Review Article

Dealing with pediatric glaucoma: from medical to surgical management—a narrative review

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Abstract: Pediatric glaucoma is a potentially sight-threatening disease and is considered the second leading cause of treatable childhood blindness. Pediatric glaucoma is a clinical entity including a wide range of conditions: primary congenital glaucoma, glaucoma secondary to ocular (e.g., aniridia, Peter's anomaly), or systemic disease (e.g., Sturge Weber) and glaucoma secondary to acquired condition (pseudophakic, traumatic, uveitic glaucoma). The treatment algorithm of childhood glaucoma is a step-by-step approach, often starting with surgery, as in primary congenital glaucoma cases. Medical therapy is also crucial in the management of pediatric glaucoma. Here we reported the results of the randomized, controlled, clinical trials carried out in children treated with topical anti-glaucoma drugs. It is worth knowing that prostaglandin analogues showed an excellent systemic safety profile, while serious systemic events have been reported in children taking topical beta-blockers. Angle surgery is the first surgical option in patients diagnosed with primary congenital glaucoma, with ab interno and ab externo approaches showing similar outcomes. Trabeculectomy in children can be troublesome, as mitomycin C (MMC) can lead to bleb complications and a higher endophthalmitis rate than in adults. Glaucoma drainage devices (GDD) are no longer a last resort and can be considered a suitable option for the management of uncontrolled pediatric glaucoma after angle surgery failure.

Keywords: Pediatric glaucoma; anti-glaucoma medication; angle surgery; trabeculectomy; glaucoma drainage device (GDD)

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Introduction

Pediatric glaucoma is one of the most challenging condition physician have to deal with. This is because of the patient is a child, with a long life expectancy, the disease is potentially sigh-threatening and because treatment, especially surgery, is often disappointing.

The term pediatric glaucoma includes a variety of conditions. Primary congenital glaucoma is the most common form (1,2) and is considered the second cause of preventable blindness in children (3,4).

Among the other forms of pediatric glaucoma we can remember the juvenile glaucoma, with an onset ranging from 4 to 16 years, and the secondary forms of glaucoma including the pseudophakic glaucoma, occurring in children who underwent surgery for pediatric cataract, the glaucoma due to systemic disease, like in the Sturge Weber patients, the glaucoma due to ocular anomalies, like in aniridia and Peter's anomaly, and the glaucoma associated with acquired conditions like the steroid, the traumatic, and the uveitic glaucoma (5).

Intraocular pressure elevation (IOP), increase in axial

length and optic nerve cupping and corneal changes, including corneal edema and Haab striae are the clinical hallmark of pediatric glaucoma. As a consequence of the IOP elevation, loss of retinal ganglion cells occurs.

The diagnosis of pediatric glaucoma, depending on the age of the patient, is made by under sedation examination (commonly in children younger than 4 years) or during a slit lamp exam (children older than 4–6 years).

The treatment of the pediatric glaucoma is a step-by-step approach, starting with drugs and often ending up with surgery. We discussed here the algorithm treatment of the childhood glaucoma, from the medical to the surgical management. We present the following article in accordance with Narrative Review reporting checklist (available at http://dx.doi.org/10.21037/aes-21-5).

Methods

Search strategy and trials selection

For this non-systematic review, we conducted a systematic search of peer-reviewed literature in PubMed and Cochrane Library through April 3, 2020. We limited the search to clinical studies and reviews.

We used the following keywords for the computerized search: pediatric glaucoma, glaucoma children, childhood glaucoma, anti-glaucoma medication, angle surgery, trabeculotomy, goniotomy, trabeculectomy, glaucoma drainage device (GDD), glaucoma valve, glaucoma tube valve, glaucoma shunt, Ahmed valve, Baerveltd valve, Molteno valve, aqueous shunt device.

We included in our work: review; retrospective or prospective clinical study carried out with patients with glaucoma younger than 18 years under medical therapy or who underwent angle surgery, trabeculectomy, or aqueous shunt surgery.

The search was limited to papers in the English language published since 1980. We also considered the references of relevant papers for the analysis.

Discussion

Medication

It is well known that primary congenital glaucoma is handled by surgery, as well as glaucoma due to ocular anomalies. However, the role of anti-glaucoma drugs is crucial for the management of children with glaucoma. Patients with juvenile glaucoma can be primarily treated with medications, and children with glaucoma due to acquired secondary forms. In addition, anti-glaucoma drugs can be used preoperatively to lower IOP while waiting for surgery and postoperatively to optimize the IOP control after partially successful glaucoma surgery. A large trial carried-out in children who underwent glaucoma surgery showed that the percentage of patients achieving a target IOP increased from 60% to 94% when patients started to use anti-glaucoma drugs (6).

Large, randomized, controlled clinical trials (RCTs) carried out in adults in the last two decades showed the efficacy and safety of glaucoma medical management in adults. IOP lowering approach has been proven to be effective in reducing the risk of glaucoma development in subjects with ocular hypertension (7) and the rate of disease worsening in subjects with glaucoma (8-11).

The results of these RCTs have been reported in two meta-analyses (12,13).

Active agents commonly used in adults have been widely used to manage pediatric glaucoma; however, data about safety and efficacy largely went from small and retrospective studies (14-27).

It was not until the study by Ott and coauthors was performed in 2005 that we had the first RCT investigating the safety and efficacy of medical therapy in children with glaucoma (28). In this study, the authors compared the efficacy and safety of dorzolamide with 0.5% timolol gel. Three years later, Whitson and coauthors published a RCT comparing brinzolamide with 0.5% levobetaxolol (29).

Three different beta-blockers were compared in the RCT by Plager and colleagues (0.25% betaxolol, 0.25% timolol gel, and 0.5% timolol gel) (30). Latanoprost and 0.50% timolol were compared in the RCT published by Maeda-Chubachi and coauthors (31), and travoprost and 0.50% timolol were compared in the RCT by El Roy Dixon (32).

We have gathered the results of these 5 RCTs in a recent review on the role of medical treatment of pediatric glaucoma (33).

The IOP lowering efficacy of the active agents, as reported in these 5 RCTs, was comparable with the known efficacy in adults, being up to 23% for carbonic anhydrase inhibitors, to 36% for beta-blockers, and to 27% for prostaglandins analogs (33).

The percentage of patients with an IOP lowering effect greater than 20% (responders) was 50% for carbonic anhydrase inhibitors, ranging from 38% to 74% and from 60% to 83% for beta-blockers and prostaglandins,

respectively (33).

The safety profile of prostaglandins analogues was excellent, as none of the young patients assuming this class of drug experienced systemic adverse events.

Conversely, two medical records reported serious systemic events occurred in children under timolol, one who experienced bradycardia and one pneumonia.

It is known that beta-blockers can lead to a potentially serious event as bradycardia, systemic hypotension, and bronchospasm. The caregiver of a pediatric subject under beta-blockers should be aware of timolol, even as eye drops can lead to systemic events.

Taking into account the potential systemic effects of beta-blockers, it is worth knowing that systemic absorption of drugs can be reduced using the lowest dose of medication (0.25% timolol rather than 0.50% is recommended in children), as well as a gel formulation. To decrease the systemic exposure of the anti-glaucoma drug, a temporarily lacrimal punctum occlusion can also be considered (34).

Surgery

Surgery is the first-line approach for the management of congenital glaucoma and is the mainstay in the childhood glaucoma treatment algorithm in patients showing an uncontrolled IOP despite medical therapy and progressive disease, despite an apparently controlled IOP.

Angle surgery is generally the first choice for the management of primary congenital glaucoma. The goal of this approach is to overcome the increased resistance to aqueous outflow due to trabecular dysgenesis. Angle surgery includes goniotomy and trabeculotomy. The former technique aims to open the trabecular meshwork by an ab interno approach. The latter aims to open the angle structures getting through the Schlemm canal by an ab externo approach.

The success rate of goniotomy and trabeculotomy are comparable, ranging from 70–90% (35).

After unsuccessful angle surgery, trabeculectomy, cyclodestructive procedures, or GDD can be considered (36,37).

Trabeculectomy is considered the gold standard surgical procedure in the adult population (38); however, trabeculectomy prognosis can be disappointing in a pediatric population.

Moreover, in pediatric patients who underwent trabeculectomy, mitomycin C (MMC) can increase the rate of complications, including avascular, thin blebs, and endophthalmitis reported with a rate as high as 6.7% (39).

Although the implantation of GDD in children is more challenging than in adults (40), GDD can be a suitable option for the control of IOP in children, especially when the initial angle surgery has failed (41) and can be considered a viable alternative to trabeculectomy.

The valved Ahmed GDD (42-59) is more commonly used than the non-valved Baerveldt GDD (36,37,60-62) for the management of pediatric glaucoma.

Both Ahmed and Baerveldt GDD effectively reduce IOP, with a final IOP ranging from 12.27 to 21.3 (42-59) and 13.8–18 (36,37,60-62) in studies carried out with Ahmed and Baerveldt GDD, respectively. At one year, the success rate has been reported to range from 50% to 94.7% (42-59) and from 72% to 94.5% (36,37,60-62) with Ahmed and Baerveldt GDD, respectively.

Although GDDs are considered the best options for the management of refractory, uncontrolled pediatric glaucoma, it is worth knowing that they can lead to several complications (36,37,42-62).

Among the complications to be aware of, hypotony is the more common. Children are more prone to hypotony because of a more elastic scleral tissue compared to adults (36,42,43,45,55). In addition to the complications commonly related to filtering surgery, including cataract development (42,48,61), endophthalmitis (42,43,49,58), hemorrhagic choroidal detachment (45,54), and retinal detachment (36,49,60-62), GDD can lead to tube-related complications, as tube exposure and malpositioning, tube obstruction by vitreous or iris, corneal decompensation and to valve plate-related complication as strabismus (36,37,42-55,60-62). Interestingly only in a few studies, MMC was used intraoperatively (44,45,46,49,50). Al-Mobarak and colleagues compared 16 eyes who underwent an Ahmed valve augmented with MMC with 15 eyes treated with a non-augmented Ahmed valve. The final IOP and the rate of failure were higher in the MMC group (46). As no conclusive data are coming from randomized trials comparing the safety and efficacy of the intraoperative use of MMC during GDD surgery, the use of MMC is not recommended so far, and it remains at the surgeon's discretion.

Mini-invasive glaucoma surgery (MIGS) is a broad term, first used in 2012 (63) and referred to glaucoma surgery techniques requiring a lesser degree of tissue manipulation, faster recovery, and greater safety profile than traditional, major filtering surgery.

MIGS with subconjunctival drainage have been used in pediatric glaucoma. In a case series of three pediatric

patients, Smith and colleagues reported the XEN gel implant outcome in one patient with glaucoma following congenital cataract surgery, one patient with congenital glaucoma, and one patient with pediatric glaucoma secondary to retinopathy of prematurity (64).

Although this small case series reported a good outcome after XEN gel implant and studies carried out in the adult population also reported good outcome and safety profile after this subconjunctival device, more data coming from randomized, large, and controlled studies in adults and hopefully in the pediatric population are needed before recommending this mini-invasive approach for the treatment of pediatric glaucoma (65).

Pediatric glaucoma outcome and rehabilitation

Pediatric glaucoma is considered one of the primary causes of childhood blindness. In a recent cross-sectional survey, more than half of the patients had a vision in the better eye lower than 20/60, and 30% were lower than 20/200 (66).

Pediatric patients with glaucoma are known to have a low vision-related quality of life than healthy children (67). The ultimate goal of glaucoma treatment is to maintain the visual function and the vision-related quality of life.

Studies reported that a higher visual acuity is associated with higher vision-related quality of life (66,68). In light of that, after elevated IOP has been controlled by therapy (including drugs, surgery, and laser), any efforts should be made to minimize the amblyopia by correcting any ametropia, using patching (34) and low vision aids (69,70) in order to improve the final visual function of the patients.

Conclusions

In conclusion, pediatric glaucoma includes a wide range of clinical entities, ranging from the most common congenital glaucoma to the secondary and syndromic ones.

We want to stress that topical medical therapy is of great importance in pediatric glaucoma treatment algorithm (6,28,71): in a percentage of children medical approach will be the first-line step, and a relevant proportion of children will eventually need medical therapy after a partially successful surgery (20,71,72).

Angle surgery is often the first surgical approach. In case of angle surgery failure, the pediatric ophthalmologist should be aware of the bleb-related complications following trabeculectomy, and that tube can be used to handle uncontrolled childhood glaucoma in order to minimize the MMC and bled related complications.

Finally, it is worth that ophthalmologist, parents, and caregiver know that pediatric glaucoma is one of the most challenging ocular disorder, requiring a step-by-step approach, several examinations, often multiple surgeries, and lifelong care. We believe that a strong alliance between eye care staff and family is of paramount importance in this challenging but also rewarding journey.

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Footnote

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