Trachoma as Cause of Blindness: Literature Review

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Abstract

This is a literature review that used as database articles in websites like Bireme, SciELO, LILACS, Journals and Webartigos.

Development: Trachoma is an ocular inflammatory disease, whose etiological agent is Chlamydia trachomatis, which affects the conjunctiva and cornea causing a chronic relapsing keratoconjunctivitis, in the course of time may lead to the formation of entropion, trichiasis and possible blindness. Its transmission occurs in the home environment, directly or indirectly. The occurrence of trachoma is mostly where hygiene and lifestyle habits are precarious. According to the World Health Organization, there are six million people currently infected.

Conclusion: The study shows the importance of knowledge about trachoma, so that Brazil is able to achieve the global goal of eliminating the disease by 2020.

Introduction

Although millenary known, Trachoma is still one of the diseases of concern to the world, and is present especially in developing countries. In 2003, the World Health Organization (WHO) estimated that there are 84 million people with active trachoma in the world, 76 million with trachoma trichiasis and five million with serious risks for their vision and potential development of blindness. Moreover, 80 million children had inflammatory trachoma that could potentially cause severe visual impairment [1, 2].

The word trachoma (Greek Tráchomas) means rough, lumpy or swollen, describing the appearance of the tarsal conjunctiva affected. Tra-
choma is the etiological agent caused by Chlamydia trachomatis, gram-negative, low infectivity, but its distribution in the world is wide. Natural or acquired immunity to the infection by this bacterium is not verified [3].

Trachoma is considered by the international health organizations a neglected disease, and since others are also classified as such, there is little or no investment by the industry in the development of new diagnostic techniques, drugs, vaccines, and is also neglected by Colleges, which can be seen by the small number of studies and publications. (4) Is included among the causes of blindness that can be prevented by making part of the GET 2020 (Global Elimination of Trachoma) of WHO, which aims to eliminate preventable causes of blindness in the world by the year 2020 [4, 5].

It is considered an inflammatory eye disease a relapsing chronic keratoconjunctivitis that with the course of time, produces scars on the upper eyelid conjunctiva, which may lead to the formation of entropion (eyelid with the turn-edge in the eye) and trichiasis (eyelash in faulty position the edges eyelid, touching the eyeball). The active, infectious stage takes place predominantly at preschool age with blindness risks in the future in these highly endemic areas. The scarring inactive phase is found in adults [6].

The diagnosis of trachoma is essentially clinical, evaluating changes of the eyelids, eyelashes, tarsal and bulbar conjunctiva and cornea. The upper eyelids are everted and the upper conjunctiva carefully examined. WHO advises that the diagnosis of trachoma should be given when at least two of the following clinical signs are present: follicles on the upper tarsal conjunctiva, follicles in limbo or pits Herbert, typical conjunctival scarring and pannus in the upper limb [4, 7].

Methods
This research has nature of literature review, using articles from the years 2001-2014, the databases of the websites Bireme, SciELO, LILACS, Journals and virtual articles. In addition, academic books and manuals updated the Ministry of Health were used.

Literature Review
Disease History
Trachoma is the second cause of blindness in the world, keeping itself in hyperendemic levels in various regions, such as Asia, Africa and the Middle East.

In the Americas, there are several outbreaks in the region located in southern Mexico, Guatemala, Bolivia, Peru and northeastern Brazil [8, 9]. The first citations of this eye disorder were in 1556 B.C, on a papyrus in the ancient scriptures it was discovered only in 1892 by George Ehers. The disease came to be described in Egypt in 525 B.C during the Persian invasion, and in 48 BC, Cicero said that in Rome several doctors cured the trichiasis, trachoma and performed cataract operations [6-9].

The occurrence of trachoma has increased considerably with the masses and hygiene conditions of these environments with the end of the Agricultural Revolution and the beginning of the Industrial Revolution (10). Over the past century, trachoma was highly prevalent in Europe and North America and was the main cause of blindness in those regions. Trachoma disappearance of developed countries has been accelerated by the introduction of sulfa drugs in 1930 and antibiotics in the 1940s (10). In this century, the disease was gradually disappearing due to multiple changes in living conditions and health care [6, 9].

In Brazil, trachoma arrived in the eighteenth century between 1718 and 1750, with the colonization of Portuguese and Europeans, because until then the disease did not exist in the native populations of the country. It was developed initially in the Northeast, specifically in Cariri in Ceará, where there is the oldest outbreak of disease in Brazil. In addition to this, two other outbreaks contributed decisively to the spread of trachoma: Rio Grande do Sul and
São Paulo. Both started in the late nineteenth century also with the colonization of foreigners coming from endemic countries of the Mediterranean (Italy and Spain), expanding to other regions [6, 9, 11].

The first measure of control Trachoma adopted in Brazil was the initiative of the Government of the State of São Paulo, which in 1904 banned the entry of immigrants with trachoma in the Port of Santos, similar to what was done in the United States. But this measure was not successful, due to pressure from the coffee farmers, in need of immigrant labor. Thus, the ban was replaced by a fine to the owner of the ship that brought immigrants with trachoma [4].

In the national level, the first control measure was taken in 1923 when enacted the "Regulations of the National Department of Public Health," which prohibited the landing of immigrants with trachoma. A measure that was taken after such a long time because back then the disease found itself widespread in the country and no longer depended on immigration to maintain this condition [4].

But only in 1990, trachoma control activities at a national level became part of the duties of the National Health Foundation - FNS and until today, the Ministry of Health has maintained control actions in regions with higher prevalence, through FNS. However, the idea of eradicating trachoma still remains dominant among the Brazilian scientific community [4, 12].

The occurrence of trachoma in the world today is restricted almost exclusively to the populations of developing countries and within them, the rural and poor population, marginalized from the benefits of socioeconomic development. The World Health Organization (WHO) points 53 countries as endemic for trachoma [13, 14].

Several studies have demonstrated the occurrence of trachoma in most parts of Brazil, with cases found in all regions and in different communities, both in urban centers and in rural areas, coastal cities or Amazon, as well as in remote indigenous communities. Since trachoma is most prevalent where hygiene conditions, lifestyle habits and socioeconomic conditions are precarious added to a high density of flies looking for ocular areas [6, 15, 16].

Ciclo of the disease

The causative organism of trachoma is a Gram negative obligate intracellular bacteria Chlamydia trachomatis, which has a single chromosome from about 1 Mbp and multiple plasmid copies which functions as a virulence factor [17]. The endemic trachoma is caused by C. trachomatis serovars A, B, Ba and C. The genital tract infection is usually caused by serovars D to K, which can also infect the eye, causing ophthalmia neonatorum in newborns or adults conjunctivitis. The basis for the tissue tropism of the serotypes was not fully elucidated [18].

It is known that the main form of transmission is direct, eye to eye, person to person. However, there is also a form of indirect transmission through contaminated objects (towels, handkerchiefs, pillowcases). It is still possible that some insects such as housefly (Musca domestica) and / or eyeslickers (Hippelate ssp.), May act as mechanical vectors, contributing to the spread of the disease. Transmission is possible only when there are active lesions, being higher at the beginning of the disease and the occurrence of associated bacterial infections [3, 9, 15].

Pathophysiology

Trachoma is the result of a complex interaction between chlamydia infection and the immune res-
response occurring over many years [22]. It begins in the form of follicular conjunctivitis (active follicular trachoma), with papillary hypertrophy and inflammatory cells infiltrating the conjunctiva (lymphocytes, macrophages, neutrophils, and plasma cells) punctuated by lymphoid follicles (B cells surrounded by a mantle of T0 cells) [23], which extends throughout the conjunctiva, especially in the upper tarsal conjunctiva.

In microscopic examination of the cornea reveals epithelial keratitis, subepithelial infiltrates and extent of the limbal vessels of the cornea. The inflammatory response to primary infection of the conjunctiva by Chlamydia trachomatis leads to a mild, self-limited frame conjunctivitis, called inclusion conjunctivitis. Not observed natural or acquired immunity to infection. Some experimental studies show that there is some resistance after the first episode of infection, but a partial resistance because after a new inoculation, a new infection is developed [9, 24].

Trachoma is manifested in successive conjunctival reinfection because the individual lives where the disease is endemic, which favors the possibility of reinfection. Repeated infections lead to a hypersensitive immune response to Chlamydia antigens, causing an inflammatory response becomes increasingly lush and leading to the succession of pathophysiological phenomena that characterize trachoma [14, 18]. The infected children have increased expression of IFN-y and IL12p40 genes, suggesting an immune response mediated by lymphocytes (Th1) [25].

In hyperendemic areas, a subgroup of children, about 8-10%, seem to have constant infection and persistent severe inflammation (26-28). The incidence of scarring is nearly five times higher in these children than in children with active trachoma, but without severe inflammation [29]. In addition, scar formation can continue to develop in people living in areas that are not endemic [30], suggesting that the tissue damaged by infection with chlamydia can undergo progressive healing after injury by other bacterial pathogens [31].

Matrix metalloproteinases are an integral part of tissue homeostasis and are also involved in tissue destruction and fibrosis. These proteolytic enzymes are produced by inflammatory cells, fibroblasts, and epithelium. In the active trachoma and scarring caused by trachoma occurs increasing the amount of matrix metalloproteinases 7, 9, and 12 [25, 32, 33]. These findings suggest a role for matrix metalloproteinases in scar formation, corneal opacities and loss of vision [34].

The fibrosis formed in response to the agent to exert traction upper eyelid, leading to a distortion, entropion, causing the eyelashes to touch the eye (trichiasis), which can cause ulcers. Therefore, scarring and corneal opacification can lead to varying degrees of decreased visual acuity to blindness [1, 3, 4, 7, 18]. Vision loss can occur within one year in up to one third of individuals with trichiasis untreated [34]. Even without loss of vision, trichiasis leads to substantial disability and reduced quality of life [35, 36].

Follicles also appear in the limbus region, when necrosam, leave small depressions known as Herbert’s pits. The appearance of keratitis in the upper limb region and neovascularization is often and is clinically as trachomatosus pannus [9].

The symptoms associated with inflammatory trachoma include tearing, foreign body sensation, photophobia and mild purulent discharge in small quantities, there will only be a lot of purulent when other bacterial conjunctivitis associated with trachoma. In older and more serious infections conjunctiva can become thickened and edematous. A large proportion of cases of trachoma, especially among younger children are asymptomatic. Patients with entropion, trichiasis and those with corneal ulcerations refer constant pain and intense photophobia [9, 16].

We observe two types of conjunctival inflammation reaction in trachomatous: follicles and diffuse infiltration which can occur simultaneously. For purposes of classification, define degrees of tracho-
matous inflammation of the conjunctiva, according to the criteria below: Predominantly Follicular inflammation, trachoma Follicular - (TF); Predominantly Infiltration and Diffuse thickening of the conjunctiva, the Trachoma Intense--(IT). The other signals for diagnosis are: Healing Trachomatous Conjunctival Tarsal Superior-(TS); Trachomatous trichiasis-(TT); and Corneal - (CO).

All these signs are not mutually exclusive, but may also occur in the same patient and the same eye. Thus, one should always register their presence or absence. Trachoma is considered Follicular (TF) where there is the presence of at least five follicles of at least 0.5 mm diameter in the upper tarsal conjunctiva. Follicles are rounded elevations of the conjunctiva, bright and fainter than the conjunctiva around. They should be distinguished from changes caused by small scars and degenerative deposits in the conjunctiva. Small scars are not round, having angled edges, while the follicles have poorly defined borders. Degenerative deposits include conjunctival aggregates, which are yellow or white opaque masses with well-defined edges and cysts that appear as tiny clear bubbles in the conjunctiva [9, 15, 37].

Inflammation intense trachomatous (IT) is characterized by marked thickening of the upper tarsal conjunctiva, which appears reddish wrinkled and not allowing the viewing of more than 50% deep tarsal vessels. In the healing Conjunctival Trachomatous (TS), the conjunctiva has a milky appearance, fibrous, with straight edges, angular or stellate. It is considered Trichiasis Trachomatous (TT) when at least one of eyelashes rubs the eye when there is recent evidence removal of inverted eyelashes associated with the presence of scars in the upper tarsal conjunctiva (TS) indicative of trachoma. The Corneal (CO) trachomatous of origin, characterized by a clear view on the pupil with sufficient strength to obscure at least part of the pupillary margin [9, 37].

In endemic areas, children are infected early in life, developing TF and, depending on the reinfection frequency of severity and association with other bacterial conjunctivitis, may develop IT and later scarring conjunctival trachoma (TS). The prevalence of active inflammatory forms (TF and TI) decreases with age. So even in highly endemic areas, are rare cases of inflammatory trachoma among adults. The prevalence of cicatricial forms (TS) and sequelae (TT and CO) tends to increase with age [4, 7, 9].

Diagnosis

The diagnosis of Trachoma is essentially clinical, and is usually done by the external eye exam using binocular loupe 2.5 fold increase. By examining the eye for diagnosis of trachoma, one should initially observe the eyelids and the cornea, verifying the presence or absence of entropion, trichiasis and corneal opacities. Then, should evert the upper eyelid and examine the central area of the tarsal conjunctiva, despising the edges of the eyelids and the corners. The normal conjunctiva is smooth, thin, transparent and pinkish in color [4, 9, 38].

In clinical diagnostics there is also the laboratory diagnosis of trachoma which is not considered essential, since no other ocular diseases where it would be necessary to perform a differential diagnosis occurs with the same epidemiological characteristics of trachoma, an endemic disease with spatial clustering cases. The standard laboratory technique for the diagnosis of Chlamydia trachomatis is by the culture. Chlamydia is a microorganism obligatorily intracellular life, therefore only grows in cell culture. There are few laboratories in Brazil that routinely develop cell cultures for diagnosis of Chlamydia. This is a complex and expensive procedure, which is not available for a routinely use of the trachoma control program [9].

The differential diagnosis of trachoma is to be done considering the other follicular conjunctivitis, such as folliculoses; toxic follicular conjunctivitis; inclusion conjunctivitis; acute follicular conjunctivitis and other less common versions [9].
**Treatment**

The goal of treatment is to cure the infection, with consequent interruption of the transmission chain of the disease. Antibiotics azithromycin oral or topical tetracycline are used to reduce the number of Chlamydia in endemic communities. Azithromycin (20 mg/kg to 1 g) is the preferred treatment. Topical treatment with tetracycline is made 1% - used ophthalmic ointment twice a day for six weeks, or in case of absence thereof, or hypersensitivity to drugs, sulfa - drop should be taken four times a day for six weeks. Patients with intense trachoma (TI) or cases of TF and TI do not respond well to topical medication, should make use of systemic treatment [14].

Despite the limited evidence in randomized trials, the overwhelming evidence from cohort studies, the rate of clinical disease and infection rates fall after the mass distribution of antibiotics (39-43). The mass distribution is indicated when the proportion of children aged 1-9 years with follicular trachoma (TF) is more than 10% in assessed community. In areas where the prevalence rate is 5-9%, it is recommended a focal approach. WHO recommends that, an initial prevalence of 10-30% mass distribution of antibiotics should continue for three years before a new prevalence study be conducted [14].

Clinical signs may persist long after the infection has cleared [44], and so the existence of clinical disease with no detectable infection has led some to question whether the clinical signs should be the criterion to determine when to stop treatment [45].

All cases of eyelid entropion and trachoma trichiasis should be submitted to corrective surgical evaluation of the eyelids. The abrasive action of the cilia on the cornea is to be repaired by surgical correction of the eyelid margin (46). The trichiasis surgery slightly improves vision, reduces pain, and in some cases reduces the severity of corneal opacity [47-50]. The success of many surgical programs is hampered by the recurrence rates of infection which can be as high as 60% in three years [48, 51-56].

**Control and Prevention**

It is clear that the treatment’s interventions should be coupled with promotion and prevention of trachoma. If the basic hygiene factors that allowed trachoma thrive on the site are not controlled, the disease will return once the mass distribution of antibiotics ceases. The trachoma interventions are planned at the district level with actions in the community and family level to interrupt transmission of the infection and minimize the reintroduction of infection in already treated communities. The local trachoma prevalence study is used to identify which programs are needed [14].

Studies dealing with the return of infection after use of azithromycin, show that the disease reappears in households within 6 months, but can take up to a year to be evident in the community [57]. The measures to promote personal and family hygiene, such as: clean keep the faces of children and proper garbage disposal, contributes to decreased concentration of flies, may have a significant impact in reducing the prevalence and severity of cases [9, 58, 59]. Overcrowding is a risk factor for trachoma, the number of children with active disease when increases proportionally if there are more people per room [60].

Routine lack of facial hygiene has been consistently associated with trachoma [10, 61, 62]. Improvement in facial cleaning also decreases the severity of active disease, probably by reducing the probability of reinfection [63]. Facial cleanliness and control strategies of environmental components for Trachoma are so important that were developed by WHO to “SAFE” strategy (S = corrective surgery for trichiasis; The antibiotics =; F = cleaning face; E = sanitation ), based on fairly simple measures that involve personal care, accompanied by improvements in living conditions (4). But the proportion of countries with trachoma that had implemented these components is daunting; while 61% have started the surgery and distribution of antibiotics programs, only 34% had also implemented facial cleanliness and environmental control measures adopted [64].
The trachoma control policy should be integrated with both water treatment and sanitation programs, as well as health programs of children and adolescents. Surgery and antibiotic distribution should be linked to hygiene and sanitation programs; and the implementation of hygiene and sanitation programs should be included in the monitoring and, consequently, in the trachoma elimination certification [65].

Although there are funds for research related to neglected diseases, the knowledge produced does not translate into therapeutic advances, for example, new drugs, diagnostic methods and vaccines. One reason for this situation is the low interest of the pharmaceutical industry on this issue, justified by the low potential lucrative perspective for the industry, since the target population is not wealthy and present, mostly in developing countries [4, 66].

The expectation is to create various strategies to mobilize prominent scientific groups in the country dedicated to the theme. Thus, new knowledge about the different aspects - biological, clinical, social and others will be more efficiently produced, contributing to the fight against these diseases, both in respect of sick or exposed individuals, as well as to respect the communities and their living conditions [66].

Conclusion
Trachoma should be a concern of health systems, since it can lead to blindness, and is easy to diagnose and has an inexpensive initial treatment. Because it is a disease with easy contamination it is found in large proportions worldwide and reaches more people with low socioeconomic status and living in poverty, where there are few hygiene, garbage accumulation and lack of water. These conditions favor the increase of the number of flies that act as vectors of disease in those environments. To be able to think of the global eradication of trachoma, it is necessary the implementation of sanitation programs in disadvantaged areas.

Another aspect worth mentioning is the importance of a detailed ophthalmological external physical examination. Health professionals are primarily responsible for providing guidelines for the prevention and carrying out the diagnosis of forms of trachoma. Even in communities where the disease is combated with active systematic search and treatment of cases and communicating, the disease is still present. The lack of knowledge on the subject leads to the current situation, and the training of health care professionals enables early recognition of trachoma, treatment and reduces the risk of complications and blindness. Only then will be possible to meet the objective of extermination of Trachoma by the year 2020 as the WHO goal.

References
1. Araújo FAM, Cruz AAV. Alterações de cílios no Hospital das Clínicas da Faculdade de Medicina de Ribeirão Preto-USP. Arq Bras Oftalmol 2002; 65:343-9.


