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Glaucoma drainage devices implantation in uveitic glaucoma: a systematic review



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ABSTRACT

Background: Uveitis is broadly defined as inflammation of the uvea. Glaucoma is the third most common complication of uveitis. Uveitic Glaucoma (UG) is known to be refractory, and multiple surgeries are often required for proper treatment. The purpose of this study is to determine the effectiveness of Glaucoma Drainage Device (GDD) implantation as a surgical procedure in UG patients.

Method: We conducted a systematic search of electronic databases from PubMed, Science Direct, and SpringerLink using a combination of relevant keywords was performed by 5 independent reviewers. Various search terms, including 'glaucoma drainage device', 'glaucoma drainage implants', 'glaucoma filtration implants', 'aqueous shunts', 'uveitic glaucoma',

'inflammatory glaucoma'.

Result: A total of 143 articles were retrieved, but only 14 articles were eligible for data extraction. There are 631 eyes from 583 patients who had UG, 442 eyes underwent GDD implantation. Overall, intraocular pressure and the use of glaucoma medication were reduced. Mean IOP preoperative is 31.57 mmHg, and IOP postoperative is 14.48 mmHg. There is a reduction in IOP of an average of 17.09 mmHg. The number of glaucoma medications has decreased from 3.24 to 1.29 postoperatively.

Conclusion: UG has been shown to be managed successfully by GDD implantation. GDD implantation may be considered a long-term effective surgical option for patients with UG.

Keywords: glaucoma drainage device, refractory glaucoma, uveitic glaucoma

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INTRODUCTION

Uveitis is broadly defined as inflammation of the uvea. The uvea consists of the middle, pigmented, vascular layer of the eye and includes the iris, ciliary body, and choroid. The etiology of uveitis is infectious or inflammatory and is variably associated with systemic disease.¹

Uveitis is responsible for approximately 10% of all blindness in the United States and Europe and up to 25% of blindness worldwide. Uveitis incidence peaks between 20 and 60 years of age. Recent data suggests that it may also increase over the age of 65. Women have slightly higher rates of uveitis overall. Prevalence is about five to tenfold lower in children than in adults. Anterior uveitis is the most common type of uveitis, representing 70-80% of cases, followed by pan uveitis,

posterior uveitis, and intermediate uveitis¹

Glaucoma is the third most common complication of uveitis after cystoid macular edema and cataract, and it is seen in 10-20% of patients with uveitis develop.^{2,3} Considerably higher rates of glaucoma (30-50%) have been described in eyes with specific uveitic syndromes, including juvenile-rheumatoid-arthritis-associated iridocyclitis, Fuchs' heterochromic iridocyclitis, Lyme-associated uveitis, and cancer-associated uveitis.⁴

The intraocular pressure is usually below normal in uveitis because the inflamed ciliary body is functioning poorly.⁵ The underlying mechanism of uveitic glaucoma (UG) has not been fully understood.² However, the elevation of intraocular pressure may

also occur through a number of different mechanisms.⁵ Etiology of uveitis, inflammatory mechanism, and steroid treatment have impacts on glaucoma development.²

UG is known to be refractory, and multiple surgeries are often required for proper treatment.⁶ Medical management of UG requires aggressive control of both intraocular inflammation and IOP, as well as prevention of glaucomatous optic nerve damage and visual field loss.¹ Surgical intervention may be indicated if intraocular pressure (IOP) cannot be adequately controlled by medication alone.³

Trabeculectomy is the most widely performed surgical procedure in refractory glaucomas, but its long-term success rate is limited in UG.² Prior literature suggests

that trabeculectomy has good outcomes in UG in the short term, the risk of failure is relatively high in the long term.³ The major complication of this procedure is bleb fibrosis. Although the application of anti-fibrotic agents such as mitomycin C has been used in surgery, the success rate of filtration surgery remains unsatisfactory.⁷

In recent years, aqueous drainage devices have been widely used to treat uveitic glaucoma.⁷ Glaucoma drainage implants have been shown to be effective for long-term success in uveitic glaucoma.⁸ The purpose of this study is to determine the effectiveness of GDD implantation as a surgical procedure in uveitic glaucoma patients.

METHOD

Literature Research

We conducted a systematic review on the effectiveness of glaucoma drainage device implantation for uveitic glaucoma patients. This study was performed following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A systematic search of electronic databases from PubMed, Science Direct and SpringerLink using a combination of relevant keywords was performed by 5 independent reviewers. Various search terms, including *glaucoma drainage device, glaucoma drainage implants, glaucoma filtration implants, aqueous shunts, uveitic glaucoma, inflammatory glaucoma*.

To formulate eligibility criteria, we used the SPIDER model for clinical questions (sample, phenomenon of interest, design, evaluation, and research type). SPIDER tool allows researchers to focus on a specific question and determine specific exclusion and inclusion criteria that are used when selecting studies to be included in the systematic review.

Inclusion Criteria

1. From any country
2. Studies in the human eye
3. Published from 10 years ago to the present day
4. Published in English
5. Appropriate study design: clinical trials, case report, case series, RCT, retrospective, prospective study, comparative study, observational study.

Exclusion Criteria

1. Non-research: commentaries, editorials, letters, methodology papers, editorial and narrative review articles
2. Research: systematic review, meta-analysis
3. Non-English article/publication
4. Subject(s) had other ocular or non-ocular conditions
5. Flawed study design

Data Analysis

From the retrieved studies, titles and abstracts were scanned, then the full-text was read, and the reference lists from all identified studies were scanned

in the same way to find other eligible studies. We descriptively analyzed all data included in this study. We recorded intraocular pressure (IOP), visual acuity (VA), inflammation, number of glaucoma medications, and number of anti-inflammatory medications preoperative and postoperative.

RESULT

A total of 143 articles were retrieved by searching the previously mentioned databases. After screening, there were 14 articles eligible for data extraction. The PRISMA flow diagram demonstrating the selection process is displayed in **Figure 1**.

Table 1. SPIDER Tool

Sample	Patient with uveitic glaucoma
Phenomenon of Interest	Effectiveness of GDD implantation for uveitic glaucoma
Design	Systematic review
Evaluation	Outcome after GDD implantation
Research Type	Qualitative method

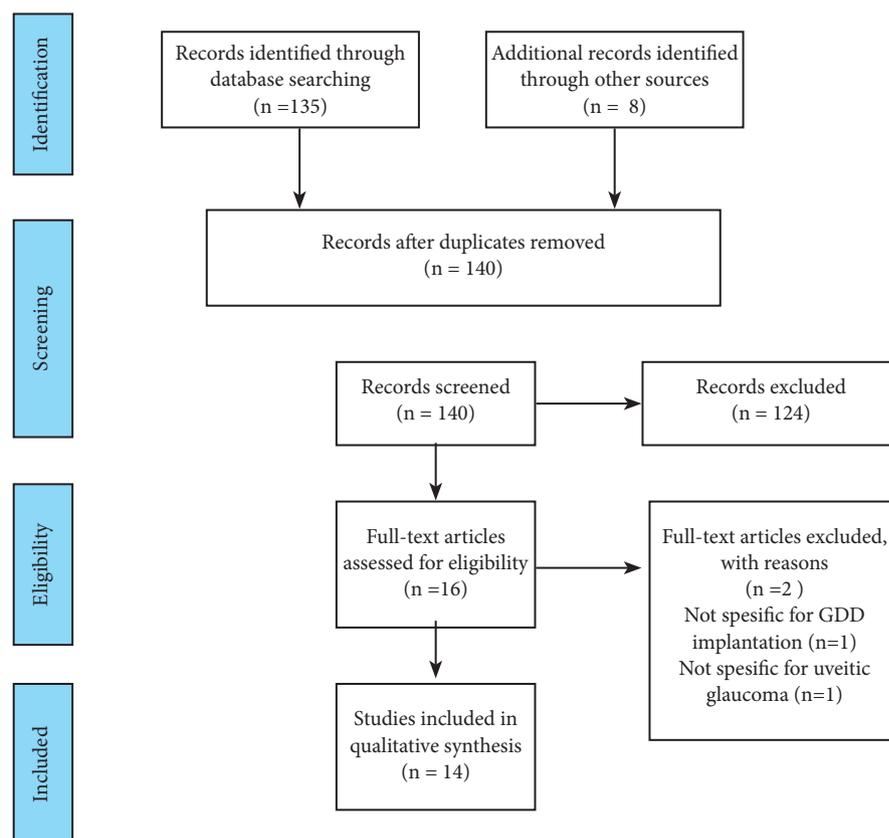


Figure 1. PRISMA Flow Diagram

A total of 631 eyes from 583 patients had uveitic glaucoma, 442 eyes underwent glaucoma drainage device implantation. Follow-up duration was varied between 6 months to five years. Of the 14 studies, 5 studies compared GDD implantation to trabeculectomy, 3 studies compared GDD implantation to a combination of GDD and fluocinolone implantation, 1 study compared GDD implantation to goniotomy, and 5 studies reported the outcome of GDD implantation for uveitic glaucoma patients. In this study, we focused on efficacy and outcome GDD implantation for treated uveitic glaucoma.

Table 1 demonstrates the demographic characteristics of included studies. Studies were conducted in 12 different countries. There was variation in the type of GDD, valve and non-valve implant. The study population included adult and pediatric uveitic glaucoma patients. All articles were published between 2013 and 2020. In this study, we determined the efficacy and outcome of GDD implantation due to comparison in intraocular pressure (IOP), visual acuity (VA), inflammation, number of glaucoma medication, and number of anti-inflammatory medication preoperative and postoperative.

We summarize our research data in **Table 2**. Overall, IOP was reduced as the effect of GDD implantation, as seen in **Figure 2**. Mean IOP preoperative is 31.57 mmHg, and IOP postoperative is 14.48 mmHg. There is a reduction in IOP of an average of 17.09 mmHg. Not all studies record changes in VA. Most of the studies show there was no significant improved VA postoperatively.

Bohnsack et al. quantified inflammation uniformly by the number of cells per high-power field; at the final examination, one eye showed no inflammation postoperatively, but the rest of the eyes remained the same.⁹ Sevgi et al. found the presence of inflammation did not change significantly in the Ahmad Glaucoma Valve (AGV), the only group compared to the AGV+ fluocinolone implant group.¹⁰ In line with Sevgi et al., Zivney et al. found fluocinolone implant had better control intraocular inflammation.^{10,11}

Figure 3 showed the number of glaucoma medications was decreased postoperatively in all studies on average

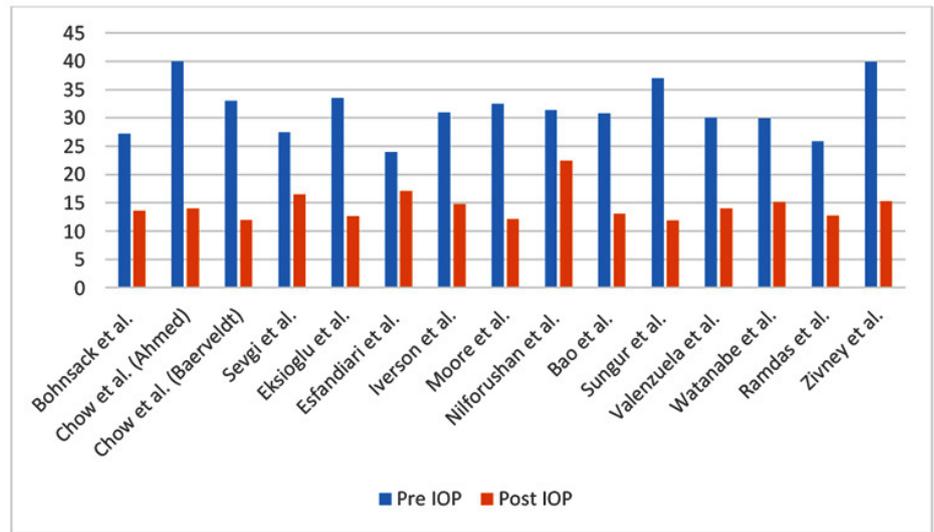


Figure 2. Preoperative and Postoperative IOP

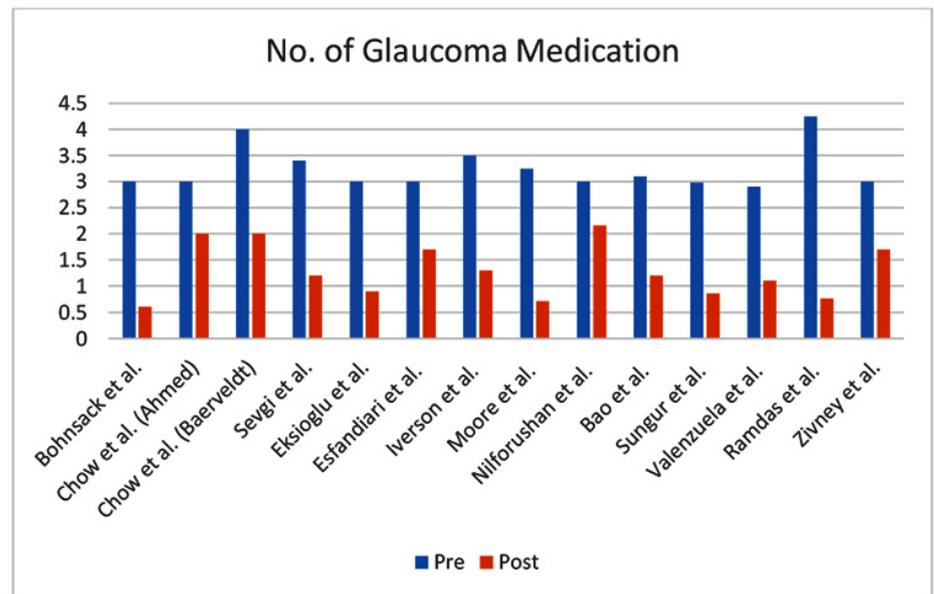


Figure 3. Preoperative and postoperative number of glaucoma medication

decrease from 3.24 to 1.29. Bohnsack et al. and Chow et al. found that there was no difference in anti-inflammatory medication use before and after surgery.^{3,9}

Generally, common complications were hypotony, choroidal effusion, hyphema, shallow anterior chamber, blocked tube, and corneal edema.

DISCUSSION

Uveitis is a common cause of blindness and is characterized by recurrent

intraocular inflammation of the eyes. One of the major complications is glaucoma.⁷ Patients with both glaucoma and uveitis have a higher risk of severe visual impairment.¹² Elevation of intraocular pressure may occur through a number of different mechanisms. The trabecular meshwork may become blocked by inflammatory cells (trabeculitis). One of the most causes of raised intraocular pressure in individuals with uveitis is the use of topical steroids. Chronic or

Table 2. Demographic characteristic of included study

No.	Author (Year)	Location	Study Design	Sample Size	Eyes	Male	Female	Population	Follow Up
1	Bohnsack et al. (2013)	Chicago	Retrospective case series	36	36	13	23	Pediatric uveitic glaucoma patients (mean age 11.1±4.4 years old)	5.6±4.8 years
2	Chow et al. (2018)	California	Retrospective comparative study	147	147	64	83	Uveitic glaucoma patients (19-96 years old)	1 year
3	Sevgi et al. (2017)	Massachusetts	Retrospective comparative study	13	18	7	6	Uveitic glaucoma patients (mean age 56.5 years old)	1 year
4	Eksioglu et al. (2017)	Turkey	Retrospective case series	11	16	8	3	Pediatric uveitic glaucoma patients (mean age 14 years old)	64.46±33.56 months
5	Esfandiari et al. (2018)	Tehran	Retrospective comparative study	26	26	14	12	Uveitic glaucoma patients (mean age 46.6 years old)	33.7±17.8 months
6	Iverson et al. (2015)	Miami	Retrospective comparative study	42	42	15	27	Uveitic glaucoma patients (mean age 62.5 years old)	5 years
7	Moore et al. (2015)	Durham	Retrospective interventional study	60	62	29	31	Uveitic glaucoma patients (mean age 47.5 years old)	2 years
8	Nilforushan et al. (2018)	Tehran	Retrospective cohort study	28	28	15	13	Patients with Fuchs uveitis syndrome (mean age 44.5 years old)	23.06±12.03 months
9	Bao et al. (2018)	China	Retrospective non-comparative study	56	67	29	27	Uveitic glaucoma patients (24-65 years old)	53.3±8.5 months
10	Sungur et al. (2017)	Turkey	Retrospective study	39	46	17	22	Uveitic glaucoma patients (19-66 years old)	51.93±23.08 months
11	Valenzuela et al. (2018)	Spain	Retrospective case series	21	26	11	10	Uveitic glaucoma patients (13-75 years old)	53.5±31 months
12	Watanabe et al. (2020)	Tokyo	Retrospective study	41	45	24	17	Uveitic glaucoma patients	50.9±33.68 months
13	Ramdas et al. (2018)	Rotterdam	Retrospective case-control study	38	38	14	24	Uveitic glaucoma patients (mean age 44.4 years old)	1 year
14	Zivney (2016)	Portland	Retrospective comparative study	25	34	6	19	Uveitic glaucoma patients (mean age 50 years old)	6 months

Table 3. Summarize of included study

Author	Intervention	n	IOP		VA		Inflammation		No. Of Glaucoma Medication		No. Of Anti-Inflam Medication		Complication
			Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	
Bohnsack et al. (2013)	Glaucoma Drainage Device	5	27.2 ±7.6	13.6 ±3.2	0.42 ±0.11	0.39 ±0.24	1-4 cell / hpf = 4, ≥5 cell/hpf=1	0 cell/hpf=1 14cell/hpf=3; ≥5cell/hpf=1	3.0 ±1.2	0.6 ±0.9	2.0 ±1.2	2.2 ±1.3	1 secondary GDD
Chow et al. (2018)	Ahmed Shunt	22	40	14	0.6	0.5	Not stated	Not stated	3	2	1	1	18% hypotony, 9% choroidal effusion, 9% hypHEMA, 9% corneal edema, 4.5% uveitic flare, 5% erosion, 5% revision
Sevgi et al. (2017)	Ahmed Shunt	11	27.45±12.5	16.5±6.6	0.86±0.58	0.6±0.5	27.30%	9.10%	3.36 ±0.76	1.27 ±1.0	Not stated	Not stated	1 eye requiring second AGV placement 1 year after for persistently high IOP (28mmHg)
Eksioğlu et al. (2017)	Ahmed Shunt	16	33.50 ±7.30	12.69 ±3.20	Not stated	Not stated	Not stated	Not stated	3	0.96 ±1.24	Not stated	Not stated	1 eye Descemet membrane detachment, 1 hypHEMA, 2 eyes hypotony, 1 eye flat anterior chamber
Baerveldt shunt		108	33	12	0.8	0.7	Not stated	Not stated	4	2	1	1	19% hypotony, 13% choroidal effusion, 7% CME, 7% hypHEMA, 4% shallow anterior chamber, 20% corneal edema, 11% uveitic flare, 0.9% diplopia, 0.9% blocked tube, 2% erosion, 9% revision

Esfandiari et al. (2018)	Ahmed Shunt	14	24 ±7.8	17.1±2.6	0.27±0.27	0.44±0.67	Not stated	Not stated	Not stated	3±0.6	1.71±0.6	Not stated	Not stated	3 eyes hyphema, 1 eye choroidal effusion, 1 eye corneal decompensation, 1 eye endophthalmitis, 2 eyes tube exposure, 2 eyes tube cornea touch
Iverson et al. (2015)	GDD Implantation	23	31 ±12	14.8 ±5.6	0.60±0.67	Not stated	Not stated	Not stated	Not stated	3.5 ±1.0	1.3±1.4	Not stated	Not stated	Cumulative probability of failure after 5 years follow-up 25%
Moore et al. (2015)	Ahmed Shunt	16	32.53	12.1	-0.63±0.67	No significant changes	Not stated	Not stated	Not stated	3.25	0.71	Not stated	Not stated	Not stated
Nilforushan et al. (2018)	Ahmed Shunt	12	31.41±6.76	22.41 ±5.09	Not stated	Not stated	Not stated	Not stated	Not stated	3.0 ±0.95	2.16 ±0.93	Not stated	Not stated	1 eye hyphema
Bao et al. (2018)	Ahmed Shunt	67	30.8±6.8	13.1 ±3.7	0.72±0.49	0.63±0.54	Not stated	Not stated	Not stated	3.1 ±0.6	1.2 ±0.5	Not stated	Not stated	3 eyes hyphema, 12 eyes transient hypotony, 7 eyes shallow AC, 1 eye tube obstructed, 10 eyes corneal edema
Sungur et al. (2017)	Ahmed Shunt	46	37.05±9.62	11.86 ±1.35	Not stated	Not stated	13%	Not stated	Not stated	2.98 ±0.27	0.86 ±1.46	Not stated	Not stated	12 eyes hypotony, 1 eye tube exposure, 1 persistent corneal edema
Valenzuela et al. (2018)	Ahmed Shunt	26	30±11.6	14 ±6.2	1.23	1.31	Not stated	Not stated	Not stated	2.9	1.1	Not stated	Not stated	6 eyes hypotony, 2 eyes choroidal effusion
Watanabe et al. (2020)	GDD	21	29.94±10.6	15.14 ±6.57	Not stated	Not stated	Not stated	Not stated	Not stated	Not stated	Not stated	Not stated	Not stated	Not stated
Ramdas et al. (2018)	GDD	38	25.9±7.7	12.7±4.4	0.63±0.38	No significant changes	Not stated	Not stated	Not stated	4.24 ±1.19	0.76 ±1.34	Not stated	Not stated	13.2% eyes developed macular edema, 15.8% eyes hypotony
Zivney (2016)	Ahmed Shunt	17	39.9±13.8	15.3±4.8	0.55±0.74	0.35±0.29	52.90%	Not stated	35.70%	3 ±0.7	1.7 ±1.0	Not stated	Not stated	Not stated

recurrent uveitis produces permanent impairment of trabecular function, peripheral anterior synechiae, and occasionally angle neovascularization, all of which increase the chance of secondary glaucoma. Seclusio pupillae due to 360° posterior synechiae produces iris bombe and acute angle-closure glaucoma.⁵

It is one of the most difficult forms of glaucoma to manage because the ophthalmologist must simultaneously address inflammation and elevated IOP as well as prevention of glaucomatous optic nerve damage and visual field loss.^{1,12} Treatment is directed chiefly at controlling the uveitis with concomitant medical glaucoma therapy as necessary.⁵

There are many therapies used to treat uveitic glaucoma.⁷ Aqueous suppressants are generally the first-line agents. Prostaglandin analogs may be used to treat uveitic glaucoma and generally do not exacerbate intraocular inflammation, especially when used concomitantly with immunomodulatory therapy (IMT) and corticosteroids.¹ The choice of additional agents often depends on the IOP level. If this is very high, oral acetazolamide may be required. For moderate elevation (e.g. less than 35 mmHg on a beta-blocker) in the absence of significant glaucomatous damage, an alpha-adrenergic agonist or topical carbonic anhydrase inhibitor (CAI) might be adequate.¹³ Use of pilocarpine (miotic) should be avoided in uveitis, as the smaller fixed pupil may be at risk for worsening of posterior synechiae, and pilocarpine causes a breakdown of the blood-aqueous barrier.¹

When medical management fails, glaucoma filtering surgery is indicated.¹ Among the current surgical treatment options are trabeculectomy, deep sclerectomy, minimally invasive glaucoma surgery (MIGS), cyclodestructive procedures, and several types of glaucoma drainage devices (GDD).¹²

Trabeculectomy is the most widely performed surgical procedure in refractory glaucomas, but its long-term success rate is limited in UG because of early bleb failure secondary to the accelerated healing response.² The major complication of this procedure is bleb fibrosis. Although the application of anti-fibrotic agents such as mitomycin C has

been used in surgery, the success rate of filtration surgery remains unsatisfactory.⁷ Landers et al. reported 20-year results of trabeculectomy in different types of glaucomas, and they have found that UG has a significantly lower success rate after trabeculectomy than other types of glaucomas.² Cyclodestructive procedures are irreversible; hence, this treatment option is often reversed for eyes with worse visual prognosis. Therefore, GDD is currently considered a better choice in the treatment of uveitic glaucoma.¹² GDD have been shown to be effective for long-term success in uveitic glaucoma.⁸

GDD creates alternate aqueous pathways by channeling aqueous from the anterior chamber through a long tube to an equatorial plate that promotes bleb formation.¹⁴ The most commonly used GDD are the valved (Ahmed Glaucoma Valve/AGV) and the non-valved (Molteno and Baerveldt implant).¹² Molteno and Baerveldt implants offer no resistance to immediate outflow; meanwhile, AGV offers some resistance.¹⁴

A previous study found the cumulative probability of success AGV implantation of 77-94.4% at 1 year and 50-80% at 2-4 years. There is also a report evaluating Molteno implants in uveitic patients that found survival estimates between 80% and 95% at 27-48 months of follow-up. A small retrospective study of Baerveldt implantation in uveitic eyes found cumulative life-table success rates were 95.8% at 3 months and 91.7% at 6-24 months.¹⁵

In this study, we evaluate GDD implant outcomes for uveitic glaucoma patients. We recorded data on IOP, VA, eye inflammation, number of glaucoma medication, and number of anti-inflammatory medications preoperative and postoperative. Some definitions of success, using numbers such as 21 or 22 mmHg as the target IOP. According to the data we got, all of them reached the target IOP and required fewer glaucoma medications. GDD implantation appears to be reasonably effective at controlling IOP. Meanwhile, there was no significant improvement for visual acuity, inflammation, and the number of anti-inflammatory medications.

Complications of GDD surgery include

shallow anterior chamber, hypotony, suprachoroidal hemorrhage, and blockage of the drainage device by blood, fibrin, or iris. Long-term complications include device erosion through the conjunctiva, valve migration, corneal decompensation, drainage device-cornea touch, and retinal detachment. Unlike trabeculectomy, these drainage devices have proven to be robust and continue to function despite chronic, recurrent inflammation, and they provide excellent long-term IOP control in eyes with uveitic glaucoma.¹ Hypotony is the most frequently reported complication. Uveitic eyes are prone to developing hypotony in the early postoperative period secondary to ciliary body shutdown.¹⁶⁻¹⁹

This study has several limitations. We do not categorize patients by age, so it is included all uveitic glaucoma patients, pediatric and adults. It has different follow-up times, range 6 months to 5 years. We do not differentiate the type of GDD. For future research, it needs to standardize the definition of success following a glaucoma surgical procedure. Long term follow-up and prospective evaluation are needed to determine the success of GDD implantation.

CONCLUSION

Uveitic glaucoma is shown to be managed successfully by GDD implantation. It can be seen from the reduction in IOP in order to preserve vision for patients with uveitic glaucoma, and patients were on fewer glaucoma medications postoperatively. GDD implantation may be considered a long-term effective surgical option for patients with uveitic glaucoma.

CONFLICT OF INTEREST

The authors state that there is no conflict of interest in this study.

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AUTHOR CONTRIBUTION

All authors contributed equally to this study.

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