Diurnal intraocular pressure fluctuation in black adult primary open angle glaucoma patients attending Ruharo Eye Centre, South- Western Uganda

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ABSTRACT

Objective: **To study the general diurnal intraocular pressure (IOP) fluctuation in black adult patients with Primary Open Angle Glaucoma attending Ruharo Eye Centre; to determine their IOP fluctuation range and determine their 24 hour IOP fluctuation pattern.**

Design: **Descriptive cross sectional study.**

Methods: **This was a hospital based, descriptive cross sectional study. Fifty one patients with glaucoma on different treatment options (No treatment, medical treatment and post trabeculectomy) were enrolled and intraocular pressure measured every 2 hours for 24 hours. The mean fluctuation ranges, peak and trough times of intraocular pressure were recorded for each group and 24 hour fluctuation curve patterns were drawn.**

Results: **Primary Open Angle Glaucoma (POAG) patients who were not on treatment had the highest mean intraocular pressure fluctuation range 11.1mmHg (95% CI 8.3-14) followed patients on medical treatment who had the second highest mean fluctuation range 9.3mmHg (95% CI 7.5-11.1), while patients who had received trabeculectomy had the lowest mean IOP fluctuation ranges 5.3 (95% CI 3.5-7.0). The general average peak intraocular pressure time was between 11am-1pm.**

Conclusion: **Trabeculectomy was found to have the best control of IOP fluctuation in patients with POAG compared to medical treatment (timolol, pilocarpine and acetazolamide) and those not on treatment. The best time for measuring IOP in patients with POAG was found to be between 11am-1pm because most of the peaks IOPs were captured during this time.**

INTRODUCTION

Glaucomas are the second leading cause of blindness after cataract, accounting for (12%) of total blindness if uncorrected refractive errors are excluded[1]. The commonest type of glaucoma is Primary Open Angle Glaucoma (POAG)[2]. Initially, treatment of glaucoma was mainly aimed at achieving a reduction in the peak Intraocular Pressure with surgical and or medical interventions. Subsequent studies established a relationship between having large IOP fluctuations to further disease progression even after achieving reduction in peak IOP[3,4]. It was then postulated that lowering peak IOP alone was not enough in the management of POAG.

The current treatment of POAG therefore now aims at not only reducing peak IOP but modulating IOP fluctuation as well. A number of studies showed good fluctuation control with trabeculectomy[5] and a few drugs like prostaglandin analogues[6,7]. However, these studies were conducted in white populations and this may not necessarily apply for black populations. In addition, drugs such as the prostaglandin analogues are expensive and are not a feasible option in a low resource environment.

At Ruharo Eye Centre (REC), the treatment arms for POAG are medication (timolol, acetazolamide and pilocarpine) and surgical (trabeculectomy). The effect of these treatments as far as modulation of IOP fluctuation in our patients had not been studied. In addition, it was observed a proportion of POAG patients continued to have visual field loss, a sign of deteriorating glaucoma disease despite available medical and surgical interventions giving convincing clinic target IOP readings. We hypothesized that this visual field loss could be as a result of large IOP fluctuation even after controlling peak IOP with medical or surgical treatment. There was therefore need to investigate the behavior of diurnal IOP fluctuation in glaucoma patients controlled on medical or surgical treatment.

MATERIALS AND METHODS

Design: This was a hospital based, analytical cross section study.

Study site: Ruharo Eye Centre (REC) located in Mbarara municipality, southwestern Uganda. The eye hospital receives patients mainly from south western Uganda, parts of north western Tanzania, Rwanda and eastern Congo. It serves a population of about 5 million people.

Target population: All African adult patients presenting for treatment at Ruharo Eye Centre during

the study period May – July 2013. Adult patients with a diagnosis of POAG treated at Ruharo. We estimated a minimum sample size of 50 eyes.

Case definition: The criteria for suspecting glaucoma was similar to a study by Mbumba *et al*[8] in the same population.

Inclusion criteria: All black adult patients, attending REC with POAG who consented to participate in the study.

Exclusion criteria

(i) Those patients who were difficult to examine.
(ii) Patients with a different type of glaucoma
(iii) Patients with history of eye surgery apart from glaucoma filtration surgery
(iv) Patients with glaucoma and any other ocular pathology
(v) Patients who developed tonometry indunced corneal abrasion

Study materials:

Machines: Biomicroscope (Slit lamp) + Calibrated Goldman tonometer, Henson perimeter CFA 2000, Pachmeter.

Lenses: Goldman goniolens and 90 dioptres lens.

Others: Data collection forms, optotypes, topical anaesthetic (drops), tropicamide (drops), viscoelastic and torch.

Data collection instrument: A questionnaire was administered for data collection, recording socio-demographic data, glaucoma clinical data, clinic IOP readings, serial 2 hourly IOP readings. The times at which the IOP readings were taken were recorded as well.

Sampling process: Every clinician at REC was sensitized on the objectives, recruitment procedures, ethical issues and tools of the study. Clinicians at REC referred all patients suspected to have glaucoma to the researcher.

Procedure: Patients were registered, and visual acuity was taken. Their eyes were examined by the clinicians using a biomicroscope. Fundoscopy with non-dilated pupil was performed to assess the optic disc. IOP was taken using a calibrated Goldman applanation tonometer. Those found to have an IOP of 22 mm Hg or more and/or abnormal looking optic discs were referred to the principal investigator for further examination, refraction, central corneal thickness and visual fields. Gonioscopy was done to type the glaucoma depending on if the anterior chamber angles were open or closed. Fundoscopy with dilated pupil using 90 diopters lens and indirect ophthalmoscope was performed to confirm glaucomatous damage on the optic disc.

At this stage, once the type of glaucoma had been diagnosed, the patient with POAG was introduced to the study. When the patient had been exposed to, and had understood all information about the study and was willing to be recruited, he/she was asked to sign the consent form. He/She retained the patient information sheet for further reference.

More information pertaining to the patient's condition was obtained using the questioneer. The patient was admitted in the hospital for a period of 24 hours. While admitted, 2 hourly IOP readings were taken in a similar pattern to the Robert David study[9]. Only one eye was considered per patient, the worst eye was selected and where both were eligible; one eye was randomly selected by tossing a coin. IOP readings were taken three times per reading and an average entered into the data, where the individual readings exceeded 3mmHg in variation, then tonometry was repeated until all the readings are less than 3mmHg. Patients were discharged from the study after completing 24 hour phasing and appropriate management plan was drawn in consultation with the glaucoma fellow at REC.

Quality control: The questionnaire was pre-tested on 5 patients. These were not included in the study. The researcher examined all glaucoma suspects and made a diagnosis. All the patients were presented to the ophthalmologist on duty before management decisions were made. All tonometers were standardized before their use.

Data analysis: Data collected was entered on Microsoft excel and later imported into STATA-11 for analysis. The level of significance was set at 0.05. For purposes of analytical comparison, the subjects were analyzed by different groups according to which treatment regimen they were on at the time of enrolling into the study. There were therefore three groups: patients on no treatment, treatment and surgery group. The mean fluctuation ranges, peak and trough times of IOP were reported for each group and compared and their 24 hour fluctuation curve patterns were drawn.

Limitations: Five patients who were unwilling to be admitted in hospital were excluded from the analysis. The study was not able to capture IOP readings for all the 24 hours because the patients had to be allowed to sleep at 11pm.

Ethical consideration: Approval was sought from the Research and Ethics Committee of Mbarara University of Science and Technology (Approval Number: 07/03-13). Informed consent was obtained from the patient.

Complications: Patients reported slight corneal epithelial irritation from application of drops and applanation. Only four patients developed corneal abrasions but recovered fully following padding.

RESULTS

General demographics: The total number of eyes included in the study was 51. The mean age of patients was 65 years, SD 1.96. All groups were comparable; there was no statistically significant difference in mean age by sex, eye and treatment group (Table 1).

Table 1: Distribution of patients by treatment group (n=51)

	Medical treatment	Trabeculectomy	No treatment	Total
Male	10	9	15	34
Female	4	2	11	17
Total	14(28%)	11(22%)	26(50%)	51

Mean diurnal IOP fluctuation: Trabeculectomy showed the least IOP fluctuation followed by medical treatment while patients not on treatment had the highest IOP fluctuation range (Table 2).

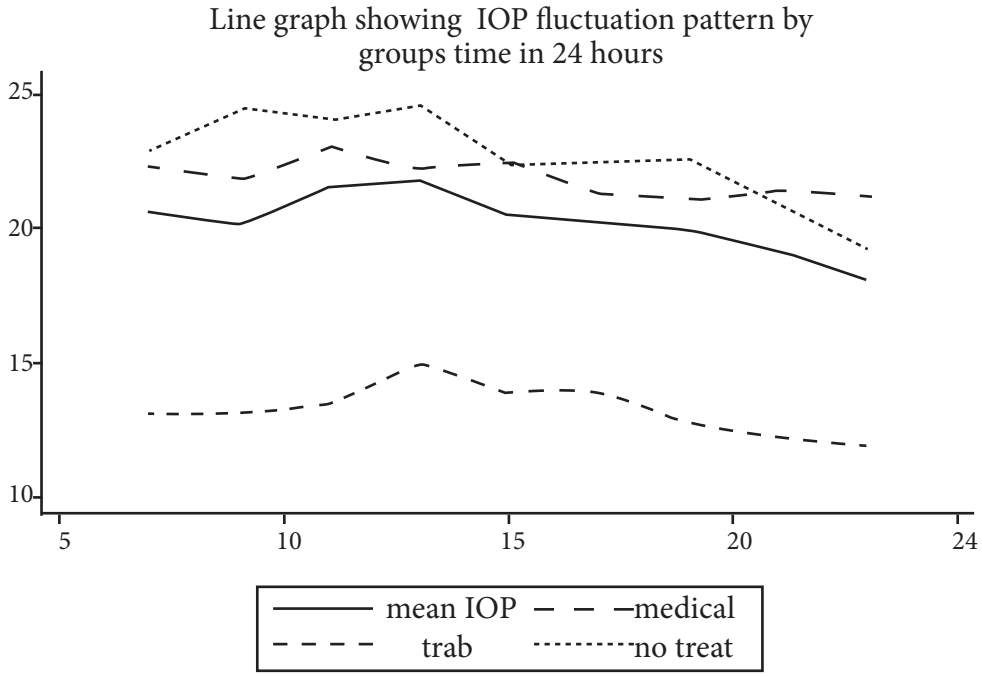
There was a statistically significant difference in mean lowest IOP between medical treatment vs. trabeculectomy (p value =0.0046) and trabeculectomy vs. no treatment (p value 0.0476). However their was no statistical significant difference between those on medical treatment vs. no treatment (0.6861). There was a statistically significant difference in the mean peak IOP between medical treatment vs. trabeculectomy (p value=0.0014) and trabeculectomy vs. no treatment (p value=0.0035) but no statistically significant difference between those on medical treatment and no treatment (p value =0.7464). There was a statistically significant difference in the fluctuation range between medical treatment vs. trabeculectomy (p value=0.0047) and trabeculectomy vs. no treatment (p value=0.0410) but no statistically significant difference between those on medical treatment and no treatment (p value =0.3742).

Table 2: Mean lowest IOP, mean peak IOP and mean fluctuation IOP amongst study participants (n=51)

	Mean lowest IOP(95% CI) mmHg	Mean peak IOP (95% CI) mmHg	Mean IOP fluctuation (95% CI) mmHg
Medical treatment	17.3 (13.8-20.8)	26.6 (21.8-31.3)	9.2 (7.4-11.2)
Trabeculectomy	10.6 (7.9-13.3)	15.9 (12.0-20.0)	5.3 (3.2-7.3)
No treatment	16.2 (12.8-19.7)	27.7 (23.0-32.5)	11.11 (8.2-14.0)
P values	(2,3=0.0046) (2,4=0.6861) (3,4=0.0476)	(2,3=0.0014) (2,4=0.0035) (3,4=0.7464)	(2,3=0.0047) (2,4=0.0140) (3,4=0,3742)

Diurnal fluctuation IOP pattern: Generally, the peak IOP was recorded in the morning, between 11am-1pm while the least IOP was recorded in the evening, between 9pm-11pm (Figure 1).

Figure 1: Fluctuation pattern of IOP over 24 hours



By proportions, majority of patients (90%) had their peak IOP in the morning and early afternoon (Table 3).

Table 3: Proportions in percentages of IOP peaks by groups (n=51)

	Morning peak (7-11am)	Afternoon peak (1-5pm)	Evening peak (7-11pm)
General	43	45	12
Medical treatment	57	28	15
Trabeculectomy	36	64	0
No treatment	39	46	15

DISCUSSION

In this study, we noted that patients who had received trabeculectomy had the least IOP fluctuation range, followed by those who were on medical treatment while those who were not on treatment had the largest IOP fluctuation range. This was by and large similar to most studies which looked at IOP with the similar research strategy[9-11].

By treatment groups, patients who were not on any treatment showed the highest fluctuation that was in double digits, this was much higher than recorded in other studies of which the highest recorded was 8.3 mmHg[10]. This could be explained by the fact that most of the patients in this group had advanced glaucoma with late presentation and therefore could have had underlying large diurnal fluctuations.

Patients who were on medication for glaucoma also showed a higher fluctuation than noted in other studies which reported fluctuation of 5.5 (95% CI 2.9-8.1) mmHg amongst POAG patients on timolol[9]. 5.4 (95% CI 2.3-8.5) mmHg amongst POAG patients on timolol twice a day and latanoprost once a day[12]. 2.7 (95% CI 1.7-3.7) mmHg amongst patients using latanoprost[13] and almost similar findings in POAG patients on various preparations of prostaglandin analogues[7,14,15]. The findings in our population were higher for obvious reasons; No patient in our population was on prostaglandin analogues which were found to have the best IOP modulations amongst the glaucoma drugs[16] and the adherence rates to treatment in our population might not have been adequate. This explains why there was no statistically significant difference in diurnal fluctuation with those who were not on anti glaucoma medication.

Patients who received trabeculectomy had the least IOP fluctuation compared to the other groups (Table 3). However, in terms of actual IOP fluctuation, our study had higher post trabeculectomy fluctuations compared to the other studies which found a fluctuation of less than 2.5mmHg[5,11]. This could be explained by the fact that perhaps that is the pattern in the population due to surgery associated factors which should be investigated. Also to note is that most of these studies had a different design in patient inclusion as they only included patients who had good post-operative outcomes.

The pattern of diurnal IOP was found to be higher in the morning and lower in the afternoon and evening. This was similar to many other studies which noted morning peaks and afternoon or evening troughs[9,17]. The average peak IOP was recorded between 11am -1pm in about 90% of patients while the average lowest IOP was recorded between 9pm-11pm. This trend followed a normal circadian rhythm, IOP readings taken in the mornings and early afternoon were found to provide a more representative picture of patients peak IOP.

CONCLUSIONS

Trabeculectomy was found to provide significantly better control of IOP fluctuation than medical treatment and could be the recommended option in our setting. However, a randomized controlled clinical trial should be conducted to ascertain this finding.

Medical therapy currently used for management of POAG was found not to provide good control of IOP fluctuation in our setting. This should be reviewed both in terms of adherence and efficacy of controlling IOP fluctuation. Drugs which have been known to provide a better control of IOP fluctuation such as prostaglandin analogues should be co opted in patients who are able to afford. However, a study should be conducted to find out the adherence rates to treatment and reasons why patients may not be adhering to treatment as they should. It will be of benefit also to find out why most POAG patients especially the new ones present very late.

In a routine glaucoma clinic, IOP measurements should be planned to be taken between 11am and 1pm as this provides the best opportunity of "capturing" true peak IOP levels in majority of POAG patients. These measurements can be assumed to be peak IOP readings.

Progressive optic nerve damage could be due to failure of current treatment in reducing the range of IOP fluctuation independent of target IOP control. However, the patients in study had not had their baseline IOP controlled and so the findings could represent both the effect of uncontrolled baseline IOP and wide fluctuation range

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