects the importance of primary and secondary prevention of childhood visual impairment in the country. Early screening and holistic intervention programs are crucial to prevent childhood visual impairment, especially among children below 1 year old. This could be achieved by improving awareness among paediatricians, family physicians, nurses, the public, and most importantly, among expectant mothers. Further research is required in establishing clinical guidelines to be incorporated into the national health program to reduce the national health care burden.

Declarations

Ethics approval and consent to participate
This study was conducted in accordance with the Declaration of Helsinki and, consent and prior ethical approval was obtained from the Medical Research and Ethics Committee of the Malaysian Ministry of Health (NMRR ID NMRR-21-1768-60877).

Competing interests
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Paediatric optic neuritis: experience from a tertiary referral centre in Malaysia

Sharifah Azira binti Mohd **Taufik**[1], Lakana Kumar **Thavaratnam**[2], Norlina binti Mohd **Ramli**[1]

[1]UM Eye Research Centre, Department of Ophthalmology, University of Malaya, Kuala Lumpur, Malaysia; [2]Department of Ophthalmology, Kuala Lumpur General Hospital, Kuala Lumpur, Malaysia

Abstract

Background: Optic neuritis typically presents with acute or subacute onset of mild or profound blurring of vision. There are very limited reports regarding optic neuritis in the paediatric population compared to adults from the South Asian region. We report a series of 7 cases of paediatric optic neuritis.
Methods: All optic neuritis cases aged less than 12 years old in 2016 were studied retrospectively.
Results: Out of 44 patients with optic neuritis, 7 of them were of paediatric age. The mean age was 9.9 years. All patients had sudden onset profound vision loss (range 3/60 to hand movement). Four patients had bilateral involvement, all had reduced colour vision. Three had underlying acute disseminated encephalomyelitis. All were treated with high-dose intravenous corticosteroids. Five patients made full recovery, one patient had partial recovery, and one patient had no visual recovery. Interestingly, none of them had multiple sclerosis (MS) or neuromyelitis optica (NMO) at the time of diagnosis.
Conclusion: Prognosis is generally good for isolated cases of paediatric optic neuritis. Outcome of cases secondary to ADEM depends on the degree and extent of demyelination. A diagnosis of chronic relapsing inflammatory optic neuropathy can be considered in recurrent cases that are steroid responsive. None of our cases had underlying MS or NMO during the study period.

Correspondence: Dr. Sharifah Azira SM Taufik, MBBS (UM), Department of Ophthalmology, University of Malaya Medical Centre, 59100 Kuala Lumpur, Malaysia.
Email: sharifah.azira@gmail.com

Keywords: paediatric optic neuritis, Malaysia

Optik neuritis pediatrik: pengalaman dari pusat rujukan tertiari di Malaysia

Abstrak

Latarbelakang: Optik neuritis adalah keadaan yang selalu hadir dengan permulaan subakut kekaburan mata yang melampau. Didapati tiada laporan berkenaan pediatrik optic neuritis di kalangan penduduk Asia Selatan. Kami melaporkan satu kes siri yang melibatkan tujuh pesakit pediatrik optic neuritis.
Kaedah: Semua kes optic neuritis yang berusia kurang dari 12 tahun dikaji secara retrospektif.
Keputusan: Terdapat empat puluh empat pesakit yang menghidapi optic neuritis, tujuh adalah golongan kanak-kanak. Min usia untuk mereka ialah 9.9 tahun. Kesemua pesakit datang dengan kehilangan penglihatan yang melampau secara megejut (dari 3/60 ke HM). Terdapat empat pesakit yang melibatkan kedua-dua mata. Kesemua mengalami pengurangan dari segi penglihatan warna. Tiga pesakit turut mengalami penyakit ensefelitis demielinasi secara akut (*acute disseminated encephalomyelitis* - ADEM). Semua pesakit telah dirawat dengan intravena kortikosteroid berdos tinggi. Lima pesakit mendapat penyembuhan yang sepenuhnya, seorang mempunyai penyembuhan separa dan seorang lagi tidak langsung mendapat pemulihan dari segi penglihatan. Menariknya, tiada seorang pun yang mendapat penyakit multiple sclerosis (MS) atau neuromyelitis optica (NMO) semasa diagnosis dibuat.
Kesimpulan: Kes optic neuritis pediatrik mempunyai prognosis yang baik. Hasil kejadian disebabkan yang oleh ADEM bergantung pada darjah dan keterukan demielinasi. Diagnosis keradangan optik neuropati yang berulang dan kronik (chronic relapsing inflammatory optic neuropathy – CRION) boleh dipertimbangkan sekiranya terdapat situasi yang berulang serta responsif terhadap steroid. Tiada satu pun kes kami yang mengalami MS atau NMO sewaktu kajian dilaksanakan.

Kata kunci: peditrik optik neuritis, Malaysia

Introduction

Optic neuritis (ON) can be a potentially devastating condition. It usually presents with acute or subacute onset of blurring of vision, usually to a severe degree. There are limited data regarding ON in Malaysia, but in one retrospective study, the average age of onset was 21–30 years.[1] ON in children differs from adult-onset ON in some clinical features, aetiology, and prognosis.

ON in children is reported to have more bilateral involvement and greater visual acuity loss compared to adults.[2] Children tend to have disc oedema, with good visual prognosis.[3] Contrary to adults, ON is often associated with recent immunization. The risk of subsequent development of multiple sclerosis (MS) is greater in older children seen in white matter lesions on magnetic resonance imaging (MRI).[4]

This retrospective chart review presents our observations of seven children seen over a 1-year period to mainly to illustrate the aetiology, clinical presentation, and outcome of ON. Its relationship to demyelinating conditions in the paediatric population is also explored.

Methods

This is a retrospective review of cases over a 1-year period (October 2015–October 2016) treated at the neuro-ophthalmology clinic in Hospital Kuala Lumpur (HKL), a tertiary referral centre located in an urban setting with a population of more than 1.5 million. The medical records of patients diagnosed with ON in children aged 12 years and below were traced. The minimum follow-up period was 3 years. The clinical presentation, aetiologic factors, and outcome were analysed in each patient.

Results

A total of 44 cases of optic neuritis were seen, and seven (15.90% prevalence) were found to be in the paediatric age group. Table 1 shows the patients' clinical data and investigations. The mean age of the patients was 9.86 years. The most common symptoms were sudden onset bilateral blurring of vision with pain on eye movement. All affected eyes had reduced colour vision. Six patients had papillitis, while only one patient showed retrobulbar involvement.

Common risk factors include a preceding episode of infection, which can be as trivial as a history of upper respiratory tract infection (URTI) 2 weeks prior to onset of symptoms or ongoing sinusitis, or can be more disease-specific, namely, acute disseminated encephalomyelitis (ADEM). One patient had a history of URTI, whilst another patient had ongoing sinusitis. Three patients had ADEM; the cause for the other two patients was unknown.

Table 1. Summary of clinical features and investigations in children with optic neuritis

Case	Age/ Sex	Eyes	Associated symptoms	Colour vision	Disc appearance	Imaging	CTD/LP
1	7/F	BE	Headache	R: 3/15 L: 1/15	Hyperaemic, swollen bilateral discs	Optic sheath enhancement over coronal section	-
2	12/M	RE	Pain on eye movement	R: 0/15 L: 15/15	Hyperaemic swollen right disc	R ON enhancement, possible L thalamic, midline mamillary signal abnormality, possible AQP4 demyelination. Repeat MRI 6 months later: normal	-
3	11/F	BE	Unable to differentiate colours, pain on eye movement, neck and shoulder pain, severe headache	R: 1/15 L: 0/15	Bilateral discs not swollen, normal in appearance	Multiple T2 hyperintense areas in bilateral cerebellum, parietal, occipital, vertex region, suggestive of ADEM. Bilateral ON normal.	-
4	12/M	BE	Pain on eye movement	BE: 0/15	Hyperaemic, swollen bilateral discs	Normal, no evidence of demyelination	CTD: normal LP: normal, negative oligoclonal band
5	11/M	RE	Nil	R: 0/15 L: 15/15	Mildly swollen right disc	R intraorbital ON slightly swollen. Hyperdensity in L frontal sinus.	-
6	10/F	LE	Nil	BE: strong deutan	Left disc swollen, hyperaemic	White plaque-like lesion in occipitoparietal area, suggestive of ADEM.	
7	6/F	BE	Fever, vomiting, headache	R: 0/15 L: 1/15	Bilateral swollen discs	Multiple T2 hyperintense lesions involving deep and subcortical white matter, lentiform nuclei bilaterally, R thalamus and bilateral ON showing ADEM.	CTD: normal LP: normal, negative oligoclonal band

F: female; M: male; BE: both eyes; R: right; L: left; ON: optic nerve; ADEM: acute disseminated encephalomyelitis; CTD: connective tissue disease; LP: lumbar puncture

Table 2. Diagnosis, risk factors, treatment, and initial and final visual acuity

Case No.	Diagnosis	Initial VA	Risk factors/ comorbidities	Treatment	Final VA
1	Isolated bilateral ON secondary to viral URTI	R: 3/60 L: 3/60	Viral URTI	IV Methylprednisolone	RE: 6/6 LE: 6/6
2	Steroid-dependent ON 2 episodes of recurrences	R: CF L: 6/9	Epilepsy	IV Methylprednisolone	R: 6/6 L: 6/7.5
3	Bilateral ON 2' ADEM	R: 2/60 L: CF	ADEM	IV Methylprednisolone	R: 6/6 L: 6/6
4	CRION	R: CF L: CF	Nil	IV Methylprednisolone, no immunomodulators given	After 7 episodes R: 6/12 L: 6/24
5	Right ON 2' acute sinusitis	R: HM L: 6/9	Sinusitis	IV Methylprednisolone	R: 6/6 L: 6/6
6	ON 2' ADEM	R:6/6 L: HM	ADEM	IV Methylprednisolone	R: 6/6 L: 6/6
7	Bilateral ON 2' ADEM	R: 3/60 L: CF	ADEM	IV Methylprednisolone	R: NLP L: 2/60

ON: optic neuritis; URTI: upper respiratory tract infection; ADEM: acute disseminated encephalomyelitis; CRION: chronic relapsing inflammatory optic neuropathy; VA: visual acuity; R: right; L: left; CF: counting fingers; HM: hand movement; NLP: no light perception

None of the children had neuromyelitis optica (NMO), as all patients were negative for anti-aquaporin 4 on blood investigation. None of the patients had evidence of MS on imaging studies. The imaging studies of five patients showed ON, while the other two did not. All patients were admitted and treated with high-dose steroid based on Optic Neuritis Treatment Trial (ONTT) criteria. Five patients regained their baseline visual acuity while two did not due to multiple recurrences and ADEM with severe demyelination. Diagnoses, risk factors, initial and final visual acuity, and treatment are noted in Table 2.

Discussion

Paediatric ON is a rare medical condition. Annual incidence was 1.04 (95% confidence interval [CI], 1.01–1.07) per 100,000 pediatric individuals and 3.29 (95% CI, 3.28–3.30) per 100,000 adults.[5] The constellation of signs and symptoms leading to a diagnosis of ON include visual acuity loss, presence of pain on activity of the extrinsic eye muscles, relative afferent pupillary defect, dyschromatopsia, and swelling of the optic nerve head in anterior ON and normal appearance of the nerve in retrobulbar ON. In this retrospective chart review, the mean age of presentation was 9.8 years old, with bilateral presentation compared to unilateral in adulthood. They also tended to have papillitis rather than retrobulbar involvement, with profound blurring of vision of 6/60 or worse. This finding is in agreement with Shatriah *et al.*, who compared paediatric ON in Asian countries.[6]

Although the exact mechanism in unknown, the proposed pathophysiology for ON is immune-mediated, delayed-type IV hypersensitivity reaction from a peripheral activation of T-cells that cross the blood brain barrier and causes destruction of the myelin sheath involving axonal degeneration and death of neural cells. Precipitating risk factors include autoimmune diseases such as systemic lupus erythematosus, infectious or parainfectious causes (tuberculosis), syphilis, inflammatory (sinusitis, gum infection, URTI), post-vaccination immunological response, and post-vaccination states. In this chart review, two of seven patients had risk factors, which were sinusitis and viral URTI.

MRI of the brain and orbit may be performed to confirm diagnosis, which includes enhancement and enlargement of the optic nerve and retro-orbital fat streakiness. Of the seven patients, six showed classical findings of ON on imaging while one patient did not. MRI of the brain was not done for all cases, only when significant changes were found needing further detailed examination of soft tissue to rule out demyelinating diseases. Global and longitudinal enhancement of the nerve is the typical pattern seen in ON and its extension has been seen to correlate with visual impairment and with visual prognosis.[7] Of the seven patients, five showed good visual recovery while the other two remained visually impaired: one due to extension of severe demyelination as shown in imaging studies, while the other due

to multiple attacks of neuritis secondary to chronic relapsing inflammatory optic neuropathy (CRION). Recurrent attacks of ON may cause poor visual acuity outcome due to progressive loss of the myelin sheath after repeated episodes of inflammation.

The aetiology for most of the children in this retrospective chart review was idiopathic, similar to earlier reports from Singapore, China, and India.[8] Although the aetiology of ON is usually idiopathic, it is commonly associated with demyelination, including MS, NMO, and ADEM. In our observation, three of the seven children had ADEM, but none had any other demyelinating conditions. In the literature, many children with single or recurrent episodes of ON following ADEM had myelin oligodendrocyte glycoprotein antibodies.[9] In ADEM, there is a tendency for longer intervals between attacks (more than 5 years), unlike in children with MS.[10]

Treatment of ON generally is based on the ONTT criteria since there are no clinical trials on paediatric ON to date. Based on ONTT, intravenous high-dose steroids can hasten visual recovery within the first week but does not affect long-term outcome. Current management of paediatric ON involves intravenous methylprednisolone (4–30 mg/kg per day divided in three doses per day) for 3 or 5 days, depending on visual recovery, followed by a more prolonged, tapered course of oral corticosteroid to avoid recurrence, which is rather common in this age group.

Paediatric ON generally has a good prognosis. Over a few weeks after an insult, resolution of inflammation and visual recovery occurs while remyelination takes place, although this process is usually not complete. As seen in the cases above, only two children had poor recovery, one due to severe demyelination in ADEM while the other had repeated episodes of neuritis. This is due to the aftermath of persistent demyelination and axonal loss, as well as rearrangement of sodium channels over demyelinated segments, which improves conduction but can make surviving axons prone to damage.[11] However, in cases which are recurrent, the prognosis is poorer. Recurrence is defined by new symptoms happening more than 2 weeks after the first presentation.[12]

In conclusion, prognosis is generally good for isolated cases of paediatric ON. However, the outcome for cases secondary to ADEM depends on the degree and extent of demyelination. A diagnosis of CRION can be considered in recurrent cases that are steroid responsive.

Declarations

Ethics approval and consent to participate

Given this was a retrospective study based on reviewing medical charts, ethics approval was not required.

Competing interests
None to declare.

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Prevalence and pattern of refractive error in a tertiary health facility in southwest Nigeria

Taibat Olusola **Otulana**[1,2], Olubunmi Temitope **Bodunde**[1,2], Haroon Adetunji **Ajibode**[1,2], Oluwatoni Olaide **Onabolu**[1,2]

[1]Department of Ophthalmology, Olabisi Onabanjo University Teaching Hospital (OOUTH), Sagamu, Ogun State, Nigeria; [2]Department of Surgery, Faculty of Clinical Sciences, Olabisi Onabanjo University, Sagamu, Ogun State, Nigeria

Abstract

Background: Globally, uncorrected refractive error (RE) is a major cause of blindness, visual impairment (VI), and low vision.
Aim: To determine the prevalence, pattern, and level of visual impairment among clinic patients with refractive error in a tertiary health facility.
Methods: This was an analytical cross-sectional study conducted on patients who presented at a tertiary health facility in Ogun State, Nigeria. The biodata of the patients, level of education, occupation, the symptoms, and signs including the visual acuity (at presentation and after correction), and diagnosis were considered. Lenses that gave the patient the best vision were recorded as the type and magnitude of refractive error for that individual.
Results: The prevalence of RE was 10.6%. Children and adolescents comprised 23.3% of the cases of refractive error while traders comprised 17.1%. Those who did not have formal education were 3.7%. Blurring of vision for near was the most common presenting symptom. Normal visual acuity (6/6) and better was 33.4% at entry and 77.4% with correction. Myopia was observed to be the most common type of RE in children and adolescents. The prevalence of VI and blindness was 6.7%.
Conclusion: RE is a major cause of blindness and VI, with the prevalence of Myopia higher in age group thirty years and below: lack of formal education may be a barrier for uptake of refractive error services in population with low literacy level.

Correspondence: Dr. Taibat Olusola Otulana, Department of Ophthalmology, Olabisi Onabanjo University Teaching Hospital, Sagamu, Ogun State, Nigeria.
E-mail: solyotulana@gmail.com

Keywords: Nigeria, prevalence, refractive error, tertiary health facility, visual impairment

Kadar kelaziman dan corak ralat biasan di kalangan pesakit yang menghadiri pusat kesihatan tertiari di barat selatan Nigeria

Abstrak

Latarbelakang: Secara global, ralat biasan tanpa pembetulan merupakan penyebab utama kebutaan, cacat penglihatan dan penglihatan rendah.
Tujuan: Untuk menentukan kadar kelaziman, corak dan tahap penglihatan rendah di kalangan pesakit yang mempunyai ralat biasan di sebuah pusat kesihatan tertiari.
Kaedah: Ini merupakan kajian keratan rentas secara analitikal dijalankan ke atas pesakit di sebuah pusat kesihatan tertiari di negeri Ogun, Nigeria. Biodata pesakit, tahap pendidikan, pekerjaan, gejala dan tanda-tanda termasuk ketajaman penglihatan (semasa kehadiran yang pertama dan selepas pembetulan) dan diagnosis yang diberikan. Jenis dan magintud kanta yang memberi penglihatan yang terbaik direkodkan untuk setiap individu. Data yang diperolehi dicerakin dengan menggunakn SPSS versi 21.
Keputusan: Kadar kelaziman untuk ralat biasan adalah 10.6%. Kanak-kanak dan remaja menyumbang 23.3% untuk kes ralat biasan sementara pesakit tanpa pendidikan yang formal adalah 3.7%. Gejala paling biasa ialah kekaburan pada jarak dekat. Untuk kumpulan yang mempunyai ketajaman penglihatan yang normal dan lebih baik, kadar kelaziman adalah 33.4% di saat permulaan dan 77.4% selepas pembetulan dilakukan. Di kalangan kanak-kanak dan remaja, miopia merupakan ralat biasan yang kerap berlaku. Kadar kelaziman untuk cacat penglihatan dan kebutaan adalah 6.7%.
Kesimpulan: Ralat biasan merupakan penyebab utama kebutaan dan cacat penglihatan dengan kadar kelaziman miopia adalah tinggi dalam kumpulan berusia 30 tahun ke bawah. Kekurangan pendidikan yang formal mungkin menjadi benteng untuk peningkatan perkhidmatan ralat biasan di dalam populasi yang mempunyai kadar celik huruf yang rendah.

Kata kunci: astigmatisme, cacat penglihatan, kadar kelaziman, pusat kesihatan tertiri, miopia, ralat biasan tanpa pembetulan

Introduction

Refractive error (RE), also called ametropia, is failure of the eye's refractive system to focus images sharply on the retina, thus causing blurred vision in an otherwise normal eye. It is the second leading cause of avoidable/treatable blindness and visual impairment (VI) after cataract and the most common cause of optically corrected visual impairment and blindness. Globally, 2.3 billion people in the world suffer from poor vision due to RE, of which 670 million are considered visually impaired.[1] It is estimated that 153 million people are either blind or have low vision from uncorrected RE.[2]

RE is a significant cause of low vision in African countries but available data are limited.[3] In Nigeria, uncorrected RE along with cataract and glaucoma are the leading causes of blindness, VI, and low vision.[4] The Nigerian National Blindness and Visual Impairment survey indicated that uncorrected RE accounts for 57.1% of moderate VI.[4,5] RE affect all ages, gender, races, and professions.[2,6] Genetic and environmental factors play a role in the aetiology of RE.[7,8] The three main types of refractive errors, myopia, hypermetropia, and astigmatism, all have in common blurring of vision for far, near, or both, and other complaints depend on the type of RE the individual has.

Uncorrected RE is of public health importance because it can result in poor academic performance, and thus loss of education and employments opportunities, low productivity, and impaired quality of life.[2] The global burden in terms of annual economic loss is reported to be $269 billion dollars.[9] RE is thus a priority for the World Health Organization's (WHO) VISION 2020: The Right to Sight campaign. Prescription of appropriate corrective lenses is the treatment of choice,[2] which in the form of spectacles is one of the most cost-effective interventions in eye health.[4] There is paucity of regional and state data on RE, especially among the adult population, as well as studies that considered both children and adults in Nigeria. To the best of our knowledge, no study has been conducted on the prevalence of RE in our health facility. Uncorrected RE contributes to the burden of VI in communities, particularly in poor-resource parts of the developing world where access to specialized care is highly restricted by lack of awareness, low priority of eye care, poor availability of eye care facility, unaffordable cost, and poor accessibility of care.

The aim of this study was to determine the prevalence, pattern of refractive error, and level of VI among clinic patients in our health facility. Given that hospital-based studies represent the small proportion of people who present themselves for examination, the results may not reflect the true magnitude of the problem. However, the study may provide baseline information on the status of RE in the environment, and this information may constitute the basis for larger community-based research. The outcomes of this study may be used to plan an intervention program in the locality.

Methods

This is a cross-sectional, hospital-based study of consecutive patients who presented with symptoms and signs of RE at the Olabisi Onabanjo University Teaching Hospital (OOUTH), the only state-owned tertiary health facility in Ogun state, located in Sagamu local government in Remo. It serves all the people in the state and surrounding areas. Ethical approval for this study was obtained from the Ethics and Research Committee of the OOUTH.

All the patients who presented at the general eye clinic of the hospital between January 2016 and December 2017 were first seen and examined by the consultant ophthalmologists. Biodata regarding age, sex, level of education, and occupation were obtained. A detailed history was obtained for symptoms and duration, as well as history of spectacle use in patient and family members. Symptoms of blurring of vision for near included difficulty reading tiny letters, threading a needle, soldering of tiny things when repairing electronics or phones, and picking of beans at home. A thorough examination including the presenting visual acuity for far was done using the Snellen chart/Tumbling E chart and Lea symbol for the very young. Near vision was checked with a near vision chart, slit lamp biomicroscopic examination, and fundoscopy using either a direct or an indirect ophthalmoscope. Those who were suspected to have RE and those who had complaints with their glasses in the absence of any eye disease were referred to the refraction clinic.

The patients who presented to the eye clinic with symptoms and signs of RE in the absence of other ocular morbidities/comorbidities were included in the study, as were those who presented with issues with their glasses (broken, misplaced, or ineffective glasses, intolerability, scratched lenses, and poor vision even with glasses) in the absence of any eye disease; these latter patients were categorised as wanting to change their glasses. A combination of two or more of the following symptoms of redness, photophobia, eye ache and pain, closing and squeezing the eye in an individual was regarded as asthenopia.

Patients for whom the cause of poor vision was not RE were excluded, *i.e.*, cataract, cataract surgery, and cataract-related problems including aphakia and pseudophakia, glaucoma, and those with evidence of ocular disease.

Ages were categorized in groups of tens. Age groups 0–10 years and 11–20 years were regarded as children and adolescents; age groups 41–50 years and 51–60 years were categorized as middle aged; and those from age 71 years were categorized as elderly.

Objective refraction was obtained with the aid of autorefractometer and/or streak retinoscopy. All children 7 years and below had cycloplegic refraction with 1% atropine. Subjective refraction was done by interposing lenses using the trial frame, trial lenses, illuminated Snellen chart, and near vision chart. The lens that gave the patient the best vision was taken as the RE and was prescribed. Myopia was taken as spherical error of ≤ -0.50 D, hypermetropia was taken as spherical error of ≥ +0.50

D, while astigmatism was cylindrical error of ≥ 0.50 D cylinder. Simple spherical RE was taken as error of ≥ 0.50 to 5.00 D while high spherical error was taken to be >5.00 D. Simple astigmatic error was ≥0.50 to 1.00 D of cylinder and higher values were regarded as high cylinder. Even though some patients presented with more than one type of RE, the more significant RE based on the patients' complaints and needs were considered for analysis.

The intraocular pressure (IOP) was checked with Goldman applanation tonometry where indicated, and those with persistent IOP greater than 21 mmHg were referred for glaucoma screening. Data were generated and recorded in a spread sheet and analysed using SPSS version 21.

Highly skilled professionals were doctors, engineers, lawyers, nurses, teachers etc.; skilled professionals were tailors, brick layers, motor mechanics, etc.; and unskilled were food vendors, cleaners, etc.

Results

A total of 13,689 new patients including children were seen during the study period. Males were 6,204 (45%) while 7,485 (55%) were females with male-to-female ratio 1:1.2. There were 1,450 patients diagnosed with RE, with a prevalence of 10.6%. The age of the patients with REs ranged from 6 months to 86 years. Male-to-female ratio was 1:1.8. There were 223 children (6 months to 15 years), 32 (14.3%) less than 7 years. The gender, presenting symptoms, and magnitude of refractive errors are presented in Table 1. The level of education and occupation are presented in Table 2. The gender of three patients, presenting complaints of 16, and level of education in 177 patients were missing.

All types of REs were more common in females across all age groups except those 10 years and younger, where myopia was predominant among males. High astigmatism was more common in males than females. The frequencies of the different age categories with respect to their sex and type of RE are as shown in Table 3. The pattern of RE according to age categories is shown in Figure 1. High myopia was 2.7% while high hypermetropia was 0.9%. Simple myopic astigmatism predominated the types of astigmatism as shown in Table 4. There was very little difference in RE between both eyes. VI due to uncorrected RE based on presenting visual acuity was recorded in 920 (63.5%) patients, giving a prevalence of 6.7%. After best correction of the RE with lenses, the prevalence of VI according to the WHO definition was reduced to 2.2% (Table 5).

There were 864 (59.6%) patients who had presbyopia with and without underlying RE. IOP was greater than 21mmHg in the right eye of 28 (1.9%) patients and in the left eye of 24 (1.7%) patients. The highest recorded values were 44 mmHg and 35 mmHg in the right and left eye, respectively. Anisometropia of ≥ 2 DS was found in 28 (1.9%) patients

Table 1. Sociodemographic characteristics of the patients and magnitude of refractive error

Variables	Frequency	Percentage (%)
Gender		
Male	510	35.2
Female	937	65.6
Missing	3	0.2
Presenting complaints		
Blurring of vision for near	641	44.2
Blurring of vision for far	455	31.4
Asthenopia	119	8.2
Eye ache and pain	90	6.2
Blurring of vision for both far and near	74	5.1
Change of glasses	67	4.6
Watering/itching	25	1.7
Squint/double vision	24	1.7
Headache	12	0.8
Nystagmus	4	0.3
**Others	41	2.8
Missing	16	1.1
Magnitude of refractive error		
Astigmatism	490	33.8
Hypermetropia	467	32.2
Myopia	338	23.3
Presbyopia	155	10.7

**Others include photophobia, redness, foreign body sensation, squeezing of eyes, peppery sensation, and those who came for (vision test) eye screening for schooling and drivers' license.

Table 2. Occupations and level of education

Variables	Frequency	Percentage (%)
Occupation		
Student	289	19.9
Trader	248	17.1
Highly skilled professional	181	12.5
Retiree	104	7.2
Civil servant	66	4.6
Skilled professional	62	4.3
Farmer	40	2.8
Unskilled	33	2.3
Cleric	28	1.9
Level of education		
No formal education	53	3.7
Primary	162	11.2
Secondary	390	26.9
Post-secondary	103	7.1
University undergraduate	23	1.6
Tertiary	487	33.6
Postgraduate	34	2.3
Indeterminate	21	1.4
Missing	177	12.2

Table 3. Prevalence of refractive errors according to age category and sex

Age group (years)	SM		HM		SH		HH		A		HA		Total	%
	M	F	M	F	M	F	M	F	M	F	M	F		
0–10	20	14	04	02	11	12	01	02	06	14	03	00	89	6.1
11–20	18	76	05	10	13	42	00	00	20	54	02	09	249	17.2
21–30	17	20	03	02	01	14	02	00	12	12	06	01	90	6.2
31–40	04	14	00	03	17	33	02	01	22	24	03	02	125	8.6
41–50	09	19	01	02	46	96	00	01	39	66	08	05	292	20.1
51–60	17	22	01	03	32	77	01	00	30	46	02	02	233	16.1
61–70	11	12	01	01	16	33	00	01	25	24	04	05	133	9.2
71–80	09	11	01	00	06	04	01	00	10	12	10	02	66	4.6
81 ≥	02	02	00	00	01	01	00	00	01	01	01	02	11	0.7
Others*	01	01	00	00	00	00	00	00	01	02	01	01	07	0.4
Total	**108**	**191**	**16**	**23**	**143**	**312**	**07**	**05**	**166**	**255**	**40**	**29**	**1295**	**89.2**

SM: simple myopia; HM: high myopia; SH: simple hypermetropia; HH: high hypermetropia; A: astigmatism; HA: high astigmatism
**Others were those whose ages were not available.

Table 4. Frequencies of the different types of astigmatism with respect to age categories

Age group (years)	SMA	CMA	SHA	CHA	MA
0-10	6	6	2	4	5
11-20	39	20	8	8	10
21-30	8	10	7	2	4
31-40	17	12	11	4	7
41-50	36	13	26	32	11
51-60	19	9	14	26	12
61-70	9	11	9	22	7
71-80	9	6	3	7	9
81≥	1	1	0	1	2
Others*	2	1	1	0	1
Total (%)	146 (29.8)	89 (18.2)	81 (16.5)	106 (21.6)	68 (13.9)

SMA: simple myopic astigmatism; CMD: compound myopic astigmatism; SHA: simple hypermetropic astigmatism; CHA: compound hypermetropic astigmatism: MA: mixed astigmatism
*Others were those whose ages were not clearly documented.

Table 5. Magnitude of visual impairment before and after correction (uncorrected and corrected visual acuity)

Visual acuity	Uncorrected (%)	Corrected (%)
6/6 & better	483 (33.4)	1122 (77.4)
6/18-6/9 (mild VI)	582 (40.1)	249 (17.2)
6/60-6/24 (moderate VI)	231 (15.9)	40 (2.8)
3/60 5/60 (severe VI)	43 (3.0)	5 (0.3)
2/60 & worse (Blind)	64 (4.4)	7 (0.5)
Others*	47 (3.2)	27 (1.9)
Total VI	**920 (63.5)**	**301 (20.8)**

VI: visual impairment
*Others included preverbal children, those whose visual acuities could not be assessed, and those with either missing or illegibly documented visual acuities.

Discussion

The results of the present study show that RE was responsible for 10% of the total clinic attendance; more than 90% of these cases were uncorrected at presentation. RE affects all ages. Adolescents and adults comprised most of the patients, while children were less than one-fifth of the population study. The reason for the low presentation of children cannot be readily explained because it's beyond the scope of the study, but may be due to the theory of emmetropisation propounded by Flitcroft *et al.*[10] It could be because children are at the mercy of their parents for seeking eye health in developing countries. The reasons given by Velibanti *et al.* in Swaziland,[11] which included poor health literacy, parents not wanting their children to wear spectacles, socioeconomic factors, and lack of knowledge and awareness of existing eye care facilities, may be applicable to all developing countries including Nigeria. Those in middle age were the most represented in the study. Difficulty in reading because of presbyopia was responsible for the large number of patients attending the clinic in this age group.

Among the adult population, the elderly from age 71 years and older were least represented. The reason for this is that most of them did not meet the inclusion criteria due to the associated ocular comorbidities usually found in these age groups.

There were twice as many females as males in the study. This could be because many more females attended the general clinic (where those with RE were recruited), and by extension, attended the refraction clinic. On the other hand, the large number of females who were traders and highly skilled professionals may be able to explain these findings. This supports past studies that found that

more women access health and eye care facilities than men.[12, 13] Those who were traders and those on shift duties, who were predominantly females, might have found it easier to create time to access health and eye care to be able to function effectively in their duties. Possible reasons for reduced male attendance could be tight schedules and that males are more likely to attend private clinics, where the waiting time is shorter, during their own free time when they finish work. They are more likely to be able to afford the cost of private health care, which is usually higher than that of public health institutions. All types of REs were more common in females because of the same reason adduced earlier, although Yoo *et al.* found no sex difference in his study,[14] while Yekta *et al.* reported more males with RE in their study. [15]

Less than one-tenth of the study population had no formal education while one-third had tertiary education. This may mean that only those who could read and write were those who accessed eye care. These patients were more likely to have information about eye health, its availability and accessibility. The simple inference from this result is that access to eye care depends not only on availability and cost but also access to health information, which may be linked to educational attainment. The implication of this finding is that there are likely many more people in the community who may be blind or visually impaired from uncorrected RE but cannot access eye care due to lack of information and awareness. A community-based intervention study may be necessary to identify such people, and provide information on eye health and the need for use of appropriate spectacle in those who are blind or visually impaired from uncorrected RE if VISION 2020 is to be a reality.

Students dominated the population of those who presented for RE services in this study probably because the hospital where the study was conducted shares the same premises as the college of health sciences, where good vision is a requirement for good academic performance. This finding is similar to those in the study by Malu *et al.*, where students comprised the majority of those who accessed their refraction facility.[16]

Blurred vision for near was the most common presenting symptoms in this study. This can be explained by the large number of middle-aged and literates who were hypermetropic and presbyopic; these results are similar to those of Ayanniyi *et al.*[17] Less than 5% of the study population presented because they wanted to change their spectacles. This is a pointer to the fact that spectacle coverage is very low in semiurban Nigeria, where this study was conducted. It is possible that barriers to spectacle uptake may be an unidentified problem in this area. Ezelum *et al.*[4] reported similar findings, while change of spectacles was the most common reason for presentation in Ayanniyi's report.[17]

Anisometropia of ≥ 2.0 DS was very low compared with the findings of Malu *et al.*,[16] which is likely to be due to difference in the population and ethnicity of the two studies.

Astigmatism was the most common type of RE observed in this study, as similarly reported by other authors.[18,19] Even though the prevalence of astigmatism found by Rim *et al.* is similar, they reported it as second to myopia.[20] Contrary to our observation, Gomez-Salazar *et al.* found a decreasing trend in astigmatism with age.[21] Simple myopic astigmatism was the most common variant of astigmatism in this study. Myopic astigmatism (simple and compound) was the most prevalent type in children. A study done in Osogbo in Nigeria on RE in children also supported this finding.[22]

The distribution pattern of astigmatism and hypermetropia were similar in the different age groups, with dual peaks at 11–20 years and 41–50 years. The greater peak at 41–50 years may be related to the high proportion of hypermetropia and hypermetropic astigmatism, which make near work difficult. Vitale *et al.*[23] reported a very low prevalence of hypermetropia among the American population, as they studied hypermetropia of +3 D and higher, thus excluding a large proportion of those with lower error.

Myopia was the least common type of RE in this study, matching the findings of Ferraz *et al.*[24] Other studies found myopia to be the most common RE, and this was attributed to changes in lifestyle.[16,25-27] Myopia appeared to decrease with age, which has been similarly reported by Natung *et al.* in India[28] and Assefa *et al.*[29] Less myopia was recorded from age 41 years and older because people with myopia in these age groups are not likely to have reading difficulty, which was identified as an important reason for presentation. This defers from the study by Onua *et al.*[30] in Nigeria where highest prevalence was reported among the age 50–59 group, probably due to the community nature of their study.

High REs, especially myopia, were more common in this study than in reports from other authors.[4] Sarma *et al.* reported no case of high myopia in their study.[31] The reason was due to their classification of moderate myopia with spherical error extending to -6 00 DS, which was regarded as high myopia in this study.

VI was an important presentation of uncorrected RE in this study, evident by 63.4% of the study population with VI at presentation. This percentage was reduced to 20.8% after correction with appropriate lenses. The relatively low prevalence of VI of 6.7% was due to the hospital-based nature of this study. A study done in Onitsha[32] reported a similar prevalence of VI due to RE, but it was conducted among school children. A prevalence of 9% was reported by Reidy *et al.*[33] in a community-based study in North London, while a much lower prevalence was reported by Resnikoff *et al.*,[2] who categorized their findings according to age group. A larger community-based study will be needed to reveal the true prevalence of VI induced by uncorrected RE in our area. Improvement in best-corrected visual acuity was recorded in all the different stages of VI, as reported by Ferraz *et al.*[34]

One of the limitations of the study was its hospital-based nature, which may not capture the real magnitude of uncorrected RE in our area; thus, this report might just represent the tip of the iceberg. Another limitation was the poor, inadequate,

and illegible documentation in the patients' case notes, which made access to all the needed information difficult and was responsible for most of the missing data.

In conclusion, the prevalence of RE remains high at 10.6%; myopia peaked in the teenage years and declined gradually with increasing age, while hypermetropia and astigmatism have dual peaks, which corresponded with middle age. Some of the recommendations to reduce the burden of uncorrected RE would be increasing its awareness and taking refraction services to the rural underserved communities with a view to making spectacles (low cost but durable) available and affordable by all.

Declarations

Ethics approval and consent to participate

Ethical approval for this study was obtained from the Ethics and Research Committee of the Olabisi Onabanjo University Teaching Hospital (OOUTH).

Competing interests

None to declare.

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Water drinking test in glaucoma management: a review of the literature

Khoo Phong Yue, **Cheng** Teck Chee, Norshamsiah **Md Din**

Department of Ophthalmology, Universiti Kebangsaan Malaysia Medical Centre, Cheras, Kuala Lumpur, Malaysia

Abstract

Purpose: To describe the methods of performing the water drinking test (WDT) and its applications in glaucoma management.
Methods: This review is based on pertinent publications retrieved by a selective search in PubMed, supplemented by further articles chosen by the authors.
Results: Intraocular pressure (IOP) changes throughout the day. IOP peak has been identified as a risk factor in glaucoma onset and progression. WDT is a simple stress test used by many researchers to elicit IOP peaks in assessing response to glaucoma treatments.
Conclusions: Studies have shown the reproducibility and promising results of WDT in various pharmacological and surgical treatments of glaucoma. It is an important tool in glaucoma management.

Keywords: intraocular pressure, glaucoma, water drinking test

Correspondence: Associate Professor Dr. Norshamsiah Md Din, Department of Ophthalmology, Universiti Kebangsaan Malaysia Medical Centre, Jalan Yaacob Latif, 56000 Cheras, Kuala Lumpur, Malaysia.
Email: shamsiahdr@hotmail.com

Ujian minum air dalam rawatan glaukoma: kajian tinjauan literatur

Abstrak

Tujuan: Untuk menerangkan kaedah menjalankan ujian minum air (WDT) dan aplikasinya dalam rawatan glaukoma.
Kaedah: Kajian ini adalah berdasarkan penerbitan jurnal berkaitan yang diperoleh melalui carian terpilih dalam PubMed, ditambah dengan artikel lanjut yang dipilih oleh pengarang.
Keputusan: Tekanan intraokular (IOP) berubah sepanjang hari. Puncak IOP telah dikenal pasti sebagai faktor risiko dalam pembentukan dan perkembangan penyakit glaukoma. WDT ialah ujian yang digunakan oleh ramai penyelidik untuk mendapatkan puncak IOP dalam menilai tindak balas terhadap rawatan glaukoma.
Kesimpulan: Berdasarkan tinjauan literatur, WDT menunjukkan kebolehulangan dan menunujukkan peranan WDT yang memberangsangkan dalam pelbagai rawatan farmakologi dan pembedahan glaukoma. WDT merupakan ujian yang penting dalam rawatan glaukoma.

Kata kunci: glaukoma, kesihatan dan kesejahteraan yang baik, tekanan intraokular, ujian minum air

Introduction

Intraocular pressure (IOP) is the main modifiable risk factor that contributes to glaucoma progression.[1] The Early Manifest Glaucoma Trial (EMGT) showed that the risk of glaucoma progression decreased by 10% with each 1 mmHg of IOP reduction from baseline.[2] However, IOP is not a fixed value, but varies throughout the circadian cycle. Twenty-four-hour IOP profile studies have shown that two-thirds of patients experienced peak IOP outside of the regular clinic hours.[3] Hence, some glaucoma patients still progress with IOP apparently within the target range during clinic visits.

Diurnal and 24-hour IOP curves have been useful to determine peak IOP. Methods to measure 24-hour IOP such as the modified diurnal tension curve (four to five IOP measurements during office hours from 8 AM to 6 PM), home tonometry, and contact lens sensor are time- and resource-intensive.

The water drinking test (WDT) has been suggested as a practical and easy test to estimate the diurnal IOP profile more feasibly. It was originally described as a diagnostic test for glaucoma but was eventually abandoned due to its low

sensitivity, low specificity, and low diagnostic value.[4] However, it has since been revamped into a stress test to detect IOP instability and predict IOP peaks.[5] This concept has led to a growing interest in the WDT. Many researchers have used the WDT to compare the effects of different clinical and surgical treatment modalities in glaucoma.

How to perform the WDT

Currently, the WDT is widely used to predict peak IOP and IOP fluctuation. It also serves as a reliable tool to assess the efficacy of different glaucoma treatments. Concomitant systemic diseases such as cardiac diseases, renal diseases, and urinary retention are the contraindications to this test. Prior to the test, participants are required to refrain from food and liquid intake for at least 2 hours. This is to avoid any possible influence of previous liquid ingestion on the results. This is particularly important for patients who are on special high-sugar or high-salt diets. Unfortunately, there is no recommendation on the washout period for patients who are on diuretics as of now. Most researchers performed WDT during office hours. However, it is advised to perform WDT within a fixed time of the day to minimise diurnal variation.

Essentially, IOP fluctuation is independent of the positioning during measurement. However, a study concluded that IOP values obtained in the supine position during practice hours were more appropriate for the estimation of nocturnal IOP peaks than measurements made in the sitting position.[6] Therefore, IOP measurements in both sitting and supine positions are recommended.

Firstly, the patient's baseline IOP is measured. Then the patient drinks a given volume of water within 5 minutes. Following water ingestion, patients are required to rest at a sitting or supine position. Subsequently, another four IOP measurements are taken at 15-minute intervals (15, 30, 45, and 60 minutes after water ingestion). One examiner measures the IOP. The average of three measurements is recorded and the measurement is repeated if the difference between the three measurements is greater than 3 mmHg. In a meta-analysis, of all available tonometers when compared with the Goldmann applanation tonometer, the least amount of variability in IOP measurement (mean difference of 0.2 mm Hg) was seen with non-contact tonometers.[7]

The volume used in WDT has not been standardized. Some authors use a fixed volume of water, whereas others use a volume adjusted to body weight. It is not yet clear whether the use of 1000 mL, 800 mL, or 10 mL/kg body weight improves the correlation or predictive value of the WDT.

A volume of 10 mL of water/kg of body weight has been used in an attempt to correct the effect of body mass and shift of fluid between intravascular, intracellular, and interstitial spaces.[8] It is presumed that a fixed volume, for example, 1000

mL, is likely to have a different physiological effect in a 100 kg patient compared to a 50 kg patient. WDT based on body weight-adjusted volume is known to induce a significant IOP response that correlates to diurnal IOP peak as well as the ingestion of 800 mL, but not 500 mL. A comparison between the ingestion of 1000 mL or 500 mL of water demonstrated that the latter failed to estimate the peak diurnal pressure.[9] Current preference is based on personal experience and scientific principles. Most recent studies use 800 mL or 10 mL/kg of body weight. Unfortunately, there is a lack of consensus regarding the maximum volume of water allowed to be consumed in this test.

Mechanism of action

The exact mechanism behind WDT has not been established. Studies have suggested that an increase in episcleral venous pressure, blood-aqueous osmotic pressure gradient, choroidal expansion, and autonomic nerve stimulation may lead to the IOP changes post-WDT.[10-13]

Previously, it was thought that the rapid ingestion of a relatively large amount of water affects blood and ocular osmotic gradients. Nongpiur *et al.* demonstrated that a significant decrease in serum osmolality occurred after water intake in WDT, and this was significantly correlated with changes in IOP.[10] This may be explained by the osmotic gradient causing water movement into the aqueous humour with a subsequent increase in IOP.

Water intake has also been shown to be associated with an increase in blood pressure and peripheral vascular resistance. Haemodynamic changes may be associated with increased episcleral venous pressure (EVP), which leads to decreased outflow facility. Aqueous fluorophotometry and estimation of the EVP using manometry following a 1000 mL WDT has been measured in young healthy volunteers.[11] Estimated EVP more than doubled within 10 minutes of the water load and was maintained at this level for 90 minutes, at which time measurement was stopped. At the same time, increased fluorescein concentration was detected in the aqueous at 10 minutes. It subsequently returned to baseline 60 minutes after the water load. The explanation for increased fluorescein concentration is unclear, but it may represent negative flow or reflux of fluorescein from Schlemm's canal. These findings suggest a role for increased EVP in the WDT response, hence explaining the rationale for performing the test over 60 minutes.

More recent studies focus on the role of choroidal expansion. The rapid water ingestion would lead to a transient increase in hydrostatic pressure and a decrease in osmotic pressure, which shifts fluid from the systemic circulation to the choroidal space due to the osmotic gradient. De Moraes *et al.* suggested that systemic fluids are transmitted into the choroidal space, causing the choroid to expand and increase the IOP.[12] This pressure gradient causes increased outflow

of aqueous humour from the anterior chamber into the trabecular meshwork. In a more recent study involving swept-source optical coherence tomography, Mansouri *et al.* found an increase of 5.7% in the peripapillary choroidal thickness and 4.3% in the macular choroidal thickness after water intake by healthy participants.[14]

The autonomic nervous system is also thought to be involved in IOP regulation. Yan *et al.* showed that aerobic exercise causes sympathetic nervous system stimulation, consequently causing the expansion of Schlemm's canal, which in turn causes IOP reduction.[13] Sasamoto *et al.* observed many unmyelinated nerves containing substance P in the inner wall of Schlemm's canal, which indicates that parasympathetic nerves may be involved in the regulation of Schlemm's canal.[15] It has been proven that water intake accelerates parasympathetic activation. Chen *et al.* later showed that the WDT could cause parasympathetic nervous system stimulation, which may cause the collapse of Schlemm's canal, leading to increased IOP post-WDT.[16]

Regardless of the mechanism that increases IOP following WDT, an intact outflow facility should be associated with rapid IOP recovery, whereas an impaired outflow facility is more likely to lead to sustained IOP elevations.

Interpreting the results

Following IOP measurement at baseline and four other measurements at 15, 30, 45, and 60 minutes, these parameters are assessed: trough IOP (lowest IOP after drinking water), peak IOP (highest IOP after drinking water), mean IOP (the mean of the four IOPs after drinking water), IOP fluctuation (difference between peak IOP and baseline), IOP range (difference between peak IOP and lowest IOP reading after drinking water), and end-pressure difference (IOP at 60 minutes *versus* baseline).

Several studies have shown that the peak IOP obtained with this test is strongly correlated and in agreement with the IOP peaks that occur during the day.[17,18] Eyes with higher IOP peaks after water ingestion take longer to return to baseline levels than eyes with lower IOP peaks, which may reflect the state of the drainage system in the eye. The factors influencing time to peak IOP following WDT are less certain, as reported findings are inconsistent. For example, Mansouri *et al.* reported that the highest mean peak IOP from 58 healthy eyes occurred at 15 minutes.[14] Similarly, Ulas *et al.* have shown that IOP elevation after WDT in healthy eyes occurs within the first 10 minutes and recovers quickly.[19] Tran *et al.* reported mean peak IOP was highest at 45 minutes after water ingestion in patients with primary open-angle glaucoma (POAG),[20] whereas Hatanaka *et al.* found that mean peak IOP was highest at 30 minutes in subjects with ocular hypertension and open-angle glaucoma.[21] It has been postulated that a more rapid return to baseline IOP following WDT may reflect an improved outflow facility.

Clinical and research applications

The WDT helps us to further understand how IOP-lowering treatments work and why glaucoma progresses. Researchers evaluated the WDT-IOP profile of glaucoma patients treated with medications and those who had undergone glaucoma procedures such as trabeculectomy, deep sclerectomy, peripheral laser iridotomy, and glaucoma drainage device (GDD) implantation.

In a comparison between latanoprost and the fixed combination of dorzolamide and timolol, patients who received latanoprost showed significantly smaller elevations in their IOP levels following the WDT.[22] The authors demonstrated that prostaglandin analogues that act on the outflow system of the eye are associated with better IOP stabilization during WDT compared to drugs that decrease aqueous humour production, such as β-blockers and carbonic anhydrase inhibitors.

Some drugs may demonstrate similar IOP reduction but different effects on blunting IOP spikes that occur during the day. Although timolol 0.5% showed similar IOP reduction to brimonidine 2.0%, IOP was more stable on brimonidine than with timolol. Eyes treated with timolol had an earlier IOP spike, higher mean IOP peak (3.5 mmHg), and longer return to baseline in WDT compared to brimonidine.[23]

Waisbourd *et al.* suggested a role for WDT in assessing response to peripheral laser iridotomy in primary angle-closure suspects.[24] Although no significant change in peak IOP was reported before and after laser peripheral iridotomy, a more rapid recovery in the IOP curve was seen after treatment. The authors postulate that this is due to the enhanced outflow facility that accompanies reduced iris-trabecular apposition.

In recent years, WDT was also performed on glaucoma patients who were treated surgically. Medeiros *et al.* reported that IOP change in 30 patients with one or two trabeculectomies was significantly lower than that of a group of patients with medicallycontrolled glaucoma.[25] Razeghinejad *et al.* studied the effects of WDT on patients with Ahmed glaucoma valve and those treated with trabeculectomy. They concluded that both groups had IOP increases, despite showing seemingly stable IOPs in a standard clinical setting. However, the WDT-IOP profile was lower in the trabeculectomy group.[26] Subsequently, Razeghinejad *et al.* also assessed primary congenital glaucoma patients who had undergone trabeculotomy and GDD implantation. Interestingly, the authors revealed a smoother WDT-IOP profile in their GDD group.[27] Martinez *et al.* revealed that subjects who had undergone either trabeculectomy or tube shunt surgery showed similar IOP responses to the WDT.[28] Studies have also shown that patients on glaucoma medications have a greater IOP increase following WDT when compared to patients who have undergone filtration surgery despite similar baseline IOP.[25,29]

A test must be reproducible to be considered clinically applicable. IOP peaks detected by WDT performed 24 hours apart in untreated patients with ocular

hypertension, showed excellent reproducibility.[21] Similarly, outstanding reproducibility was observed by the same research group in a cohort of treated POAG patients with a mean interval of 4.85 (range 3–6) months between tests. By performing WDT on 34 treated POAG patients in two consecutive visits without any change in the treatment regimen, Babic *et al.* demonstrated better reproducibility for IOP peaks than IOP fluctuation.[30]

There are certainly some limitations to the WDT. It cannot be used as a diagnostic test for glaucoma. IOP response to this test may be affected by prior topical antiglaucoma treatment, as some medications can reduce IOP peaks by improving aqueous humour drainage. Another study also demonstrated that eyes with worse glaucomatous lesions experienced higher IOP fluctuations than the contralateral eyes, even when equally treated with topical medication.[31] There are no reports of systemic complications related to WDT. However, some side effects such as corneal oedema, hyperaemia, and discomfort have been associated with its use.

Conclusion

There has been increased attention on IOP peaks being risk factors for glaucoma onset and progression. More studies are being carried out to establish a target IOP peak or target IOP peak range instead of a single target IOP level. Better methods to evaluate the IOP profile over 24 hours are warranted.

The practicability of current 24-hour IOP monitoring devices remains doubtful. Meanwhile, the WDT is reproducible and shows clinically relevant results validated several times by a series of peer-reviewed studies. It can be an important tool for IOP profile assessment in glaucoma management, particularly in treatments that aim to improve outflow facility. Further studies on the 24hour diurnal curve and WDT after glaucoma surgery, including microinvasive glaucoma surgery, will provide more insights into the IOP profile after filtration surgery.

Declarations

Ethics approval and consent to participate
Not required, as this is a literature review.

Competing interests
None to declare.

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Ultrasound cycloplasty: a case series examining the efficacy on a local Malaysian cohort of patients

Shankari **Sothirachagan**, Jemaima **Che Hamzah**

[1]*Department of Ophthalmology, Universiti Kebangsaan Malaysia Medical Centre, Kuala Lumpur, Malaysia*

Abstract

Introduction: Ultrasound cycloplasty (UCP) is commercially available in Europe. It has been shown to have less side effects than its trans-scleral diode laser cyclophotocoagulation counterpart in reducing intraocular pressure (IOP) in refractory glaucoma patients.
Case presentation: This retrospective case series followed seven patients treated with UCP for refractory glaucoma at the Ophthalmology Clinic, Hospital Universiti Kebangsaan Malaysia. Patients were aged 52–80 years, with baseline IOP 14–27 mmHg. All patients received sequential activation of the transducers lasting 8 seconds. Postoperatively, patients were followed-up at 1 week, 1 month, and 3 months. No complications or changes in best-corrected visual acuity were recorded postoperatively. One patient underwent a trabeculectomy 3 months post-procedure, whilst the others continued regular medication.
At 1-month postoperative, there was IOP reduction of 6–10 mmHg in six patients. At the 3-month follow-up, IOP returned to the preoperative levels. Conservative power and duration of the shots were used to ensure patients safety.
Conclusion: Most studies on UCP safety and efficacy have been conducted on Caucasian populations. A longer duration of UCP may be necessary in the Asian population. Further studies are required to determine the efficacy of UCP in the Asian population.

Keywords: Malaysia, refractory glaucoma, ultrasound cycloplasty

Correspondence: Jemaima Che Hamzah, PhD, Department of Ophthalmology, Universiti Kebangsaan Malaysia Medical Centre, 9th floor, Clinical Block, Jalan Yaacob Latif, 56000 Cheras, Kuala Lumpur, Malaysia.
E-mail: jemaima@ppukm.ukm.edu.my

Sikloplasti ultrasound: kajian kes siri ke atas efikasi dikalangan pesakit setempat di Malaysia

Abstrak

Pengenalan: Kaedah baru siklokoagulasi ultrasonic (UCP) terdapat di pasaran komersil di Eropah.. Menurut kajian, kaedah ini mempunyai kesan sampingan yang lebih rendah berbanding kaedah laser diode trans-skleral siklofotokoagulasi dalam pengurangan tekanan intraocular (IOP) bagi pesakit glaukoma refraktori.
Pembentangan kes: Satu kajian retrospektif kes bersiri dijalankan atas tujuh pesakit dengan glaukoma refraktori di Klinik Oftalmologi, Pusat Perubatan Universiti Kebangsaan Malaysia. Kesemua pesakit terlibat berumur di antara 52 dan 80 tahun dengan IOP 14-27mmHg. Mereka menerima pengaktifan transduser berturutan selama 8 saat. Selepas prosedur ini, temujanji rawatan susulan teleh diberikan selepas seminggu, sebulan dan 3 bulan. Didapati tiada perubahan dalam ketajaman penglihatan terbaik (BCVA) dan tiada komplikasi dicatatkan sepanjang temujanji selepas prosedur. Hanya seorang pesakit perlu menjalani pembedahan trabekulektomi tiga bulan selepas prosedur, manakala yang lain meneruskan rawatan yang ditetapkan. Sebulan selepas pembedahan, enam pesakit menunjukkan penurunan IOP sebanyak 6-10mmHg. Walau bagaimanapun, pada rawatan susulan bulan ketiga, IOP kembali ke paras sebelum prosedur. Bagi melindungi pesakit, hanya kuasa laser dan jangka masa yang konservatif diaplikasikan ke atas pesakit.
Kesimpulan: Kebanyakkan hasil kajian menunjukkan kaedah ini adalah efektif dan selamat dalam menurunkan IOP dengan kesan sampingan yang mínima di kalangan pesakit orang kulit putih. Pesakit dari populasi Asia mungkin memerlukan durasi prosedur yang lebih lama. Kajian yang lebih mendalam diperlukan untuk menilai keberkesanan UCP bagi populasi Asia.

Kata kunci: glaukoma refraktori, Malaysia, sikloplasti ultrasound

Introduction

Glaucoma is one of the leading causes of blindness in the world and it is estimated to reach 76 million cases worldwide in 2020, and to increase to 111 million cases by 2040.[1,2] The main risk factor, although not exclusive, is an elevated intraocular pressure (IOP). IOP reduction is currently the only treatment that has been proven effective in slowing down the progression of glaucoma.[2,3] Medical treatment is considered the first-line therapy, whilst the gold-standard surgical approach, trabeculectomy, is typically reserved for advanced, drug-intolerant cases.

In refractory glaucoma, destruction of the ciliary body (CB) is considered the treatment of last resort to control IOP. The coagulation techniques that decrease aqueous humour (AQH) production use a variety of energy sources including laser, microwave, cryotherapy, and ultrasound.[2,3] As cyclodestruction is associated with several disadvantages, it is considered an end-stage procedure.

Trans-scleral diode laser cyclophotocoagulation (TSCPC) is the most applied cyclodestructive procedure,[3,4] although it is associated with side effects such as chronic uveitis, hypotony, and serous retinal detachment.[2,4,5] In the last decades, high-intensity focused ultrasound (HIFU) has been studied as a cyclodestructive procedure.[2,3] This method causes a transient hyperthermia focused on the desired area of the CB, sparing damage to the surrounding tissue.[2,3]After a series of successful clinical trials in Europe, ultrasound cycloplasty (UCP) was approved for the treatment of refractory glaucoma and made commercially available. The aim of this study was to determine the efficacy of UCP on our cohort of refractory glaucoma patients.

Case presentation

Methods

This is a retrospective case series conducted on seven patients recruited from the Ophthalmology Clinic at Hospital Universiti Kebangsaan Malaysia. Patients were included in the study if they were > 18 years, had refractory glaucoma on maximum topical antiglaucoma therapy, and had evidence of glaucoma progression. Patients who had surgical and laser intervention in the 3 months prior to surgery or previous CB ablation were excluded.

At baseline, patients underwent best-corrected visual acuity (BCVA), slit lamp microscopy examination, Goldmann applanation tonometry, fundus examination with 78 D or 90 D, biometry, and visual field testing (24-2 and 10-2 full threshold test). Biometry was done as the size of the ultrasound probe is determined by axial length and white-to-white measurements. These measurements determine probe size, as the diameters correspond to the CB focal zones to be targeted. Ocular anatomy presents normal variations, including the limbal-ciliary body distance. To account for these differences, three probe sizes (11, 12 and 13 mm) are commercially available.

The procedure was done under aseptic technique in the operation theatre. Once supine, peribulbar anaesthesia was given. All procedures were conducted by the same surgeon. The coupling cone, connected to a suction ring, was placed directly onto the ocular surface aligned with the optical axis. The ultrasound beam was focused at a 2 mm depth beneath the sclera, which corresponded to the CB. The suction ring kept the cone in direct contact with the eye to prevent ocular movement and misalignment. The space between the eye and the coupling cone/

probe was filled with balanced salt solution. The following parameters were used: suction ring, 70 mmHg; number of sectors activated, six; duration of each of the six shots, 8 seconds; and time between each shot, 20 seconds.

Patient 1 received four sectors, while patients 2–6 received six sectors. Patient 1 had a previous failed trabeculectomy in the affected eye and subsequently opted for UCP treatment instead of a revision of the trabeculectomy. Patients 2–6 were given the option of surgery first but refused.

Patient 3 had ocular hypertension and was the only patient given acetazolamide 250 mg QID until UCP, in addition to maximum topical antiglaucoma medication. He had uncontrolled IOP in his only functioning eye despite good compliance. In this case, systemic medication did not help in IOP reduction, as the patient subsequently required a trabeculectomy.

Postoperatively, patients received gutt prednisolone acetate 1% and ciprofloxacin hydrochloride 0.3% every 2 hours, and neomycin/polymyxin B sulphate and dexamethasone ointment at night for 2 weeks. Medications were tapered gradually over a 2-month period. Preoperative hypotensive medications were unaltered throughout the course of the follow-up. Follow-up was done at 1 week, 1 month, and 3 months. Earlier appointments were given if required.

Results

Table 1 presents the patient demographics, clinical findings, glaucoma diagnosis, and visual field test results. Table 2 presents preoperative and postoperative values at all follow-up points for BCVA and IOP.

The patients who had high IOP on follow-up were managed accordingly with oral and intravenous antiglaucoma medication. Patient 3, who had IOP of 32 mmHg at the 3-month follow-up underwent a trabeculectomy. Patient 6 defaulted the 1-month follow-up and Patient 5 defaulted the 3-month follow-up. No complications were found postoperatively.

Discussion

IOP reduction can be achieved by reducing production or increasing outflow of AQH. The two mechanisms can be modified reversibly via topical and systemic medication, or permanently with laser procedures and surgery[5]. Cyclophotocoagulation (CPC) is the most common cyclodestructive procedure used in clinical practice[5] and involves the destruction of the CB epithelium by coagulative necrosis.

The diode laser (810 nm wavelength) is better absorbed by CB melanin pigment and therefore has more targeted tissue destruction.[5] Generally, TSCPC and endoscopic cyclophotocoagulation (ECP) are indicated for refractory glaucoma,

Table 1. Patient demographics, clinical findings, diagnosis, and visual field test results

P	Demographics (age, ethnicity, sex)	Comorbidities	Diagnosis	Baseline mean VF MD
1	52, Malay, M	ESRF, HTN, hepatitis C, asthma	Advanced POAG	-29.69 dB
2	54, Malay, F	DM, HTN	Advanced POAG	-20.44 dB
3	63, Malay, M	HPL	Ocular hypertension	-0.74 dB
4	73, Chinese, M	HTN, HPL, gout	Advanced POAG	-16.62 dB
5	80, Malay, M	HTN	Advanced POAG	Unable to perform VF
6	75, Chinese, M	HTN, CKD, IHD, stroke, adrenal adenoma	Advanced POAG	-17.54 dB
7	59, Chinese, M	HTN	Angle recession	-23.08 dB

P: patient; ESRF: end-stage renal failure; HTN: hypertension; HPL: hyperlipidaemia; CKD: chronic kidney disease; IHD: ischaemic heart disease, POAG: primary open-angle glaucoma; VF: visual field; MD: mean deviation

Table 2. Preoperative and postoperative best-corrected visual acuity and intraocular pressure

P	Preoperative		Postoperative follow-up					
	BCVA (unaided/ pinhole)	IOP	1 week		1 month		3 months	
			BCVA	IOP	BCVA	IOP	BCVA	IOP
1	6/24 (6/24)	17	6/60 (6/60)	13	6/36 (6/36)	09	6/36 (6/24)	17
2	6/6	17	6/18 (6/9)	11	6/6	16	6/6	18
3	6/9 (6/9)	20	6/12 (6/12)	20	6/12 (6/9)	28	6/12 (6/9)	32*
4	6/12 (6/9)	24	6/18 (6/12)	14	6/18 (6/12)	12	6/18 (6/12)	14
5	CF	27	HM	12	CF	16	-	-
6	6/18 (6/18)	20	6/18 (6/12)	16	-	-	6/18 (6/12)	18
7	3/60	14	3/60	14	3/60	30	3/60	16

P: patient; BCVA: best-corrected visual acuity; IOP: intraocular pressure, HM: hand movement; CF; counting fingers
*Patient underwent trabeculectomy after the 3-month follow-up.

or eyes with significantly compromised visual acuity or poor visual potential.[5] The previous coagulation techniques have two major drawbacks: (i) the inability to deliver focused energy at a specific target organ site, which leads to surrounding tissue damage; and (ii) the unpredictable dose-effect relationship which prevents the titration of the treatment.

UCP is the latest technology to induce CPC, which is applied as a system of minitransducers. There is rapid sequential activation that produces six focused ultrasound beams, which stimulate six segments of linear CB tissue coagulation; these areas undergo focal thermal necrosis.[1] The focused beams allow controlled transmission through optically opaque ocular media[1] and minimise structural damage to adjacent tissue. This technique is faster, simpler, safer, and less invasive than previous methods such as TSCPC and ECP.[2-4]

These features enable UCP to be done as an outpatient procedure. UCP has been found to lower IOP by (i) necrosing CB epithelium, which decreases the AQH production,[1-3] and (ii) stimulating the unconventional drainage pathway via the suprachoroidal and trans-scleral portions of the uveoscleral pathway. Mastropasqua *et al.* observed anatomical changes in the microarchitecture of the sclera.[4] They found an increase in the intrascleral hyporeflective spaces with anterior segment optical coherence tomography and presence of microcysts on histology. Microcysts were initially described in the epithelial wall of the functioning bleb in trabeculectomy as an indicator of transconjunctival AQH filtration.[2,3,6,7]

Minimal surrounding tissue destruction and a smaller ocular surface involvement ensures a faster postoperative recovery.[3] Furthermore, the effect is not dependent on the degree of CB pigmentation.[1] There is less postoperative inflammation; even though the CB epithelium is remodelled, the blood-aqueous barrier remains intact.[4] Other advantages include a better safety profile with less complications, such as persistent hypotony and phthisis bulbi.

The TSCPC approach is essentially a 'blind' procedure, commonly reserved for patients who are unfit for filtering surgery or who refused filtration surgery.[9] There is disruptive tissue damage (microexplosions heard as audible "pops") and tissue ischaemia.[9] These can lead to complications such as anterior chamber inflammation (due to blood-aqueous barrier breakdown), hyphaema, hypotony, cataract progression, and rarely, sympathetic ophthalmia.[5,9] Although TSCPC has been used successfully to reduce IOP in patients with advanced glaucoma, the thermal damage to surrounding tissues and associated complications have resulted in TSCPC being used as a last resort in refractory glaucoma.[9]

Subsequently, transpupillary CPC allowed direct visualisation of the CB. Unfortunately, the clear visual axis and dilated pupil requirement along with unpredictable postoperative outcomes[10-12] made it unpopular amongst surgeons.

ECP, a newer CPC technique, enabled the CB epithelium to be accessed via a limbal or pars plana approach. The former is proposed in patients with pre-existing cataract and is planned to receive combined ECP and cataract removal with

intraocular lens implantation surgery. The pas plana approach is commonly reserved for pseudophakic patients and provides the most inclusive view of the ciliary processes. Anterior vitrectomy is performed in this approach. ECP is reported to be superior to TSCPC because: (i) it allows better visualisation of the ciliary processes; (ii) cyclodestruction can be delivered in a targeted manner, minimising collateral tissue damage; and (iii) the laser can be delivered in a highly titratable manner. To date, there are no long-term randomised prospective studies comparing ECP to TSCPC and trabeculectomy.[6,13] The risks of ECP combined with cataract surgery include hypotony, ciliary block glaucoma, and phthisis bulbi.[7,13] As ECP is an invasive procedure, it can be complicated by postoperative infections.[8] Variable postoperative refractive outcomes may occur with an ECP combined surgery.[8] More myopic shifts were reported in eyes with angle closure after a combined operation.[8,14] Postoperative inflammation has been suggested to be more intense after a combined ECP procedure than when performed alone.[8] Surgeons must also be extremely selective when performing a combined operation to minimise the risk of cystoid macular oedema.

To our knowledge, we are the first to conduct UCP in Malaysia. Prior to the procedure, all patients had an IOP of < 30 mmHg and were on at least three, if not maximum, topical antiglaucoma medications. No changes in visual acuity occurred postoperatively. At the 1-week and 1-month follow-up, an IOP reduction of 6–10 mmHg was noted in six patients. However, by the 3-month follow-up, the IOP had returned to preoperative levels. There may be several reasons for this. To ensure the safety of this procedure in our patients, we used a conservative power and duration of the shots, based on protocols defined in studies performed on Caucasian populations. As our cohort of patients are of an Asian origin, a higher power and longer duration may be required to achieve the same outcome as in those studies.

Several limitations were identified. This case series consists of small number of patients with preoperative IOP < 30 mmHg. Giannacare *et al.* postulated that UCP would be more effective in patients with a higher preoperative IOP. Therefore, a higher preoperative IOP value may result in a bigger IOP reduction. The study also reported that a quarter of patients did not respond to UCP treatment, and an estimated half required subsequent surgery to further control IOP.[15] It may be possible that the selected patients given this treatment were not responsive and may not be a true reflection of the efficacy of UCP. Aptel *et al.* stated that selected patients may be classified as early failures.[14,16] Hypothetical models of failure can be classified into early or late depending on the time of onset.[14,16] Early failures may reflect an insufficient circumferential amount of coagulated ciliary tissue during the procedure, whilst late failures imply possible re-epithelialisation of the ciliary processes with recovery of its function[15] or the gradual reduction of the stimulated unconventional outflow pathway.[14,16]

Insufficient treatment may be possible in our patients. Giannacare *et al* noted an improved efficacy with the 8-second treatment, commonly used in Europe.[15]

Although Deb-Joardar *et al.* found no significant difference between an 8- and 10-second protocol in a cohort of Indian patients, it may be useful for future research to consider a longer duration of 10 seconds instead of the 8 seconds of application in our patients.[2] This may aid in determining if the 10 second protocol is beneficial in our cohort. Furthermore, the number of sectors could be increased from six to eight.

Therefore, re-treatment in our patients may be necessary. Given the nature of UCP, minimal postoperative inflammation and quicker recovery further supports re-treatment. Several studies have sought to evaluate the efficacy and safety of repeated UCP treatments in patients with a previous failed first UCP procedure. Aptel *et al.* found that patients who underwent re-treatment demonstrated good IOP reduction at 1 and 3 months post-repeat procedure. However, only one of the four patients re-treated showed sustained IOP reduction at 1 year post-procedure.[16]

With the recent Covid-19 pandemic, clinics were severely reduced in patient load and many of our patients were reluctant to be reviewed. This made it difficult to follow up patients and to review IOP trends at the established follow-up time points. As mentioned previously, the first 3 postoperative months are critical to classify a patient as a success or failure. The team had to rely on patient claims regarding their compliance to the postoperative topical steroid medication.

Conclusion

UCP has been proven to be effective in IOP reduction with minimal postoperative side effects. The CB epithelium is remodelled while the blood-aqueous barrier remains intact. This not only reduces postoperative inflammation but supports the option of re-treatment, especially in patients where the desired IOP is yet to be achieved. Our series may not have reflected a positive outcome, but it remains a procedure that has been proven to be safer, less invasive, and with a faster recovery period compared to traditional cyclodestructive procedures. Further studies are required to determine the efficacy of UCP in the Asian population.

Declarations

Ethics approval and consent to participate
As a retrospective case series, this study did not require ethics approval.

Competing interests
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Case report
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Uveitis masquerade syndrome as an early manifestation of precursor B-cell acute lymphoblastic leukaemia: a case report

Dharshana **Thiagarajan**[1,2], Sangeetha **Tharmathurai**[1], Mae-Lynn Catherine **Bastion**[2], Norhafizah **Hamzah**[3], Rohanah **Alias**[1], Jamalia **Rahmat**[1]

[1]Department of Ophthalmology, Hospital Kuala Lumpur, Ministry of Health Malaysia, Kuala Lumpur, Malaysia; [2]Department of Ophthalmology, Faculty of Medicine, Hospital Canselor Tuanku Muhriz, Kuala Lumpur, Malaysia; [3]Department of Ophthalmology, Hospital Tuanku Azizah, Ministry of Health Malaysia, Kuala Lumpur, Malaysia

Abstract

Background: To report a case of paediatric precursor B-cell acute lymphoblastic leukaemia (ALL) presenting as uveitis masquerade syndrome.
Case presentation: A 3-year-old girl with neutropenic sepsis presented with poor fixation and right preferential gaze. Vision was light perception and counting fingers in right (OD) and left (OS) eyes with bilateral panuveitis, and OS Roth spots, retinal haemorrhages, and exudates. Vitreous biopsy was negative for organisms, malignant cells, and blasts. Bone marrow aspiration and trephine biopsy (BMAT) was inconclusive for leukaemia and orbital magnetic resonance imaging showed no infiltration. She improved with antimicrobials and steroids. However, during rehospitalization six months later for neutropenic sepsis, repeated BMAT showed 80% blasts confirming B-cell precursor ALL, requiring chemotherapy. OD vision remained poor with band keratopathy, keratoconjunctivitis sicca, seclusio pupillae, cataract, and vitreous haemorrhage. OS vision improved partially with a macular scar.
Conclusion: Paediatric precursor B-cell ALL may present as uveitis masquerade syndrome. Prompt diagnosis and treatment may increase survival and visual potential.

Correspondence: Dharshana Thiagarajan, MD, Department of Ophthalmology, Hospital Kuala Lumpur, Jalan Pahang, 50586 Kuala Lumpur, Malaysia.
E-mail: srk_dharshana@yahoo.com

Keywords: paediatric acute lymphoblastic leukaemia, uveitis, uveitis masquerade syndrome

Sindrom penyamaran uveitis sebagai manifestasi awal sel B pelopor leukemia limfoblastik akut laporan kes

Abstrak

Latar belakang: Melaporkan satu kes melibatkan kanak-kanak dengan sindrom penyamaran uveitis sebagai manifestasi awal sel B pelopor leukemia limfoblastik akut (ALL).
Persembahan kes: Seorang kanak-kanak perempuan berusia tiga tahun yang dijangkiti sepsis neutropenik mengalami tumpuan penglihatan yang lemah dan cenderung menglihat ke arah kanan. Penglihatan mata kanannya (OD) adalah hanya persepsi kepada cahaya, sementara mata kiri (OS) hanya dapat mengira jari. Hasil dari pemeriksaan, kedua-dua mata mendapat radang panuveitis serta terdapat bintik Roth, pendarahan retina, dan eksudat pada OS. Biopsi dari vitres tidak menunjukkan kehadiran sebarang organisma, sel barah mahupun blas. Pemeriksaan sum-sum tulang dan biopsi (BMAT) serta pengimejan resonan magnetik bahagian orbit tidak menunjukkan penyusupan leukemia. Rawatan dengan ubat antibiotik dan steroid adalah berkesan pada peringkat ini. Malangnya, kanak-kanak ini dimasukkan semula ke hospital enam bulan kemudian untuk sepsis neutropenia. Hasil dari BMAT yang kedua menunjukkan kehadiran 80% sel blas yang mengesahkan sel B pelopor ALL. Kanak-kanak ini dirawat dengan kemoterapi, malangnya penglihatan OD tidak dapat dipulihkan dengan kewujudan keratopati jalur, keratoconjunktivitis sicca, seklusio anak mata , katarak, dan pendarahan vitreous. Manakala penglihatan OS pulih sebahagiannya dengan parut di bahagian titik peka.
Kesimpulan: Sindrom penyamaran uveitis mungkin merupakan tanda awal sel B pelopor ALL di kalangan kanak-kanak. Pengesanan awal dan rawatan segera mungkin boleh meningkatkan jangka hidup dan potensi penglihatan.

Kata kekunci: leukemia limfoblastik akut (ALL), sindrom penyamaran uveitis, uveitis,

Introduction

Acute lymphoblastic leukaemia (ALL) is the commonest childhood malignancy of which precursor B-cell ALL is the commonest form.[1] The annual incidence is 35 per million children below 14 years.[2] Although ALL has a bimodal distribution affecting children and middle-aged adults, 80% of cases occur in children.[3] It is due to abnormal proliferation and malignant transformation of lymphoid progenitor cells in the bone marrow, peripheral blood, and extramedullary sites.[3] Patients present with constitutional symptoms and bone marrow failure due to leukemic infiltration.[1] Ocular infiltration in leukaemia accounts for only 5% of paediatric uveitis cases.[4] Ocular manifestation as an initial presenting feature of ALL, especially those involving the anterior segment as well, is extremely rare with only three cases previously described to our knowledge.[1] We now present a case of a child with bilateral uveitis as a presenting feature of precursor B-cell ALL.

Case presentation

A 3-year-old girl with no comorbidities presented with 1 week of fever, cough, and lethargy associated with 1 day of vomiting and reduced consciousness. On examination, she was in septic shock and had hepatosplenomegaly, skin bruises, and generalized lymphadenopathy. She required inotropes and intubation for airway protection. Full blood picture (FBP) showed severe anaemia (haemoglobin 2.1 g/dL) with leucocytosis (13.8 K/μL), neutropenia (absolute neutrophil count 0.73 K/μL), and thrombocytopenia (5 K/μL) with an absence of blasts. She was treated with broad-spectrum antibiotics and antifungals following a diagnosis of febrile neutropenic bicytopenia with liver and splenic microabscesses. Blood, urine, tracheal aspirate, and cerebrospinal fluid cultures were negative. She improved hemodynamically with treatment. However, she required intravenous dexamethasone 9 mg and nebulized budesonide 1 mg BD for 1 day for stridor after extubation. Subsequently, she underwent a bone marrow aspiration and trephine (BMAT) biopsy that showed a borderline B-cell precursor blast count of 4–5%, which was insufficient to diagnose leukaemia. BMAT was not repeated as she improved clinically and repeated FBP showed normalizing counts.

Three weeks later, she was referred for poor fixation with a right preferential gaze. There was no eye redness, swelling, discharge, or pain. She had no previous visual problems. Vision was light perception in the right eye (OD) and counting fingers in the left eye (OS). Red reflex was poor bilaterally (OU) without leukocoria or relative afferent pupillary defect. There were fine keratic precipitates with occasional anterior chamber cells without hypopyon OU. Fundus OD showed dense vitritis whereas OS showed inferior vitritis, submacular haemorrhage, Roth spots, and retinal haemorrhages with exudates. There was no vasculitis or optic

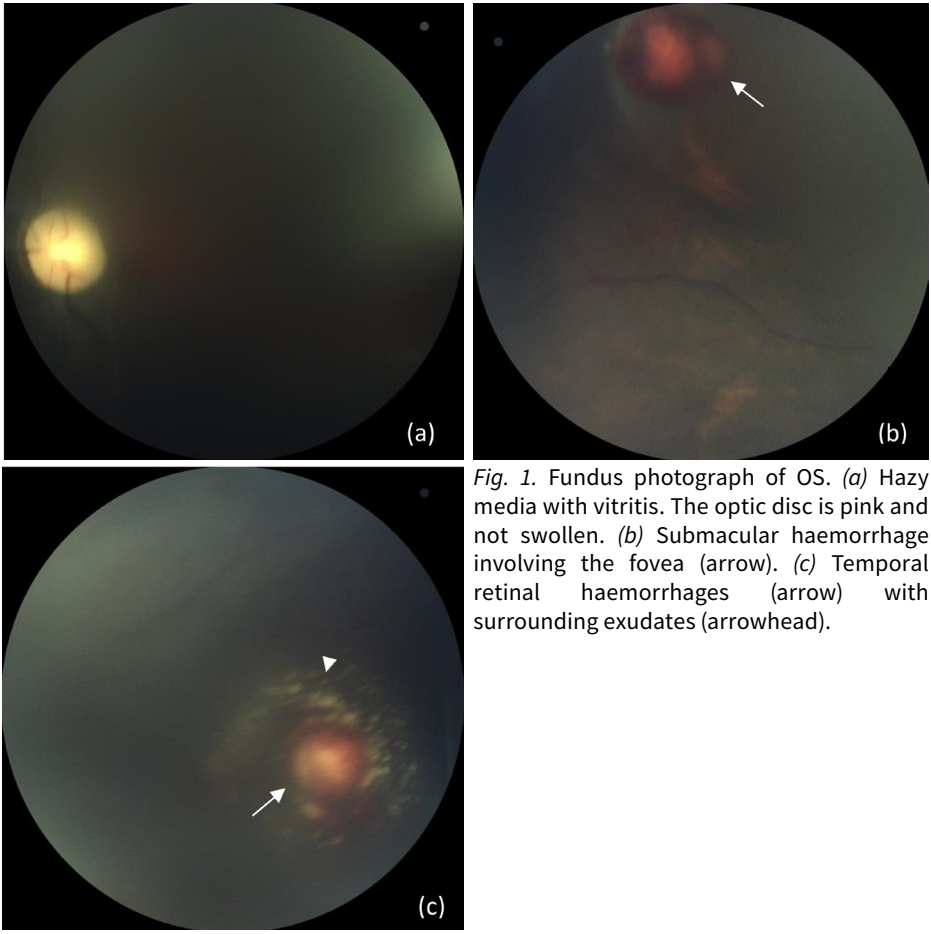

Fig. 1. Fundus photograph of OS. *(a)* Hazy media with vitritis. The optic disc is pink and not swollen. *(b)* Submacular haemorrhage involving the fovea (arrow). *(c)* Temporal retinal haemorrhages (arrow) with surrounding exudates (arrowhead).

disc swelling (Fig. 1). The intraocular pressure (IOP) was normal bilaterally. B-scan OD showed a flat retina with vitritis without loculation. The child was started on intensive empirical topical antibiotics and steroids. Magnetic resonance imaging (MRI) of the orbits showed hyperintense irregular intraocular lesions at the posterior aspect of both globes, suggestive of haemorrhage. However, there were no enhancing lesions that might indicate leukemic infiltration.

At this juncture, in the presence of dense vitritis OD, there was a diagnostic dilemma between leukemic infiltration and endogenous endophthalmitis secondary to immunosuppression, or both. Hence, she underwent right 23-G diagnostic and therapeutic pars plana vitrectomy. Intraoperatively, there was dense vitreous haemorrhage with pre- and submacular haemorrhage. Vitreous biopsy showed few pus cells with no bacteria or fungi on direct smear. Cytology

showed neutrophils admixed with a few atypical lymphocytes, which were likely reactive, consistent with a chronic inflammatory process. However, no malignant cells or blasts were seen. Vitreous culture and cytomegalovirus polymerase chain reaction (PCR) were negative. In view of normalizing FBP, clinical improvement after antimicrobial treatment, and inconclusive ocular investigations for malignancy, her uveitis was attributed to infective endogenous endophthalmitis, likely related to the liver and splenic abscesses.

Two months later, her vision remained light perception OD, whereas OS improved to 3/60. Fundus OD showed persistent diffuse organized vitreous haemorrhage with a flat retina on B-scan. Fundus OS showed a vitreous opacity overlying the macula with retinal fibrosis at the inferotemporal arcade without retinal traction and resolution of retinal haemorrhages.

Six months after the initial presentation, she was readmitted for 2 days of fever, cough, lethargy, and poor oral intake. The FBP showed bicytopenia and leucocytosis with 65% blasts. A repeated BMAT showed 80% blasts consistent with B-cell precursor ALL. Bone marrow cytogenetics revealed a t(12; 21)(p13; q22) translocation and *ETV6-RUNX1* gene fusion. There was no central nervous system involvement. Although her vision had improved to 6/9.5 OS, OD vision remained light perception only. OD examination showed a quiet anterior chamber, seclusio pupillae, white cataract, and contracting vitreous haemorrhage via B-scan. OS examination was unremarkable except for a vitreous band overlying the inferior macula. The OD was treated with topical steroid and cycloplegic agents.

The patient responded well to chemotherapy. Unfortunately, she developed band keratopathy and keratoconjunctivitis sicca OD and was given lubricants. She also developed transient raised IOP OU, which responded to a short course of single IOP-lowering agent and discontinuation of topical steroid. During the last review, OD vision remained status quo with light perception, whereas OS vision was 6/24 with a macular scar.

Discussion

ALL in children occurs typically between the ages of 2 and 5 years.[5] This child fits the age group, being 4 years old at the point of diagnosis. The incidence of ocular manifestations in patients with leukaemia varies significantly from 9% to 90% due to the transient nature of findings that vary with the course of the disease.[5] However, ocular manifestations are commoner in adults and in myeloid leukaemia than in lymphoid leukaemia.[5]

Ocular manifestations of leukaemia are divided into primary (direct infiltration) and secondary (indirect involvement). Direct infiltration, including uveal, retinal, orbital, and optic nerve infiltration, is rare and may present as uveitis, proptosis, and optic disc swelling.[4,5] Ocular infiltration occurs most frequently in the choroid

due to its high vascularity. Uveitis due to direct infiltration of ocular tissues by leukemic cells is termed uveitis masquerade syndrome.[6] The vitritis present in this patient could be due to uveal infiltration by leukemic cells causing intense inflammation. However, there was no radiological or cytological evidence of orbital, optic nerve, or vitreous infiltration.

Indirect ocular involvement may be due to haematological abnormalities (thrombocytopenia, anaemia, and hyperviscosity) that lead to leukemic retinopathy. This is the commonest ocular finding in ALL and may manifest as retinal and vitreous haemorrhage, Roth spots, and vascular occlusion.[4,5] Ocular toxicity due to chemotherapy and the effects of immunosuppression may lead to secondary ocular manifestations such as infections, keratoconjunctivitis sicca, conjunctivitis, corneal opacity, glaucoma, and cataract.[4,5]

Unfortunately, this child developed many of the ocular manifestations mentioned above. She displayed leukemic retinopathy evidenced by the presence of vitreous and retinal haemorrhages, Roth spots, and retinal exudates.[5] The cause of IOP elevation was likely multifactorial, including steroid and chemotherapy administration. Leukemic infiltration of the trabecular meshwork by blasts should be considered as well. Severe inflammation as a cause is unlikely as both anterior chambers were quiet. She developed white cataract, keratoconjunctivitis sicca, and band keratopathy, which were likely sequelae of intense, prolonged ocular inflammation and chemotherapy.[5] The cataract could also be attributed to the vitrectomy itself.

The diagnosis of uveitis masquerade syndromes was initially considered given her suspicious FBP and BMAT findings in addition to the unresolved bilateral vitritis. Furthermore, infection, as in her case, is a common presentation in the prodromal phase of leukaemia, where an initial BMAT may be negative in the presence of cytopenia.[7] However, the vitreous tap and biopsy were inconclusive for malignant cells and did not yield any organisms. We postulate that the negative cytology results may be either due to the masking effect of topical and systemic steroids administered before sampling, or due to an insufficient vitreous sample or cell lysis caused by the vitreous cutter. Hence, the vitreous sample should be taken undiluted before turning the vitrectomy infusion on and with a low cut-rate setting. Her FBP had also normalized by then, leading to the possibility of spontaneous remission before vitreous sampling. Repeated vitreous sampling should be considered after discontinuation of topical steroids for 3 weeks in the interest of a conclusive diagnosis in the absence of one from BMAT, such as in this case.[8]

The poor ocular prognosis OD of this patient is multifactorial. Chronic severe intraocular inflammation, combined with leukemic retinopathy, vitrectomy sequelae, and toxicity of steroids and chemotherapy led to irreversible damage to the ocular structures and amblyopia. Hence, visual rehabilitation of the fellow eye is essential.

This patient had a t(12; 21)(p13; q22) translocation with *ETV6-RUNX1* gene fusion, the commonest molecular genetic aberration in childhood ALL, occurring in 25% of cases.[9] Traditionally, patients with specific orbital or ocular lesions had poor prognosis, and short overall survival since eye involvement often denoted leukemic relapse.[10] On the contrary, *ETV6-RUNX1* gene fusion has been associated with relatively low relapse rates and a favourable prognosis.[9]

Conclusion

A high index of suspicion for uveitis masquerade syndrome is required in cases of severe paediatric uveitis unresponsive to steroids. Early diagnosis may increase survival rates and visual prognosis in children with ALL. Children with persistent uveitis, whose investigations are inconclusive, should be closely monitored for new clinical manifestations which may aid the diagnosis.

Declarations

Consent for publication
The guardian provided informed consent for the use of the clinical images and information contained in this case report.

Competing interests
None to declare.

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None to declare.

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A perspective on neural tissue measurements in glaucoma

Shiivaa Manjare **Birapadian**, Norshamshiah **Md Din**

Department of Ophthalmology, Universiti Kebangsaan Malaysia Medical Centre (UKMMC), Kuala Lumpur, Malaysia

Given the present advancement in the management of glaucoma, in comparison to retinal nerve fibre layer (RNFL), neural tissue parameters are much more reliable and accurate in discriminating glaucomatous and non-glaucomatous changes. Pertaining to the article titled *Retinal nerve fibre layer thickness measured by spectral domain optical coherence tomography amongst early primary open-angle glaucoma patients at Hospital Melaka*, published in Malaysian Journal of Ophthalmology issue 2-3, it was concluded that optical coherence tomography (OCT) of the RNFL is not suitable to be used as a diagnostic tool alone to detect early glaucomatous changes.

Here we would like to suggest the use of neural tissue parameters such as Bruch's membrane opening-minimum rim width (BMO-MRW) and prelaminar neural tissue thickness (PNTT) to assess these changes reliably (Fig. 1). As Bruch's membrane ends around the optic nerve head (ONH), it forms Bruch's membrane opening (BMO), *i.e.*, an aperture for the passage of retinal ganglion cells (RGC) as they exit

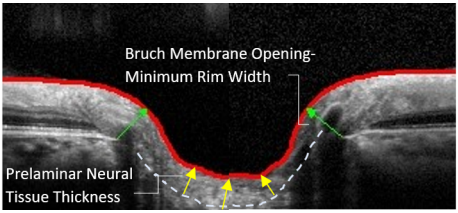

Fig. 1. Bruch's membrane opening-minimum rim width (green arrow) and prelaminar neural tissue thickness (yellow arrow).

Correspondence: Associate Prof Dr Norshamshiah Md Din (PhD), Department of Ophthalmology, Universiti Kebangsaan Malaysia, Jalan Yaacob Latif, Bandar Tun Razak, 56000 Cheras, Kuala Lumpur, Malaysia.
E-mail: shamsiahdr@hotmail.com

to pass through the choroidal and scleral openings to leave the orbit. Among the three openings, BMO is said to remain stable over time and is a more reliable area to be monitored in glaucoma compared to conventional ONH margin.[1] The prelaminar neural tissue, on the other hand, consists of neural components such as astrocytes and RGC axons with connective tissue (CT), including capillaries and extracellular matrix. [2,3]

In patients with glaucoma, increased intraocular pressure (IOP) results in stretch of Bruch's membrane, damaging the RGCs and astrocytes lining the ONH. The severity of this damage is dependent on both the properties of the peripapillary sclera and the dynamic changes within the lamina cribrosa (LC).[2] Due to alteration of the CT matrix and remodelling of the ONH, there is a reduction in blood supply to the axons and RGC death causing LC thinning, deepening, and widening.[2] Measurement of the RNFL in glaucoma may be affected by peripapillary atrophy, myopia, ONH drusen, congenital disc anomalies, oxidative damage, aging, or even inflammatory cascade, thus providing inaccurate readings.[3,4]

BMO-MRW is used to assess the neuroretinal rim thickness, and measures the shortest distance from the BMO to the internal limiting membrane.[4,5] Precise measurement of the BMO area highly correlates with visual field changes compared to RNFL.[5] Additionally, it may return to the previous value in subjects if the IOP is lowered, since it is dependent on the strain on RGC and acts as an anatomical measure of ONH compliance.[4]

PNTT on the other hand, can be affected by IOP, cup-to-disc ratio, depth of cup, and disc area.[3] It is measured from the anterior surface of the prelaminar neural tissue to the anterior border of the LC,[5] and is evaluated by quantifying the perpendicular distance between the anterior lamina border and BMO.[3] In a study conducted by Jung *et.al.*, three measurements for PNTT were obtained manually; central, nasal, and temporal, and the average was derived. Cup-to-disc ratio and glaucoma progression directly affect the thickness of the neural layer and results in reduction of PNTT.[3]

In conclusion, most dynamic alterations occur in the early stages of glaucoma; neural tissue measurements allow detection of the minute changes and effectively produce accurate data at different severities of glaucoma. These features make neural tissue parametersmore reliable than the conventional RNFL OCT in detecting early changes that may occur in a glaucomatous ONH.

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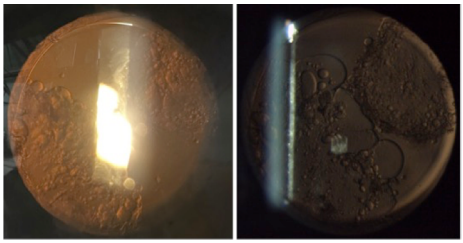
Growing pearls in the eye

Siti Farhah 'Adilah Binti Basiron, Adeline **Khaw** Mae Li, **Ch'ng** Tun Wang

Department of Ophthalmology, Hospital Raja Permaisuri Bainun, Ipoh, Perak, Malaysia

Clinical context

An 18-year-old female with underlying idiopathic intermediate uveitis developed cataract. She had an uneventful lens aspiration and intraocular lens implantation (IOL) surgery. Two years after the surgery, her vision deteriorated due to posterior capsule opacity (PCO). The rapid progression of PCO from Figure 1a to 1b occurred over a period of 2 weeks.



Question 1
What is the pathophysiology of the condition seen in Figure 1?

Question 2
What are the preventive measures for PCO formation?

Answer 1
The wound-healing response post-cataract surgery triggers the residual lens epithelial cells (LEC) to proliferate and migrate across the posterior capsule, where they undergo lens fibre regeneration and epithelial-to-mesenchymal transition that gives rise to Elschnig pearls.[1]

Correspondence: Siti Farhah 'Adilah Binti Basiron, MD, Department of Ophthalmology, Hospital Raja Permaisuri Bainun, Jalan Raja Ashman Shah, 30450 Ipoh, Perak, Malaysia.
E-mail: sitifarhahadilah@gmail.com

Answer 2

The preventive measures for PCO formation are:

- Surgical technique: Thorough cortical removal by polishing the lens capsule.[2]
- Pre- and post-cataract operation control of inflammation: Patients with concomitant uveitis are prone to an intense inflammatory response due to the impaired blood-aqueous barrier. The resulting chemical mediators stimulate LECs mitotic activity, which eventually leads to the formation of PCO.[3]
- IOL design and material:
  - IOL design with a square, truncated optic edge acts as a mechanical barrier, hindering LEC migration across the posterior capsule.[4]
  - Hydrophobic IOLs have a lower rate of PCO formation compared to hydrophilic IOLs.[5]

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