Editorial

Clinical classification and medical treatment options in childhood glaucoma

Clasificación clínica y opciones de tratamiento médico en el glaucoma en la infancia

C. Mendez-Hernandez a,b,*, G. Arcos-Villegas a, J. Garcia-Sanchez a,b, J. Garcia-Feijoo a,b

a Servicio de Oftalmología, Hospital Clínico San Carlos, Instituto de Investigación Sanitaria del Hospital Clínico San Carlos (IdISSC), Universidad Complutense de Madrid, Madrid, Spain
b Red Temática de Investigación Cooperativa en Oftalmología (RETICS), Instituto de Salud Carlos III, Madrid, Spain

The International Expert Consensus on Childhood Glaucoma was presented at the 5th International Glaucoma Congress (Vancouver, July 2013) as a diagnostic and therapeutic guide for said disease.

Childhood glaucoma diagnostic is established when at least two of the following criteria are fulfilled:

- Intraocular pressure (IOP) ≥ 21 mmHg.
- Papillary cup increase/ asymmetry.
- Increased corneal diameter or Haab striations.
- Progressive myopia.
- Glaucomatous scotoma in campimetry.

IOP is the most variable diagnostic as it could be due to multiple factors (tonometer type, ocular movements, patient cooperation, anesthesia or corneal condition). Reference tonometry is Goldmann's tonometer, although the Perkins tonometer (Haag-Streit AG, Bern, Switzerland) was utilized on multiple occasions as it enables IOP readings in supine position and with uncooperative patients. Other tonometers such as Tono-Pen (Reichert Ophthalmic Instruments, Depew, NY, USA), pneumotonometer (Ocular Response Analyzer, ORA) (Reichert Ophthalmic Instruments, Depew, NY, USA) or the rebounding tonometer (iCare and iCare Pro) (Tiolat Oy, Helsinki, Finland) tend to overestimate IOP. Pachymetry is a significant parameter although it should not be utilized as an IOP-correcting factor. Patients with primary congenital glaucoma or juvenile glaucoma tend to have thinner corneas. In contrast, patients with aniridia or aphakia after congenital cataract surgery frequently have thicker pachymetries.

Characteristic signs such as Haab's striations (ruptures of Descemet's membrane due to IOP increase, present in primary congenital glaucoma which develops in the first years of life), posterior embryotoxon, increased corneal diameter and corneal edema or opacification are frequently observed in these patients.

Corneal diameters over 13 mm in any child, of 12 mm in children under 1 year of age or 11 mm in newborns are signs of suspected glaucoma.

Gonioscopy allows the identification of characteristic angle changes and goniodysgenesiae present in primary or juvenile congenital glaucoma, and enables the diagnostic of secondary glaucoma and consequently the establishment of the most adequate therapeutic approach.


* Corresponding author.
E-mail address: cdmendezh@gmail.com (C. Mendez-Hernandez).
2173-5794/© 2015 Sociedad Española de Oftalmología. Published by Elsevier España, S.L.U. All rights reserved.
One of the most relevant parameters for the diagnostic and follow-up of childhood glaucoma is the condition of the optic nerve. A cup/papilla ratio above 0.3 in Caucasian children under 1 year or over 0.5 in children over 1 year must lead the specialist to suspect the presence of glaucoma.

Changes in refraction such as hypermetropia reduction and presence of myopia or astigmatism with oblique or irregular axis are also suggestive of childhood glaucoma.

Most explorations in these children are carried out under general anesthesia. Some studies have demonstrated possible adverse effects in brain development and neurocognitive changes. For this reason it is recommendable to restrict examinations as much as possible and even to operate at diagnostic.

Nearly all anesthetics and sedatives reduce IOP with the exception of ketamine, benzodiazepine and chloride hydrate. It is recommendable to measure IOP at the beginning and the end of the examination, when the child is not fully unconscious, to minimize the effects of the anesthetic on IOP measurements.

Tables 1 and 2 comprise the childhood glaucoma classification developed by the expert consensus. Fig. 1 shows the scheme to be followed to reach diagnostic when childhood glaucoma is suspected.

A significant part of said consensus relates to the medical treatment. Even though the therapeutic basis is surgery, medical treatment plays a very important role. Table 3 summarizes indications for medical treatment and the most frequent side effects.

Aqueous production suppression diminishes IOP and corneal edema while facilitating angle surgery. On the other hand, medical treatment is necessary in many patients to maintain post-surgery IOP within normal ranges. For this reason, medical treatment is frequently maintained while awaiting angle surgery as well as being applied as adjuvant treatment for refractory glaucoma.

There are important differences between the medical treatment for adults and children, both in pharmacokinetics and adverse reactions. In addition, children are more vulnerable to adverse effects as they are frequently unable to express the symptoms they are feeling. In addition, adverse effects can occasionally express in children as nocturnal coughing when betablockers are applied. For this reason, parents must be informed about the possible side effects that may occur and instruct them on how to reduce systemic absorption by means of simple maneuvers such as closing the eyelids, clearing drop surplus or occluding the lacrimal point.

Medical treatment is the first therapeutic line for juvenile and open angle secondary glaucoma. In congenital glaucoma, it is used to improve corneal transparency in preparation for surgery. In addition, it is used as adjuvant treatment for pressure control when surgery has had only relative success.

Some topical treatments such as pilocarpine are used preoperatively due to the fact that miosis facilitates angle surgery and reduces peripheral anterior synchiae in the post-surgery. For this reason, some surgeons prescribe pilocarpine twice or three times a day in the post-surgery period for 2 or 3 weeks. Apart from these indications, recurrences with the use of miotics is infrequent due to their adverse effects such
as induction of myopia, headaches, diarrhea, sweating, hyper-salivation or retinal detachment.

Younger children exhibit poorer response to ocular hypotensors and are more susceptible to exhibiting more adverse effects due to metabolic immaturity and lower plasma volumes.

Topical betablockers are usually the first choice of treatment in younger children due to their higher hypotensive efficacy (reduction of 20–25%). It is recommendable to begin with the lowest concentration of 0.1% timolol in gel formulation which facilitates administration. Topical betablockers are not recommended for newborns and premature due to the risk of apnea and bradycardia, and they are contraindicated in patients with bradycardia, 2nd or 3rd degree AV blockage and bronchial constriction history. Some children may exhibit bronchial spasms and persistent coughing, worsening of asthma and even epinep episodes.

Carbonic anhydrase inhibitors can be considered as a first line when betablockers or prostaglandins are contraindicated. They are not generally applied orally except preoperatively in the presence of very high IOP and exceptionally as adjuvant treatment due to their significant adverse effects such as metabolic acidosis and respiratory alkalosis, lethargy, loss of appetite, diarrhea and allergy crossed with sulfamides. As for topical carbonic anhydrase inhibitors, brinzolamide is preferred over dorzolamide because it produces less irritation when instilled and is better tolerated. Loss of weight or appetite in a child in treatment with carbonic anhydrase inhibitors could be a symptom of metabolic acidosis. In addition, said inhibitors are contraindicated in patients with corneal edema or decompensation and low endothelial count.

Alpha-adrenergic agonists such as apraclonidine and brimonidine are utilized as a 2nd or 3rd therapeutic line or as pre- and post-angle surgery advitant to prevent bleeding. Brimonidine is contraindicated in children under 2 years of age or children in topical treatment with betablockers due to the severity of its adverse effects (sleepiness, apnea or coma).

Preoperative apraclonidine reduces angle bleeding although it must be used with caution in children in treatment with topical betablockers.

Prostaglandins are the first therapeutic line in juvenile glaucoma. Latanoprost was the first drug to be used in a multicenter clinical trial in children in the European Union. Tolerance to bimatoprost is lower compared to latanoprost and travoprost.

Even though data is insufficient, fixed combinations are indicated in patients with multi-therapy or non-cooperative children.

Topical preservative-free treatment must be considered in patients with ocular surface inflammation, blepharitis,
Table 3 – Indications, contraindications and side effects of hypotensive medication in childhood glaucoma.

<table>
<thead>
<tr>
<th>Medication</th>
<th>Indications</th>
<th>Contraindications/adverse effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Betablockers</td>
<td>- First line in PCG</td>
<td>Systemic effects: bronchial spasm, bradycardia</td>
</tr>
<tr>
<td></td>
<td>- 2nd line in JG</td>
<td>Avoid in premature and children with reactive airways history</td>
</tr>
<tr>
<td></td>
<td>- Non-cardioselective more effective.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Use cardioselective beta blockers in asthma patients</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- B1 selective (betaxolol)</td>
<td></td>
</tr>
<tr>
<td>Carbonic anhydrase inhibitors</td>
<td>- First and 2nd line in PCG</td>
<td>Starting with lowest concentration dose of 0.1%</td>
</tr>
<tr>
<td></td>
<td>- Topical (dorzolamide or brinzolamide) 2–3 times a day</td>
<td>- Systemically safe topical</td>
</tr>
<tr>
<td></td>
<td>- Topical is better tolerated but not as efficient.</td>
<td>- Avoid in corneal decompensation.</td>
</tr>
<tr>
<td></td>
<td>- Oral (acetazolamide 10–20 mg/kg/day, 2–4 times a day, metazolamide)</td>
<td>- Dorzolamide less tolerated than brinzolamide</td>
</tr>
<tr>
<td>Miotics</td>
<td>Pilocarpine after angle surgery and sometimes in juvenile glaucoma, less efficient in congenital glaucoma</td>
<td>- Possible metabolic acidosis with oral therapy.</td>
</tr>
<tr>
<td></td>
<td>Rarely used. Limited preoperative efficacy and angle surgery and postoperative corneal transplant</td>
<td>- Systemic effects: diarrhea, headache, myopization and possible retina detachment</td>
</tr>
<tr>
<td>Adrenergic agonists</td>
<td>- Apraclonidine 0.5%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Brimonidinone 0.1%</td>
<td></td>
</tr>
<tr>
<td>Alpha-2 agonists</td>
<td>Preoperatively in angle surgery and postoperative corneal transplant</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- 2nd and 3rd line in juvenile glaucoma</td>
<td></td>
</tr>
<tr>
<td>Prostaglandins</td>
<td>1st, 2nd and 3rd line in juvenile glaucoma</td>
<td>Red eye, growth of eyelashes, orbital fat atrophy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Do not use in uveitis</td>
</tr>
</tbody>
</table>

PCG, primary congenital glaucoma; JG, juvenile glaucoma.

allergic conjunctivitis, limbar insufficiency, aniridia and history of numerous glaucoma operations.

Therapeutic indications, according to the type of childhood glaucoma, are as follows:

**Primary childhood glaucoma**

**Primary congenital glaucoma**

*When surgery has to be delayed*

- Betablockers: preferably in low doses (timolol 0.1 or 0.25%) and gel formulations.
- Carbonic anhydrase inhibitors: brinzolamide is better tolerated than dorzolamide.
- Prostaglandin analogs: no significant role as initial treatment but significant as adjuvant.

**Open angle juvenile glaucoma**

- First line: better response to hypotensive treatment than primary congenital glaucoma. Prostaglandins would be the first choice due to their higher hypotensive effect. Betablockers would be the 2nd choice, followed by carbonic anhydrase inhibitors in fixed combination with beta blockers, and finally adrenergic agonists would be considered.
- Adjuvant treatment if surgery is required.

**Secondary childhood glaucoma**

- First line of treatment for open angle glaucoma.
- Adjuvant treatment after anti-glaucomatous surgery.
- In closed angle secondary glaucoma (pupil blockage in uveitis) which does not usually respond to treatment.

- In open angle glaucoma secondary to cataract surgery, the therapeutic scheme is similar to that of juvenile glaucoma. Although infrequent in clinical practice, the risk of macular edema must be borne in mind when using prostaglandin analogs. Pilocarpine can be useful in some cases.

**REFERENCES**