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ORIGINAL RESEARCH

Clinical Research for Inherited Retinal Disease Related Pediatric Blindness: A Preliminary Descriptive Analysis Based on ClinicalTrials.gov

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Background: Childhood blindness is a significant global health concern, consistently identified in existing research as stemming from rare genetic and congenital disorders. With the technological advances of the 21st century which have positively impacted many areas of human life, healthcare included, recent advances in gene therapy and pharmacological interventions have served to spur clinical research in this area. The primary focus of the current study was to use data from ClinicalTrials.gov to carry out a preliminary exploration and and descriptive analysis of clinical trials focusing on the treatment of childhood blindness.

Methods: A cross-sectional analysis was conducted using data from ClinicalTrials.gov. The initial search for data in ClinicalTrials.gov yielded a total of 110 studies under blindness-related conditions. Upon further cross-examination of these studies based on the inclusion criteria, only five interventional trials (published between 2012 and 2023) specifically targeting childhood blindness met the inclusion criteria and were therefore included. Key trial characteristics studied conditions, intervention types, outcome measures, study phases, and enrollment sizes were extracted and analyzed descriptively.

Results: Across the five included trials, a majority of trials investigated rare genetic conditions, including Leber Congenital Amaurosis, Wolfram Syndrome, and Osteoporosis Pseudoglioma. On interventions, the most commonly used approaches for handling childhood blindness include gene therapy vectors like AAV RPE65, antisense oligonucleotides like QR-110, and repurposed pharmacological agents such as lithium and dantrolene sodium. All studies included children within their target populations, and most were early-phase (Phase 1/2) trials with small sample sizes (11–26 participants). Primary outcomes focused on safety, while secondary outcomes assessed visual function and biochemical changes.

Conclusion: Although limited in number, current clinical trials represent a promising shift toward targeted therapies for childhood blindness. The dominance of early-phase studies highlights the need for expanded, multicenter, and later-phase trials. Future research should aim to improve trial accessibility, standardize outcome measures, and ensure ethical conduct in pediatric populations.

Keywords: childhood blindness, pediatric ophthalmology, clinical trials, gene therapy, Leber Congenital Amaurosis, X-linked retinitis pigmentosa, achromatopsia, Leber hereditary optic neuropathy, Usher syndrome

Introduction

Childhood blindness is a devastating condition that can significantly affect a child's development, education, and quality of life, leading to disability. According to Keeffe,[1] childhood blindness is a major health concern in that while more adults suffer vision loss and blindness than children, the actual impact of vision loss and blindness as measured in disability-adjusted life years (DALY) positions childhood blindness second only to cataracts across the global burden of eye disease. Further, childhood blindness has for years remained among the top five core priority areas for the World Health Organization (WHO) in regard to the right to sight. Blindness has the effect of compromising quality of life, especially when experienced in the early childhood years where it can negatively impair child development and restrict

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not only their participation in social activities but also have major consequences on their education and later employment opportunities.[2,3] Globally, it is estimated that 1.4 million children are blind, with the majority residing in low-income countries. However, congenital and genetic causes of blindness, such as Leber's Congenital Amaurosis (LCA), Wolfram Syndrome, and Osteoporosis Pseudoglioma Syndrome, are also prevalent in higher-income countries and present unique therapeutic challenges.[4,5] Across the current literature on blindness, researchers agree that early-onset blindness often arises from hereditary retinal degenerations, optic nerve hypoplasia, or metabolic syndromes and deficiencies, making it a focus of genetic and pharmacologic research.[6–8]

In recent years, novel therapeutic approaches including gene therapy, RNA-based drugs, and pharmacological agents have shown promising results.[9,10] Aniz-Girach et al (2022) agreed that although certain traditional conditions, such as inherited retinal diseases (IRDs), remain incurable and individuals suffering from them can only receive supportive care, advancements in understanding of the genotype-phenotype correlations associated with these conditions are facilitating the development of appropriate therapeutic measures and strategies.[11] Similarly, Saw and Song (2024) emphasized that recent advancements in addressing childhood and adulthood blindness have identified RNA molecules as exceptionally promising due to their ability to target undruggable proteins and molecules with minimal side effects and a high level of precision.[12] In a study investigating recent applications of RNA therapeutics in clinics, Ha Thi et al (2023) found that these approaches offer high specificity and the ability to target particular gene-related proteins associated with the condition while delivering cost-effective benefits in the production process.[13] The FDA's approval of voretigene neparvovec-rzyl (Luxturna) for RPE65 mutation-associated retinal dystrophy was a landmark moment in ophthalmic gene therapy.[14] With the emergence of such breakthroughs, an increasing number of clinical trials have been specifically aimed at understanding treatment approaches for blindness in children, many of which are registered on ClinicalTrials.gov, a global database of privately and publicly funded clinical studies.

Despite advancements in therapeutic options for childhood blindness, there is a scarcity of research on specific findings on which methods yield optimal outcomes and should consequently be recommended among relevant stakeholders. The purpose of the current study was to explore the characteristics of clinical trials focusing on childhood blindness, analyze the type and phase of interventions being tested, and assess the current research landscape using data from ClinicalTrials.gov. This analysis provides valuable insight into the direction of pediatric ophthalmic research and the therapeutic areas that are gaining momentum. It is vital to note that the key strength of this study is its exclusive focus on registered trials on a niche that includes clinically significant subgroup. In particular, by systematically analyzing trial attributes such as intervention type, study phase, and outcome measures, the study offers a consolidated snapshot of current research directions in gene therapy for childhood IRDs. It is the researchers view that unlike prior literature focused on specific conditions or therapies, this preliminary descriptive analysis maps the broader clinical research, highlighting critical gaps and early-stage trends in pediatric IRD trial development.

Methods

On March 15, 2025, the researchers carried out a descriptive cross-sectional analysis through the use of data extracted from ClinicalTrials.gov. The data search was conducted using the following keywords or their combinations: child blindness, treatment, biological, and gene therapy. As the initial search did not produce trials for common inherited retinal diseases like X-linked retinitis pigmentosa, achromatopsia, Leber hereditary optic neuropathy, and Usher syndrome, a second search was carried out later including these specific conditions as part of the search terms and phrases.

Inclusion and Exclusion Criteria

For a trial to be included in the current study as a data source, it had to be an interventional clinical trial research and one in which the authors targeting blindness-related conditions in children completed studies with results. The dataset included information such as NCT numbers, study titles, conditions, interventions, outcome measures (both primary and secondary), age groups, phases, and enrollment numbers, as well as the completion date of the trial. Only trials involving children (as per the age field) were selected. On the other hand, trials were excluded from this study if they only targeted fully adult populations, were observational in nature, did not contain fully published and accessible results, or addressed non-treatment-focused aspects (for example diagnostic tools or screening alone). The particular search period for the included trials was limited to 2012 and 2023 with the aim of getting trials that had been carried out and completed over the decade period in between and identify emerging trends and patterns on the published trials. All included trials had to be published in the ClinicalTrials.gov database.

The data extraction was carried out by the principal researcher assisted by two other researchers. The process included first determining the suitability of the emerging studies by screening the titles, abstracts, and findings to confirm that their findings could be of importance in the collection of the relevant data for the current study. An initial screening of study titles and summaries was conducted, followed by a full review of the detailed study entries on ClinicalTrials.gov. Discrepancies in study selection or classifications were resolved through discussion and consensus. Data from all included studies were extracted using the same criteria employed in the search, encompassing numerical values and string variables related to treatment type and frequency, NCT number, primary and secondary outcomes, trial completion date, conditions and interventions, as well as the phases of the included intervention allowed approaches in each trial. Overall and for the purpose of ensuring relevance and consistency, trials included in this study were limited to interventional studies specifically targeting blindness-related conditions in pediatric populations, with completed status and publicly available results. Each study had to report treatment-focused interventions, not diagnostic or observational aims. Trials were selected based on strict screening of study descriptors, age criteria, and intervention relevance. Figure 1

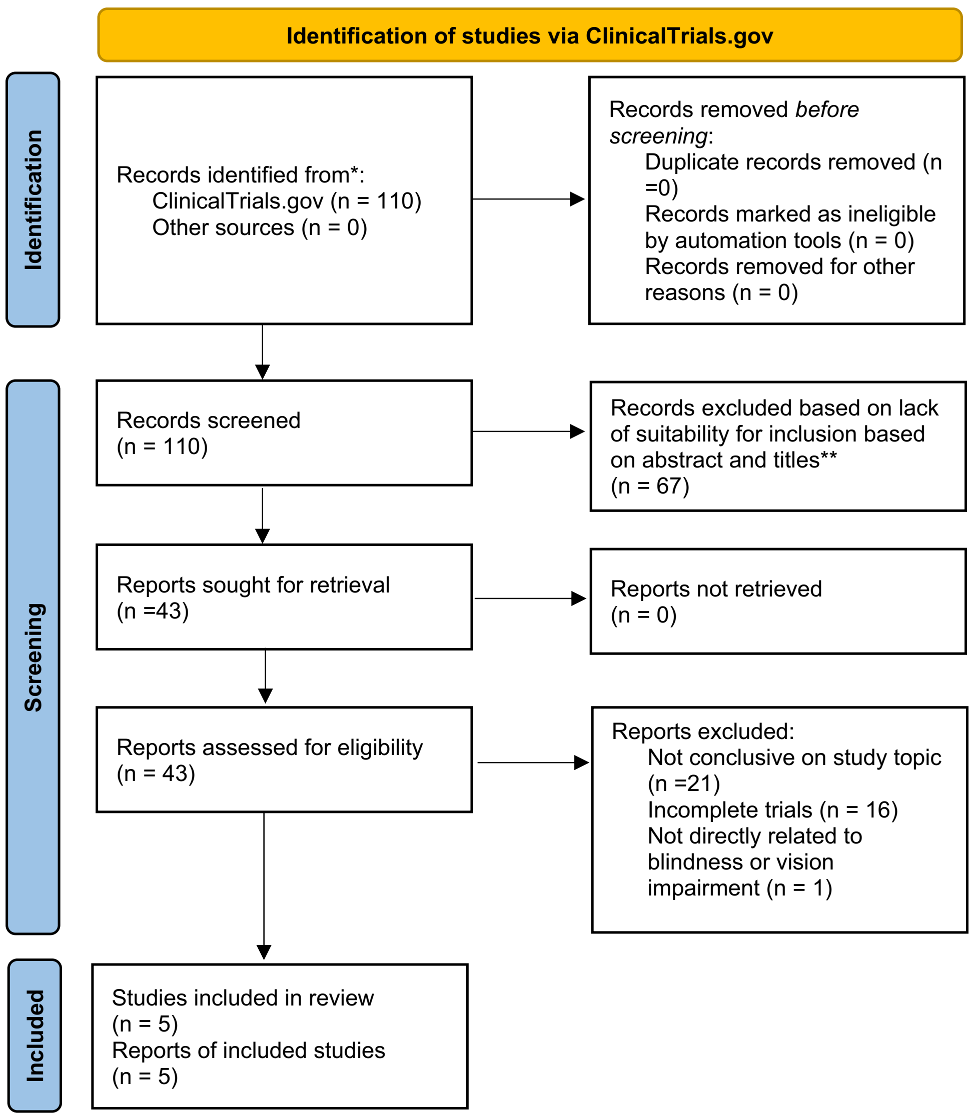

Figure 1 PRISMA Chart for Identification of Trials for Inclusion. Adapted from Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ.* 2021;372(71). Creative Commons.[15]

is the PRISMA flow chart diagram for the selection and screening of the studies to capture the five included trials. This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines by Page et al[15]

Data Analysis

A descriptive analytical approach was applied. Frequency distributions and simple tabulations were used to characterize the types of conditions studied, intervention strategies, and clinical trial phases. Graphical summaries and tables were created where appropriate to aid in visualizing the current research landscape in pediatric blindness therapy. The study did not include inferential statistics as part of the data analysis as the researchers were interested in establishing the current status based on previously published trials.

Ethical Approval

As this study did not directly include human participants or any tests, ethical approval was not required. As earlier indicated, all data were sourced from publicly available, anonymized clinical trial registries.

Results

Only five clinical trials focusing on childhood blindness were identified from a total of 110 studies on ClinicalTrials.gov. These studies examined a number of uncommon genetic and metabolic conditions which impair vision in young people (Table 1). Leber Congenital Amaurosis (LCA) was the most often examined condition, appearing in three out of the five investigations. Other disorders included Wolfram Syndrome, which is frequently linked to diabetes mellitus and optic nerve atrophy, and Osteoporosis Pseudoglioma Syndrome. The trials examined a range of treatment modalities. Adeno-associated viral (AAV) vectors, such as rAAV2-CB-hRPE65 and AAV RPE65, were employed in three gene therapy experiments to introduce functional genes into the retina. One study looked into QR-110, an antisense oligonucleotide medication intended to fix RNA splicing errors in CEP290 mutations (Table 2). Lithium carbonate and dantrolene sodium, two pharmacological treatments with possible neuroprotective or cellular stabilizing effects related to congenital blindness, were evaluated in two more trials. Figure 1 depicts the intervention distribution across the five studies.

All five studies established age eligibility criteria encompassing children (<18 years), with some additionally including adults and older persons. The majority of the trial stages (Phase 1/2) were preliminary, indicating an emphasis on assessing initial efficacy and safety; one trial, however, did not specify the phase being studied. Given the rarity of the disorders being investigated and the early stage of the studies, enrollment sizes were modest, ranging from 11 to 26 patients. The main results evaluated safety measures, namely the frequency of systemic or ocular adverse events. Secondary outcomes, where reported, included functional measures such as changes in visual fields, biochemical markers

Table 1 Descriptive Details from the Included Trials

NCT Number	Conditions Investigated	Phase	Number of Participants
NCT00749957	Leber Congenital Amaurosis	1 and 2	12
NCT02781480	Leber Congenital Amaurosis	1 and 2	15
NCT03140969	Leber Congenital Amaurosis	1 and 2	11
NCT01108068	Osteoporosis Pseudoglioma	Not reported	26
NCT02829268	Wolfram Syndrome; Diabetes Mellitus; Optic Nerve Atrophy; Ataxia	1 and 2	21

Table 2 Description of the Included Trials, Titles, Outcomes, and Completion Time

NCT Number	Study Title	Primary Outcome Measures	Secondary Outcome Measures	Date
NCT00749957	Phase 1/2 Safety and Efficacy Study of AAV-RPE65 Vector to Treat Leber Congenital Amaurosis	Number of Participants Experiencing Ocular or Non-ocular Adverse Events, 2 years	Participants With Changes in Visual Fields, Improvement in the central 30 degree visual field, measured by static perimetry, at one or more time points after treatment, that was greater than the limit of agreement for baseline values., 2 years; Participants With Changes in Best Corrected Visual Acuity, Increase in BCVA of 7 or more letters at Year 2 visit compared to average baseline value, 2 years	9/22/2017
NCT02781480	Clinical Trial of Gene Therapy for the Treatment of Leber Congenital Amaurosis (LCA)	Overall Safety of Adeno-Associated Virus Vector (AAV-OPTIRPE65) - Number of Participants With a Safety Event, Safety was defined as an advanced therapy investigational medicinal product (ATIMP) related: - Reduction in visual acuity by 15 Early Treatment Diabetic Retinopathy Study (ETDRS) letters or more. - Severe unresponsive inflammation. - Infective endophthalmitis. - Ocular malignancy. - Grade III or above non-ocular suspected unexpected serious adverse reaction (SUSAR)., 6 months		2018-12
NCT03140969	Study to Evaluate QR-110 in Leber's Congenital Amaurosis (LCA) Due to the c.2991+1655A>G Mutation (p.Cys998X) in the CEP290 Gene	Frequency and Severity of Ocular Adverse Events in the Treatment and Contralateral Eyes, 1 year	Frequency and Severity of Non-ocular Adverse Events, 1 year|Change in Best-corrected Visual Acuity (BCVA), 1 year|Change in Full-field Stimulus Test (FST), Average Red Light Score, 1 year|Change in Full-field Stimulus Test (FST), Average Blue Light Score, 1 year	10/2/2019
NCT01108068	Trial of Lithium Carbonate for Treatment of Osteoporosis-pseudoglioma Syndrome	pQCT of Lower Leg, pQCT will be done at baseline for all OPPG participants and unaffecteds. The Z-score indicates the number of standard deviations away from the mean of age matched controls. A Z-score of 0 is equal to the mean, with negative numbers indicating values lower than the mean and positive values higher. A positive change in Z-score indicates a favorable outcome., Baseline	pQCT Z-score in OPPG Participants at Baseline and 6 Months After Lithium, The Z-score indicates the number of standard deviations away from the mean of age matched controls. A Z-score of 0 is equal to the mean, with negative numbers indicating values lower than the mean and positive values higher. A positive change in Z-score indicates a favorable outcome.Z-score of pQCT variable was noted for the in two OPPG participants who received lithium and were also able to get pQCT scans. The "n" of 2 was too small to do statistical analyses. Of the 5 OPPG who were on lithium, 2 were too small for the machine (eventhough over age 4) and 1 had rods in his legs and could not have pQCT, baseline, 6 months	2014-07

(*Continued*)

Table 2 (Continued).

NCT Number	Study Title	Primary Outcome Measures	Secondary Outcome Measures	Date
NCT02829268	A Clinical Trial of Dantrolene Sodium in Pediatric and Adult Patients With Wolfram Syndrome	Number of Participants With Treatment-related Adverse Events as Assessed by Liver Function Tests, The investigators assess the safety and tolerability of dantrolene sodium administered orally at upper end of therapeutic dose range for 6 months in patients with Wolfram syndrome. More specifically, the investigators perform liver function tests to check the levels of certain enzymes and proteins in participants' blood. Levels that are higher or lower than normal can indicate liver problems. The liver function tests include: Alanine transaminase (ALT), Aspartate transaminase (AST), Alkaline Phosphatase (AP), and bilirubin., 6 months	Changes in C-peptide Levels in Participants Assessed by the ELISA Assay, The investigators determine the effect of dantrolene sodium on residual beta cell functions. The investigators monitor base-line C-peptide levels in participants' blood. The investigators also monitor C-peptide levels in participant's blood during the oral mixed meal tolerance test. The night before the oral mixed meal tolerance test, the participants will turn their insulin pump basal rate to 50% of the normal rate at midnight or take half of their evening dose of Lantus insulin and fasted from midnight until the test at 8 a.m. The mixed meal consists of 6 mL/kg (maximum 360 mL) of Boost Original (SociÃ©tÃ© des Produits NestlÃ© S.A., Vevey, Switzerland). Blood for glucose and C-peptide measurement will be drawn at time 0 (fasting) and 30 minutes after the Boost. If a subject's fasting glucose exceeds 11.1 mmol/l, the test will not be performed, but fasting glucose and C-peptide will be obtained., 6 months|Changes in Visual Functioning in Participants Assessed by Visual Functioning Questionnaire-25., Changes in Visual Functioning in participants assessed by Visual Functioning Questionnaire-25. The Visual Functioning Questionnaire-25 (VFQ-25) is divided into several subdomains, each assessing a specific aspect of visual functioning and its impact on an individual's life. There are a total of 11 subdomains in the VFQ-25. To calculate the total score on the VFQ-25, we follow these steps: 1. Calculate Subdomain Scores, 2. Weighted Sum, 3. Calculate Total Score VFQ-25 provides scores that range from 0 to 100. The total score represents the overall impact of visual functioning on the individual's quality of life, with higher scores indicating better quality of life and less impact from vision problems., 6 months|Changes in Best-corrected Visual Acuity in Participants Measured by LogMar Score, Best-corrected visual acuity is assessed using the Snellen optotype and then converted into LogMar Scores (Minimum: −0.30, Maximum: 3.0). A higher LogMar score signifies poorer vision., 6 months|Changes in Neurological Functions in Participants Assessed by the Wolfram Unified Rating Scale (WURS), Neurological functions are assessed by the Wolfram Unified Rating Scale (WURS). The WURS is divided into the following subscales: Physical Assessment and Behavioral Assessment. Physical Assessment (34 items rated on a scale from 0 = no symptoms to 4 = highest severity, minimum: 0, Maximum: 136) and Behavioral Assessment (9 items rated on frequency and severity from 0 = normal behavior to 3 = highest severity, Minimum: 0, Maximum: 27). Subscale scores are summed to calculate the total scores (minimum: 0, Maximum: 163). Higher total scores indicate more severe neurological manifestations., 6 months	2023-02

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(eg, C-peptide levels), or imaging-based assessments (eg, pQCT for bone density). Table 1 captures the conditions, phases, and number of participants in the included trials.

The primary completion dates of the trials ranged from 2014 to 2023, indicating that while some studies are completed, others are ongoing or recently concluded.

Discussion

The findings in this study reveal a diverse range of clinical trials and interventions as being available and designed to target blindness in pediatric populations from different therapeutic perspectives. This study is among the few to provide a consolidated overview of interventional trials specifically targeting pediatric IRDs, offering a real-time snapshot of current translational research efforts. Leber Congenital Amaurosis was the most frequently studied condition, consistent with its prominence as a leading cause of inherited blindness in children.[12] Three of the five trials included gene therapy vectors such as AAV-RPE65, which are designed to restore function in defective retinal cells. This reflects the growing reliance on molecular and gene-based therapies in addressing hereditary ocular diseases. In a notable way, the identification of LCA as the leading target among IRDs also suggests a prioritization of conditions with well-characterized genetic underpinnings, making them more amenable to gene-targeted treatments.

The presence of drugs such as QR-110 (now known as sepofarsen) and dantrolene sodium demonstrates the breadth of therapeutic strategies being explored and aligns well with current research supporting the use of pharmacological approaches as one of the core interventions in dealing with pediatric blindness. According to Beharry et al (2016), various drugs such as methylxanthines, antioxidants, VEGF inhibitors, and others are among the key pharmacological interventions employed in treating childhood blindness conditions, particularly retinopathy of prematurity.[16] In the findings of the current study, drugs like QR-110 emerged as an antisense oligonucleotide that has increasingly been tried and targets a common mutation in the CEP290 gene found in LCA10 patients. In this regard, this drug is being developed to bypass the mutation at the RNA level and can, in the long run, present significant benefits in helping in the effective management of childhood blindness.[17] Dantrolene sodium, traditionally used for muscle disorders, is being repurposed for Wolfram Syndrome due to its potential to stabilize calcium homeostasis in endoplasmic reticulum stress-related conditions.[18] Abreu et al (2021) contended that this pharmacological product, through its capacity to reduce ER stress, presents as a potential solution that can help preserve pancreatic beta-cell function and slow the progression of diabetes mellitus, one of the syndrome's hallmark symptoms.[19] Further, and in alignment with the findings of the current study, early clinical trials suggest that it could also improve neurological outcomes by mitigating neurodegeneration linked to disrupted calcium signaling.[19] This diversity in therapeutic modalities in a special way emphasize the multidimensional nature of pediatric blindness, where different molecular mechanisms may require distinct, tailored interventions.

Many previous studies have focused on the safety of various interventions used to treat pediatric blindness. For instance, Bennett et al (2016) asserted that there is every need to understand the safety associated with childhood blindness interventions such as AAV2-hRPE65v2. Consequently, it is unsurprising that the current investigation reveals safety as a fundamental key outcome measure across multiple trials.[20] Despite the evident innovations in the interventions currently being employed to treat childhood blindness, it was notable that most trials were in preliminary (Phase 1/2) stages, which is an indication of a high degree of alignment with the current literature and indicates that safety and dosing remain the primary focus of research. The limited sample sizes as few as 11 participants in one study highlight the challenges of conducting trials in rare pediatric populations. Multicenter and international collaborations may help address recruitment barriers and improve statistical power. Moreover, the narrow participant pools observed across trials underscore the rarity of these conditions and the logistical challenges of recruiting pediatric participants with specific genotypes. These recruitment limitations further pinpoints the importance of global patient registries and genomic screening programs, which can accelerate patient identification and facilitate earlier trial enrollment.

Notable existing studies have explored different short-term efficacies of various interventions on childhood blindness. In a 2009 study, Gogate et al noted that despite a substantial increase in the number of studies being published on interventions around pediatric blindness, attention remained mainly focused on safety as a short-term measure of how effective these interventions can be.[21] In alignment with this observation by Gogate et al, the findings in the current study indicated that most of the outcome measures were mostly safety-related, with few trials measuring long-term efficacy or visual function improvement.[22] This gap emphasizes the need for extended follow-up studies and the integration of quality-of-life measures in future protocols. Incorporating patient-reported outcomes and functional vision assessments has the potential to provide richer insights into the real-world impact of these interventions beyond laboratory metrics. In addition, ethical considerations in pediatric trials, such as consent, minimal risk standards, and equitable access, must be carefully navigated as more high-cost gene therapies enter clinical testing.

The predominant focus of most clinical trials on short-term outcomes for interventions addressing childhood blindness indicates that, despite ongoing innovation in this field, there remains a need for more comprehensive, large-scale, and late-phase studies.[3,22] Through the mapping of therapeutic trends across genetic, pharmacologic, and molecular approaches, this study contributes a foundational layer for guiding future trial design, funding priorities, and clinical decision-making. The findings further do suggest that cross-disciplinary collaboration, one that entails bridging ophthalmology, neurology, molecular biology, and bioethics, will be key in shaping robust, patient-centered trial designs. Regulatory support, funding mechanisms, and advocacy for rare pediatric disorders are and will continue to be essential for the purpose of transitioning promising therapies from experimental stages to widespread clinical application.[23,24]

Limitations and Future Directions

When evaluating the results, it is important to consider several notable limitations of this study. Of the 110 blindness-related research studies identified on ClinicalTrials.gov, only five specifically focused on pediatric blindness. The findings' generalizability is limited by the small number of eligible trials, which might not accurately reflect the state of research on treating juvenile blindness worldwide. Second, ClinicalTrials.gov was the only source of data used in the study. Selection bias may have resulted from the probable omission of pertinent studies that were recorded in other trial registries, such as the EU Clinical Trials Register or the WHO International Clinical Trials Registry Platform. The very focus on ClinicalTrials.gov could also have limited the studies covering common inherited retinal diseases like X-linked retinitis pigmentosa, achromatopsia, Leber hereditary optic neuropathy, and Usher syndrome all of which are relevant conditions in the current study. Additionally, the quality of reporting by trial sponsors determines how accurate and full the data are, and some entries lacked specific information, particularly regarding secondary outcome measures or research phase classification. Third, although children were enrolled in all included studies, several also included adults and older individuals. This age overlap limited the capacity to accurately assess the benefits of child-focused treatments by making it challenging to isolate pediatric-specific outcomes.

Notwithstanding these drawbacks, the results point to significant patterns and knowledge gaps in the study of juvenile blindness. More clinical trials with a specific focus on children and pediatric outcomes are needed going forward. In order to verify the safety and effectiveness of new treatments, future research should prioritize late-phase (Phase 3) trials. Additionally, studies should use standardized end measures for visual function in order to increase study comparability. Prioritizing long-term follow-up is also necessary to evaluate the long-term safety profile and the durability of therapeutic benefits, particularly for gene treatments and experimental medications. Furthermore, growing multicenter trial networks and international collaboration could aid in overcoming obstacles associated with rare disease recruitment and small sample sizes. Lastly, in order to fully analyze the effects of treatment in juvenile groups, future research should incorporate quality-of-life evaluations and patient-reported outcomes.

Conclusion

This document provides an overview of clinical research related to the treatment of childhood blindness as listed on ClinicalTrials.gov. Despite the limited number of trials that fulfilled the inclusion criteria, they show encouraging developments in molecular treatments, pharmacological interventions, and gene therapy for uncommon pediatric ocular illnesses. Preliminary phase studies are more common, highlighting the continuous efforts to determine safety and dosage in these vulnerable populations. The research findings also show an increasing interest and creativity focused on addressing inherited and congenital causes of blindness in children, notwithstanding the small number of trials. Nonetheless, small sample sizes, insufficient data directly relating to children, and the necessity of long-term outcome evaluation remain obstacles. Future initiatives must focus on broadening the scope of trials, enhancing accessibility, and encouraging partnerships in order to hasten the creation of safe, efficient, and easily available treatments for pediatric blindness.

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Disclosure

The authors report no conflicts of interest in this work.

References

1. Keeffe J. Childhood vision impairment. *Br J Ophthalmol*. 2024;88(6):728–729. doi:10.1136/bjo.2003.040006
2. Loh L, Prem-Senthil M, Constable PA. A systematic review of the impact of childhood vision impairment on reading and literacy in education. *J Optom*. 2024;17(2):100495. doi:10.1016/j.optom.2023.100495
3. Rainey L, Elsman EBM, van Nispen RMA, van Leeuwen LM, van Rens GHMB. Comprehending the impact of low vision on the lives of children and adolescents: a qualitative approach. *Qual Life Res*. 2016;25(10):2633–2643. doi:10.1007/s11136-016-1292-8
4. Gilbert C, Foster A. Childhood blindness in the context of VISION 2020—The Right to Sight. *Bull World Health Organ*. 2001;79(3):227–232.
5. Hoyt CS, Good WV. The many challenges of childhood blindness. *Arch Dis Child*. 2001;85(6):452–453. doi:10.1136/adc.85.6.452
6. Garcia-Filion P, Borchert M. Optic nerve hypoplasia syndrome: a review of the epidemiology and clinical associations. *Curr Treat Options Neurol*. 2013;15(1):78–89. doi:10.1007/s11940-012-0209-2
7. Igoe JM, Lam BL, Gregori NZ. Update on clinical trial endpoints in gene therapy trials for inherited retinal diseases. *J Clin Med*. 2024;13(18):5512. doi:10.3390/jcm13185512
8. Maccora I, Marrani E, Pagnini I, et al. Challenges and management of childhood noninfectious chronic uveitis. *Expert Rev Clin Immunol*. 2023;19(6):599–611. doi:10.1080/1744666X.2023.2198210
9. Shrestha M, Bhandari G, Kamalakannan S, et al. Evaluating the effectiveness of interventions to improve the follow-up rate for children with visual disabilities in an eye hospital in Nepal: nonrandomized study. *JMIR Pediatr Parent*. 2023;6:e43814. doi:10.2196/43814
10. Wu KY, Kulbay M, Toameh D, Xu AQ, Kalevar A, Tran SD. Retinitis pigmentosa: novel therapeutic targets and drug development. *Pharmaceutics*. 2023;15(2):685. doi:10.3390/pharmaceutics15020685
11. Girach A, Audo I, Birch DG, et al. RNA-based therapies in inherited retinal diseases. *Ther Adv Ophthalmol*. 2022;14:25158414221134602. doi:10.1177/25158414221134602
12. Simonelli F, Ziviello C, Testa F, et al. Clinical and molecular genetics of Leber's congenital amaurosis: a multicenter study of Italian patients. *Invest Ophthalmol Vis Sci*. 2010;51(7):3399–3406. doi:10.1167/iovs.09-4752
13. Ha Thi HT, Than VT. Recent applications of RNA therapeutic in clinics. *Prog Mol Biol Transl Sci*. 2024;203:115–150. doi:10.1016/bs.pmbts.2023.12.015
14. Russell S, Bennett J, Wellman JA, et al. Efficacy and safety of voretigene neparvovec (AAV2-hRPE65v2) in patients with RPE65-mediated inherited retinal dystrophy: a randomized, controlled, open-label, phase 3 trial. *Lancet*. 2017;390(10097):849–860. doi:10.1016/S0140-6736(17)31868-8
15. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372(71). doi:10.1136/bmj.n71
16. Beharry KD, Valencia GB, Lazzaro DR, Aranda JV. Pharmacologic interventions for the prevention and treatment of retinopathy of prematurity. *Semin Perinatol*. 2016;40(3):189–202. doi:10.1053/j.semperi.2015.12.006
17. Dulla K, Aguila M, Lane A, et al. Splice-modulating antisense oligonucleotide therapy for ocular atrophy associated with CEP290 mutations. *Nat Med*. 2018;24(12):1796–1806. doi:10.1038/s41591-018-0260-0
18. Lu S, Wang X, Thelin WR, Paudel HK. Dantrolene improves abnormal Ca^{2+} signaling in neurons derived from patients with Wolfram syndrome. *J Biol Chem*. 2014;289(24):17365–17376. doi:10.1074/jbc.M114.562694
19. Abreu D, Stone SI, Pearson TS, et al. A phase Ib/IIa clinical trial of dantrolene sodium in patients with Wolfram syndrome. *JCI Insight*. 2021;6(15):e145188. doi:10.1172/jci.insight.145188
20. Bennett J, Wellman J, Marshall KA, et al. Safety and durability of effect of contralateral-eye administration of AAV2 gene therapy in patients with childhood-onset blindness caused by RPE65 mutations: a follow-on phase 1 trial. *Lancet*. 2016;388(10045):661–672. doi:10.1016/S0140-6736(16)30371-3
21. Gogate P, Kalua K, Courtright P. Blindness in childhood in developing countries: time for a reassessment? *PLoS Med*. 2009;6(12):e1000177. doi:10.1371/journal.pmed.1000177
22. Barker PM, Reid A, Schall MW. A framework for scaling up health interventions: lessons from large-scale improvement initiatives in Africa. *Implement Sci*. 2016;11(1):12. doi:10.1186/s13012-016-0374-x
23. Hansen ED, Hartnett ME. A review of treatment for retinopathy of prematurity. *Expert Rev Ophthalmol*. 2019;14(2):73–87. doi:10.1080/17469899.2019.1596026
24. Saw PE, Song E. Advancements in clinical RNA therapeutics: present developments and prospective outlooks. *Cell Rep Med*. 2024;5(5):101555. doi:10.1016/j.xcrm.2024.101555