Graefe's Archive for Clinical and Experimental Ophthalmology (2019) 257:1079–1089
https://doi.org/10.1007/s00417-019-04256-8

REVIEW ARTICLE

Surgical treatment of neovascular glaucoma: a systematic review and meta-analysis

Zakhar Shchomak[1] · David Cordeiro Sousa[2] · Inês Leal[2] · Luís Abegão Pinto[2]

Received: 11 November 2018 / Revised: 11 November 2018 / Accepted: 24 January 2019 / Published online: 6 February 2019

Abstract

Purpose This literature review and meta-analysis aims to compare intraocular pressure (IOP) lowering efficacy, failure rates and loss of light perception (LP) rates 6 months after an IOP-lowering surgical procedure in neovascular glaucoma (NVG) eyes.
Methods MEDLINE and EMBASE were used as data sources. Only studies including NVG patients who underwent two different surgical approaches were considered. The treatment effect measures were (i) weighted mean difference (WMD) for IOP reduction, (ii) risk ratio (RR) for failure rates and (iii) risk difference (RD) for loss of LP. Outcome measures were reported with a 95% confidence interval (CI) and $P < 0.05$ was considered statistically significant. Analysis was performed using RevMan v5.0.
Results No RCT were retrieved. Seven comparative non-randomised studies were eligible. In glaucoma drainage devices (GDDs) vs cyclophotocoagulation arm, there was no statistical difference in IOP-lowering efficacy (WMD = − 3.63; CI [− 8.69, 1.43], $P =$ 0.16), although failure rates and loss of LP were lower in the GDDs group (RR = 0.64, CI [0.41, 0.99], $P = 0.05$; and RD = − 0.15, CI [− 0.25, − 0.05], $P = 0.004$, respectively). In the Ahmed glaucoma valve (AGV) vs trabeculectomy arm, there was no statistical difference in IOP-lowering efficacy and loss of LP (WMD = 0.78, CI [− 2.29, 3.85], $P = 0.62$ and RD of 0.04, CI [− 0.05, 0.14], $P =$ 0.34, respectively), but failure rates were lower in trabeculectomy group (RR of 2.25, CI [1.14, 3.71], $P = 0.02$).
Conclusions There is lack of high-quality evidence on the subject as no RCT were retrieved comparing two different IOP-lowering procedures in NVG patients. Our findings are based, therefore, on non-RCT studies and should be interpreted with caution. There appears to be no difference in IOP-lowering efficacy between GDDs and cyclophotocoagulation, although GDDs appear to be safer. AGV and trabeculectomy also seem to provide similar IOP-lowering results with trabeculectomy showing lower failure rates.

Keywords Neovascular glaucoma · Glaucoma drainage devices · Trabeculectomy · Cyclophotocoagulation

Introduction

Neovascular glaucoma (NVG) is an aggressive type of glaucoma generally associated with poor visual prognosis [1]. NVG is secondary to a number of diseases that affect the eye, the most common being diabetic retinopathy, ischemic central retinal vein occlusion and ocular ischemic syndrome [2]. The common feature to all is a hypoxic posterior segment, which leads to increased vascular endothelial growth factor (VEGF) formation. In turn, this cytokine-rich environment promotes the formation of fibrovascular tissue over the trabecular meshwork, resulting in aqueous humour (AH) outflow impairment and consequently increased intraocular pressure (IOP) [3]. While initially an open-angle condition, the myofibroblasts proliferation eventually creates a synechial angle-closure and further IOP elevation [4].

The management of NVG includes both controlling of the underlying ischemic process and decreasing IOP [5]. The first one is directed at reduction of ischemic drive that induces formation of new blood vessels, usually by panretinal photocoagulation or intravitreal anti-angiogenic administration [6]. The second key aspect is the successful IOP management [6]. This can be achieved with medical therapy and surgery, when ocular hypotensive drugs are insufficient.

Surgical options include cyclodestructive procedures, filtering surgery and glaucoma drainage devices (GDDs). Most

✉ Luís Abegão Pinto
abegaopinto@gmail.com

1 Faculdade de Medicina da Universidade de Lisboa, 1649-028 Lisbon, Portugal

2 Department of Ophthalmology, Hospital Santa Maria, Av Prof. Dr. Egas Moniz, 1649-035 Lisbon, Portugal

cyclodestructive techniques are based on partial destruction of the ciliary body which decreases AH production, and therefore lowers the IOP [5]. Several procedures are available, such as cryotherapy, ultrasound cycloplasty and transcleral/endophotocoagulation [5]. Alternatively, both filtering surgery and GDDs create an alternative route for AH drainage, thus bypassing the blockade and restoring the AH outflow. The most commonly performed filtering surgery is trabeculectomy. However, NVG alone is considered a risk factor for bleb failure after trabeculectomy [7]. In consequence, GDDs have gained popularity as their success is less dependent on control of intraocular inflammation and the failure of filtering bleb [8]. Various GDDs (e.g. Molteno implant, Baerveldt implant, Ahmed glaucoma valve [AGV]), have been tried in the treatment of NVG. However, there is no evidence of superiority of one over another [6]. All in all, current evidence comparing surgical techniques in NVG is limited and the selection of the surgical procedure is based primarily on the individual surgeon's judgement and consideration of patients' variables [1].

The purpose of this review was to compare the best available evidence on the comparative efficacy and safety of the surgical techniques used in NVG.

Material and methods

Eligibility criteria for considering studies for this review

Studies including patients with NVG who underwent a surgical intervention for IOP control were included. Only studies comparing two groups with different surgical approaches were included. Both randomised clinical trials (RCTs) and non-randomised studies were included. No restrictions were made based on patients' age, ocular comorbidities or NVG aetiology. The primary outcome was the mean difference in IOP reduction 6 months after surgery, with or without anti-glaucoma medication. Our secondary outcomes were the rates of surgical failure and loss of light perception (LP) at the last visit.

Search methods for identifying studies

Search protocols were elaborated for MEDLINE and EMBASE databases (see Appendix 1 and 2 for detail). We electronically searched Journals@Ovid Full Text <March 18, 2018>, Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily, Ovid MEDLINE and Versions, EMBASE Classic and EMBASE <1947 to 2018 March 18. The last electronic search was performed on the 18th of March of 2018. No data or language restrictions were used. Additionally, a manual search throughout the bibliography of relevant studies was performed to include other potential studies.

Study selection

Two reviewers independently screened the titles and abstracts of studies identified by electronic and manual searches. Each reviewer classified the results as "Yes", "Maybe" or "No" on whether to include or not to include studies for full text analysis. The differences in classification were resolved through mutual consensus, and whenever needed, a third reviewer was consulted. The same procedure was applied to full text analysis. All studies excluded from our review were excluded with reasons (see Fig. 1—PRISMA flow diagram). Whenever needed, additional information was requested from study investigators.

Data collection and risk of bias assessment

The risk of bias assessment was performed using ROBINS-I tool for non-randomised studies of interventions [9]. The first reviewer performed data extraction which included methods (study design, number of participants, randomisation, case matching), intervention details (definitions and time points) and outcome details (i.e. IOP at different time points, success and failures rates and proportion of patients with loss of LP). The second author reviewed the extracted data and existing conflicts were resolved by consensus.

Data synthesis and analysis

The measures of treatment effect were weighted mean difference (WMD) for IOP reduction, risk ratio (RR) for failure rates and risk difference (RD) for loss of LP. Outcome measures were reported with a 95% confidence interval (CI). $P < 0.05$ was considered statistically significant for the overall effect. Data analysis was performed with RevMan v5.0.

Results

Search results and baseline characteristics

A total of eight studies were analysed in this review (Fig. 1). No RCTs were retrieved (see Table 1 for baseline characteristics of the included studies). Of the eight eligible studies, six were retrospective and two were prospective in nature. The risk of bias assessment is summarised in Table 2. The studies were aggregated into two groups based on the type of intervention. The first consisted of three studies comparing GDDs with cyclophotocoagulation: (i) Chalam 2002 [10] compared pars plana modified Baerveldt valve with neodymium: YAG cyclophotocoagulation; (ii) Eid 1997 [11] compared tube-shunt surgery (which included eight eyes with double-plate Molteno implant, eight with AGV,

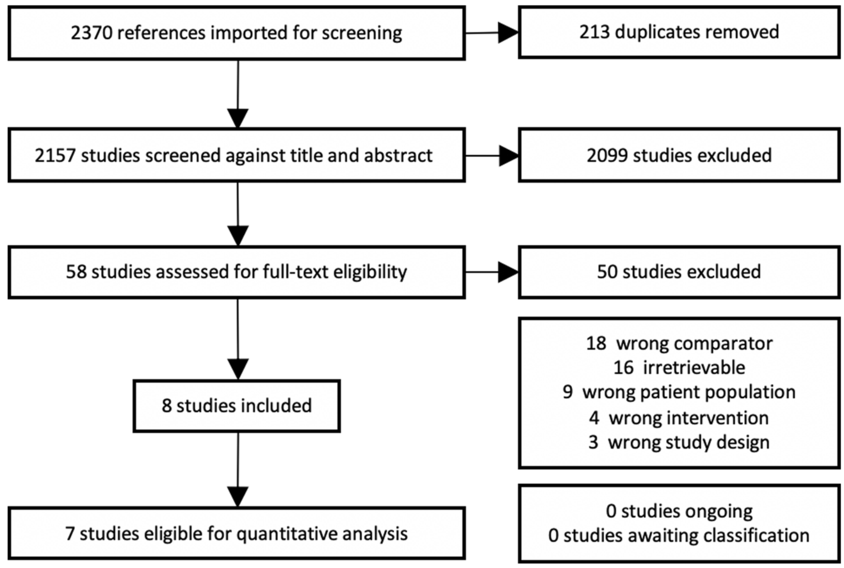

Fig. 1 PRISMA flow diagram of the search for eligible studies

six with Baerveldt valve and 2 with Schocket procedure) with neodymium: YAG cyclophotocoagulation; and (iii) Yildirim 2009 [12] compared AGV with diode laser cyclophotocoagulation. The second group consisted of four studies comparing AGV with trabeculectomy: (i) Engin 2011 [13] compared trabeculectomy with AGV; (ii) Liu 2011 [14] compared trabeculectomy combined with ranibizumab and mitomycin C (MMC) with AGV; (iii) Shen 2009 [15] compared trabeculectomy combined with MMC with AGV and (iv) Sun 2017 [16] compared intravitreal ranizumab with panretinal photocoagulation followed by trabeculectomy with AGV.

Yalvac 2007 [17] study, a retrospective study that compared AGV and Molteno valve in NVG, being the only identified study to compare two different GDDs was not considered for quantitative analysis, as data from this study could not be pooled with any of the two existing groups.

GDDs vs cyclophotocoagulation

IOP reduction

Mean IOP before and after surgical intervention at various time points was considered for quantitative analysis. In order to reduce bias, we selected only the common follow-up time point between all studies: mean IOP reduction 6 months after surgery. No statistically significant difference was observed between the two interventions (WMD = − 3.63; CI [− 8.69, 1.43]; $P = 0.16$) (Fig. 2).

Failure rates

In addition to IOP reduction, we also analysed failure rates in each study, which take into consideration not only IOP reduction, but also other factors such as loss of LP, necessity of an additional procedure and occurrence of complications (e.g. hypotony or *phthisis bulbi*). However, as seen in (Fig. 3), the criteria of failure applied in the reports were slightly heterogeneous. In cases in which no clear failure criteria were presented, we considered as a failure the cases that did not achieve the success criteria. We did not use the authors' success rates in our analysis, due to an even wider heterogeneity.

Data concerning failure rates at several time points was extracted, but because there was no common time point, we used information available at the last visit for statistical analysis (Fig. 4) which showed RR favouring the GDDs group (RR = 0.64, CI [0.41, 0.99], $P = 0.05$).

Loss of LP

We also analysed the rates of loss of LP in each group. We considered the data available at the last visit for statistical analysis (Fig. 5). The results showed RD favouring the GDDs group (RD = − 0.15, CI [− 0.25, − 0.05], $P = 0.004$). However, heterogeneity was significant in this case ($I_2 = 90\%$).

AGV vs trabeculectomy

IOP reduction

Data concerning mean IOP values before and after surgical intervention was extracted for various time points. Shen 2011 study was excluded from this analysis due to missing data at the intermediary time points. No statistically significant difference was observed between two interventions (WMD = 0.78; CI [− 2.29, 3.85], $P = 0.62$) (Fig. 6).

Failure rates

As in the first case, failure rates were analysed for each intervention. Similarly, in cases in which no clear failure criteria

Table 1 Baseline characteristics of included studies

Author (year)	Design	Case matching	Type of intervention	Intervention groups in each study	N° of eyes	Follow-up time (in months)	Baseline IOP (mean and SD)		
Chalam (2002)	Non-RCT	No	GDDs vs Cyclo	Pars plana Baerveldt	18	6	62.8 (11)		
				Nd: YAG	30	6	53.87 (9.3)		
Eid (1997)	Non-RCT	Yes	GDDs vs Cyclo	Pool of 4 different GDDs*	24	16.9 ± 14.6	51.4 (10.2)		
				Nd: YAG	24	15.2 ± 11.8	54.9 (10.5)		
Yildirim (2009)	Non-RCT	Prospective	GDDs vs Cyclo	AGV	33	24	43.3 (7.49)		
				Diode lase	33	24	43.44 (11.98)		
Author (year)	Design	Case matching	Type of intervention	Intervention groups in each study	N° of eyes	Adjunctive anti-VEGF	Adjunctive MMC	Follow-up time (in months)	Baseline IOP (mean and SD)
Engin (2011)	Non-RCT	No	AGV vs Trab	AGV	10	No	No	12	50.2 (7.4)
				Trab	23	No	No	12	52.8 (8.6)
Liu (2016)	Non-RCT	Prospective	AGV vs Trab	AGV	18	No	No	6	49.8 (11.8)
				Trab	20	Ranibizumab	Yes	6	57.1 (8.88)
Shen (2011)	Non-RCT	Yes	AGV vs Trab	AGV	20	No	No	31	47.7 (10.2)
				Trab	20	No	Yes	25	47.8 (11.3)
Sun (2017)	Non-RCT	No	AGV vs Trab	AGV	23	Ranibizumab	No	12	44.9 (4.67)
				Trab	22	Ranibizumab	Yes	12	43.45 (3.9)

Non-RCT, non-randomised clinical trial; *GDDs*, glaucoma drainage devices; *Cyclo*, cyclophotocoagulation; *AGV*, Ahmed glaucoma valve; *Trab*, trabeculectomy; *SD*, standard deviation; *8 double-plate Molteno implants, 8 AGVs, 6 Baerveldt valves and 2 Schocket procedures, *AGV*, Ahmed glaucoma valve; *Trab*, trabeculectomy; *VEGF*, vascular endothelial growth factor; *MMC*, mitomycin C

Table 2 Risk of bias assessment using ROBINS I tool for non-randomised studies of interventions

Bias domains	Chalam 2002	Eid 1997	Yildirim 2009	Engin 2011	Liu 2016	Shen 2011	Sun 2017
1. Bias due to confounding	Moderate	Moderate	Low	Moderate	Moderate	Moderate	Moderate
2. Bias in selection of participants into the study	Low	Moderate	Moderate	Low	Low	Low	Low
3. Bias in classification of interventions	Low	Low	Low	Low	Low	Low	Low
4. Bias due to deviations from intended interventions	Low	Moderate	Low	Low	Moderate	Moderate	Low
5. Bias due to missing data	Low	Low	Moderate	Low	Low	Low	Low
6. Bias in measurement of outcomes	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate
7. Bias in selection of the reported result	Low	Low	Low	Low	Low	Low	Low
Overall risk	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate

Study or Subgroup	Valve Mean	Valve SD	Valve Total	Cyclo Mean	Cyclo SD	Cyclo Total	Weight	Mean Difference IV, Fixed, 95% CI
Chalam 2002	−46.4	16.65	18	−32.87	15.2	30	28.9%	−13.53 [−22.95, −4.11]
Eid 1997	−32.5	13.669	21	−29.2	18.228	23	28.6%	−3.30 [−12.77, 6.17]
Yildirim 2009	−23.58	11.6476	33	−26.44	16.99185	25	42.6%	2.86 [−4.90, 10.62]
Total (95% CI)			**72**			**78**	**100.0%**	**−3.63 [−8.69, 1.43]**

Heterogeneity: $Chi^2 = 6.94$, df = 2 (P = 0.03); $I^2 = 71\%$
Test for overall effect: Z = 1.41 (P = 0.16)

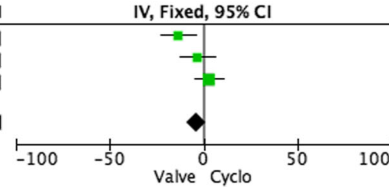

Fig. 2 IOP reduction from baseline at 6 months after the intervention

were presented, we considered as a failure the cases that did not achieve the success criteria. Once again, the criteria of failure were not homogeneous (Fig. 3) and we did not use the authors' success rates in our analysis, due to an even wider heterogeneity.

We extracted data concerning failure rates at several time points for each group, but because there was no common time point, we used data available at last visit for statistical analysis which showed RR favouring the trabeculectomy group (RR = 2.25, CI [1.14, 3.71], $P = 0.02$) (Fig. 7).

Loss of LP

Rates of loss of LP were analysed for both interventions. We considered the number of eyes with loss of LP at last visit to run the statistical analysis. It showed no statistically significant difference between the two groups (RD = 0.04, CI [− 0.05, 0.14], $P = 0.34$) (Fig. 8).

Discussion

In the present review and meta-analysis, seven non-RCT studies in which two different IOP-lowering procedures compared head-to-head were analysed. In GDDs vs cyclophotocoagulation group, we found no statistically significant difference in IOP-lowering capacity between the two techniques. However, failure rates and proportion of patients with loss of LP were favourable to the GDDs group. The fact that all the three studies in this group were non-RCTs creates a potential selection bias, since cyclophotocoagulation procedures are traditionally reserved for patients with more advanced NVG and

Chalam 2002	- IOP of ≤ 6 mmHg - phthisis - loss of light perception - another operation to achieve adequate intraocular pressure control (IOP≤21)
Eid 1997	- uncontrolled IOP (>25 mmHg) over three consecutive visits while on maximally tolerated medications; - persistent hypotony (IOP < 6 mmHg) or phthisis bulbi; - additional glaucoma procedures other than revision of the tube-shunt or repetition of Nd: YAG-CPC; - any complication requiring removal of the implant or leading to enucleation. - loss of light perception was not used as a criterion of failure in this study
Yildirim 2009	surgical success: - IOP less than 21mmHg and greater than 5mm Hg - without additional glaucoma surgery - without loss of light perception. - postoperative use of antiglaucoma medications was not accepted as a criterion of success or failure.
Engin 2011	complete success: - IOP between 5 to 20 mmHg - without additional medical therapy - IOP <5 as hypotony - no mention of loss of light perception or re-operation
Liu 2016	- IOP ≥ 21 mmHg even with anti-glaucoma medicines - additional surgical treatment was needed to control IOP - loss of light perception.
Shen 2016	complete success: - 6≤IOP≤21 mmHg, with or without glaucoma medications - without further glaucoma surgery including cyclophotocoagulation or complications that required removal of the Ahmed implant - without loss of light perception - IOP ≥ 21 mm Hg in two consecutive visits - laser suture lysis and bleb needling to improve bleb function were not considered failure of the procedure.
Sun 2017	- IOP > 21 mmHg despite the use of maximum medication - additional IOP-lowering surgical treatment - no mention of loss of light perception

Fig. 3 Failure criteria applied in each study. In the studies that had no definition of surgical failure, the failure was presumed to be as not achieving success

Study or Subgroup	Valve Events	Valve Total	Cyclo Events	Cyclo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Chalam 2002	1	18	7	30	15.8%	0.24 [0.03, 1.78]
Eid 1997	8	24	19	24	57.1%	0.42 [0.23, 0.77]
Yildirim 2009	12	31	9	31	27.1%	1.33 [0.66, 2.70]
Total (95% CI)		**73**		**85**	**100.0%**	**0.64 [0.41, 0.99]**
Total events	21		35			

Heterogeneity: $Chi^2 = 6.93$, df = 2 (P = 0.03); $I^2 = 71\%$
Test for overall effect: Z = 2.00 (P = 0.05)

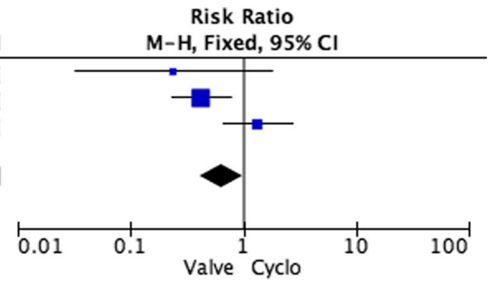

Fig. 4 Comparison of failure rates at last post-operative encounter in the GDDs vs cyclophotocoagulation arm

already limited visual acuity, whereas GDDs are normally implanted in patients thought of having better prognosis and in whom there is still some preserved visual acuity [8]. Thus, our results are consistent with the mainstream practice, as GDDs were superior concerning the failure rates and loss of LP, translating more serious complication profile of cyclophotocoagulation. However, GDDs is a non-specific term, covering at least three types of GDDs, each with its specificities, ranging from different plate sizes to valved and non-valved mechanisms. The fact that different types of GDDs were used make the GDDs vs cyclophotocoagulation comparison even more difficult. In regard to this, several authors conducted literature reviews with an objective to compare different GDDs [18] and a recent a Cochrane review found no evidence of superiority of one over another [19]. It is worth mentioning that all the above included mixed glaucoma patients (primary and secondary) and none was directed exclusively to NVG patients. In this specific segment of patients, Yalvac 2007 [12] found both AGV and single-plate Molteno implants to be successful in early and intermediate IOP control, although long-term follow-up showed that both implants had poor results in maintaining clinical success. A recent RCT by Christakis et al. [20] compared AGV with Baerveldt implants in inadequately controlled glaucoma and in patients with previously failed trabeculectomy that included 50 NVG patients and had a follow-up of 5 years. A univariate analysis reported NVG to be a risk factor for failure in this study. Notwithstanding, a multivariate analysis showed no difference in success rates between devices for neovascular cases. In our case, the results concerning the IOP-lowering capacity need a more attentive interpretation due to a possible selection bias, as previously stated. In addition, heterogeneity, as seen by I^2 values, was high in the results. Variability in success and failure criteria applied among the studies may account partially for it. Another potential source is the fact that different types of cyclophotocoagulation were used in this arm, although literature supports the concept that diode laser and Nd-YAG to be equivalent in terms of efficacy [21].

In the AGV vs trabeculectomy arm, there was also no statistically significant difference in IOP-lowering capacity between the two procedures, and while we did not identify any significant difference in LP rates, there was a statistically significant difference in failure rates, which favoured the trabeculectomy group. These results are surprising, given that recently published data from a Survey of the American Glaucoma Society shows a substantial increase in the use of GDDs with proportional decrease in trabeculectomies [22]. Nevertheless, our results should be interpreted with caution. The non-RCT nature of the retrieved studies is a potential source of selection bias, since the severity of the disease may have influenced the choice of surgical procedure. Just as in the previous case, the criteria defining surgical success and failure were heterogenous among the studies. Another aspect that should be mentioned is the differences seen in adjuvant administration of anti-VEGF agent and MMC. Engin 2011 [13], for instance, did not use MMC in trabeculectomies, a practice that is uncommon nowadays. Anti-VEGF administration also varied among the studies. As such, prospective controlled studies are needed to clarify this question.

One of the most importing findings in our study is probably the fact that very little high-quality evidence exists concerning surgical procedures in NVG patients. We

Study or Subgroup	Valve Events	Valve Total	Cyclo Events	Cyclo Total	Weight	Risk Difference M-H, Fixed, 95% CI
Chalam 2002	1	18	7	30	30.0%	-0.18 [-0.36, 0.01]
Eid 1997	4	24	11	24	32.0%	-0.29 [-0.54, -0.04]
Yildirim 2009	0	33	0	25	38.0%	0.00 [-0.07, 0.07]
Total (95% CI)		**75**		**79**	**100.0%**	**-0.15 [-0.25, -0.05]**
Total events	5		18			

Heterogeneity: $Chi^2 = 20.12$, df = 2 (P < 0.0001); $I^2 = 90\%$
Test for overall effect: Z = 2.86 (P = 0.004)

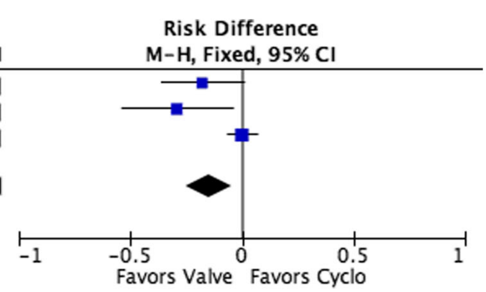

Fig. 5 Comparison of loss of light perception at last post-operative encounter in GDDs vs cyclophotocoagulation arm

Study or Subgroup	Ahmed Mean	Ahmed SD	Ahmed Total	Trab Mean	Trab SD	Trab Total	Weight	Mean Difference IV, Fixed, 95% CI
Engin 2011	−29.7	7.508	10	−33.1	8.73	25	28.2%	3.40 [−2.38, 9.18]
Liu 2016	−27	16.26899	19	−37.4	11.4954	18	11.5%	10.40 [1.36, 19.44]
Shen 2011	−34	16.6027	20	−31.3	15.7	20	0.0%	−2.70 [−12.71, 7.31]
Sun 2017	−29.8	6.8	23	−27.51	6.73	22	60.2%	−2.29 [−6.24, 1.66]
Total (95% CI)			**52**			**65**	**100.0%**	**0.78 [−2.29, 3.85]**

Heterogeneity: Chi² = 7.46, df = 2 (P = 0.02); I² = 73%
Test for overall effect: Z = 0.50 (P = 0.62)

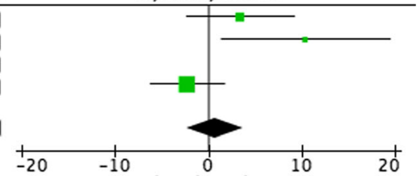

Fig. 6 IOP reduction from baseline at 6 months after the intervention

Study or Subgroup	Valve Events	Valve Total	Trab Events	Trab Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Engin 2011	5	10	7	25	33.0%	1.79 [0.74, 4.32]
Liu 2016	6	19	1	18	8.5%	5.68 [0.76, 42.70]
Shen 2011	8	20	3	20	24.8%	2.67 [0.82, 8.62]
Sun 2017	4	23	4	22	33.7%	0.96 [0.27, 3.36]
Total (95% CI)		**72**		**85**	**100.0%**	**2.05 [1.14, 3.71]**
Total events	23		15			

Heterogeneity: Chi² = 2.69, df = 3 (P = 0.44); I² = 0%
Test for overall effect: Z = 2.39 (P = 0.02)

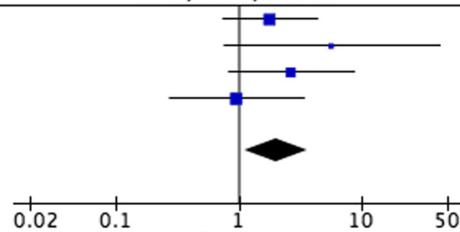

Fig. 7 Comparison of failure rates at last post-operative encounter in the Ahmed vs trabeculectomy arm

conducted an extensive electronic search for articles comparing different IOP-lowering surgical procedures in NVG population; however, not a single RCT was retrieved, meaning that current practice is largely based on case series and expert opinions, rather than well-designed clinical trials. Our study also highlights the heterogeneity of the success and failure criteria in the retrieved studies. More standardised definitions should be used in the upcoming studies to allow future systematic reviews and meta-analyses. Also, limited duration of the follow-up is another issue that should be addressed in the future studies, as it seems that most of the surgical procedures are effective in early post-operative time; however, little information exists regarding their long-term efficacy. Over the last years, there has been a significant increase in use of anti-VEGF agents for NVG, both as stand-alone or adjunctive agents to photocoagulation, trabeculectomy or GDDs [23]. Despite its widespread use, there is still lack of high-quality evidence regarding its role in the treatment of NVG, as seen by recently conducted Cochrane systematic review by Simha et al. [24]. The authors studied the role of anti-VEGF agent in NVG and not a single study was retrieved meeting their inclusion criteria.

Conclusion

There is lack of high-quality evidence on the subject as no RCT were retrieved comparing two different IOP-lowering procedures in NVG patients. Our findings are based, therefore, on non-RCT studies and should be interpreted with caution. There appears to be no difference in IOP-lowering efficacy between GDDs and cyclophotocoagulation; however, GDDs seem to be associated with a smaller number of complications. Trabeculectomy and AGV also showed a similar IOP-lowering capacity, with failure rates favouring the trabeculectomy group. Given the non-RCT nature and heterogeneity of included studies, these results need to be interpreted with caution. There is a great need of prospective controlled trials, using well-established reporting protocols from the International Ophthalmological Societies to clarify which is the best surgical option in NVG.

Study or Subgroup	Valve Events	Valve Total	Trab Events	Trab Total	Weight	Risk Difference M-H, Fixed, 95% CI
Engin 2011	1	10	0	25	19.0%	0.10 [−0.11, 0.31]
Liu 2016	2	19	1	18	24.6%	0.05 [−0.12, 0.22]
Shen 2011	4	20	3	20	26.6%	0.05 [−0.18, 0.28]
Sun 2017	0	23	0	22	29.9%	0.00 [−0.08, 0.08]
Total (95% CI)		**72**		**85**	**100.0%**	**0.04 [−0.05, 0.14]**
Total events	7		4			

Heterogeneity: Chi² = 1.39, df = 3 (P = 0.71); I² = 0%
Test for overall effect: Z = 0.96 (P = 0.34)

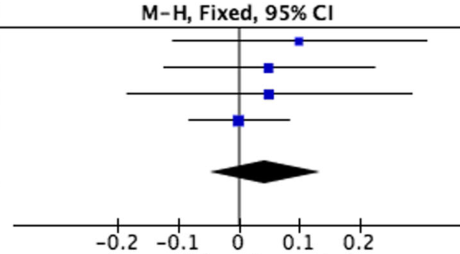

Fig. 8 Comparison of loss of light perception at last post-operative encounter in AGV vs trabeculectomy arm

Acknowledgments We thank Joana Alarcão MD for her contribution in elaborating the search strategy for this review. We also thank Filipe Rodrigues MD for assistance in the electronic search.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants performed by any of the authors.

Abbreviations IOP, intraocular pressure; LP, light perception; NVG, neovascular glaucoma; WMD, weighted mean difference; RR, risk ratio; RD, risk difference; CI, confidence interval; GDDs, glaucoma drainage devices; AGV, Ahmed glaucoma valve; VEGF, vascular endothelial growth factor; AH, aqueous humour; RCTs, randomised clinical trials; MMC, mitomycin C

Appendix 1. MEDLINE search strategy

1. exp. neovascular glaucoma/
2. ((glaucoma* or angle* or iris or anterior) adj4 neovascular*).tw.
3. (NVG or NVI or NVA).tw.
4. 1 or 2 or 3
5. exp. filtering surgery/
6. filtering surgery.tw.
7. glaucoma surgery.tw.
8. trabeculectomy.tw.
9. exp. glaucoma drainage implants/
10. exp. molteno implants/
11. (drainage adj2 (valve or implant or device or shunt)).tw.
12. (ahmed adj2 (valve or implant or device or shunt)).tw.
13. (molteno adj2 (valve or implant or device or shunt)).tw.
14. (krupin adj2 (valve or implant or device or shunt)).tw.
15. exp. angiogenesis inhibitors/
16. (macugen* or pegaptanib* or lucentis* or rhufab* or ranibizumab* or bevacizumab* or avastin* or aflibercept* or eylea*).tw.
17. (anti adj2 VEGF*).tw.
18. (baerveldt adj2 (valve or implant or device or shunt)).tw.
19. 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18
20. 4 and 19
21. (animal$ not human$).sh,hw.
22. 20 not 21

Appendix 2. EMBASE search strategy

1. exp. neovascular glaucoma/
2. ((glaucoma* or angle* or iris or anterior) adj4 neovascular*).tw.
3. (NVG or NVI or NVA).tw.
4. or/1–3
5. exp. filtering surgery/
6. filtering surgery.tw.
7. glaucoma surgery.tw.
8. trabeculectomy.tw.
9. exp. glaucoma drainage implants/
10. exp. molteno implants/
11. (drainage adj2 (valve or implant or device or shunt)).tw.
12. (ahmed adj2 (valve or implant or device or shunt)).tw.
13. (molteno adj2 (valve or implant or device or shunt)).tw.
14. (baerveldt adj2 (valve or implant or device or shunt)).tw.
15. (krupin adj2 (valve or implant or device or shunt)).tw.
16. exp. angiogenesis inhibitors/
17. (macugen* or pegaptanib* or lucentis* or rhufab* or ranibizumab* or bevacizumab* or avastin* or aflibercept* or eylea*).tw.
18. (anti adj2 VEGF*).tw.
19. or/5–18
20. and/4,19
21. (animal$ not human$).sh,hw.
22. 20 not 21

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