www.jcimcr.org

JCIMCR OPEN ACCESS Journal of Clinical Images and Medical Case Reports

ISSN 2766-7820

Case Report

Open Access, Volume 2

Targeted next generation sequencing gene panels used to improve diagnosis of congenital cataract and current treatment strategies

Elewys Hearne, MB ChB[1]*; Susan Lightman, FRCP(UK) PhD FRCOphth[2]

[1]BMedSci ST4 Severn Deanery, United Kingdom.

[2]Professor of Clinical Ophthalmology UCL/IOO, Professor of Ophthalmology University of the Highlands and Islands

***Corresponding Author: Elewys Hearne, MB ChB**
BMedSci ST4 Severn Deanery, United Kingdom
Email: ellieghearne@gmail.com

Received: Mar 26, 2021
Accepted: Apr 26, 2021
Published: Apr 29, 2021
Archived: www.jcimcr.org

Abstract

There is huge potential in using targeted Next Generation Sequencing (NGS) gene panels to improve diagnosis of congenital cataract, however the many difficulties in incorporating it into routine clinical care are explored. Treatment options for children with congenital cataract are described.

Keywords: Congenital; Cataracts; Genetics; Treatment.

Introduction

Congenital cataract can cause lifelong visual loss and by 15 years of age has an incidence of 3.5 per 10,000 [1]. 27-39% of congenital cataracts are thought to be inherited [2], and they may be autosomal-dominant, autosomal-recessive or X-linked. Over 100 genes are currently associated with cataract, and there is a predominance of autosomal dominant inheritance [3]. Congenital cataracts can be either isolated or related to other syndromic conditions or ophthalmic abnormalities [4].

Timely diagnosis of the cause facilitates prompt referral into appropriate multidisciplinary care. Optimal visual outcomes are achieved by early identification and swift surgical intervention, combined with amblyopia treatment. Bilateral congenital cataracts have better visual outcomes post-surgery than unilateral cataract [5].

Current management and investigation pathways yield a low proportion of cases in which the underlying cause is found [6]. Referral to a clinical geneticist is only recommended if the child is dsymorphic. Targeted Next Generation Sequencing (NGS) gene panels used in research shows promising results in increasing the percentage of underlying causes found in patients with congenital cataracts.

Aims

To investigate the potential use of NGS testing for the diagnosis of congenital cataract in clinical care

Objectives

To identify how useful NGS testing is compared to current care pathways in the diagnosis of congenital cataract. To explore the limitations of NGS testing in the diagnosis of congenital cataract.

Methods

Pubmed was used to identify peer reviewed literature, using the search terms 'Congenital Cataract' and 'next generation sequencing'. Studies using NGS panels for congenital cataract were selected.

Discussion

Early removal of congenital cataracts is essential to stop deprivation of vision during the sensitive and critical period of vision development [7]. There are a few options that can be undertaken to correct the resulting aphakia; primary intraocular lens (IOL) implantation, the use of spectacles or contact lenses, or secondary IOL implantation.

Primary IOL implantation, whereby cataract surgery and IOL implantation occur in the same operation has the following severe complications due to the proceeding ocular growth and axial length elongation; myopia shift, intense posterior capsular opacification, and excessive inflammation [8]. This does however reduce the amount of time the child spends under general anaesthetic. The other practice is to let the child remain aphakic after cataract removal and wear contact lenses instead to avoid amblyopia. They can then go on to have secondary IOL implantation months or years later. Contact lenses are extremely inconvenient in infants and children leading to noncompliance and secondary IOL implantation has been known to cause its own complications including secondary membrane formation, IOL decentration, and secondary glaucoma [9]. Most paediatric ophthalmologists agree that primary IOL implantation is the best treatment for children over 2 years old, however the surgical option for children under 2 years of age with congenital cataracts remains controversial [8].

Identification of a causative mutation of congenital cataract through NGS facilitates a timely treatment plan and can offer opportunities in reproductive planning.

Within the research setting NGS testing gave a positive diagnosis in 70% of congenital cataract cases [10]. One study incorporated NGS testing into routine clinical care, at Manchester Eye Hospital and found an increase of congenital cataract diagnosis from 26% to 71% in a 6 month period [6]. Both of these studies were in single centers and had small samples of patients so therefore their results cannot be generalized.

Difficulties in incorporating NGS panel testing in routine clinical care for congenital cataract include:

- Variation in genes available in NGS panels and prices at different centers.
- Pediatric ophthalmologists being unfamiliar with genetic tests.
- Communication barriers between clinical geneticists, paediatric ophthalmologists and genetic scientists.
- There is only a limited amount of evidence available to portray the clinical utility and cost effectiveness of NGS panel testing in congenital cataract.
- There are inconsistencies between clinical molecular laboratories in their variant classification.

Conclusion

Primary IOL implantation is the most common treatment for children over 2 years old with congenital cataracts but the best surgical option for children under 2 years of age remains controversial.

NGS panel testing presents a promising technology in increasing diagnosis of congenital cataract. Standardised genes for these panels need to be made and incorporated into guidelines which are regularly updated and clinical molecular laboratories need to standardise their variant classification. Paediatric ophthalmologists need to be educated into the potential of this new and exciting technology. More studies are required to illustrate the clinical utility and cost effectiveness of targeted NGS panel testing.

References

1. Rahi JS DC. Measuring and interpreting the incidence of congenital ocular anomalies: lessons from a national study of congenital cataract in the UK. Investigative ophthalmology & visual science. 2001; 42: 1444–1448.
2. Haargaard B, Wohlfahrt J, Fledelius HC, Rosenberg T, Melbye M. A nationwide Danish study of 1027 cases of congenital/infantile cataracts: etiological and clinical classifications. Ophthalmology. 2004; 111: 2292-2298.
3. http://cat-map.wustl.edu/.Accessed 10/02/21
4. Hejtmancik JF. Congenital cataracts and their molecular genetics. Semin Cell Dev Biol. 2008; 19: 134-149.
5. Louison S, Blanc J, Pallot C, Alassane S, Praudel A, Bron AM, et al. Visual outcomes and complications of congenital cataract surgery. J Fr Ophtalmol. 2019; 42: 368-374.
6. Wirth MG R-EI, Craig JE, Elder JE, Mackey DA. Aetiology of congenital and paediatric cataract in an Australian population. The British journal of ophthalmology. 2002; 86: 782–786.
7. Lambert SR, DuBois L, Cotsonis G, Hartmann EE, Drews-Botsch C. Factors associated with stereopsis and a good visual acuity outcome among children in the Infant Aphakia Treatment Study. Eye (Lond). 2016; 30: 1221-1228.
8. Zhang S, Wang J, Li Y, Liu Y, He L, Xia X. The role of primary intraocular lens implantation in the risk of secondary glaucoma following congenital cataract surgery: A systematic review and meta-analysis. PLoS One. 2019; 14: e0214684.
9. Mataftsi A, Prousali E, Kokkali S, Haidich AB. Complications and Visual Outcomes After Secondary Intraocular Lens Implantation in Children. Am J Ophthalmol. 2015; 160: 1087.
10. Gillespie RL OSJ, Ashworth J, Bhaskar S, Williams S, Biswas S, et al. Personalized diagnosis and management of congenital cataract by next-generation sequencing. Ophthalmology. 2014; 121: 2124–37.e1-2.