OUTCOME OF TRABECULECTOMIES WITHOUT ADJUNCTIVE ANTIMETABOLITES

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SUMMARY

Background: The effectiveness of trabeculectomy in the management of glaucoma is well known. It is the most common intervention for most glaucoma cases treated in the Upper East region. In this region trabeculectomies are, however, performed without adjunctive antimetabolites.

Objective: To report on the outcome of trabeculectomy without adjunctive antimetabolites in controlling the intraocular pressures of eyes with Primary Open Angle and Normal Tension Glaucomas.

Design: Retrospective, non-comparative interventional case study

Method: Records of 191 eyes of 164 patients who had undergone standard trabeculectomy were retrospectively analyzed.

Outcome Measure: Successful intraocular pressure control defined as IOP less than 22 mmHg or a reduction of 30% if pre-operative pressure was already less than 22mmHg.

Results: There were 185 (96.8%) eyes with Primary Open Angle glaucoma and 6 (3.2%) with the Normal Tension variant. Mean age of patients was 50.6 years (Range 17-85) with 22% aged below 40 years. There was a statistically significant difference between the mean pre-op and post-op intraocular pressures (38.09, SD=6.11 versus18.97, SD=7.28 mmHg respectively); p=0.0001. The procedure was effective in controlling the intraocular pressures to below 22mmHg in 88.46% and below 18mmHg in 67.95% of OAG eyes at six months. In eyes with NTG only one out of six (16.7%) achieved a successful 30% target pressure reduction.

Conclusion: Trabeculectomy alone was effective in controlling IOPs to less than 22 mmHg in POAG. Lower IOP levels needed to control progressive visual field loss may require the use antimetabolites.

Keywords: Intraocular Pressure, Target Pressure, Open Angle Glaucoma, Normal Tension Glaucoma, Applanation Tonometry.

INTRODUCTION

Glaucoma continues to be a major cause of irreversible blindness in the world. The number of people currently affected is estimated to be in the region of 66.8 million with 6.7 million people already blinded from it[1]. In Ghana, a recent study reported that primary open angle glaucoma (POAG) affects 7.7%, and 8.5% of people 30 and 40 years or over, respectively[2]. For many years the level of the intraocular pressure (IOP) has been the common connecting feature in the pathogenesis of glaucoma. Although frequently raised, the IOP is currently thought of as a major risk factor and no longer the only defining characteristic[3,4]. Notwithstanding this, the management of glaucoma still largely centres on lowering the intraocular pressure either by medication, laser applications or filtration surgical procedures with or without antimetabolites as wound healing modulating agents[5]. All these modalities have been used in Ghana with variable successes[6,7].

Trabeculectomy remains the established and most performed fistulising procedure for glaucoma refractory to medical treatment. Wound healing modulating agents, usually anti-metabolites like 5-Fluorouracil and Mitomycin C which inhibit the natural healing response and scar formation are used to reduce trabeculectomy failure. However, they exhibit serious potential complications and, as such, are normally used in the presence of known risk factors for trabeculectomy failure.

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At the Bawku hospital eye unit in the Upper East Region, filtration surgery of trabeculectomy is our preferred treatment for most glaucoma cases. This is largely because of its proven efficacy, coupled with the high cost, high resistance and low compliance in the use of anti-glaucoma drugs. Adjunctive anti-metabolites, however, are not normally used. In this paper we present the results of our trabeculectomy outcomes, with focus on intraocular pressure control and discuss the potential for using antimetabolites.

MATERIALS AND METHOD

This was a retrospective interventional case study involving 191 eyes of 164 patients operated at the Bawku hospital eye unit between January 2001 and December 2003. Included were 27 patients who underwent bilateral non-simultaneous trabeculectomy. Records of all patients with Primary Open Angle Glaucoma (POAG) and Normal Tension Glaucoma (NTG) who had undergone standard trabeculectomy with fornix-based conjunctival flap and a rectangular sclerostomy were retrospectively analyzed. All the surgical procedures were performed by one surgeon (AOD) either as a primary procedure or on failure of medical treatment. All patients were given Gutt. Atropine 1% BD, and one of Gutt. Maxitrol or Betnesol –N qds post-operatively.

Case Definition and Diagnosis

The diagnosis of glaucoma was based on finding a characteristic excavation of the optic nerve head (glaucomatous cupping) using the direct ophthalmoscope and indirect biomicroscopy with the 90D Volks lens. Gonioscopy was performed on all eyes to determine the anterior chamber angle configuration. A hundred and seventy eight eyes had visual field assessment using the Friedmann Visual Field Analyzer. Fields could not be done on thirteen eyes of thirteen patients due to poor cooperation.

Inclusion and Exclusion Criteria

Only patients who attended one or more post-operative reviews with IOP measured using the standard Goldmann Applanation tonometer were included in the study. Patients who failed this or who attended a review but had no IOP measurement taken were excluded. Also excluded were eyes that received combined phacotrabeculectomy. Visiting periods were grouped into four categories: those that occurred within the first post-operative month, between the second and third months, fourth to fifth month and finally visits that occurred from the sixth month and beyond.

Outcome

The principal outcome of interest was the intraocular pressure (IOP), measured by the Goldmann Applanation tonometer. We elected not to perform/analyze serial fields as it would be difficult to make meaningful comparisons because of variability of subject performances, and the low likelihood of demonstrating significant change in visual fields within the short study period. We also elected not to include secondary outcomes in the analysis because the few patients who were put on post-op supplemental medication had problems with compliance as a result of high cost of drugs and unavailability.

Success

Successful intraocular pressure control was defined as a decrease of post-operative IOP below 22mmHg without supplemental anti-glaucoma medication or a decrease of at least 30% of the initial IOP if this was already lower than 22mm Hg[8,9].

Data Analysis

The Epi-Info 2002 and Intercooled Stata-7 were used in the statistical analysis. Student's t-test was used to compare pre-operative and post-operative intraocular pressures where necessary.

RESULTS

During the period under review, 316 glaucomatous eyes were operated in the unit. Out of this only 191 eyes (60.4%) of 164 patients met the set of inclusion criteria. The mean age was 50.6 years with a range of 17 to 85 and a standard deviation of 13.9. There were 131 (68.6%) eyes of 111 male patients and 60 (31.4%) of 53 female patients; forty two eyes (22.0%) were of patients younger than 40 years. The right eye was affected in 99 (51.8%) of cases and the left 92 (48.2%). Out of the 191 eyes, 6 (3.2%) had normal tension glaucoma (NTG) with pre-operative IOP range of 17-21 mmHg, while 185 (96.8%) had elevated pressures above 21 mmHg. Five out of the 191 eyes (all with POAG) had either received Pilocarpine or Adrenaline prior to presentation at our clinic, and in each case, the duration was up to two months. Four eyes among the POAG group developed over-filtration secondary to scleral flap leakage in the early post-operative period but were successfully managed conservatively with pressure patching.

Out of the 191 eyes that were studied 169 were reviewed within the first month. This figure fell

dramatically in the subsequent months reaching 78 by the sixth month review. Table 1 shows the comparison between the intraocular pressures during these visits and those taken pre-operatively in the same subjects. At all times post-operatively up to 6 months the IOPs were significantly lower than the pre-operative levels ($p< 0.0001$).

Table 1 Mean Pre- and Post-op IOPs of POAG eyes.

Period [months]	Observation (%)	Pre-op [mmHg]*	Post-op [mmHg]*	T-statistic	P-value
1	169 (88.48)	38.31 ± 5.91 R=24-59	17.06 ± 8.36 R=6-59	28.64	0.000
2-3	91 (47.64)	38.15 ± 5.22 R=24-50	16.99 ± 5.49 R=7-46	25.88	0.000
4-5	61 (31.94)	39.11 ± 4.67 R=24-50	18.23 ± 6.01 R=7-41	20.84	0.000
6	78 (40.84)	38.09 ± 6.11 R=23-59	18.97 ± 7.28 R=8-52	17.4	0.000

*: Mean ± SD
R: Range

Table 2 summarizes the distribution of eyes that met the definition of successful IOP control. There was a significant decrease in the mean intraocular pressure by the sixth post-operative month following trabeculectomy ($p=0.000$) with success (post-operative IOP < 22mmHg) achieved in 88.46% of eyes at the last examination at six months. There was a gradual increase in the mean IOP achieved as time elapsed post-operatively although the measurements were largely within the "normal" 21mmHg limit. Only 67.95% of eyes achieved IOP levels of <18mm Hg at the 6th month.

Table 2 Distribution of post-op eyes with successful IOP control

Period	Observation (%)	IOP<22 mmHg	%	Mean IOP ±SD (mmHg)
1	169 (88.48)	148	87.57	14.55±3.61
2-3	91(47.64)	85	93.41	15.87 ± 3.2
4-5	61(31.94)	53	86.89	16.39±3.26
6	78(40.84)	69	88.46	16.64±2.86

NB: IOP<18mmHg =67.95% at 6 months

Normal Tension Glaucoma

There were 6 eyes of six patients (M: F=1) in this group. Mean age was 62 years (range 49 to 69) with a standard deviation of 8.4 and mean pre-operative IOP of 19mmHg (SD=2.19). Only one eye (out of 6) met the case definition of success with post-op IOP of 8mmHg while in another eye the IOP actually shot up to 41mmHg due to filtration failure. This eye failed to respond to conservative management and surgical revision was considered non-beneficial at the time of review. Table 3 below summarizes the results.

Table 3 Intraocular pressure distribution in patients with NTG at the 6th month

Pre-op IOP (mmHg)	Target IOP (mmHg)	Post Op IOP (mmHg)
17	11.9	15
21	14.7	17
21	14.7	15
21	14.7	8
17	11.9	15
17	11.9	41

DISCUSSION

Previous studies have reported that glaucoma was a common problem in Ghanaian populations and occurred in 7.7% of the population 30 years and over [2]. The mean age of 50.6 years in the present study was consistent with these previous studies, and with that in other Black populations such as the St. Lucia and the Barbados Eye Study which showed an earlier onset of open angle glaucoma among Black subjects compared to Caucasians[10,11]. It is interesting to note in this particular study, however, that as high as 22% of the oper-

ated eyes were of subjects below the age of 40 years. This figure parallels the findings of Wormald and Foster who studied the same population in 1990. In their paper, they reported that 21% (7/34) of the studied subjects who had trabeculectomy were below the age of 40 years[12]. Similarly, Verrey et al (1990) reported that as high as 26% of glaucoma patients operated in the North Eastern Ghana were below the age of 40 years[8]

The significant drop-out rate in post-operation attendance especially after the first visit reflects the problems associated with glaucoma care in this region. Similarly low post-operation attendance (19%) was reported at six months by Verrey et al (1990)[8]. Outreach or domiciliary follow-up visits by the ophthalmic team have not been possible due to the extensive geographical barriers including inaccessible villages stretching from the Brong Ahafo region to Burkina Faso, and logistics constraints.

The high success rates of trabeculectomy without the use of adjunctive antimetabolites have been reported in a smaller study from the same population previously[8,12]. This, we believe are more likely to be due to surgical techniques rather than a gene pool phenomenon as similar high success rates have been reported in other populations elsewhere[13,14]. Such variations in surgical technique (as practiced by different surgeons) include the size of the excised deep scleral flap with trabeculum which has been shown to determine a successful IOP control[15]. Standard flaps were fashioned in all our eyes.

It is important to state however that merely keeping the post-op IOP below the theoretical 22mmHg limit should not be the goal of filtration surgeries. Although we were unable to evaluate visual field changes in this study, one should aim at reducing the IOP sufficiently enough as to maintain the health of the optic nerve head so as to control the progression of field loss. This, according to Pojda et al (2001)[15] is only possible if the intraocular pressure is kept at 13-18mmHg. Anand et al (2001) established in a Nigerian population that trabeculectomies alone (i.e. non-augmented) were effective in keeping the intraocular pressure below 22 but not less than 16mmHg[16]. In our study, the mean postoperative IOP of 18.97mmHg attained by the 6th month was above the 16mmHg mark postulated by Anand et al[16] as achievable only with adjunctive antimetabolites. In addition, only 67.95% achieved IOP levels below the 18mmHg upper limit suggested by Pojda[15] as necessary to control progressive field loss, by the 6th month. Higher success rates may, therefore, require a form of augmentation.

The controversy over the use of wound healing modulating agents continues. With a small sample size in a placebo-control trial, Leyland et al (2001) found no significant difference in trabeculectomy outcomes at least in low risk cases[17]. Similar works by Tsai et al (2003) reported that in juvenile primary open angle glaucoma trials there was no clinically significant difference in cumulative success rates between cases that received Mitomycin-C and those who had trabeculectomy alone[18]. These findings have been supported by Spaeth and Mutlukan (2001)[19] who argue that the rapid acceptance of antimetabolites in glaucoma filtration surgeries may be explained by reasons other than the anticipated increase in success. They suggest that their usage may be at least a consequence of changing medico-social and economic factors rather than the desire of physicians to improve the success of glaucoma surgery and highlight the need to re-evaluate the proper place of antimetabolites in association with filtration surgery[19].

IOP control was less successful in the few NTG cases included in our study. This probably underscores the fact that antimetabolites may at least be necessary in order to attain the low IOPs deemed as targets in NTG. Using a Pointwise Linear Regression Analysis, Membrey et. al (2001)[20] established a positive correlation between the percentage reduction in IOP and the subsequent risk of progressive visual field loss in NTG cases undergoing filtration surgery with adjunctive antimetabolites. The risk was significantly higher in cases that received MMC compared with those on 5-FU, despite the greater fall in IOP for the MMC group, hazard ratio=1.51 (p=0.001). Such visual field deterioration was attributed to the functional loss produced by late postoperative complications which have been reported at a higher rate among cases given perioperative MMC. The use of perioperative 5-FU, they suggest, maintains a suitable target IOP with preservation of visual function without the additional complications and associated visual field deterioration seen with adjunctive MMC.[20] However, especially in a population where patient follow-up is erratic and attendances fall off with time, it must be remembered that antimetabolites, especially MMC have significant side effects.

CONCLUSION

This study has shown that controlled intraocular pressures in Open Angle Glaucoma can be achieved using trabeculectomies without adjunctive antimetabolites. Achieving levels low enough to control progressive visual field loss may, however, call for their usage. This is especially so for Normal Tension Glaucoma cases as these demand a much lower IOP target pressure setting. We appreciate the fact that the number of cases in the NTG group was too small to draw definitive conclusions on their outcomes. We also acknowledge that the follow-up period was rather short and the drop-out rate significantly high but these were beyond our control. We hope that this report will pave the way for well-powered randomized control trials to establish the proper place and conditions for using adjunctive antimetabolites in glaucoma filtering surgeries in the Ghanaian/African setting.

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REFERENCES

1. Quigley HA. Number of people with glaucoma worldwide. *Br J Ophthalmol* 1996; 80: 389.

2. Ntim-Amponsah CT, Amoaku WM, Ofosu-Amaah S, Ewusi RK, Idirisuriya-Khair R, Nyatepe-Coo E, Adu-Darko M. Prevalence of glaucoma in an African population. *Eye* 2004; 18: 491-497.

3. Johnson GJ, Minassiam DC, Weale R. Epidemiology of Eye Diseases, Chapman and Hall, London, 2nd Ed 1998; 159.

4. Sommer A. Intraocular Pressure and Glaucoma. *Am J Ophthalmol* 1989; 107: 186-188.

5. Kanski JJ. *Clinical Ophthalmology: A systemic Approach*. Butterworth Heinemann, London. 5th Ed 2003; 256-267.

6. Egbert PR, Fiadoyor S, Budenz DL, Dadzie P, Byrd S. Diode Laser Transscleral cyclophotocoagulation as a Primary Surgical Treatment for Primary Open-Angle Glaucoma. *Arch Ophthalmol* 2001; 119: 345-350.

7. Singh K, Byrds S, Egbert P R, Budenz D. Risk of hypotony after primary trabeculectomy with antifibrotic agents in a Black West African population. *J Glaucoma* 1998; 7: 82-85.

8. Verrey J D, Foster A, Wormald R, Akuamoah C. Chronic Glaucoma in Northern Ghana – a Retrospective study of 397 patients. *Eye* 1990; 4:115-120.

9. Das JC, Sharma P, Chaudhuri Z, Bhomaj S. A comparative study of small incision trabeculectomy avoiding tenon's capsule with conventional trabeculectomy. *Ophthalmic Surg Lasers*. 2002; 33: 30-36.

10. Mason, R.P., Kosoko, O., Wilson M.R. et al. National Survey of the prevalence and risk factors of glaucoma in St. Lucia, West Indies. Part 1. Prevalence findings. *Ophthalmology* 1999; 96: 1363-1368.

11. Leske, M.C., Connell, A.M.S., Schacht, A.P. et al The Barbados Eye Study. Prevalence of open angle glaucoma. *Arch Ophthalmol* 1994; 112: 821-829.

12. Wormald R, Foster A. Clinical and pathological features of chronic glaucoma in north-east Ghana. *Eye* 1990; 4: 107-114.

13. Edmunds B, Thompson JR, Salmon JF, Wormald RP. The National Survey of Trabeculectomy. II. Variations in operative technique and outcome. *Eye* 2001; 15: 441-448.

14. Bekibele CO. Evaluation of 56 trabeculectomy operations at Ago-Iwoye, Ogun State, Nigeria. *West Afr J Med*. 2001; 20: 223-226.

15. Pojda SM, Herba E, Zatorska B, Pojda-Wilczek D, Rycerska A, Plech A, Jedrzejewski W. The long-term follow up after trabeculectomy. *Klin Oczna*. 2001; 103: 161-164.

16. Anand N, Mielke C, Dawda VK. Trabeculectomy outcomes in advanced glaucoma in Nigeria. *Eye* 2001; 15: 274-278.

17. Leyland M, Bloom P, Zinicola E, McAlister J, Rassam S, Migdal C. Single intraoperative application of 5-Fluorouracil versus placebo in low-risk trabeculectomy surgery: a randomized trial. *J Glaucoma*. 2001; 10: 452-457.

18. Tsai TC, Chang HW, Kao CN, Lai IC, Teng MC. Trabeculectomy with Mitomycin C versus trabeculectomy alone for juvenile primary open angle glaucoma. *Ophthalmologica*. 2003; 217: 24-30.

19. Spaeth GL, Mutlukan E. The use of antimetabolites in trabeculectomy: a critical appraisal. *J Glaucoma*. 2001; 10: 145-151.

20. Membrey WL, Bunce C, Poinooswamy DP, Fitzke FW, Hitchings RA. Glaucoma surgery with or without adjunctive antiproliferatives in normal tension glaucoma. 2. Visual field progression. *Br J Ophthalmol* 2001; 85:696-701.