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ETHICAL AND LEGAL ASPECTS ON PREVENTION, EARLY DIAGNOSIS AND TREATMENT OF CHILDHOOD GLAUCOMA

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Abstract: ***Introduction.*** The purpose of this review is to identify the ethical considerations associated with the assessment, diagnosis, and management of childhood glaucoma, also known as pediatric glaucoma. This condition, characterized by a diverse range of disorders affecting the eye's anterior segment, can lead to blindness. However, it is treatable if recognized, diagnosed, and treated efficiently in a timely manner.

Methods. To gather information, a comprehensive literature search was conducted on databases and professional websites for clinical practice guidelines related to pediatric glaucoma published in English.

Results. The search using the term "pediatric glaucoma" yielded varied results across different databases. However, when the keyword "ethic" was combined with "pediatric glaucoma," 21 results were obtained from PubMed, 3 from Web of Sciences, and 6 from Elsevier (SCOPUS). After removing duplicates and reviewing titles and abstracts, twenty-five papers were selected and analyzed. The review addressed the significant challenges associated with the diagnosis and clinical management of this group of conditions that affect a vulnerable population—children and young adults. The ethical principles outlined by Beauchamp and Childress, upon which physicians base their clinical practice, were utilized.

Conclusions. This review has raised several questions, some of which are still awaiting answers. Future directions are anticipated to focus on minimizing the side effects of management, improving visual prognosis, and enhancing the quality of life for pediatric glaucoma patients. Effective communication between the healthcare team and parents or legal guardians of the children is crucial for a successful approach to this chronic condition.

Keywords: childhood glaucoma, congenital glaucoma, medical treatment, surgical treatment, ethics.

INTRODUCTION

Childhood glaucoma, also referred to as "pediatric glaucoma," encompasses a diverse range of disorders affecting the anterior segment of the eye, resulting in the obstruction of normal aqueous humor flow and an increase in intraocular pressure (IOP> 21 mmHg) [1, 2]. These alterations, occurring either at birth or later in life, have the potential to cause damage to the optic nerve and, more broadly, the entire eye [3]. The two primary types of pediatric glaucoma are Primary Childhood Glaucoma, which includes congenital glaucoma (PCG) and juvenile open-angle glaucoma (JOAG), and Secondary Childhood Glaucoma, which is linked to non-acquired ocular anomalies, systemic diseases or syndromes, acquired conditions such as ocular injury, eye inflammation/infection, medication use, or glaucoma following cataract surgery [4].

The management of this group of disorders is a challenge for ophthalmologists, from diagnosis through the timing and choice of the most appropriate surgical approach, to long-term follow-up.

Fortunately, pediatric glaucoma is a relatively rare condition, with congenital glaucoma reported worldwide in the range of 1:68,000 to 1:10,000 live births [5, 6]. However, it is a treatable cause of blindness if identified, diagnosed, and promptly treated. Recognizing the severity of its consequences, pediatric glaucoma has been designated as a priority eye condition for inclusion in the WHO's Package of

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Eye Care Interventions [7]. Early diagnosis, surgical treatment, and vigilant monitoring can effectively prevent blindness in the majority of affected children [8].

In order to establish a prompt diagnosis there are some steps that healthcare providers should take into consideration when evaluate children with suspicion of glaucoma [4]. Primarily, the historical assessment encompasses indicators and manifestations (e.g., epiphora without discharge, blepharospasm, and photophobia), age of onset, and gestational details such as maternal infection and forceps delivery. Beyond considering family history (including glaucoma and parental consanguinity) and ocular history, attention should also be directed toward general pediatric and syndromic aspects, including developmental milestones [9,10], cardiac or genitourinary issues, congenital infections, and atopic disease (with steroid use).

Following the historical analysis, the examination entails an assessment of general appearance, visual behavior, visual acuity, and intraocular pressure (IOP) measurements. Additionally, diagnostic methodologies encompass an anterior segment examination (evaluating corneal diameter, presence of Haab striae, gonioscopy, lens opacity, and central corneal thickness) and posterior segment examination, focusing on optic disc assessment. Cycloplegic refraction may reveal significant changes in hyperopia or myopia progression [11]. When considering examination under anesthesia, IOP should be measured as close to induction as possible, given that many induction agents used tend to reduce IOP.

Investigative procedures include measuring axial length, utilizing optical coherence tomography for both the anterior segment and optic nerve, and employing ultrasound biomicroscopy. Corneal biomechanics changes are of growing interest, although further studies are imperative to establish their significance in pediatric glaucoma [10].

In spite of the great number of publications on childhood glaucoma, the ethical and medico-legal aspect involved in dealing with glaucoma in this vulnerable group of population, children and young people, were insufficiently addressed. Therefore, the objective of this review is to explore diagnostic approaches, both surgical and non-surgical treatment options as well as long-term monitoring and complications' prevention of childhood glaucoma, analyzing the ethical and legal aspects and the requirement of a standard of care based on individual pathology.

METHODS

Search strategy

PubMed/MEDLINE, Web of Science (WOS) and SCOPUS databases were assessed for articles in English language using as key-words "childhood glaucoma", "pediatric OR paediatric glaucoma", "congenital glaucoma", "infantile glaucoma", "ethical", "legal", malpractice" with the Boolean operators AND, OR and NOT. A manual search in relevant journals such as Eye, Acta Ophthalmologica, Ophthalmology, British Journal of Ophthalmology, in Romanian Journal of Legal Medicine, and in the references of the identified articles, was also performed.

RESULTS AND DISCUSSION

The search strategy "pediatric glaucoma" in PubMed revealed 2039 results, 1171 in WOS and 2006 in SCOPUS. The overview of the linked key words of the published articles using the open access software VOSviewer, created by van Eck and Waltman at Leiden University's Centre for Science and Technology Studies (CWTS)[12], is displayed in Figure 1. When the key word "ethic" was associated with "pediatric glaucoma", 21 results were obtained from PubMed, 3 from WOS and 6 results from Elsevier (SCOPUS).

Upon eliminating duplicates and reviewing titles and abstracts, twenty-five papers were selected for analysis. However, from the analyzed results, when referred to diagnostic and treatment of childhood glaucoma, no article was found to directly address the four principles of biomedical ethics: beneficence, nonmaleficence, autonomy, and justice stated by Beauchamp and Childress in their book entitled Principles of Biomedical Ethics [13], principles upon physicians base their clinical practice [14].

This paper will examine the application of the four ethical principles, focusing specifically on their relevance to the management of childhood glaucoma.

The principle of beneficence, which underscores the physician's duty to act in the patient's best interest, preventing harm and addressing conditions that may cause harm, is exemplified in the primary goal of medical and surgical interventions for pediatric glaucoma. This goal involves reducing intraocular pressure (IOP) and implementing long-term monitoring to enhance the quality of life for young patients [15].

When dealing with childhood glaucoma, there are more questions than answers. Some of the questions posed are: Why some of the young patients "heal" after

a single surgery and others need multiple interventions with suboptimal results? What associate medication will work better? What is the type of screening in the general population which will ensure early diagnosis and successful treatment outcome? What is the target population for such screening? And so on.

Examining asymptomatic children in the population could enhance the likelihood of early detection and management of childhood glaucoma, considering its potential occurrence in various ocular and systemic conditions [7].

The classical triad of symptoms at presentation: epiphora without discharge (watering), photophobia and blepharospasm, due to the effects of elevated IOP on the cornea, unilateral or bilateral [4] are major reasons for the pediatrician to urgent refer the patient to a pediatric glaucoma center for diagnostic and adequate treatment.

The evaluation of suspected glaucoma children is very challenging, requiring sedation for uncooperative children and infants. IOP measurement can be altered by obtaining increase values- if the child is not calm, is crying or squeezing or decrease values - when anesthetic is use, except for ketamine, chloral hydrate and benzodiazepines [4].

What would be better to use (or more accurate): minimally invasive approach in diagnosis or the entire investigation protocol under general anesthesia? This is another important dilemma when dealing with childhood glaucoma.

Childhood glaucoma cases often necessitate frequent anesthesia administrations to monitor progression until children can cooperate for slit-lamp examination and intraocular pressure (IOP) measurement. The repeated exposure to anesthesia has been shown to impact not only brain development but also cognition, behavior, and memory. Various sedative agents such as chloral hydrate, pedicloryl, midazolam, and ketamine are employed for short-term procedures with varying success rates. A more recent sedative, dexmedetomidine, has demonstrated superior success rates compared to chloral hydrate, and it is notable for not causing side effects commonly associated with other sedatives. A major advantage is that it can be administered intranasally, without causing any irritation and avoiding the cannulation [8].

The second ethical principle, known as nonmaleficence or "primum non nocere", entails the physician's duty to avoid causing harm to the patient. When medical professionals are dealing with childhood glaucoma weighing the benefits against treatment's burdens is a very difficult task. Some of the questions are: What is the best documented option as surgical technique? What are the risks involved in the surgical procedures? Surgery vs medication what would be better? Pressure-lowering drops or surgery?

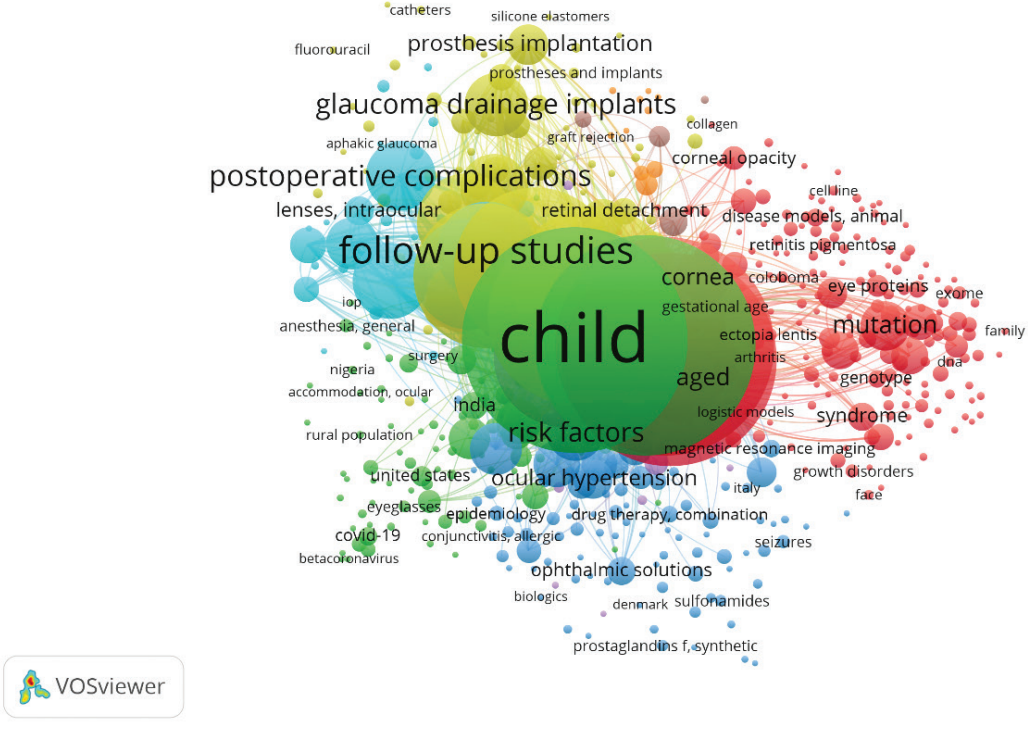

Figure 1. Key word links for "pediatric glaucoma" search in PubMed.

Randomized clinical trials (RCT's) on glaucoma medication in children are difficult to be undertaken due to the low power (low number of participant included – low sample size) as well as study's design and ethical questions raised by Ethical Committees when shaking for approval [16]. According to Sacci et al., in a review performed in 2020, only five RCT's on medical therapy for childhood glaucoma could be considered, however, all underpowered (with reduced number of participants). The investigations conducted comparisons involving dorzolamide with 0.5% timolol gel [17]; brinzolamide with 0.5% levobetaxolol [18]; 0.25% betaxolol, 0.25% timolol gel, and 0.5% timolol gel [19]; latanoprost with 0.5% timolol [20]; and travoprost with 0.5% timolol [21]. Based on the above-mentioned studies, it appears that the effectiveness of glaucoma medications in children is comparable to that observed in adults. The authors concluded that for topic medication in pediatric patients a more frequent follow-up is required and more focused on safety in RCT's design [16].

To date, surgical intervention remains the primary treatment approach for childhood glaucoma, considering medical treatment as a temporary measure for intraocular pressure (IOP) control until surgery can be performed. Glaucoma surgery aims to reduce IOP, and this reduction is linked to alterations in various ocular factors, including axial eye length shortening, lamina cribrosa repositioning, and increased ocular blood flow [22]. The extent of these ocular changes is contingent on the biomechanical properties of the eyeball and impacts ocular refraction [10]. The selection of treatment is influenced by the glaucoma subtype and the condition of the anterior chamber angle. For instance, angle surgery is typically the primary consideration for primary congenital glaucoma, while medication is often employed before surgical intervention in juvenile open-angle glaucoma (JOAG) and secondary glaucoma with open angles. The challenges of glaucoma surgery in children are heightened due to distorted anatomy in buphthalmic eyes, a more aggressive inflammatory and healing response, and the lack of postoperative cooperation for monitoring [16]. Considering the existing challenges in surgical treatment, future studies are imperative to enhance the success rates of techniques and minimize postoperative complications [23].

When discuss the principle of autonomy in pediatric glaucoma, is more likely to evaluate parent's or legal tutor's opinion regarding child's wellbeing and the treatment to be administrated.

The visual prognosis for these patients is contingent on the timing of their presentation and treatment. Prolonged delays in presentation, diagnosis, and management can result in severe visual consequences. The delayed presentation is primarily attributed to a lack of awareness of the disease among caregivers and clinicians.

Seeking professional consensus and establishing clear recommendations can alleviate the sense of families bearing the full burden of decision-making [24].

The concept of a "zone" of parental discretion, wherein parents have the authority to make decisions regarding their children's treatment, is a subject of widespread debate. Various countries may have different extents of parental discretion, with some granting broader or more restricted autonomy. For instance, the United Kingdom (UK) appears to accord greater importance to professional opinions, aiming to safeguard the interests of children [24]. In the UK, if the treatment's benefit (relative to cost/burden) is deemed sufficiently high, it will be administered even if parents decline consent. Conversely, if the benefit is low or the procedure poses too much risk, treatment will not be provided, even if parents express a desire for it.

However, due to the lack of competence to act autonomously, infants and children's treatment requires parents or legal tutors' informed consent for any type of investigations and treatment procedures [25]. The healthcare professionals' team has a key role, not only in treatment plan and follow-up procedures, but also to clearly explain to the parents the importance of continuous monitoring of this severe chronic condition. In pediatric glaucoma, even if the IOP is controlled, the child can lose vision if the refractive error is not corrected. In certain cases, lifelong follow-up maybe required, and disease progression may still occur in spite of surgical intervention and the children's caregivers need to be aware of this unfortunate event [26].

The application of the justice principle, emphasizing fair, equitable, and appropriate treatment, proves challenging in the context of childhood glaucoma. This difficulty arises from the chronic care demands of the condition, coupled with the significant burden on caretakers and elevated per capita economic costs [6]. A geospatial service coverage analysis was conducted by Vu *et al.* in the USA utilized ArcGIS Pro (Esri) software, geocoding the locations (1-hour drive time areas) of service providers (specialists), using data from the American Glaucoma Society and American

Association for Pediatric Ophthalmology and Strabismus, overlaid these regions with demographic data. The analysis revealed that an estimated 14 to 94 new cases per year may face delayed diagnosis risks due to residing in "service desert" areas [6].

Efforts are required to facilitate the application of the justice principle, particularly given the challenges posed by relatively poor socioeconomic status, limited healthcare access, and extended travel times to pediatric ophthalmic centers in managing childhood glaucoma. It is imperative for healthcare policies, especially in developing countries or regions with limited resources, to implement educational initiatives aimed at enhancing caregivers' awareness regarding the importance of early intervention in childhood glaucoma and ensuring the prompt detection of the disease [2]. Additionally, effective referral patterns need to be established for underserved or less resourceful regions since children with glaucoma in these areas face the additional hurdle of limited access to specialists.

To overcome parents and caregiver's challenges involved in the chronic care of the children with this heterogenous group of disorders, a Childrens' Glaucoma Passport was proposed and developed in UK by Bruynseels *et al.* to record the details of treatment plans, including drug/drop regimens, glasses prescription for refractive error and amblyopia treatment plans [27].

Given the significant challenges associated with living with childhood glaucoma, initiatives have been undertaken to engage both children and their parents in disease management, aiming to enhance self-care practices and optimize overall quality of life [27].

In conclusion, childhood glaucoma can result in substantial vision impairment, attributed to causes such as amblyopia, optic nerve damage, or other ocular comorbidities. Amblyopia, encompassing refractive, strabismic, or sensory classifications, stands out as the primary etiology for vision impairment in these patients, followed by glaucomatous optic atrophy.

The World Health Organization's VISION 2020 program has identified pediatric glaucoma as the third most prevalent cause of severe visual impairment and blindness in childhood, contributing to 5% of childhood blindness globally. Children with glaucoma typically experience a significant decline in both vision-related and health-related quality of life compared to their normally sighted counterparts. This decline is attributed to the administration of numerous eyedrops, multiple surgical procedures, and frequent general anesthetics.

Addressing pediatric glaucoma necessitates a multidisciplinary approach, fostering collaborations among ophthalmologists, pediatricians, anesthesiologists, and geneticists to enhance clinical management. Effective communication between the healthcare team and the parents or legal guardians of the children is crucial for successfully managing this chronic condition.

Looking ahead, future efforts are anticipated to concentrate on minimizing side effects of management, achieving improved visual prognosis, and enhancing the overall quality of life for individuals affected by pediatric glaucoma.

Conflict of interest

The authors declare that they have no conflict of interest.

References

1. Saavedra C, Rios HA, Belalcazar S, Rosenstiehl SM. Characteristics of Pediatric Glaucoma in a Latin American Reference Center. J Curr Glaucoma Pract. 2020;14(1):10-15.
2. Shen R, Li VSW, Wong MOM, Chan PPM. Pediatric Glaucoma-From Screening, Early Detection to Management. Children (Basel). 2023;10(2):181.
3. Hoguet A, Grajewski A, Hodapp E, Chang TC. A retrospective survey of childhood glaucoma prevalence according to Childhood Glaucoma Research Network classification. Indian J Ophthalmol. 2016;64(2):118-123.
4. Karaconji T, Zagora S, Grigg JR. Approach to childhood glaucoma: A review. Clin Exp Ophthalmol. 2022;50(2):232-246.
5. Papadopoulos M, Cable N, Rahi J, Khaw PT; BIG Eye Study Investigators. The British Infantile and Childhood Glaucoma (BIG) Eye Study. Invest Ophthalmol Vis Sci. 2007;48(9):4100-4106.
6. Vu DM, Stoler J, Rothman AL, Chang TC. A Service Coverage Analysis of Primary Congenital Glaucoma Care Across the United States. Am J Ophthalmol. 2021;224:112-119.
7. Lingham G, Thakur S, Safi S, Gordon I, Evans JR, Keel S. A systematic review of clinical practice guidelines for childhood glaucoma. BMJ Open Ophthalmol. 2022;7(1):e000933.
8. Kaushik S, Dhingra D, Pandav SS. Current management of pediatric glaucoma. Adv. Ophthalmol. Optom. 2021; 6: 69-85.
9. Dragosloveanu CDM, Potop V, Coviltir V, Dinu V, Păsărică M, Ducan IL, Maier C, Dragosloveanu Ş. Prematurity-Risk Factor or Coincidence in Congenital Glaucoma? Medicina (Kaunas). 2022;58(3):334.
10. Potop V, Coviltir V, Schmitzer S, Corbu C, Ionescu IC, Burcel M, Dăscălescu D. The Relationship Between Corneal Hysteresis and Retinal Ganglion Cells - A Step Forward in Early Glaucoma Diagnosis. Med Sci Monit. 2020;26:e924672.
11. Coviltir V, Burcel M, Cherecheanu AP, Ionescu C, Dascalescu D, Potop V, Burcea M. Update on Myopia Risk Factors and Microenvironmental Changes. J Ophthalmol. 2019;2019:4960852.
12. van Eck NJ, Waltman L. Software survey: VOSviewer, a computer program for bibliometric mapping. Scientometrics. 2010;84(2):523-538.
13. Beauchamp TL, Childress JF. Principles of biomedical ethics. Oxford University Press, USA. 2001; ISBN 0195143310.
14. Curcă PF, Tătaru CI, Burcea M, Tătaru CP. Ethical considerations in laser-assisted refractive surgery. Rom J Leg Med. 2022; 30: 133-142.
15. Varkey B. Principles of Clinical Ethics and Their Application to Practice. Med. Princ. Pract. 2020; 30: 17-28.

16. Sacchi M, Lizzio RAU, Villani E, Monsellato G, Lucentini S, Cremonesi E, Luccarelli S, Serafino M, Nucci P. Medical management of pediatric glaucoma: lessons learned from randomized clinical trials. Graefes Arch Clin Exp Ophthalmol. 2020;258(8):1579-1586.
17. Ott EZ, Mills MD, Arango S, Getson AJ, Assaid CA, Adamsons IA. A randomized trial assessing dorzolamide in patients with glaucoma who are younger than 6 years. Arch Ophthalmol. 2005;123(9):1177-1186.
18. Whitson JT, Roarty JD, Vijaya L, Robin AL, Gross RD, Landry TA, Dickerson JE, Scheib SA, Scott H, Hua SY, Woodside AM, Bergamini MV; Brinzolamide Pediatric Study Group. Efficacy of brinzolamide and levobetaxolol in pediatric glaucomas: a randomized clinical trial. J AAPOS. 2008;12(3):239-246.e3.
19. Plager DA, Whitson JT, Netland PA, Vijaya L, Sathyan P, Sood D, Krishnadas SR, Robin AL, Gross RD, Scheib SA, Scott H, Dickerson JE; BETOPTIC S Pediatric Study Group. Betaxolol hydrochloride ophthalmic suspension 0.25% and timolol gel-forming solution 0.25% and 0.5% in pediatric glaucoma: a randomized clinical trial. J AAPOS. 2009;13(4):384-390.
20. Maeda-Chubachi T, Chi-Burris K, Simons BD, Freedman SF, Khaw PT, Wirostko B, Yan E; A6111137 Study Group. Comparison of latanoprost and timolol in pediatric glaucoma: a phase 3, 12-week, randomized, double-masked multicenter study. Ophthalmology. 2011;118(10):2014-2021.
21. Dixon ER, Landry T, Venkataraman S, Gustafson N, Salem C, Bradfield Y, Aljasim LA, Feldman R. A 3-month safety and efficacy study of travoprost 0.004% ophthalmic solution compared with timolol in pediatric patients with glaucoma or ocular hypertension. J AAPOS. 2017;21(5):370-374.e1.
22. Popa-Cherecheanu A, Iancu RC, Schmetterer L, Pirvulescu R, Coviltir V. Intraocular Pressure, Axial Length, and Refractive Changes after Phacoemulsification and Trabeculectomy for Open-Angle Glaucoma. J Ophthalmol. 2017;2017:1203269.
23. Munteanu M, Munteanu G, Zolog I, Giuri S, Coviltir V, Stanca H, Cretu O. Okuläre Dekompressions-Retinopathie nach kombinierter tiefer Sklerektomie und Trabekulotomie [Ocular decompression retinopathy after combined deep sclerectomy and trabeculotomy]. Klin Monbl Augenheilkd. 2012;229(8):830-1. German.
24. Wilkinson D, Savulescu J. Ethics, conflict and medical treatment for children: from disagreement to dissensus; Elsevier. 2018; ISBN 0702077836.
25. Curcă G.C. Dilemmas regarding the informed consent in the informative model of the doctor-patient relationship. Rom J Leg Med 2014; 22: 137-143.
26. Kantipuly A, Pillai MR, Shroff S, Khatiwala R, Raman GV, Krishnadas SR, Lee Robin A, Ehrlich JR. Caregiver Burden in Primary Congenital Glaucoma. Am J Ophthalmol. 2019;205:106-114.
27. Bruynseels A, Cross V, Sii F, Shah P, Abbott J. Developing a children's glaucoma passport: mapping innovations in healthcare. Eye (Lond). 2017;31(12):1635-1638.