THE EFFECT OF MEDICAL THERAPY ON IOP CONTROL IN GHANA

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SUMMARY

Background: To investigate IOP control following twelve months of continuous medical therapy in Ghana.

Methods: This retrospective case series included 163 glaucoma patients diagnosed at a referral eye center between 1996 and 2006. Information collected included age, gender, IOP at presentation, six months and one year post treatment and types of anti-glaucoma medications prescribed. Optimal IOP control was defined according to results from the Advanced Glaucoma Intervention Study (AGIS), which demonstrated arrest of visual field progression in patients with IOP < 18 mmHg at all visitations: Level 1 (post-treatment IOP ≤ 21 mmHg); Level 2 (≤ 18 mmHg) and level 3 (≤ 16 mmHg). The principal outcome measure was the achievement of IOP <18 mmHg at six months and twelve month visitations.

Results: One hundred sixty three patients were analyzed. These included 68 males (41.7%) and 95 females (58.3%). The mean age was 57±16 (median 59 years; range 7 – 95 years). There was no significant difference in age (p=0.35) or mean IOP (p=0.08) between genders. The mean pre-treated IOP of 31.9±8.9 mmHg significantly decreased to 21.3±6.6 mmHg at 6 months (p=0.001), with 57.4% of eyes at Level 1 IOP control, 25.3% at Level 2 and 15.4% at Level 3 and decreased further at 12 months to 20.7±6.9 mmHg (p=0.48) with 69.7% of eyes at Level 1, 34.4% at Level 2, and 12.4% at Level 3.

Conclusions: Current medical regimen is insufficient to reduce IOP to target levels as defined in the Advanced Glaucoma Intervention Study.

Keywords: Glaucoma, POAG, IOP, Ghana, intraocular pressure

INTRODUCTION

Glaucoma is the second most important cause of blindness in Ghana surpassed only by cataract.[1] It is estimated to account for 20.6% of all causes of blindness in the country.[2] Blindness from the disease, unlike that of cataract, is irreversible making it the most common cause of irreversible blindness. Worldwide the disease, in its various forms affects some 66.8 million people out of which 6.7 million are presumed blind from it.[3] Primary open angle glaucoma (POAG) is the most common variant in Africa and has been shown in Black populations to have an earlier onset and run a more aggressive course.[4] This variant is reported to affect nearly one out of every ten (8.5%) people aged 40 years and above living in Ghana.[5] Medical therapy aimed at reducing the intraocular pressure (IOP) is the primary treatment for POAG, however it is unknown if medical therapy alone is sufficient to achieve target levels in Ghanaian patients.

The Advanced Glaucoma Intervention Study (AGIS) in particular demonstrated that lower IOP is associated with reduced progression of visual field defect. AGIS found that eyes with 100% of visits with IOP <18 mmHg over 6 years had mean changes from baseline in visual field defect score close to zero during follow-up, whereas eyes with less than 50% of visits with intraocular pressure less than 18 mm Hg had an estimated worsening over follow-up of 0.63 units of visual field defect score (P =.083).[6] Using the results from AGIS as a benchmark for successful IOP control, we developed the first study to investigate the outcome of medical treatment at achieving target IOP levels in patients with POAG.

MATERIALS AND METHODS

Study Design

A retrospective case series involving the review of clinical records of all 'first-time' glaucoma cases treated at the Emmanuel Eye Centre, Accra, Ghana between 1996 and 2006. Information collected included age, IOP documented at presentation, six months and one year; and types of anti-glaucoma medications given at presentation, six months and one year to achieve IOP control. In all 163 patients were reviewed. All patients were of African descent, older than 18 years of age, and presented with elevated IOP (IOP >21 mmHg as measured with Goldmann applanation tonometry).

Case Definition and Diagnosis

Case definitions were based on the working protocol used in the clinic. Glaucoma was diagnosed by the finding of a characteristic optic disc excavation (glaucomatous cupping) in the presence of elevated IOP with or without matching visual fields and no secondary cause of glaucoma identified. Ocular hypertension (OHT) was defined as persistent presenting IOP higher than 21 mmHg in the absence of ocular hypotensive medications and optic nerve head damage. Optic disc evaluations, as is the practice of the hospital, were all done with either the Volk 78 or 90 Diopter condensing lenses. All the cases were diagnosed and managed by experienced ophthalmologists and all IOPs were measured using the slitlamp-mounted Goldmann applanation tonometer.

Inclusion and Exclusion Criteria

Only untreated cases that received their required medications from the clinic and were followed up to one year with IOPs measured at times of visitations were included in the study. All cases of true congenital and secondary glaucoma were excluded. Also excluded were patients who had had glaucoma filtering surgery, glaucoma-specific laser procedures or patients with medically controlled IOPs (prior to first visitation). We elected not to include records of angle closure glaucoma due to the different mechanism of elevated IOP in this disease.

Principal Outcome and Measure of Success

The principal outcome of interest was the IOP, measured at presentation, six months and at twelve month visits. Successful IOP control was defined using three levels of success designed by our team and based in part on results from the Advanced Glaucoma Intervention Study (AGIS). With this information, we designed three levels of IOP control for subjects in this study: Level 1 (borderline control), where the mean post-treatment IOP was measured at 21 mmHg or less at the time of visit; Level 2 (moderate control), where the mean IOP was measured at 18 mmHg or lower; and level 3 (high control), at 16 mmHg or lower.

Drug Administration

As a clinical protocol in this facility, all first-time untreated POAG or OHT patients presenting with IOPs of 30mmHg or higher were prescribed two medications, the type of which depended on a number of factors that related to both the patient and facility. The most important facility factor was the availability of the prescribed medication at the time of presentation. Where this was unavailable, a drug prescription form was given to the patient to purchase from a pharmacy shop. Patient factors in regards to treatment efficacy therefore included one's ability to pay for the prescribed medications or known adverse reactions to the drug or similar agents. For example, patients who reported an allergy to sulphonamides were not prescribed acetazolamide preparations. In this current study, only patients who received all their required medications from the hospital were enrolled into the study.

Types of anti-glaucoma drugs prescribed in this hospital setting covered nearly the entire spectrum of commonly used ocular anti-hypertensive topical medications. These included emerging drugs (at that time) like prostaglandin analogues, prostamides and fixed combination preparations.

From the reviewed clinical notes, no specific target pressures were set for any of the patients, however the doctors sought to control the pressures to the so-called 'normal pressure' of 21mmHg, which is currently known to be inadequate in forestalling disease progression.[6] Once a patient failed to achieve this end-point, the medications were modified by adding new ones, substituting existing ones or by doing both.

Data Analysis

Data were entered and checked using Microsoft Excel©. Epi Info™ 3.4.1 and Stata™ 8.1 were used for the analysis; these two tools were complimentary. For continuous variables, the mean and the standard deviation were reported and where necessary, the median was also reported. For continuous variables with two groups, the Student's t-test was used while the one-way analysis of variance (ANOVA) was employed for more than two groups. Where multiple comparisons were done, the Bonferroni Correction was applied. All statistical tests were two-sided and an alpha level < 0.05 was considered a statistically significant result. The 95% confidence intervals and Fisher's exact test for cells with less than five entries were also used where appropriate.

RESULTS

In all, records of 163 patients with either OHT or POAG were analyzed. These were made up of 68 males (41.7%) and 95 females (58.3%). The mean age of the studied population was 57±16 with a median of 59 and a range of 7 to 95 years. The mean pre-treatment IOP was 31.9±8.9 mmHg. This was slightly higher in males (32.9±9.2 mmHg) compared to females (31.2±8.7 mmHg), but this difference was not statistically significant (p=0.08).

IOP Trend Analysis

Successful IOP control was defined using three levels of success designed by our team and based in part on results from the AGIS study which provided clear evidence that low IOP is associated with reduced progression of visual field defect.[6] There was a significant drop in the presenting mean IOP from the baseline value of 31.9±8.9 mmHg to the 6th month value of 21.3±6.6 mmHg and a further drop to the 12th month value of 20.7±6.9 mmHg following treatment. While changes from baseline IOP at initiation of treatment to the 6 month mark were statistically significant (p=0.001), there was no significant change noticed in IOPs between the sixth and twelve month (p=0.48).

Regarding IOP control, at the 6 month mark, 57.4% of the studied eyes had their IOPs controlled to a level ≤21 mmHg. Approximately one in every four patients (25.3%) were controlled to <18 mmHg and only 15.4% were controlled to <16 mmHg after continuous medical therapy. By the 12th month, 69.7% were controlled to ≤21 mmHg, 34.4% were controlled to <18 mmHg and only 12.4% were controlled to <16 mmHg. These results are graphically displayed in Figure 1.

Mean pre-treatment IOP of 31.9±8.9 mmHg decreased to 21.3±6.6 mmHg at 6 months (p=0.001), with 57.4% of the eyes at Level 1 (borderline control), 25.3% at Level 2 (moderate control), and 15.4% at Level 3 (high control), and decreased further at 12 months to 20.7±6.9 mmHg (p=0.48) with 69.7% of the eyes at Level 1, 34.4% at Level 2, and 12.4% at Level 3.

Anti-glaucoma Drug Prescription Patterns

The mean number of prescriptions patients were placed on at their initial diagnosis was calculated at 1.6±0.65 medications. This increased to 1.9±0.77 medications at the 6th month and 1.9±0.75 medications by the 12th month. Patients were placed on either one (42.3%) or two (47.5%) topical eye medications initially. As shown in Table 1, with time a higher percentage of patients were prescribed additional medications to achieve IOP control. Table 2 shows the percent distribution of medications prescribed across the period of this study. The most common medication prescribed was a topical beta blocker followed by a carbonic anhydrase inhibitor (CAI).

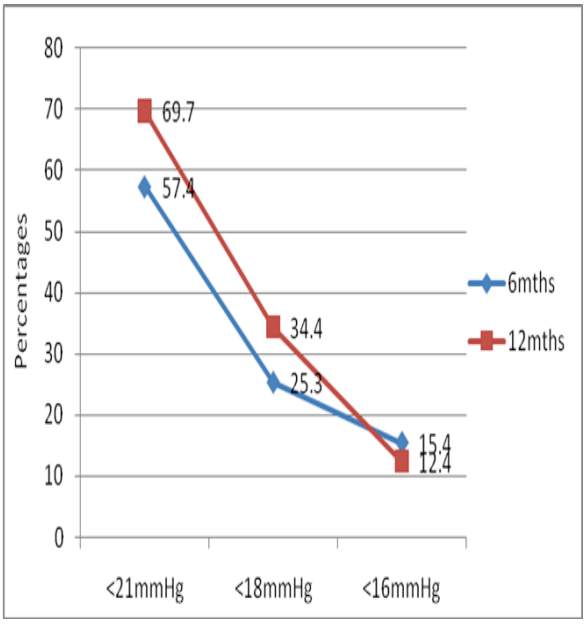

Figure 1 Stratification of IOP control at 6 and 12 month intervals

Table 1 Pattern of anti-glaucoma drug prescriptions

Drugs	At Presentation		Month 6		Month 12	
	No.	%	No.	%	No.	%
1	129	42.3	96	29.5	92	28.3
2	145	47.5	157	48.3	159	48.9
3	31	10.2	64	19.7	68	20.9
4	0	0	8	2.5	6	1.8

Table 2 Anti-glaucoma drugs prescribed

Drug Type	At Presentation	Month 6	Month 12
Beta blockers	45.6	47.7	49.6
CAIs	28.1	22.6	22
Parasympathomimetics (Pilocarpine)	17.4	18	17.6
Prostaglandins and Prostamides	6.8	7.4	8.8
Alpha agonists	0.9	1.7	0.6
Fixed combinations	0.9	0	0
Others	<1	2.6	1.7
Total	100	100	100

DISCUSSION

This study investigated outcomes of medical therapy in Ghanaian patients and found that an unsatisfactory percentage of patients achieved AGIS IOP criteria demonstrated to arrest visual field progression.[6] Persistent elevation in the IOP has been identified as the most important risk factor for the development and progression of glaucoma.[6,8,7] The findings from this study provide, for the first time in Ghana, clear evidence that medical therapy alone is insufficient for adequate control of IOP.

Reports from the AGIS Study show that patients who had their IOP controlled by laser or filtering surgery after failed medical treatment had slower progression in visual field (VF) deterioration.[6] In this study, eyes receiving medical treatment were categorized according to target IOPs into borderline control (Level 1, ≤21 mmHg), moderate control (Level 2, <18 mmHg) and high control (Level 3, <16 mmHg) with only 34.4% of the studied eyes achieving the 18 mmHg cut-off identified in the AGIS.[6] In the best performing category, (borderline control) the proportion of eyes that achieved the required cut off IOP (69.7%) was still much lower than those achieved by comparative interventions like trabeculectomy. Verrey et al previously reported in a retrospective study in Ghana that 84% of patients treated with trabeculectomy achieved target IOP levels at 6 months versus only 17% of medical treated pateints.[8] In the British national survey of trabeculectomy techniques, the overall level of unqualified success (IOP control of <21 mmHg without additional medication) was measured at 84% and qualified success (with medication) at 92% after a duration of 1 year.[9] Similarly high success rates have been found in other studies among Black West African populations.[10, 11]

To the best of our knowledge, no prior study in Ghana has investigated the medical treatment as a sole modality for achieving AGIS target levels for IOP. The baseline IOP value reported in this study of 31.9 mmHg to the 6th month value of 21.3 mmHg does not appear sufficient for adequate POAG control. Furthermore, no statistical difference in IOP was reported at the twelve-month visitation despite an increase in ocular hypotensive medication administration.

Our results agree with Verrey et al, who reported that only 17% of patients treated medical had an IOP less than 22 mmHg at six-month follow-up, but this study did not extend follow up beyond six-months and did not have the benefit of newer medications or the more recent randomized trials.[8] Francis et al compared advanced and moderate glaucoma patients and reported that advanced glaucoma patients presented with a mean IOP on first presentation greater than 30 mmHg in both eyes (OD: 30.93; OS: 32.37 mmHg), but treatment effects were not analyzed.[12] Ntim-Amponsah et al investigated risk factors for glaucoma progression and reported that initial IOP>31 mmHg was associated with advanced glaucoma at presentation, but also did not investigate the effects of medical treatment.[13]

The poor measure of control among study subjects in this study is unlikely to be a result of low efficacy of the various medications used to reduce IOP. The effectiveness of the most commonly used drugs have been extensively studied and used in the major glaucoma clinical trials with good outcomes in reducing IOP.[6, 7] Topical beta blockers, for example, were used extensively in the Ocular Hypertension Treatment Study (OHTS)[14] and the EMGT.[7]

In addition almost all the patients were on multiple medications and the number of drugs used increased as the disease progressed. The mean number of drugs initially prescribed was 1.6±0.65 and this increased to 1.9±0.77 by the 12th month.

A more likely explanation for such a high treatment failure may be related to compliance rather than drug efficacy as most of the drugs used had both international and local regulatory body's approval. In one systematic review, Olthoff and co-workers measured medical treatment non-compliance among glaucoma patients to range from 5% to as high as 80%.[15] Using qualitative study methodologies, Lacey and coworkers identified multiple barriers to anti-glaucoma medication compliance among patients in the UK.[16] Similar studies relating to compliance have been extensively studied in the United States.[17, 18] In one such study, Tsai and co-workers identified as many as 71 barriers to medication compliance and subsequently categorized these into 4 groups: Situational/environmental factors (49%), Medication regimen (32%), Patient factors (16%) and Provider factors (3%).[17]

This study did not look into barriers to treatment adherence among subjects and the authors do not intend to make any authoritative statement on this subject. On the other hand, the issue of limited patient education, low doctor/patient ratios in sub-Saharan African nations like Ghana and the absence of counseling on glaucoma eye drop application techniques cannot be overemphasized. Ghana's population now exceeds 24 million people with only 52 ophthalmologists in active clinical practice (19 million and 45 ophthalmologists respectively as of the most recent National Eye Care Report in 2004).[19] This is compounded by the absence of nurses and other health care professionals specifically trained to educate and counsel the glaucoma patient.

Limitations of this study include the retrospective design, the small number of patients enrolled and the involved of only a single large tertiary care center. Corneal pachymetry was not available at this clinic and diurnal variations in IOP were not measured, however a recent study investigating CCT in Ghana by Ntim-Amponsah et al demonstrated an average CCT of 524.28 μm for right eyes and 524.70 μm for left eyes in 253 cases of high tension glaucoma which would appear to support our Goldmann applanation measurements were not seriously affected by thinner corneas.[20]

The patient population was homogenous in their baseline demographics, however medical comorbidities that may affect IOP (diabetes, hypertension, myopia, inherited disease) were not recorded. This study did not attempt to correlate achievement of IOP level with progression or no progression of clinical disease as measured by visual field analysis, optic nerve imaging, or visual acuity and these results were therefore not included. This study did not attempt to define a threshold for progression using visual field data due to the single center and relatively small patient sample. Also taken into consideration was the low likelihood of demonstrating significant changes in visual fields within the short study period of one year. We also chose not to do comparative analysis on the effects of the various antiglaucoma medications as medications prescribed were often in combination and patient surveys were not available for this retrospective study. Patients were not stratified by baseline IOP given the elevated mean IOP for all subjects and the percent reduction of IOP for each patient likely varied.

CONCLUSION

In conclusion, the current medical regimen is insufficient to reduce IOP to levels needed to control disease progression in all Ghanaian patients receiving care. We suggest that all ophthalmologists be trained to perform safe and effective glaucoma surgical procedures when medical treatment fails to achieve target goals. Patient education and counseling, we suggest, should be an integral part of a glaucoma service and patient experience.

REFERENCES

1. Ghana Vision 2020, the Right to Sight: National Framework for Action. 2002-2006:1-87.
2. Guzek JP, Anyomi FK, Fiadoyor S, Nyonator F. Prevalence of blindness in people over 40 years in the volta region of ghana. *Ghana Med J* 2005;39:55-62.
3. Quigley HA. Number of people with glaucoma worldwide. *Br J Ophthalmol* 1996;80:389-393.
4. Mason RP, Kosoko O, Wilson MR, et al. National survey of the prevalence and risk factors of glaucoma in St. Lucia, West Indies. Part I. Prevalence findings. *Ophthalmology* 1989;96:1363-1368.
5. Ntim-Amponsah CT, Amoaku WM, Ofosu-Amaah S, et al. Prevalence of glaucoma in an African population. *Eye (Lond)* 2004;18:491-497.
6. The Advanced Glaucoma Intervention Study (AGIS): 7. The relationship between control of intraocular pressure and visual field deterioration.The AGIS Investigators. *Am J Ophthalmol* 2000;130:429-440.
7. Leske MC, Heijl A, Hussein M, et al. Factors for glaucoma progression and the effect of treatment: the early manifest glaucoma trial. *Arch Ophthalmol* 2003;121:48-56.
8. Verrey JD, Foster A, Wormald R, Akuamoa C. Chronic glaucoma in northern Ghana--a retrospective study of 397 patients. *Eye (Lond)* 1990;4 (Pt 1):115-120.
9. Edmunds B, Thompson JR, Salmon JF, Wormald RP. The National Survey of Trabeculectomy. II. Variations in operative technique and outcome. *Eye (Lond)* 2001;15:441-448.
10. Bekibele CO. Evaluation of 56 trabeculectomy operations at Ago-Iwoye, Ogun State, Nigeria. *West Afr J Med* 2001;20:223-226.
11. Gyasi M, Amoaku W, Debrah O, Awini E, Abugri P. Outcome of trabeculectomies without adjunctive antimetabolites. *Ghana Med J* 2006;40:39-44.
12. Francis AW, Gyasi ME, Deng L, Gong H. Comparison of moderate and advanced glaucoma patients in Ghana. *Clin Ophthalmol* 2012;6:297-304.
13. Ntim-Amponsah CT, Amoaku WM, Ewusi RK, Idirisuriya-Khair R, Nyatepe-Coo E, Ofosu-Amaah S. Evaluation of risk factors for advanced glaucoma in Ghanaian patients. *Eye (Lond)* 2005;19:528-534.
14. Gordon MO, Kass MA. The Ocular Hypertension Treatment Study: design and baseline description of the participants. *Arch Ophthalmol* 1999;117:573-583.
15. Olthoff CM, Schouten JS, van de Borne BW, Webers CA. Noncompliance with ocular hypotensive treatment in patients with glaucoma or ocular hypertension an evidence-based review. *Ophthalmology* 2005;112:953-961.
16. Lacey J, Cate H, Broadway DC. Barriers to adherence with glaucoma medications: a qualitative research study. *Eye (Lond)* 2009;23:924-932.
17. Tsai JC, McClure CA, Ramos SE, Schlundt DG, Pichert JW. Compliance barriers in glaucoma: a systematic classification. *J Glaucoma* 2003;12:393-398.
18. Taylor SA, Galbraith SM, Mills RP. Causes of non-compliance with drug regimens in glaucoma : a qualitative study. *J Ocul Pharmacol Ther* 2002;18:401-409.
19. Hagan M. National Eye Care Report. Accra: Ghana. Health Service Eye Care; 2004:3-5.
20. Ntim-Amponsah CT, Seidu AY, Essuman VA, et al. A study of central corneal thickness in glaucoma and nonglaucoma patients in a West African population *Cornea* 2012;31:1093-1096. ✪