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## GLAUCOMA UPDATE

# Ahmed glaucoma valve in children: A review <sup>☆</sup>

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Received 8 July 2011; revised 17 July 2011; accepted 18 July 2011

Available online 30 July 2011

### KEYWORDS

Ahmed glaucoma valve;  
Children;  
Glaucoma;  
Management

**Abstract** Pediatric glaucoma is potentially a blinding disease. Although goniotomy and trabeculotomy are associated with good early success rates, eventually 20% of these procedures fail and many children will require additional surgery to control the IOP in the long-term. In this review, we reported that adequate IOP control can be achieved with the placement of Ahmed glaucoma valve and can last 5 or more years. However, most patients will need one or more glaucoma medications at some point after surgery. In addition, the implants may be associated with pupillary irregularities, lenticular opacification as well as tube-related complications, particularly in the first year of life, as the globe is enlarging with age.

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<sup>☆</sup> The authors did not receive any financial support from any public or private sources. The authors have no financial or proprietary interest in a product, method, or material described herein.

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Peer review under responsibility of King Saud University.

doi:10.1016/j.sjopt.2011.07.002



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## 1. Introduction

Pediatric glaucoma is a potentially blinding disease, accounting for about 18% of blindness in blind institutions and 5% of overall pediatric blindness worldwide (Gilbert et al., 1994; Gilbert et al., 2003). It has heterogeneous etiologies characterized by elevated intraocular pressure (IOP). It is defined as *primary* when an isolated, idiopathic developmental anomaly of the anterior chamber angle exists, and *secondary* when aqueous outflow is impaired due to preexisting ocular or systemic disease (Papadopoulos and Khaw, 2005; Ben-Zion et al., 2010). In a recent study in the United States, the incidence of childhood glaucoma was 2.29 per 100,000 (or 1 per 43,575) residents younger than 20 years of age (Aponte et al., 2010). Acquired (traumatic or surgical, drug-induced and uveitic) and secondary (e.g. Sturge-Weber syndrome) forms of glaucoma were the most common, whereas congenital and juvenile glaucoma were rare (Aponte et al., 2010).

Primary congenital glaucoma (PCG) is the most common type of glaucoma in infancy (Taylor et al., 1999), and has been estimated to comprise  $\geq 5\%$  of the general glaucoma population of adult Caucasians (Ben-Zion et al., 2011). The incidence of PCG in Western countries has been estimated at 1 per 10,000 to 1 per 30,200 population (Taylor et al., 1999; Kipp, 2003; deLuise and Anderson, 1983; Miller, 1966; Papadopoulos et al., 2007; Bermejo and Martinez-Frias, 1998; MacKinnon et al., 2004). As the disease has an autosomal-recessive pattern of transmission, it is reported to occur more frequently in certain ethnic and religious groups where consanguineous marriage is common (Miller, 1966; Papadopoulos et al., 2007). The highest reported prevalence has been among individuals of Slovakian Roma (1 per 1250) (Genčík, 1989) and of Saudi Arabian racial descent (1 per 2500) (Jaafar, 1988).

## 2. Management

### 2.1. Surgical management of pediatric glaucoma

The mainstay of treatment in pediatric glaucoma is the surgical reduction of intraocular pressure (IOP) (Alsheikheh et al.,

2007; Turach et al., 1995), although medical therapy is often used adjunctively (Maris et al., 2005; Portellos et al., 1998; Enyedi and Freedman, 2002; Sabri and Levin, 2006). The ultimate goal of IOP reduction is to prevent progressive optic nerve damage and to maintain visual functioning. However, even with adequate IOP control, these patients, especially those with advanced stage of glaucoma, may still have poor visual function because of prolonged deprivation amblyopia, corneal opacities, high astigmatism, uncorrected high myopia, and possible lens subluxation (Ben-Zion et al., 2011; Alsheikheh et al., 2007; Robin et al., 1979).

PCG is typically treated with angle surgery first. Initial goniotomy or trabeculotomy have been found to have comparable success rates (deLuise and Anderson, 1983; Meyer et al., 2000; Yalvac et al., 2007; McPherson and Berry, 1983). Although goniotomy and trabeculotomy are associated with good early success rates, eventually 20% of these procedures fail and many children will require additional surgery to control the IOP in the long-term (deLuise and Anderson, 1983; Anderson, 1983; Tanimoto and Brandt, 2006). Furthermore, some forms of pediatric glaucoma respond poorly to angle surgery and are difficult to treat (deLuise and Anderson, 1983; Dascotte et al., 1991). Currently, there is no general agreement as to the preferred surgical algorithm after failure of angle surgery and there is a wide variation in recommended treatment by centers experienced in the treatment of PCG. Various surgical approaches have been proposed for surgical treatment of pediatric glaucoma including trabeculectomy with or without adjunctive antimetabolites (Fulcher et al., 1996; Rodrigues et al., 2004), nonpenetrating deep sclerectomy (Roche et al., 2007), combined trabeculotomy and trabeculectomy (Mullaney et al., 1999), glaucoma drainage devices (Ben-Zion et al., 2011; Netland and Walton, 1993; Budenz et al., 2004; van Overdam et al., 2006; Donahue et al., 1997; Coleman et al., 1997; Englert et al., 1999; Hamush et al., 1999; Djodeyre et al., 2001; Hill et al., 2003; Beck et al., 2003; Morad et al., 2003; Al-Torbak, 2004; Kirwan et al., 2005; Chen et al., 2005; Kafkala et al., 2005; Pakravan et al., 2007; O'Malley Schotthoefer et al., 2008; Ou et al., 2009; Al-Mobarak and Khan, 2009; Yang and Park, 2009), and cyclodestructive procedures (Al Faran et al., 1990; Phelan and Higginbotham,

**Table 1** Studies in which Ahmed glaucoma valve implants were used for the management of pediatric glaucoma.

Studies/Groups	No. of eyes (patients; male: female)	Type of glaucoma	Race	Mean age $\pm$ SD (range)	Mean follow-up time $\pm$ SD (range)	Mean preoperative IOP $\pm$ SD (mm Hg)	Mean last follow-up IOP $\pm$ SD (mm Hg)	No. of preoperative medications $\pm$ SD	No. of Last follow-up medications $\pm$ SD	Cumulative probability of success and Causes of failure
Coleman et al. 1997 <sup>38</sup>	24 (21; 11:10)	Congenital = 13 Sturge-Weber syndrome = 3 Congenital rubella = 2 Traumatic = 2 Osteogenesis imperfecta = 1 Uveitic = 1 Persistent hyperplastic primary surgery = 1 Peter anomaly = 1	Asian = 6 Hispanic = 5 Black = 4 Arab = 3 White = 3	6.61 $\pm$ 5.67 years	16.3 $\pm$ 11.2 months	30.7 $\pm$ 8 (16-46)	19.3 $\pm$ 8	1.5 (0-3)	0.8 (0-2.3)	12 months = 77.9% 24 months = 60.6% Failures = 7 (extrusion of implant = 3; inadequate IOP control = 3; suprachoroidal hemorrhage = 1)
Englert et al. 1999 <sup>39</sup>	27 (23; 10:13)	Congenital = 14 Aphakic = 7 Aniridic = 2 Uveitic = 2 Sturge-Weber Syndrome = 1 Neovascular = 1	White = 11 Black = 15 American-Indian = 1	6.44 $\pm$ 5.88 (0.3-16.8) years	12.6 $\pm$ 8.2 (3-31) months	32.8 $\pm$ 7.5	16.4 $\pm$ 6.9	2.7 $\pm$ 1	0.8 $\pm$ 0.7	12 months = 91% 24 months = 58% Failures = 4 (inadequate IOP control = 2; retinal detachment = 1; intraocular tumor = 1)
Hamush et al. 1999 <sup>40</sup>	11 (10; 5:5)	All Sturge-Weber syndrome	Hispanic = 5 Caucasian = 3 Asian = 1 Arabian = 1	10 days to 25 years	30.35 $\pm$ 19.13 months	27.7 4.6	18.5 4.4	1.5 1.4	0.9 0.7	24 months = 79% 48 months = 59% 60 months = 30% Failure = 4 (implant extrusion = 1; inadequate IOP control = 3)
Djodeyre et al. 2001 <sup>41</sup>	35 (18:17)	Congenital = 17 Sturge-Weber syndrome = 5 Persistence of fetal vasculature = 4 Congenital cataract = 3 Uveitis in Juvenile Rheumatoid arthritis = 2 Keratoplasty = 1 Pars plantitis = 1 Retinopathy of prematurity = 1 Stickler syndrome = 1	All white	4.4 $\pm$ 4.7 years	12.6 $\pm$ 10.8 months	28.8 $\pm$ 4.5 (22-40)	18.1 $\pm$ 2.4			12 months: Total = 70.1% Complete = 67.4% 24 months: Total = 63.7% Complete = 44.5% 9 failures = 6 tube malposition (4 cases tube retracted out of the AC, 1 tube block due to tube-endothelium contact and 1 tube-iris contact), 3 inadequate IOP control
Hill et al. 2003 <sup>42</sup> AGV group	38 (34) 18	Congenital = 12 Frank Kamenetsky Syndrome = 3 Reiger's Syndrome = 3	Armenians	12.5 $\pm$ 2.8 (6-16) years	18.8 $\pm$ 9.6 (6-60) months	32 $\pm$ 10.1	14.8 $\pm$ 5.4	1.9 $\pm$ 0.8	0.7 $\pm$ 0.8	Total = 16 (88%) Complete = 10 (55%); Qualified = 6 (33%); Failure = 2 (12%)
Trab with MMC group Beck et al. 2003 <sup>43</sup> AGV group	20 46 (32)	Congenital = 18 Anterior chamber anomalies = 12 Aphakia = 10 Other = 6	White	12.5 $\pm$ 2.4 (10-17) years	16 $\pm$ 12.5 (6-60) months	30.1 $\pm$ 7.4	13.5 $\pm$ 7	2.2 $\pm$ 1.1	0.4 $\pm$ 0.75	Total = 18 (86%) Complete = 16 (76%); Qualified = 2 (10%); failure = 3 (14%)
Trab with MMC group	24 (19)	Congenital = 11 Anterior chamber anomalies = 6 Aphakia = 4 Other = 3		5.3 4.8 (0.5-24) months	11.5 15 (1-60) months	36.4 $\pm$ 7.6	27.3 $\pm$ 12.2	1.6 $\pm$ 0.8	1 $\pm$ 1	12 months = 37 $\pm$ 16% 72 months = 19 $\pm$ 13%
Morad et al. 2003 <sup>44</sup>	60 (44; 25:19)	Congenital/infantile = 25/60; Aphakia = 9/60; Sturge-Weber synd = 9/60; Uveitic = 8/60; Aniridia = 4/60; Anterior segment dysgenesis = 3/60; Juvenile = 2/60		6 $\pm$ 4.9 years (1.5 months to 16 years)	24.3 $\pm$ 16 (3-60) months	32.8 $\pm$ 6.2 (21-50)	16.6 $\pm$ 8 (2-57)	4.45 $\pm$ 1.97	2 $\pm$ 2	12 months = 93% 24 months = 86% 36 months = 71% 48 months = 45%
Al-Torbak 2004 <sup>45</sup>	20 (17; 7:10)	All congenital		11.7 (2-60) months	30.9 $\pm$ 1.1 (18-60) months	32.3 $\pm$ 11.6	19.7 $\pm$ 10.6	2.35 $\pm$ 0.49	1.6 $\pm$ 1.2	2 months = 85% 24 months = 44% 48 months = 33% 100%
Kirwan et al. 2005 <sup>46</sup>	19 (13; 7:6)	Aphakic		96 (9-189) months	32 (3-84) months	29.7	12.6			

(continued on next page)

Table 1 (continued)

Studies/Groups	No. of eyes (patients; male: female)	Type of glaucoma	Race	Mean age $\pm$ SD (range)	Mean follow-up time $\pm$ SD (range)	Mean preoperative IOP $\pm$ SD (mm Hg)	Mean last follow-up IOP $\pm$ SD (mm Hg)	No. of preoperative medications $\pm$ SD	No. of Last follow-up medications $\pm$ SD	Cumulative probability of success and Causes of failure
Chen et al. 2005 <sup>47</sup>	52 (41; 20:21)	Congenital = 20/52; Aphakic aft. Cong Cat = 19/52; Sturge-Weber Syndrome = 5/52; Aniridia = 4/52; Uveitic = 2/52; Persistent hyperplastic primary vitreous = 2/52	White = 44 African-American = 3 Asian = 3 Arab = 1	4.9 $\pm$ 6.5 (0.02–18.0) years	2.2 $\pm$ 1.8 years (3 months to 7.5 years)	38.1 $\pm$ 6.4	21.6 $\pm$ 5.9	1 $\pm$ 0.8	0.6 $\pm$ 0.7	12 months = 85.1% 24 months = 63.2% 36 months = 51.7% 48 months = 41.8%
Kafkala et al. 2005 <sup>48</sup>	7 (6; 2:4)	All uveitis due to: Juvenile idiopathic arthritis associated with iridocyclitis = 4 patients Sarcoidosis = 1 patient Pars plantitis = 1 patient		11 (9–13) years	36.8 (6–60) months	37 $\pm$ 8	12.1 $\pm$ 3.4	3 $\pm$ 0.8	0.7 $\pm$ 0.7	100%
Pakravan et al. 2007 <sup>49</sup> AGV with MMC group	15 (15:2:3)	Aphakic		10.9 $\pm$ 5.1 (1.5–16) years	13.1 months	31 $\pm$ 7.5	14.4 $\pm$ 3.5	3.3 $\pm$ 0.5	1.6 $\pm$ 0.5	Complete = 20%; Qualified = 66.7%; Total = 86.7%; Failure: 2 (2 suprachoroidal hemorrhage)
Trabeculectomy with MMC group	15 (13; 6:7)	Aphakic		9.1 $\pm$ 4.1 (2–16) years	16.3 months	31 $\pm$ 10.7	14.7 $\pm$ 4	3 $\pm$ 0.6	1.7 $\pm$ 0.5	Complete = 33.3; Qualified = 40%; Total = 73.3; Failures (1 choroidal hemorrhage, 1 inadequate IOP control)
O'Malley Schotthoefler et al. 2008 <sup>50</sup> Congenital group	38 (30)					29	14			12 months = 92% 10 years = 42%
Aphakic group	41 (32)					36	15			12 months = 90% 10 years = 55%
Ou et al. 2009 <sup>51</sup>	30 (19; 12:7)	Primary congenital glaucoma	White = 8; Asian: 3; Hispanic = 8	1.8 (0.02–9.9) years	57.6 (5–166) months	28.4 $\pm$ 6.7(14–40)	17.7 $\pm$ 6.7			12 months = 63% 2–3 years = 50% 4 years = 41% 5 years = 33% Failures = 16 (5 inadequate IOP control; 1 IOP < 5 mm Hg; 10 second Ahmed valve was implanted)
Al-Mobarak and Khan 2009 <sup>52</sup> AGV with MMC group	16 (8:8)	Congenital (7/16); Aphakic (3/16); Peters anomaly (4/16); Aniridia (1/16); congenital rubella (1/16)		10.4 $\pm$ 5.3 months	24 months	35.1 $\pm$ 11.40	21.3 $\pm$ 13.1	2.38 $\pm$ 0.70	1.9 $\pm$ 1.4	24 months = 31.3%
AGV without MMC group	15 (9:6)	Congenital (10/15); Aphakic (2/15); Peters anomaly (1/15); Sturge-Weber syndrome (1/15); Steroid-induced (1/15)		11.8 $\pm$ 5.7 months	24 months	31.6 $\pm$ 7.40	18.9 $\pm$ 7.2	2.67 $\pm$ 0.70	1.13 $\pm$ 1.10	24 months: 80%
Yang and Park 2009 <sup>53</sup>	34 (29)	Congenital = 12 Glaucoma following lensectomy for congenital cataracts = 11 Aphakic = 5 Pseudophakic = 6 Aniridia = 1 Microphthalmia = 1 Axenfeld-Rieger anomaly = 3 Neovascular = 4 Developmental glaucoma with associated systemic disease = 1 Glaucoma associated with cicatricial ROP = 1		5.5 $\pm$ 4.2 (0–16) years	29.1 $\pm$ 16.2 (6–63) months	37.5 $\pm$ 7.3	22.9 $\pm$ 11.1	2.3	1.8	6 months = 89% 12 months = 68.6% 24 months = 45.7%
Ben-Zion et al. 2011 <sup>7</sup>	AVG = 6 eyes Trabeculectomy = 31 eyes	PCG	Rural Southern Ethiopia	3.3 (0.4–10) years	6 (1–11) months	54 $\pm$ 2	23 $\pm$ 2			Those who were implanted with a shunt device achieved an IOP < 22 mmHg in 75 % of cases.

SD: Standard deviation; AGV: Ahmed glaucoma valve; MMC: Mitomycin C.

**Table 2** Surgical complications following Ahmed glaucoma valve implantation in pediatric glaucoma.

Studies	Complications
Coleman et al. (1997) ( <i>n</i> = 24 eyes)	Scleral graft revision = 4; Extrusion of implant = 3; Tube revision = 3; Pupillary membrane = 2; Suprachoroidal hemorrhage = 1; Strabismus = 1; Preseptal cellulitis = 1; Amblyopia/strabismus = 1; Corneal edema = 1
Englert et al. (1999) ( <i>n</i> = 27 eyes)	Corneal-tube touch = 5; Corneal-tube contact requiring tube revision/trim = 4/27; Wound leak = 1/27; Vitreous blocking tube = 1/27; Hypotony = 1/27; Shallow AC = 3/27; Choroidal effusion 2/27; Retinal detachment 1/27; Enucleation for intraocular tumor = 1/27
Hamush et al. (1999) ( <i>n</i> = 11)	Choroidal detachment = 3 which resolved spontaneously.
Djodeyre et al. (2001) ( <i>n</i> = 35)	Tube malposition = 9; Shallow AC = 9; Lens opacity = 6; Choroidal detachment = 6; Hyphema = 4; Vitreous hemorrhage = 4; Impermeable valve capsule = 3; Ocular hypertension = 3; Motility limitation = 2; Tube occlusion = 1; Scleral dissolution = 1; Corneal decompensation = 1; Endophthalmitis = 1; Phthisis bulbi = 1
Hill et al. (2003) ( <i>n</i> = 38) AGV group ( <i>n</i> = 18)	Tube excursion = 1/18; Reposition of tube = 1/18; Transient shallow AC = 2/18; Limited choroidal hemorrhage = 2/18; Corneal blood staining = 1/18; Scleral graft thinning = 1/18
Trabeculectomy with MMC group ( <i>n</i> = 20)	Corneal blood staining = 2; Massive choroidal hemorrhage = 1; Choroidal detachment requiring drainage = 1; Shallow AC requiring reformation = 2; Aqueous misdirection = 1; Lenticular opacification = 6
Beck et al. (2003) AGV group ( <i>n</i> = 46)	Tube-cornea touch = 16; Cataract = 5; Corneal decompensation or graft failure = 4; Shallow AC = 3; Tube/implant exposure = 2; Wound leak = 1; Fibrous in-growth = 1; Serous choroidal detachments = 4; Shallow AC = 3; Late bleb leak = 3; Late endophthalmitis = 2; Corneal decompensation = 2; Cataract = 2; Chronic hypotony = 1
Trabeculectomy with MMC group ( <i>n</i> = 24)	Hypotony (< 5 mm Hg) = 14/60; Flat AC = 9/60; Choroidal detachment = 11/60; Subretinal effusion = 3/60; Exposed tube = 7/60; Tenon's cyst = 4/60; Endophthalmitis = 3/60; Retracted tube = 3/60; Wound leak = 2/60; Tub-corneal touch = 2/60; Iatrogenic Brown Syndrome = 2/60; Vitreous blocking tube = 1/60; Iris blocking tube = 1/60; Postoperative cataract = 1/60; Late migration into suprachoroidal space = 1/60
Morad et al. (2003) ( <i>n</i> = 60)	Subconjunctival scarring = 6; Endophthalmitis = 2; Retinal detachment = 2; Tube-endothelial-touch = 2; Conjunctival erosion = 1; No light perception = 1; Conjunctival dehiscence = 1; Tube migrated centrally = 1; Aqueous misdirection = 1; Phthisis bulbi = 1
Al-Torbak (2004) ( <i>n</i> = 20)	Choroidal detachment/hypotony = 2; Corneal touch = 2; Valve removal = 2; IOP ≤ 5 mm Hg on postoperative day 1 = 22; Shallow AC = 9; Tube occlusion = 7; Tube-corneal touch = 4; Tube exposure = 3; Tube-associated inflammation = 2; Postoperative cataract = 2; Tenon's cyst = 2; Hyphema = 1; Pupillary membrane = 1; Strabismus = 1; Retinal detachment = 1; Endophthalmitis = 1; Choroidal detachment = 1; None = 8
Kirwan et al. (2005) ( <i>n</i> = 19)	Hemorrhagic choroidal detachment = 2 (resolved without any surgical intervention)
Chen et al. (2005) ( <i>n</i> = 52)	Choroidal effusion = 2; Suprachoroidal hemorrhage = 2
Kafkala et al. (2005) ( <i>n</i> = 7)	Choroidal effusion = 4; Vitreous hemorrhage = 1; Endophthalmitis = 1
Pakravan et al. (2007) AGV with MMC group ( <i>n</i> = 15) Trabeculectomy with MMC group ( <i>n</i> = 15)	
O'Malley Schotthoefer et al. (2008) Congenital ( <i>n</i> = 38) Aphakic ( <i>n</i> = 41)	Pupil abnormalities = 16%; Cataract formation = 20% Pupil abnormalities = 7%
Ou et al. (2009) ( <i>n</i> = 30)	Tube-cornea touch = 4 eyes (13%); Tube exposure = 2; Transient hypotony (IOP < 5 mm Hg) = 2; Shallow AC requiring reformation = 1; Endophthalmitis = 1; Penetrating Keratoplasty = 3 eyes; Cataract extraction = 4 eyes; Cycloablative procedure = 3; Enucleation after endophthalmitis after cataract extraction = 1
Al-Mobarak and Khan (2009) AGV with MMC group ( <i>n</i> = 16)	Tube migration requiring intervention = 4; Endophthalmitis = 1; (negative culture); Preseptal cellulitis = 1
AGV without MMC group ( <i>n</i> = 15)	Tube migration requiring intervention = 6; Endophthalmitis = 1; (negative culture); Preseptal cellulitis = 1; Suprachoroidal hemorrhage = 1
Yang and Park (2009) ( <i>n</i> = 34)	Shallow AC = 3; Hyphema = 2; Hypotony (IOP < 5 mm Hg) = 1; Choroidal detachment = 1; Retinal detachment = 1; Tube exposure: 1; Tube occlusion by iris tissue = 1/34; No complication = 28/34
Ben-Zion et al. (2011) ( <i>n</i> = 6)	AGV extrusion = 2

AGV: Ahmed glaucoma valve; MMC: Mitomycin C; AC: Anterior chamber.

1995; Alvarado, 2007). In this review, we will focus on the use of Ahmed glaucoma valve (AGV) in pediatric glaucoma (Table 1).

Although success rates of trabeculectomy with mitomycin C (MMC) were reported in the range of 52–95% (Sidoti et al., 2000; Beck et al., 1998), in two clinical studies, the suc-

cess rate with AGV was better than that with trabeculectomy with MMC (Netland and Walton, 1993; Pakravan et al., 2007). Beck et al. reported a cumulative probability of success of 87% in the AGV group versus 36% in the trabeculectomy with MMC group after one year of follow-up. This decreased to 53% and 19%, respectively, after 6 years of follow-up (Beck et al., 2003). In a randomized study of eyes with pediatric aphakic glaucoma, Pakravan et al. (2007) reported success rates of 87% and 73% after a mean follow-up time of 16.3 and 13.13 months with AGV and trabeculectomy/MMC, respectively; the IOP reduction and number of glaucoma medications needed were similar in the two groups. Only eyes with trabeculectomies had postoperative endophthalmitis in both groups.

## 2.2. Predictors of surgical failure after AGV implantation in children

Although different studies have demonstrated considerable success with AGV in the management of pediatric glaucoma, it is difficult to compare surgical success rates as these studies vary widely in the populations studied, study design, definition of success and failure, prior glaucoma interventions, type and severity of glaucoma, and length of follow-up. The reported success rate ranges from 31% after 24 months in a study by Al-Mobarak and Khan (2009) and Khan to 86% at 24 months in a retrospective case series by Morad et al. (2003). The most common definition for success has been an IOP  $\leq 22$  mm Hg with (qualified) or without (complete) glaucoma medications, no additional glaucoma surgery, and no visually significant complications (i.e., suprachoroidal hemorrhage, endophthalmitis, or retinal detachment). Surgical success has been related to different factors including longer follow-up time (Table 2) (Coleman et al., 1997; Englert et al., 1999; Djodeyre et al., 2001; Beck et al., 2003; Morad et al., 2003; Al-Torbak, 2004; Chen et al., 2005; O'Malley Schotthoefer et al., 2008; Ou et al., 2009; Yang and Park, 2009), ethnic background and gender. Ou et al. (2009) demonstrated a less favorable surgical outcome in patients of Hispanic ethnicity compared with non-Hispanic patients (Ou et al., 2009). Female gender and more advanced glaucoma (with higher IOP and buphthalmos) have been associated with increased risk of failure (Ben-Zion et al., 2011; Ou et al., 2009; Al-Mobarak and Khan, 2009).

Some studies indicated that AGV has a higher rate of failure in patients with PCG compared with patients with other diagnoses (Coleman et al., 1997; Djodeyre et al., 2001; Chen et al., 2005). However, other studies have not found any correlation between surgical failure and type of glaucoma (Morad et al., 2003; O'Malley Schotthoefer et al., 2008; Yang and Park, 2009) or even reported a higher success rate with PCG in the pediatric population (Englert et al., 1999). On the other hand, Chen et al. reported that a diagnosis of aphakic glaucoma appeared to be associated with a higher success rate compared to other types of childhood glaucoma (Chen et al., 2005). Age of the patient has not been found to affect success rates (Morad et al., 2003; Ou et al., 2009). Morad et al. and Yang and Park reported that prior glaucoma surgery before AGV did not affect the success rate (Morad et al., 2003; Yang and Park, 2009). On the contrary, Djodeyre et al. (2001) noted that eyes with 2 or fewer previous glaucoma surgeries showed significantly better survival rates. The same investigators observed that more than half of their failures occurred as a result

of tube malposition. Accurate angle of tube entrance into the anterior chamber, gentle handling of the device, and adequate fixation are factors related to surgical experience.

There is limited information on whether various types of drainage devices have different success rates in pediatric glaucoma. Beck et al. (2003) did not find any statistically significant difference in IOP control, reduction in the number of glaucoma medications and success rates between the AGV (32 eyes) and the Baerveldt implant (14 eyes). On the other hand, Al-Mobarak and Khan (2009) have shown that silicone AVIs tend to survive longer than polypropylene AVIs two years postoperatively. Yang and Park also mentioned that the success rate may be limited with the AGV model S3, which has a smaller surface area (96 mm<sup>2</sup>) (Yang and Park, 2009). Hence, they proposed that a measurement of globe size with ultrasound may be useful in deciding the size of the implant to be used (Yang and Park, 2009).

One of the reasons for failure of glaucoma drainage devices is the development of encapsulated blebs around the plate. Occasionally, removal of these fibrous capsules leads to a drop in IOP, but in some patients these cysts reappear and require repeated surgical procedures (Eibschitz-Tsimhoni et al., 2005; Feldman et al., 1997; Hill et al., 2000; Trigler et al., 2006). Surgical removal of the thick capsule around the plate has been explored shortly (2–6 months) after surgery (Thieme et al., 2011). Histopathologically, the wall of these encapsulated blebs was found to be very thick (1.5–2 mm). Macroscopically, the tissue was split into 2 layers. The smooth inner surface (facing the plate of the AGV) consisted of compressed collagen fibers with signs of elastoid degeneration along with the formation of a pseudoendothelium toward the plate. There was pronounced transformation of fibroblasts into myofibroblasts in this inner layer. The outer area was highly vascularized. Electron microscopy revealed thrombosis of these vessels. There was no inflammatory response in almost all areas of the excised material (Thieme et al., 2011). Although, in the above study, encapsulation of bleb did not seem to interfere with the function of the valve, prior studies have reported on adhesions between the two membranes forming the valve and fibrovascular tissue ingrowth into the valve mechanism (Feldman et al., 1997; Hill et al., 2000; Trigler et al., 2006).

There are few data regarding the so-called hypertensive phase in pediatric population (Nouri-Mahdavi and Caprioli, 2003). The incidence of the hypertensive phase has been reported to be up to 40–59% (Chen et al., 2005; Yang and Park, 2009). Based on the definition by Nouri-Mahdavi and Caprioli (2003), Yang and Park (2009) observed resolution of the hypertensive phase in 75% of their patients, which is much higher than the reported 28% in adults (Nouri-Mahdavi and Caprioli, 2003). Chen et al. found that the presence of a hypertensive phase was associated with a significantly higher long-term rate of failure (Chen et al., 2005).

There is also limited information with regard to the efficacy of intraoperative adjunctive MMC use in pediatric glaucoma patients. Prior studies of aqueous shunt implantation with and without adjunctive MMC in adults have not shown a remarkable benefit to intraoperative MMC use in this setting. Kirwan et al. (2005) reported that there was no postoperative difference in IOP measurements or complications in patients with or without MMC. Al-Mobarak and Khan (2009) demonstrated that both the cumulative success rate and the mean sur-

vival time were better in the non-MMC group compared to the MMC group. However, because of the retrospective nature of their study, a selection bias based on the type of glaucoma and prior glaucoma surgeries could not be ruled out. Generally speaking, adjunctive MMC use for AGV does not seem to improve IOP outcomes and is better avoided, especially since there is some evidence that it may increase complications (Minckler et al., 2008, 2006).

### 2.3. Subsequent surgical procedure after AGV implantation in children

Surgical treatment of a child with a failed aqueous shunt can be very challenging. Al-Torbak reported that 45% of eyes needed subsequent surgery including valve revision in a series of patients with PCG who underwent combined AVG and penetrating keratoplasty (Al-Torbak, 2004). Other authors have reported the need for subsequent surgery in 9–50% of pediatric patients (Coleman et al., 1997; Djodeyre et al., 2001; Chen et al., 2005). Additional procedures after pediatric Ahmed valve surgery may consist of reformation of the anterior chamber, tube-related complications (e.g. extrusion of the implant), revision of the scleral graft or tube, and perivalvular capsulectomy (Coleman et al., 1997; Beck et al., 2003; Donahue et al., 1997; Chen et al., 2005). Previous studies showed lower success rates with implantation of a second glaucoma drainage device compared to the initial shunt implantation (Burgoyne et al., 2000; Godfrey et al., 2002). Ou et al. (2009), however, have demonstrated that a second AGV for further IOP control in children with prior AGV appears to be safe and effective with a 5-year success rate of 69%. Yang and Park (2009) reported that 46% of their patients underwent additional AGV without removal of the primary implant and 80% of these cases survived by the last follow-up (mean of  $26.6 \pm 12.7$  months). The investigators considered removal of the primary implant to be traumatic, and also the possibility that failed valves may still be partially functioning. Pediatric eyes with previous cyclodestruction have been noted to have a greater chance of glaucoma control with aqueous shunt devices than those without previous cyclodestruction, (Englert et al., 1999) making subsequent cyclodestruction, either ab interno or ab externo, an option in the treatment of refractory pediatric glaucoma (Semchshyn et al., 2002). Further studies are required to delineate the best surgical treatment of pediatric patients who fail an aqueous shunt procedure.

### 2.4. Medical treatment after AGV implantation in children

Although the need for glaucoma medications decreases after placement of a AGV (Coleman et al., 1997; Englert et al., 1999; Hill et al., 2003; Beck et al., 2003; Morad et al., 2003; Chen et al., 2005; Pakravan et al., 2007; Ou et al., 2009; Al-Mobarak and Khan, 2009), most patients will need glaucoma medications at some point after surgery (Table 2) (Hill et al., 2003; Pakravan et al., 2007). Ou et al. (2009) reported that the proportion of eyes requiring medications increased over 5 years of follow-up. While 63% of eyes did not require medications at 3 months, only 11% of the eyes remained off glaucoma medications at 5 years (Ou et al., 2009). Reduction of the number of topical glaucoma medications in children is important because of the potentially greater systemic side effects that

may occur due to lack of cooperation in either eyelid closure or punctual occlusion (Coleman et al., 1997; Zimmerman et al., 1984).

## 3. Complications of AGV implantation

Several devastating postoperative complications may occur following the placement of an AGV in pediatric patients requiring further surgical management (Table 2). Certain complications from glaucoma drainage implants seem to be more common in children (Djodeyre et al., 2001; Hill et al., 1991). Pirouzian and Demer reported that AGV could be associated with cosmetically significant albeit clinically insignificant pupillary irregularity, lenticular opacification as well as extrusion out of anterior chamber, particularly in the first year of life, as the globe is enlarging with age (i.e., buphthalmic process) (Pirouzian and Demer, 2008).

### 3.1. Tube-related complications

Postoperative *tube migration* (typically anteriorly) is the most common complication occurring in up to 35% of patients (Coleman et al., 1997; Englert et al., 1999; Djodeyre et al., 2001; Beck et al., 2003; Al-Mobarak and Khan, 2009). Tube migration is thought to be associated with shrinkage of the sclera and globe after IOP reduction, with the tube repositioning more anteriorly and closer to the corneal endothelium. Additionally, vigorous eye rubbing can move the tube forward toward the cornea. Moreover, as the child's eye grows, the initially well-positioned tube may rotate more anteriorly over time. It is recommended that the tube is placed at least 1 mm posterior to the limbus and that the tube is positioned parallel to the iris (Englert et al., 1999; Beck et al., 2003; Morad et al., 2003; O'Malley Schotthoefer et al., 2008).

*Tube-cornea touch* was reported in as many as 20% of childhood cases (Mullaney et al., 1999; Englert et al., 1999; Hill et al., 1991; Fellenbaum et al., 1995). Tube-cornea contact occurs with higher frequency in buphthalmic patients (deLuise and Anderson, 1983; Englert et al., 1999). Yang and Park attributed their low rate of tube-corneal touch to the application of Ahmed valve S-3 model with smaller surface area (96 mm<sup>2</sup>) in patients under 12 years old (Yang and Park, 2009). A smaller model may be preferred in pediatric patients to prevent tube-cornea contact, which tends to occur in the eyes of very young patients with low scleral rigidity. *Transcorneal migration* of a tube is an unusual complication that might result from prolonged tube-cornea touch (Rosenberg and Krupin, 1996). Reduced scleral rigidity and especially the long-term memory of the silicone tube may allow straightening of the tube with time. Reduced postoperative IOP may lead to shrinkage of the elastic young eye, shifting the tube anteriorly and causing cornea touch (Netland and Walton, 1993; Hill et al., 1991). Local corneal endothelial decompensation from tube touch has been hypothesized to potentially prompt a toxic inflammatory reaction in thin edematous corneas (Al-Torbak and Edward, 2001). These events might cause slow corneal erosion with concurrent scar formation posterior to the eroding tube, thereby preventing aqueous humor leakage. Positioning tubes as posteriorly as possible in the anterior chamber may reduce incidence of tube-cornea touch (Englert et al., 1999; Djodeyre et al., 2001).

*Tube extrusion* is mostly seen in long-standing, uncontrolled severe disease with exceptionally high IOP and large horizontal corneal diameter. Elevated IOP may exert its effect by changing scleral thickness and rigidity thereby affecting implant stability (Asejczyk-Widlicka and Pierscionek, 2008). However, the rigidity of implants (silicone vs. polypropylene) as well as the difficulty in placing scleral sutures in buphthalmic eyes may have also contributed to the high rate of extrusion (Al-Mobarak and Khan, 2009). The earlier the AGV placement is done in life, the higher the probability of tube extrusion (Pirouzian and Demer, 2008). Because it is possible that tube malposition and extrusion may result from contraction of the perivalvular fibrous tissue, placing the tube as posteriorly as possible in the anterior chamber may reduce the incidence of this complication (Englert et al., 1999; Djodeyre et al., 2001). Pirouzian and Demer proposed the tube insertion to be done through a tangentially curved corneal tunnel in the primary surgical insertion phase. Once a tube is retracted and/or extruded from anterior chamber, it is able to reinsert the tube in a straight-line method directly into the chamber in a secondary procedure circumventing the requirement for an extender (Pirouzian and Demer, 2008).

The incidence of *tube blockage* has been reported to be between 0% and 14% after AGV in pediatric glaucoma (Rodrigues et al., 2004; Roche et al., 2007; Netland and Walton, 1993; Donahue et al., 1997; Hamush et al., 1999). The blockage may occur due to iris, vitreous, or blood (Sarkisian, 2009). *Tube erosion* has been well reported in pediatric glaucoma. Tube exposure following conjunctival erosion in AGV appeared to be a major risk factor for the development of endophthalmitis (Al-Torbak et al., 2005). Conjunctival erosion occurs mostly at the limbus and other locations and it does not appear to be related to the conjunctival incision line being placed a few millimeters away from the limbus (Al-Torbak et al., 2005). Reasons for conjunctival erosion over patch grafts and tube are not totally clear and are possibly multifactorial. Most patients had multiple previous conjunctival surgeries with exposure to anti-metabolites and this may contribute to conjunctival erosion (Al-Torbak et al., 2005). Morad et al. found a significant linkage between uveitis and tube exposure (Morad et al., 2003). Although the reason is unclear, they explained that the highly active immune system in these patients overproduces cellular or humoral factors that eventually cause donor sclera melting (Morad et al., 2003). However, the high rate of exposure in this group of patients in their study did not influence the success rate in uveitic patients (Morad et al., 2003). The standard of care to prevent tube erosion is with the use of a patch graft such as sclera, pericardium, fascia lata, cornea, or amniotic membrane (Sarkisian, 2009).

Careful suturing technique, including securing the tube to the sclera, can help minimize tube-related complications. This can prevent many cases of tube and plate migration, retraction, and erosion. Periodic observation of tube position in pediatric eyes is highly recommended.

### 3.2. Ocular hypotony

The reported incidence of hypotony following AGV ranges from 11% to 25% (Coleman et al., 1997; Englert et al., 1999; Djodeyre et al., 2001; Morad et al., 2003). However, Chen et al. reported hypotony in 42% of their patients, which is comparable to studies involving non-valved implants (Chen

et al., 2005). This is higher than that reported in the adult population (<10%) (Sarkisian, 2009). In many of these cases, anterior chamber reformation or implant revision is required (Netland and Walton, 1993; Fellenbaum et al., 1995; Nesher et al., 1992). The management of flat or shallow anterior chambers is more difficult in children, as treatment may often require repeat general anesthesia.

The possible protective effect of the valve mechanism of the AGV in reducing postoperative hypotony and shallow anterior chamber is still unclear. It was suggested that the placement of the drainage tube through a smaller needle track such as a 23- (Beck et al., 2003) or 25- (Djodeyre et al., 2001) needle and partially ligating the tube (Chen et al., 2005) might lessen the chance of leakage around the aqueous drainage implant tube in patients with extremely thin scleral walls. It is also possible that a Valsalva maneuver associated with vomiting can cause hypotony or shallow anterior chamber (Coleman et al., 1997). Because the tube is placed after anterior or posterior chamber penetration by a needle, sudden and severe reduction of the IOP may occur, producing choroidal detachment and cyclitis, which can lead to hypotony. Unlike non-valved implants, a two-stage procedure is not usually required with Ahmed valve glaucoma implants. However, if there is heightened concern for postoperative hypotony, such as in cases of Sturge-Weber Syndrome or patients with a history of postoperative hypotony in the other eye, a two-stage procedure might be considered in which the plate is implanted initially and the tube will be inserted 4–6 weeks later, giving time for the fibrous capsule to provide resistance to flow. This technique also can be performed with the Ahmed glaucoma valve (Sarkisian, 2009).

### 3.3. Motility disturbances

In children, ocular motility disturbances following glaucoma drainage devices are frequent (Sarkisian, 2009). The incidence of strabismus after AGV in pediatric patients has been reported in around 3–5% of patients (Coleman et al., 1997; Morad et al., 2003). The AGV implants seem to produce a lower incidence of postoperative ocular motility disturbance than those with larger plate size (Morad et al., 2003). Probably, it is because of implanting the shunt between rather than partially under the rectus muscles with minimal manipulation of the muscles (Morad et al., 2003).

The motility problems are believed to be secondary to a mass effect from the equatorial filtering bleb, a Faden or posterior suture fixation effect, or fat adherence syndrome (Christmann and Wilson, 1992; Smith et al., 1993; Munoz and Parrish, 1992). Almost all patients with motility disturbance had a large fibrous capsule surrounding the implant plate, adjacent muscles and sclera (Sarkisian, 2009). Surgical intervention included muscle surgery, removal of the fibrous capsule around the implant, and size reduction of the implant plate (Sarkisian, 2009).

### 3.4. Infectious endophthalmitis

Infectious endophthalmitis is rare following placement of any glaucoma drainage devices in children (Hill et al., 1991; Munoz et al., 1991; Al-Torbak and Edward, 2002) and is usually delayed in onset (Al-Torbak et al., 2005). This devastating complication was reported to be the consequence of conjunctival



erosion over an implant tube, which was likely the portal of entry of the organism (Al-Torbak et al., 2005; Al-Torbaq and Edward, 2002; Gedde et al., 2001). The rate of endophthalmitis following AGV surgery in pediatric age group was reported to be five times higher than that in adults (Al-Torbak et al., 2005). Age < 18 years old has been reported to be a significant risk factor for endophthalmitis (Al-Torbak et al., 2005). Interestingly, the rate of endophthalmitis in children appears to parallel the rate of tube exposure in pediatric shunts (10–13%) (Djodeyre et al., 2001; Hill et al., 2003; Chen et al., 2005), which has been reported to be five times higher than the rate reported for glaucoma drainage devices in adults (0–2%) (Lloyd et al., 1994; Melamed et al., 1991). The most frequently detected organisms causing endophthalmitis following glaucoma drainage devices in children are *Hemophilus influenzae*, *Streptococcus pneumoniae*, or both (Al-Torbak et al., 2005). It seems that the bacillus *H. Influenza* is an important source of endophthalmitis in children because it can be part of the normal bacterial flora of the conjunctiva and upper respiratory tract, and is a common cause for infection in both tissues (Al-Torbak et al., 2005; Al-Torbaq and Edward, 2002; Gedde et al., 2001).

Recommendations for removal of the glaucoma shunt device at the time of vitrectomy in an eye with endophthalmitis remain unclear. Although Gedde et al. (2001) and Perkins (1990) recommended shunt removal at the time of vitrectomy as shunt might be a reservoir for the infectious organism, others have reported successful outcomes with intravitreal antibiotics without removal of the shunt device (Al-Torbak et al., 2005; Al-Torbaq and Edward, 2002; Ellis et al., 1993; Krebs et al., 1992). In pediatric patients, prompt revision of the exposed valve implants is recommended, as this group of patients is at a higher risk of endophthalmitis than adults, most likely due to the higher incidence of upper respiratory tract infections (Al-Torbak et al., 2005).

### 3.5. Delayed suprachoroidal hemorrhage

The incidence of delayed suprachoroidal hemorrhage after glaucoma surgery in children has been reported as 0.36% in one study (Ghadhfan and Khan, 2009), which is lower than the reported rate in adults (1.6–6.1%) (Givens and Shields, 1987; Ruderman et al., 1986; Paysse et al., 1996). Aphakia, AGV implantation, and MMC use were reported as risk factors for delayed suprachoroidal hemorrhage (Ghadhfan and Khan, 2009). The authors hypothesized that the lack of an intact posterior capsule in pediatric surgical aphakia may decrease the eye's ability to tamponade against decompression which makes delayed suprachoroidal hemorrhage more likely to develop. Theoretically, AGV implantation should reduce the incidence of postoperative hypotony and, therefore, would have been expected to decrease the potential for large rapid changes in the suprachoroidal vascular gradient and hence delayed suprachoroidal hemorrhage. Early leakage around the tube or a defective valve mechanism may have allowed IOPs to reach very low levels postoperatively (Ghadhfan and Khan, 2009).

### 3.6. Pupillary irregularities

The mechanism of pupillary peaking toward the tube area is not well understood. The most likely mechanism of iris peaking might be secondary to inflammatory response to the presence of talc on the tube or local creation of peripheral anterior

synechia (Pirouzian and Demer, 2008). Occasionally, superficial iris incarceration due to acute decompression during the creation of the needle track may lead to iris entrapment and secondary iris elevation. To cope with this adverse outcome, Pirouzian and Demer suggested manipulating the tube and inserting the tube in a tangential method posterior to the gray surgical limbus line to change the direction of the outflow (Pirouzian and Demer, 2008). Additionally, they proposed to create a surgical peripheral iridectomy, whenever possible at the entrance site of valve. This may also alter the fluid outflow pathway. Surgical iridectomy may split the flow of aqueous to the tube orifice into two separate streams emanating from posterior and/or anterior chambers (Pirouzian and Demer, 2008).

## 4. Conclusion

The treatment of primary congenital glaucoma and other childhood glaucomas remains a daunting task, even under the best of circumstances. The initial learning curve, complications, longer-term failure, the need for further surgical interventions have been major obstacles to the management of pediatric glaucoma. In this review, adequate IOP control can be achieved with the placement of AGV and can last 5 or more years. A major challenge is to continue to stimulate interest in the treatment of pediatric ocular conditions by ophthalmologists in training. Reduction of visual disability worldwide from primary congenital glaucoma will only be realized by training adequate numbers of ophthalmologists, who cannot only diagnose the condition, but are willing and able to treat it.

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