Avoidable blindness: a review on its leading causes worldwide

Cegueira evitável: uma revisão sobre suas principais causas no mundo

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ABSTRACT
Globally, blindness affects more than 7 billion people. In addition to impacting quality of life, it doubles the risk of mortality and has a significant impact on the economy, both in developed and developing countries. However, at least two-thirds of the causes of this onerous outcome are preventable. Blindness can be avoided in two forms: prevention or treatment of its etiologies. Cataract or glaucoma, for instance, are not preventable diseases, but if they are treated, blindness is prevented or reversed. Given these facts, the relevance of establishing blindness prevention strategies is evident, as they effectively are capable of transforming the situation. This article addresses the subject of avoidable blindness reviewing its leading causes worldwide, in addition to presenting a cause that has exemplary been eliminated from one country. Against the expected, the number of blind people has been increasing globally in the last decades, which is hypothesized to be related with the increase in life expectancy. Undoubtedly, an accurate knowledge dissemination of the main causes of blindness to the population, associated with investment in affordable diagnostic and surgical technology must be driven by and put into practice by governments and scientific organizations in order to reduce such large and growing numbers of this avoidable outcome.

Keywords: blindness, cataract, glaucoma, trachoma, onchocerciasis.

RESUMO
Mais de 7 bilhões de pessoas no mundo são afetadas pela cegueira. Além de impactar a qualidade de vida, ela dobra o risco de mortalidade e tem um significativo impacto na economia, tanto em países desenvolvidos quanto subdesenvolvidos. Entretanto, pelo menos dois terços das causas desse desfecho oneroso são preveníveis. A cegueira pode ser evitada de duas formas: com prevenção ou tratamento de suas etiologias. Catarata e glaucoma, por exemplo, não são doenças preveníveis; se tratadas, porém, a cegueira é evitada ou revertida. Diante desses fatos, a relevância de estabelecer estratégias de prevenção da cegueira é evidente, visto que as mesmas tem, efetivamente, capacidade de transformar a situação. Este artigo aborda o assunto da cegueira evitável revisando suas principais causas no mundo, além de apresentar uma causa que foi exemplarmente eliminada de um país. Ao contrário do esperado, o número de pessoas cegas tem aumentado globalmente nas últimas décadas, o que sustenta-se estar relacionado com um aumento na expectativa de vida. Sem dúvidas, uma disseminação de conhecimento adequeda à população sobre as principais causas de cegueira, associada com investimento em tecnologias diagnósticas e cirúrgicas acessíveis devem ser impulsionadas e colocadas em prática por governos e organizações científicas no intuito de reduzir números tão grandes e crescentes desse desfecho evitável.

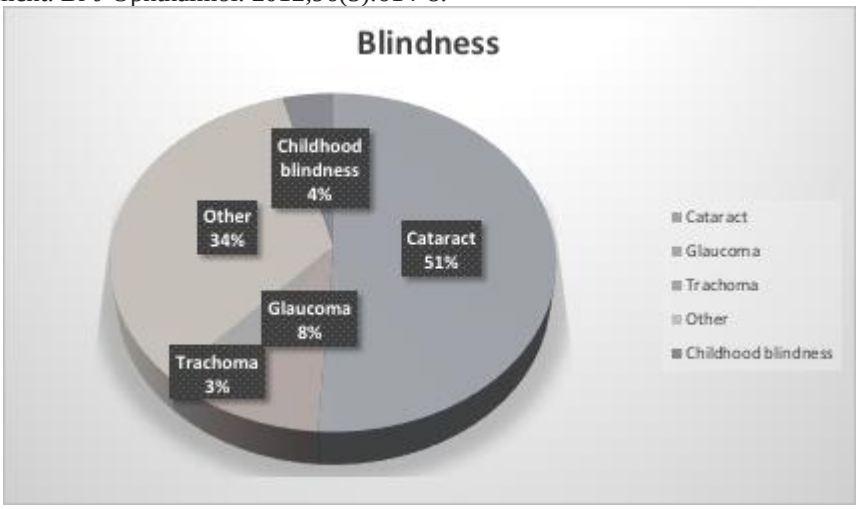
Palavras-chave: cegueira, catarata, glaucoma, tracoma, oncocercose.

1 INTRODUCTION

Recent research indicates that blindness is preventable in more than two thirds of cases[1]. This is the case because its main causes are either treatable before reaching such an outcome or even preventable. Cataract, glaucoma, uncorrected refractive errors, trachoma, age-related macular degeneration and diabetic retinopathy are pointed out by current research as the leading etiologies of blindness in the world[2]. Among the preventable causes, glaucoma, trachoma and cataract are the ones that stand out[3].

Among those three, only one can be prevented, which is trachoma. In order to stop the natural progression of the other two diseases before they cause blindness, there are two factors required. First, socio-educational orientation, whether from the government or from independent entities, so that the population can be aware of the importance of screening exams. Second, it is essential that there is technology available and affordable to actually run such exams and to perform surgery.

Figure 1: Leading causes of blindness in the world. Numerical data from: Mariotti A, Pascolini D. Global estimates of visual impairment. Br J Ophthalmol. 2012;96(5):614-8.



Besides these diseases, we bring to light the case of onchocerciasis, a very neglected cause of avoidable - but irreversible - blindness that in 2013 it was for the first time eliminated in a country, Colombia. This was proof that with the right efforts it can be eliminated from other endemic countries in the world, mainly located in Latin America and Africa[4]. Currently, there are 45 million blind people in the world, 90% of whom are in developing countries[5]. Under these circumstances, it is visible the necessity of a joint effort by these countries to raise awareness among the population, in addition to which constant investments in diagnostic infrastructure should be made.

The aim of the present study is to synthesize information obtained in research on blindness worldwide, clarifying the development, prognosis and treatment of important preventable causes: cataracts, glaucoma, trachoma and onchocerciasis. The aim is to illuminate the fact that social awareness, technological innovation and government economic support are at the heart of the solutions for achieving a reduction in the number of blind people in the world, especially in developing countries.

2 BLINDNESS

The definition of blindness by the World Health Organization is visual acuity worse than 3/60[6]. It is largely acknowledged that visual impairment has a great impact on the quality of life, but it also importantly impacts in the economy and represents an increased risk of mortality[7]. A well conducted study designed to estimate the annual loss of productivity from blindness came to the result that the "cost of blindness" (COB) in the United States is $ 2.5 billion annually. This makes it clear that even the global economy would benefit from more investments in the eye health sector.

In addition, there is evidence that even mild visual loss increases the risk of mortality by more than 2x[8]. Even with those data available, blindness has steadily increased worldwide in the last decades[9]. From 1990 to 2015, there was an increase of 17.6% of blind people[7], and the trend was expected to increase significantly until this year (data still not available). One of the causes pointed out for its growth is the expansion of life expectancy, since the elevation of the average age of the population in many countries leads to the onset of more diseases related to age, for instance, a very much prevalent cause of blindness: cataract[10].

3 CATARACT

In developed countries, there are 20 million people whose blindness is attributable to bilateral cataracts, cataract being the leading cause of blindness in the world[11]. On the African and Asian continents, there is at least 1 person per 1000, yearly, who is blinded by cataract. This disease is distributed differently between men and women, being slightly more prevalent in females. As for demographic distribution, subSaharan Africa is the region that has the highest prevalence of blindness caused by cataracts in adults[12].

It is significantly more commonly related to aging. However, there are some diseases that are risk factors for cataract, such as diabetes or uveitis. In addition, it can also be congenital[13]. Some hypotheses about congenital cataracts are still being studied, such as its relationship with maternal nutritional deficiencies[14]. And there is evidence of its relation with

congenital infections during pregnancy, such as rubella, toxoplasmosis, herpes, syphilis and cytomegalovirus[15].

The lens is composed by a delicate capsule, which is supported by zonules anteriorly and posteriorly, and it is filled with fibers[16]. Most cataracts are caused by the physiological aging of the lens, and its consequent opacification. This is due to a gradual accumulation of yellowish pigment in the lens over the years, which impairs the passage of light rays towards the retina, in addition to structural changes that are expected to occur in the organization of the lens fibers with the advancement of age[17].

Although it is not a preventable disease, its worst consequence - blindness - is avoidable. With cataract surgery, highly positive results are achieved in terms of visual recovery. For instance, after surgery, it is reported that up to 90% of patients achieve sufficient vision to acquire driving permission in most countries[18]. Thus, ensuring access to this surgery, which involves intraocular lens implants, should be a priority for governments around the world, for the cure of cataract re-establishes a fundamental capacity for the working life.

Cataract surgery is one of the most performed surgeries in the global population. In addition to the fact that the number of executions of this surgery in recent years have grown consistently, its outcomes have improved each year, with the continuous advent of technological innovations[19]. The two main obstacles to conducting the cataract surgery are the lack of awareness on the subject by the patients (thus the absence of diagnosis) and the high cost of the procedure. In underdeveloped countries, such as Nigeria, the average cost of the surgery is US $ 51. To 70% of the local population, which seems affordable, but the reality is that this cost is equal to 50 working days[20]. In Latin American countries, the economic situation is reported to be also still a barrier[21].

One of the limiting aspects in the treatment of cataracts in the world is the number of ophthalmologists able to operate. In former socialist economies the number of ophthalmologists who do not operate cataracts reaches 85% and, according to the literature, in Latin American countries, the percentage is also significantly high[12].

In addition, some patients may have limitations on outcomes due to underlying diseases, such as diabetes. After cataract extraction, patients with diabetes may experience poor visual acuity. There is ample evidence that diabetic patients develop cataracts earlier and more frequently than the non-diabetic population. Under 65, cataracts are up to 4 times more prevalent in diabetic patients. While over 65, it has twice the prevalence[19].

Nevertheless, some examples of strategies implemented in countries with high rates of blindness by cataract in the aim of reverting this scenario serve as an example to foster support

for cataract surgery. Two largely populous countries, China and India, through government programs, have managed to boost the number of patients who underwent cataract surgery in recent years, especially in the poorest sections of the population. In China, the strategy was to carry out a project entitled Free Cataract Surgeries for a Million Poor Patients. And in India, government investment in eye care has also created circumstances for improvement[12].

4 GLAUCOMA

Blindness due to glaucoma affects a population of approximately 8.4 million people in the world today. In many studies, this condition is highlighted as the second general leading cause of blindness worldwide[22]. One of the most important features in respect to this disease is its quiet development. It is reported that in developed countries, less than 50% of people who have glaucoma are aware of the disease, while in developing countries, this rate is even lower[23]. Studies suggest that 20% of glaucoma patients develop blindness, the two main characteristics of these cases being: late diagnosis/referral and disease progression even with controlled intraocular pressure[24].

Like cataract, glaucoma is also not a preventable disease. Unlike cataract, however, blindness caused by glaucoma is irreversible. In fact, this is the leading cause of irreversible blindness in the world[25]. This is because the damage is located at the nerve, which is not replaceable as it is the lens and it does not regenerate itself after injury. However, there is a possibility to avoid visual loss and blindness if the diagnosis is made in its early stages. Thus, there is great relevance of sharing information with the general population in order to motivate the reach for screening exams. Even more so because glaucoma is a disease in which structural changes occur primarily than functional changes, so the damage is happening before any symptom[26].

The term glaucoma, in fact, encompasses a set of possible etiologies for neurophthalmological conditions, and not a single entity. In order to facilitate epidemiological studies, there is a well shared proposed definition that considers the disease as an optical neuropathy identified by specific structural changes in the optic disc associated with functional deficits perceived in computerized campimetry[22].

It is important to note that increased intraocular pressure (IOP) is not actually a defining element of glaucoma, although it is the most important risk factor for glaucoma. According to studies, the first site of neurological injury is the optic nerve[27]. Since the damage to the optic nerve is permanent, no treatment can restore the portion of the vision that has already been lost.

In effect, a possible definition of glaucoma should incorporate the notion of progressive and irreversible injury to the optic nerve corresponding to loss of visual field, in addition to being frequently associated with elevated intraocular pressure. However, there are at least two main types of glaucoma: angle closure glaucoma (ACG) and open angle glaucoma (OAG). The first group includes patients with eye pain and acute visual loss. In the second group, there are patients who often do not have any symptoms[26].

Treatment for glaucoma can be pharmacological as well as surgical. The first approach is usually topical, made with eye drops with the aim of reducing intraocular pressure (IOP). The eye drops used for glaucoma are classified in five classes: prostaglandin analogues, beta-blockers, diuretics, cholinergic agonists, and alpha agonists. It is considered often as first line of treatment the use of a prostaglandin analogue or a beta-blocker[28].

There is also the possibility of injecting medications. However, in some cases the approach with drugs does not achieve the goal of reducing intraocular pressure. Laser therapies such as laser trabeculoplasty are indicated in these circumstances, and their use has greatly increased in recent years[28]. Surgery is mostly indicated when drug therapy or laser therapy are not effective as expected. In this case, trabeculectomy or other types of surgery such as "microinvasive glaucoma surgery" (MIGS) are recommended.

5 TRACHOMA

Trachoma is a disease caused by recurrent infection by Chlamydia trachomatis. In comparison with the conditions mentioned above, this is the only preventable one[29]. Nevertheless, the disease remains a public health problem in developing countries such as Brazil, as well as in different parts of the African and Asian continents.

A study published in june of 2013 points out that the majority of patients with trachoma are located in rural areas, with a prevalence of about 5% in children up to 9 years old[30]. According to the World Health Organization, trachoma is responsible for 1% of the causes of blindness globally. It is estimated that 5.9 million people in the world are blinded by trachomatous sequelae and it is believed that it is due to the precarious access to the public health system and the poor sanitation and hygiene in some rural areas[31].

Traditionally, the clinical presentation is characterized by entropion, dry eyes and trichiasis, which happens due to damage to the tear film and glandular attachments. In advanced stages, it can lead to diffuse corneal opacity, caused by glandular damage to the cornea and the predisposition to infections by other microorganisms, especially Haemophilus sp, Streptococcus sp and fungi Trachoma Control Manual[32].

The classification of trachoma by the World Health Organization is divided in 5 stages, organized within an increasing order of complexity: Follicular Inflammatory Trachoma; Intense Inflammatory Trachoma; Scar Trachoma; Trachomatous Trichiasis; and Corneal Opacity. It is the recurrence or persistence of the infection that determines the evolution of the condition, with the clinical characteristics of each stage.

It turns out that these factors activate a healing immunopathological response, known as a trachomatous scar. With the increase of the scar, the eyelid folds inwards (entropion), creating a contact between the lashes and the corneal surface, called trachomatous trichiasis[33]. The association between trichiasis, conjunctival scars and central leukoma leads to blindness secondary to trachoma[34].

The ophthalmic clinical examination is the basis for this diagnostic staging, and the eyelids, cornea, and central area of the everted tarsal conjunctiva should be evaluated. In case of long-term conjunctivitis, especially in children, associated with symptoms such as mild photophobia, small amount of eye discharge and a foreign body sensation in the eyes, should raise the suspicion of trachoma and be conducted for detailed ophthalmological evaluation[35].

Regarding laboratory tests, although cell culture is the gold standard method for detecting Chlamydia infections, due to its high cost and level of complexity, it ends up not being used routinely. Other techniques such as direct immunofluorescence, nucleic acid amplification and immunoenzymatic assay are also available, but in general they are used for the purpose of detecting the circulation of the bacteria in a group or community, not individually[36].

The diagnosis of a case should incite a search for cases in each patient's contacts, since the transmission of the disease occurs not only from direct contact with the eyes, but also from contaminated objects, such as towels or sheets. Thus, cases typically arise in groups, such as members of the same school or family.

In respect to prevention, the "SAFE" strategy is preconized, which stands for: surgery, antibiotics, facial cleansing and environmental improvements[29]. This means that access to basic sanitation and health facilities play a crucial role in reducing cases of the disease. For the treatment of sequelae, tectonic transplantation is indicated, which aims to restore ocular integrity, despite not being completely effective in restoring vision and being associated with postoperative complications[37].

Since the disease has high rates of transmissibility, the simultaneous treatment of several individuals from the same community is an important strategy for reducing the circulation of the bacteria and promoting public health. Azithromycin orally in a single dose has been indicated for the treatment of communities in which trachoma is endemic, with the advantage

of comfort in comparison with the treatment with topical tetracycline for six weeks, another therapeutic modality.

However, a recent study carried out in Nigeria revealed an increase in resistance rates to Azithromycin and other macrolide class antibiotics, when used twice a year, for four years, in children, in order to reduce infant mortality, a practice that also occurs in other African communities. This data threatens the effectiveness of early treatment of trachoma, as the areas of worst socioeconomic development are the most affected by the disease and also those that most benefit from treatment with a single dose of antibiotic[38].

Another important strategy is the promotion of school control for the diagnosis and management of trachoma. This includes education on vision and ophthalmological assessment of blind children[6]. Such measures are important because, in addition to the fact that children are the most affected population by the disease, it is assumed that the burden of bacterial infection is a relevant factor in leading to blindness, and this aspect is more relevant in children, probably because they do not have established acquired immunity[39].

6 ONCHOCERCIASIS

Onchocerciasis, also known popularly by the name of "river blindness", is a systemic disease caused by infection with Onchocerca volvulus. Its clinical presentation is mainly represented by dermal tumors, itching and eye injuries[40]. In 2017, more than 20 million people were infected with this parasite[41], leading 0.3 million people with blindness. The infection is endemic in African countries and some countries in Latin America[1].

The parasite's vector is a black fly that reproduces in streams, giving the popular name of the disease. When the fly enters in contact with a human, the nematode enters the bloodstream and contaminates him[42].

The diagnosis is made by clinical evaluation, biopsy of skin nodules, immunobiological tests and hypersensitivity or demonstration of the presence of the intraocular worm. The clinical features occur by the deposition of dead microfilariae, associated with the cellular response to them (eosinophils, neutrophil macrophages)[43].

Among the clinical features, it can be mentioned, in addition to the presence of tumors, also itching, dermatitis and skin discoloration caused by dermal atrophy. The presence of microfilariae in musculoskeletal tissues can lead to pain morbidities and atrophy. At the eye level, the infection can generate lesions in all tissues, and may present as recurrent conjunctivitis, photophobia, chronic uveitis, glaucoma, keratitis and progressive visual loss, the main consequence of which is blindness[44],[45].

Eye injuries are classified according to its locations, causing anterior or posterior involvement. When they affect the anterior chamber, they appear as punctate keratitis. It is believed that the injuries are caused due to the stimulation of bacteria Wolbachia sp., stimulated by the presence of dead microfilariae in the eye, important for the survival of the adult worm and for embryogenesis. When the insult is repetitive, it generates opacification and scarring of the cornea, known as sclerosing keratitis, related to visual loss[43].

In the posterior segment, chronic chorioretinitis, inflammation, scarring, optic atrophy and glaucoma are some consequences that can occur. They are difficult to distinguish from end-stage lesions of the optic nerve, retina and choroid. It is not yet well established whether these posterior lesions occur due to an autoimmune response, persistence of the microfilariae or an inflammatory state caused by a response between the parasitic antigen and the human retinal pathogen in the optic nerve and retinal neuronal layers. As it has an autoimmune characteristic, onchocercal chorioretinitis does not respond to treatment and the best alternative to fight it is prevention[46].

It is established that an effective therapeutic is doxycycline 100 to 200mg with a 6-week course to fight the main bacteria that causes intraocular comorbidities[47]. In addition, the use of ivermectin appears to temporarily sterilize adult worms. Thus, its use periodically, in addition to reducing transmission, prevents the appearance of new lesions in the eye and skin[45].

Prevention seems to be one of the best strategies to fight the disease. Among the strategies are the distribution of antiparasitic drugs (ivermectin) to endemic communities, establishing surveillance and monitoring mechanisms for new cases of blindness and implementing disease control programs (WHO), aiming to reduce the incidence of preventable blindness. It is believed that more than 1 million cases of blindness can be prevented with this protocol[1]. In addition, the use of repellents and protective clothing and the abolition of vector habitat are strategies described[46].

New studies and technologies are being developed in order to create a vaccine capable of developing protective immunity against this disease[48]. The prognosis of onchocerciasis, when discovered and treated early, is good. However, injuries to optic vascularization, neuronal atrophy and blindness are irreversible injuries if left untreated when evolving.

7 FUTURE PROSPECTS

Blindness affects a huge population worldwide, alters the risk of mortality, and has a significant socioeconomic impact. Fortunately, more than half of the causes of blindness are preventable. Therefore, establishing screening strategies and disseminating information on the

main etiologies of blindness seems to be the best possible alternative to combat it. In effect, this has been achieved in one country with regard to onchocerciasis. However, we are not close to the same result regarding cataract, the main cause of blindness in the world, or regarding glaucoma, the main cause of irreversible blindness in the world. Trachoma, which unlike these two is preventable, is also far from being eliminated.

It is essential that all people, both in the populations of developing and developed countries, receive instruction and guidance on the diseases most responsible for blindness. The more widespread the information, the more people are driven to conduct screening and follow-up consultations. This type of measure reduces public health costs with surgeries that could be avoided, not to mention the costs with diminished productivity. It is important to remember that the adoption of simple hygiene measures, such as hand and face washing, are extremely valuable in preventing trachoma installation, for example. Increasing access to the health system, with eye education strategies, screening for diseases in early stages and management to prevent the progression of blindness, have been advocated for decades by world organizations.

In addition to this approach, priority should also be given to the development and improvement of technologies for diagnosing eye diseases, thus making their screening even more effective. Glaucoma is an emblematic disease with regard to the impact of technological development in screening tests, since there is still a need for better tests capable of detecting more structural aspects of the disease before any functional worsening occurs. In the case of cataract, developments in innovation have made cataract surgery one of the most performed in the world and with very high success rates. Therefore, the incentive for technological advancement must be as great as the investment in the population's awareness.

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