Amblyopia: An overview

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Abstract

Amblyopia, a visual disorder with another name "lazy eye", is a form of visual development disorder. It is thought to originate from retinal image degradation associated with abnormal visual experiences during the developmental period of the visual system in infancy and early childhood. According to existing data, 2-3% of the world's population suffers from amblyopia. It is important to have visual function checks early to detect the risk of amblyopia, considering that in general amblyopia does not cause symptoms. Amblyopia can be treated if detected early and treated appropriately. This paper uses an article review method using sources such as journals and books. The following review aims to present contemporary literature regarding the definition, pathophysiology, risk factor, classification, severity, treatment, and prognosis associated with these visual deficits.

Keywords : Amblyopia, children, early detection, visual acuity

1. Introduction

Amblyopia, often referred to as lazy eye, is a condition where vision diminishes either in one or both eyes without any visible damage to the eyes themselves[1]. It is generally diagnosed when there's a discrepancy of two or more lines in visual acuity between the eyes during an optotype test, or if vision is 20/30 or worse, even with optimal eyewear[2]. Objectively, this condition is confirmed when the Best-Corrected Visual Acuity (BCVA) is below 20/40 (0.30 LogMAR) in both eyes, or if there's a variation of 0.2 LogMAR (two lines on the Snellen chart) between the eyes[3]. Amblyopia is a leading factor behind impaired vision in one eye among both children and adults[4]. The most frequent causes of this condition include strabismus (crossed eyes), anisometropia (unequal refractive power), a combination of these, and deprivation of vision[5].

2. Amblyopia

2.1 Pathophysiology

At the time of birth, the visual system is still developing, with an estimated visual acuity of about 20/400. In the initial months of life, visual acuity sharpens and the ability to perceive depth (stereopsis) begins to form. Key developments such as the myelination of the optic nerve, the maturation of the visual cortex, and the growth of the lateral geniculate nucleus occur in the first two years. Concurrently, the fovea – the part of the retina most responsive to visual stimuli – reaches its full development by approximately 4 years of age. The first 7-8 years of life, known as the critical period, are crucial for the development of the visual system, and normal visual stimulation during this time is essential for developing normal vision. The formation of visual pathways in the central nervous system is dependent on the brain receiving clear, focused images from both eyes. Any disruption or impairment in the development of these pathways, caused by abnormal visual input, can lead to amblyopia[6].

Early in life, primary visual cortex cells may lose their ability to respond to stimuli in one or both eyes, and those that remain responsive exhibit significant function. Visual cortex deficiency can explain the phenomenon of "crowding" in opotype examination, namely that sufferers more easily identify letters if they are displayed one by one rather than in a linear row with other letters. Abnormalities were also found in neurons within the lateral gicularis. body, but the retina and optic nerve in amblyopia are basically normal. Amblyopia is primarily a central visual defect, but peripheral visual fields are usually normal[7].

On MRI examination, the first changes are seen in V1, which is the anatomical location of the visual pathway. Anisometropia and deprivation of stimuli cause the formation of out-of-focus images, whereas in strabismus, the images formed are not aligned. Both conditions cause sensory deficits, but the magnitude of the deficits does not correspond to the physiological changes in V1. Therefore, in addition to disturbances in V1, amblyopia also alters processes in extrastriate areas of the brain[8].

2.2 Risk Factors

Amblyopia risk factors are categorized into ocular and nonocular types[9]. The ocular risk factors that can lead to amblyopia include conditions like anisometropia, astigmatism, strabismus, hyperopia, eye cloudiness or cataracts, and ptosis[10]. In a large multicenter randomized controlled trial (RCT) involving 409 children aged 3 to 6 years

being treated for amblyopia, the breakdown was as follows: 38% had strabismus, 37% anisometropia, 24% both strabismus and anisometropia, and 3% had less common causes like ptosis, congenital cataract, or corneal injury or dystrophy[11].

Research exploring various perinatal, socioeconomic, and demographic factors has linked non-ocular factors to amblyopia. These include maternal smoking during pregnancy, prematurity, low Apgar scores, and admission to neonatal intensive care units. Identified amblyopia risk factors also encompass maternal age at pregnancy (35 years or older), exposure to toxic substances during pregnancy, a pre-pregnancy maternal BMI below 18, and untreated congenital obstruction of the nasolacrimal duct, which is considered a modifiable factor[9].

2.3 Classification

2.3.1 Strabismic amblyopia

Strabismic amblyopia arises from the conflicting or suppressive interactions among neurons that receive incompatible inputs from both eyes[7]. To prevent double vision, the brain suppresses the activity of the retinocortical pathway from the misaligned fovea, leading to changes in the visual system and ultimately causing amblyopia[6]. In young children with strabismus, this suppression happens quickly[7].

In cases of monocular amblyopia, like anisometropic and strabismic amblyopia, the disability is often minimal with few symptoms, as the unaffected eye typically maintains good visual acuity. The most notable issues stem from reduced stereopsis (the three-dimensional perception due to differences in the two retinal images), which can impact work opportunities and reduce visual efficiency in activities requiring depth perception, such as driving, or tasks involving eye-hand coordination[12].

2.3.2 Refractive amblyopia

Refractive amblyopia occurs due to persistent blurring of the retinal image in one or both eyes. When there's a difference in the refractive error between the eyes, known as anisometropia, it leads to amblyopia in one eye. In contrast, isoametropia, where both eyes have a similar refractive error, can result in amblyopia affecting both eyes[7].

2.3.2.1 Anisometropic amblyopia

Anisometropic amblyopia occurs when there is a difference in refraction between the two eyes which causes the image on one retina to become out of focus over time. If the image in the fovea in both eyes is different in shape and size due to unequal refractive errors between the left and right, then there is an obstacle to fusion. Moreover, the more ametropic fovea of the eye will hinder the formation of images (formed vision)[13].

Hyperopic anisometropia (farsightedness) and astigmatism are more associated with decreased vision than myopic anisometropia (farsightedness)[14]. Amblyopia occurs when the refractive difference is more than 3 D in myopic anisometropia, 1.5 D in hyperopic anisometropia, and 2 D in astigmatism anisometropia[7].

2.3.2.2 Isoametropic amblyopia

Isoametropic amblyopia, also known as bilateral ametropic amblyopia, refers to a reduction in visual acuity in both eyes caused by continuous blurring of the retinal image. This blurring results from equally high uncorrected refractive errors in both eyes. Significant risk factors include hyperopia (farsightedness) greater than 4.00 to 5.00 diopters and myopia (nearsightedness) exceeding 5.00 to 6.00 diopters. Additionally, high bilateral astigmatism can lead to a specific loss in the ability to resolve details along the blurred meridians, a condition known as meridional amblyopia. Most eye specialists advise correcting astigmatism when it exceeds 2.00 to 3.00 diopters[7].

2.3.3 Deprivation amblyopia

Deprivation amblyopia, particularly in its most severe form known as visual deprivation amblyopia (also referred to as stimulus deprivation amblyopia, blyopic deprivation amblyopia, visual stimulus deprivation amblyopia, and form deprivation amblyopia), is a rare but challenging condition to treat. This type of amblyopia develops when an obstruction along the visual axis, such as opacity in the refractive media (like a cloudy cornea, cataract, or vitreous hemorrhage), drooping eyelid (blepharoptosis), or eyelid tumors, occurs during the critical period of visual cortex development. Visual deprivation amblyopia tends to worsen more rapidly and is more severe than amblyopia caused by strabismus or anisometropia. When deprivation is unilateral, the visual impairment in the affected eye is usually more pronounced than the deficits caused by bilateral deprivation, owing to the added impact of interocular competition on top of the direct effects of image degradation. Even in cases where both eyes are affected, visual acuity can drop to 20/200 or worse if not promptly treated[7].

2.4 Severity

Amblyopia's severity is typically determined by measuring the visual acuity in the impacted eye. Mild amblyopia generally corresponds to a visual acuity ranging from 6/9 to 6/12. If the visual acuity falls between worse than 6/12 and up to 6/36, it's considered moderate amblyopia. Severe amblyopia is classified as having a visual acuity worse than 6/36. While different studies may vary in their definitions of these severity levels, most agree on defining normal vision in the unaffected eye as 6/6 or better. On a standard visual acuity chart, each row of letters or symbols, which typically includes 4 or 5 characters, represents a change of 0.1 LogMAR unit[11].

2.5 Treatments

Recent research indicates that children with amblyopia, even up to the age of 15, can benefit from treatment due to the continued plasticity of the brain beyond the traditionally defined critical period[11]. The primary approach to treating amblyopia involves enhancing visual stimulation in the weaker eye. This is typically done by temporarily obstructing the vision in the stronger eye, using methods like patching (occlusion therapy) or through atropine and optic penalization[15]. The objective of these treatments is to attain clear vision and equalize visual acuity in both eyes, though it's important to note that this goal may not always be fully realized[16]. The process of treating amblyopia in children encompasses several steps[7]:

- Eliminate the causes of obstruction of the visual axis
- Correct any refractive errors
- Empower or stimulate the use of the problematic eye by limiting the use of the normal/dominant eye with occlusion and penalization.

2.5.1 Cataract surgery

Cataracts that are severe enough to cause dense amblyopia need to be addressed with timely surgical intervention. For the best chance at restoring vision, it's crucial to remove visually significant congenital cataracts in one eye within the first six weeks after birth. In cases where children develop significant cataracts at a known time, swift and thorough treatment is warranted, especially if there's a chance that the cataracts have developed recently. When it comes to dense bilateral congenital cataracts, surgery is typically advised within the first 10 weeks of life. On the other hand, smaller, partial cataracts might sometimes be managed without surgery. In such cases, using medication to dilate the pupil can enable satisfactory vision despite the presence of central opacity[7].

2.5.2 Correction of refractive errors

Refractive correction plays a key role in the treatment of all types of amblyopia, not just refractive amblyopia even anisometropic, isoametropic and even strabismic amblyopia can improve or cure with refractive correction alone[7]. The Pediatric Eye Disease Investigator Group (PEDIG) has conducted a number of randomized clinical trials of amblyopia therapy in children aged 3 – 17 years to evaluate the effectiveness of amblyopia therapy and determine optimal therapy protocols [16]. The initial treatment for amblyopia is to correct the refractive error which is assessed based on cycloplegic refraction [18]. Correction of refractive errors can be done using glasses or contact lenses. If the patient does not want to use glasses or contact lenses, refractive surgery can be performed [16].

In general, the refractive correction for amblyopia should rely on a cycloplegic refraction assessment. Full correction of hyperopia (farsightedness) is often essential, particularly when treating associated accommodative esotropia (crossed eyes due to focusing effort). For children with either unilateral or bilateral amblyopia, it may be necessary to fully or almost fully correct their hyperopia as part of their treatment, even in the absence of accommodative esotropia. Furthermore, ensuring that the non-amblyopic eye has clear distance vision, even when under the effect of cycloplegia, can help lessen the risk of amblyopia reoccurring. This risk can sometimes arise following the use of atropine for pharmacological treatment[7].

2.5.3 Occlusion therapy (patching)

For centuries, occlusion or patching therapy has been a mainstay in the treatment of amblyopia[17]. Known for being effective, affordable, and devoid of systemic side effects, occlusion therapy is particularly favored for unilateral amblyopia[16]. It involves covering the healthy eye with a patch to encourage the use of the weaker, amblyopic eye[6]. Notably, occlusion therapy can quickly reverse significant strabismic amblyopia in infants, often within a month. In contrast, older children, who may only wear the patch after school and on weekends, could require several months to see improvement in moderate conditions[7].

Full-time occlusion, which means patching during all waking hours, has the potential to cause reverse amblyopia and strabismus. For severe cases of amblyopia, part-time occlusion for about 6 hours daily can yield results comparable to full-time occlusion. The duration of patching should be tailored to the severity of the amblyopia. For more severe cases (VA 20/125–20/400), a 6-hour daily regimen is recommended, whereas for moderate cases (VA 20/100 or better), 2 hours a day may suffice. It's not necessary for patients to engage in specific activities, like close work, while wearing the patch. Follow-up frequency depends on the patient's age and the intensity of treatment. Part-time treatment requires less frequent follow-ups, typically a re-examination every 2-3 months after starting. Further appointments may be spaced out longer, depending on the initial response[7].

During diocclusion, the eyes should remain stimulated by reading. The vision of both eyes must also always be monitored, because amblyopia may occur in the occluded eye. Monitor visual acuity every 6 - 8 weeks until normal visual acuity is achieved or there is no improvement[16]. If the vision in the amblyopic eye does not improve with eye occlusion for 2 hours per day, the duration of eye occlusion can be increased to 6 hours per day[18]. Therapy can be stopped if there is no improvement within 6 months [6].

2.5.4 Penalization

Penalization involves deliberately impairing vision in the unaffected eye to encourage the use of the amblyopic eye. This can be done through medication, adjusting eyeglasses, or a combination of both[16]. A common pharmacological method is the application of 1% atropine eye drops biweekly in the healthy eye to reduce visual

clarity[19]. Atropine sulfate solution, typically at a 1% concentration, is used as a cycloplegic agent in the better-seeing eye, which prevents it from focusing[7]. Atropine drops work by temporarily blocking the parasympathetic control of the ciliary muscle and iris, leading to dilation of the pupil and loss of focus[6]. This results in blurred vision for the stronger eye, especially up close and potentially for distance vision if hyperopia is not well-corrected[7]. Atropine tends to be more effective in patients with farsightedness[6]. It's important for parents and caregivers to be aware of the possible side effects of atropine, which include sensitivity to light and risks of systemic toxicity, symptoms of which may include fever, rapid heartbeat, confusion, and dry mouth and skin[7].

Eye penalization and occlusion are equally effective[16]. Studies show that patients with moderate amblyopia who received eye occlusion therapy for at least 6 hours per day compared to patients who received 1% atropine eye drops as much as 1 drop in healthy eyes, experienced the same magnitude of visual acuity improvement, namely 3 lines or more after 6 months of therapy (79 % in the eye occlusion group and 74% in the atropine group) although visual improvement appeared to be achieved slightly more quickly in the eye occlusion group[6]. Another study also showed that using 1% atropine only on weekends for 4 months had the same effectiveness as using 1% atropine every day[18].

Apart from pharmacological penalization, there is also optical penalization using glasses or contact lenses to obscure the healthy eye[16]. Optical penalization can be used in conjunction with pharmacological penalization[6]. As with occlusion therapy, monitoring the vision of the healthy eye needs to be carried out to prevent amblyopia in the healthy eye[16].

2.5.5 Pharmacotherapy: citicoline

Citicoline, also known by its scientific name cytidine diphosphatecholine (CDP-choline), plays a key role in the creation of phospholipids for cell membranes[20]. It's believed to protect nerve cells by directly supporting cell membrane structure and function[21]. Citicoline is utilized in various neurological and ophthalmological conditions, including trauma, ischemia, and degenerative diseases[15]. Its oral form appears to enhance the effectiveness of part-time occlusion therapy in children[22].

A recent randomized controlled trial (RCT) targeting children aged 4–13 demonstrated that combining citicoline with patching significantly improved visual acuity (VA) more than patching alone within a year[23]. In a study comparing the outcomes at 12 months in 80 children with amblyopia (average age 4.5 years), both the Bangerter filter and the Bangerter filter combined with citicoline were found effective in improving VA[24]. Notably, the addition of citicoline showed a significantly greater effect[24]. However, the efficacy of citicoline remains under investigation, as another study indicated no additional benefit when combining CDP-choline with patch therapy over a 30-day period compared to patching alone[25].

2.6 Prognosis

The prognosis for amblyopia is dubia because the return to normal vision in the amblyopic eye depends on several factors, including the age at which amblyopia first occurred, the cause, severity, duration of amblyopia, history and response to previous therapy, and compliance with therapy. Therapy at critical periods of visual cortex development will provide a better prognosis. The prognosis is worse if there are factors associated with a high risk of treatment failure such as noncompliance, age 6 years or more, astigmatism of at least 1.5 D, hyperopia of more than 3 D, and initial visual acuity of 20/200 or worse[6].

The success in treating amblyopia largely hinges on the timing of the treatment and the condition's severity. It's a significant contributor to single-eye vision loss. Successful vision restoration is seen in about 75% of children who undergo occlusion therapy. Nonetheless, around half of these children may experience a minor decline in vision acuity as time goes on. Early referral typically leads to better results. However, the long-term prognosis can vary for many children as they grow older. More than 70% of individuals treated for amblyopia show considerable improvement in vision within a year. Yet, some may still see a gradual decrease in vision quality over subsequent years. Factors that can impede vision recovery include the age when treatment starts (with later treatments usually less effective), deprivation amblyopia, and initially poor vision acuity[26].

2.7 Early detection and preventions

Early detection and treatment can effectively prevent Amblyopia. It is recommended that primary health care providers conduct initial screenings in newborns within the first 4-6 weeks of life. Additionally, children who are more susceptible to the condition should undergo yearly check-ups during their formative years, from birth until around 6-8 years old. It's also important to start checking for eye issues like refractive errors and strabismus within the first year. Targeting children with a family history of strabismus or amblyopia for screening could be a cost-efficient approach. Other countries have seen significant success with amblyopia screening programs for 4-year-olds. However, in the United States, the rate of preschoolers receiving proper amblyopia screening is disappointingly low. Thus, optometrists have a crucial role in educating parents about the commonness and dangers of amblyopia, and in urging them to seek regular professional eye care for their children[12].

3. Conclusion

It can be concluded from the literature that amblyopia occurs due to disturbances in the development of vision during a critical period even with the best visual acuity correction in one or both eyes. This visual deficit can be cured with appropriate therapy according to indications. The earlier amblyopia is discovered, the better the prognosis.

Therefore, early detection through screening, one of which is in primary health care, plays a big role in the prevention and treatment of amblyopia.

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