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Short- and long-term effectiveness of interventions for improving adherence to glaucoma medications

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Background: The need for effective interventions for addressing non-adherence to glaucoma medications is fundamental in improving visual outcomes among persons with glaucoma.

Aim: The study aims to assess the effectiveness of short- and long-term behavioural, educational and mixed interventions for improving adherence to glaucoma medications.

Setting: Four eye hospitals in Accra were used for this study.

Methods: This was a prospective multi-centre randomised controlled trial involving 236 non-adherent patients with glaucoma. Participants were assigned to intervention and control groups. The intervention group received behavioural, educational and mixed interventions. Data were analysed with the IBM SPSS software version 25. Mean differences in adherence between the groups were determined at baseline, at 3 months and 6 months intervals, using the Independent-Sample-*t*-test and repeated measures for analysis of variance. *P*-values less than 0.05 were considered statistically significant.

Results: The mean age was 61.0 ± 7.9 years. Participants were similar in terms of age, intraocular pressure and cup-to-disc ratio, across the study centres ($P > 0.05$). At 3- and 6-months following intervention, the intervention group experienced an increase in adherence from 55.1% to 59.3% respectively. There was a significant difference in mean score for adherence between the intervention and control groups after 3 and 6 months with an effect size ≥ 0.80 ($P < 0.05$).

Conclusion: The interventions resulted in a significant improvement in adherence.

Contribution: Our findings support the use of multi-faceted interventions in reducing non-adherence to glaucoma medications.

Keywords: adherence; glaucoma; medication; intervention; behavioural; educational.

Introduction

Glaucoma is a major global public health concern.[1,2] The use of topical anti-glaucoma medications remains the most common method for managing glaucoma globally.[2,3] However, adherence to such medications is commonly poor, especially in developing countries, and is arguably the most significant barrier to glaucoma management.[4,5] Poor adherence to glaucoma medications can result in severe visual and ocular damage, reduced quality of life and productivity, increased health care cost and caregiver burden.[3,4,5,6] Although there is evidence to support the importance of anti-glaucoma medications in reducing progressive damages caused by uncontrolled rise in intraocular pressure (IOP) and needless additional prescriptions and surgeries,[2,3] these medications will work for only those who use them appropriately.

A significant solution for addressing non-adherence is the development and testing of the effectiveness of interventions for reducing non-adherence to glaucoma medications.[5] The World Health Organization (WHO) has indicated that 'increasing the effectiveness of adherence interventions may have a far greater impact on the health of the population than any improvement in specific medical treatment'.[7] Several studies have demonstrated the significance of multifaceted interventions that may include: simplifying medication regimens, educating patients and caregivers, encouraging patient–provider communication and use of reminder applications in improving adherence to medication.[8,9,10,11,12]

As part of this study, the authors developed behavioural, educational and mixed interventions for improving adherence to glaucoma medications.[13,14,15] These tailored

interventions (the KPM Eye App, motivational interviewing session, the glaucoma educational handout) were designed to address the multifactorial nature of unintentional and intentional non-adherence to glaucoma medications Fundamental to the development of these interventions was the need to test their effectiveness in a randomised controlled trial (RCT) that can provide the most reliable evidence on the effectiveness of the interventions since the methodologies incorporated in RCTs tend to reduce the risk of confounding factors that may influence the outcome.[16]

Therefore, the aim of this study was to test the effectiveness of short- and long-term behavioural, educational and mixed interventions for improving adherence to glaucoma medications in a Ghanaian population. These interventions, when proven to be effective, may be beneficial in improving adherence in this population known to have the second highest prevalence of glaucoma in the world.

Research methods and design

Study design and setting

A multi-centre RCT design was used to assess the effectiveness of the interventions. Four major eye hospitals in the Greater Accra region of Ghana were used in this study. These facilities were selected as they serve as major referral facilities for glaucoma care in Accra.

Trial registration and ethical considerations

The trial was registered with the Pan African Registry of trials with registration number PACTR202108476131561. Guidelines and regulations in the Helsinki Declaration of ethical principles for medical research involving human subjects were observed. The study was approved by the Biomedical Research Ethics Committee of a University in Durban (BREC/00002965/2021) and the Institutional Review Board of Teaching Hospital in Ghana (KBTH-IRB/00048/2021). Official approval was also obtained from the heads of all the eye hospitals before the commencement of data collection. The objectives of the study were explained to participants and voluntary written informed consent was obtained. Participants' information was treated confidentially by anonymising their identities through the use of assigned codes.

Selection criteria

Study participants comprised of adult patients aged 18 years and older diagnosed with glaucoma who were non-adherent to glaucoma medication following a baseline assessment of the prevalence and predictors of non-adherence to glaucoma medications. Adult patients with glaucoma aged 18 years and older, who were previously diagnosed for 1 or more years, and prescribed topical anti-glaucoma medications and had used these medications for 1 or more years, were included. In addition, these participants were expected to be able to read and understand the English language at the grade 9 level of the United States (US) educational system or its equivalence (equivalent to the basic Junior High School in Ghana), and must have access to a mobile phone with an android application.

Patients diagnosed with glaucoma who underwent glaucoma surgery and those with psychiatric disorders were excluded.

Sample size, randomisation, blinding and administration of interventions

Details of the sample size calculation for the study are reported elsewhere in a baseline study examining the prevalence and predictors of non-adherence to glaucoma medications.[12] From the baseline study, 236 (61.5%) participants were non-adherent.[13] These non-adherent participants were randomised into intervention or control group (1 – intervention: 1 – control) respectively using block randomisation with the help of a Research Randomizer software. The intervention group received behavioural (B), educational (E) and mixed (M) interventions in addition to routine standard care for patients with glaucoma.

The control group received only routine standard care for patients with glaucoma. Participants were randomly assigned to either Group B, E or M respectively by an Ophthalmic nurse independent of the masked principal investigator.

The behavioural interventions included the use of a reminder application (the KPM Eye App) installed on the mobile phones of participants and a motivational interviewing (MI) session at the clinics. The educational intervention incorporated the use of a glaucoma educational handout designed for the study.

In the development of the KPM Eye App, three stages in software development were followed: problem identification, application design and development and product testing and validation. The basis for developing this software was forgetfulness, which was one of the findings from a qualitative study involving 24 adult patients with glaucoma at the problem identification stage. A number of programmed codes were used in the App's design and development process to create its features. After 10 adult patients with glaucoma had evaluated and validated the software, suggestions for enhancing its general functionality were taken into consideration.[13]

The development and validation of the MI manual followed three phases: content development via a qualitative exploratory study involving 24 adult glaucoma patients, which identified themes related to motivators and barriers to medication adherence; validation through pre-testing and quality assessment by experts in clinical psychology, ophthalmology and health communication and the training of counsellors or interviewers.[14]

The educational handout was also developed based on five themes derived from the qualitative study described earlier in the text. These themes included; understanding of glaucoma, knowledge of non-adherence, reasons for non-adherence, utilisation of glaucoma medicine and the role of patients in glaucoma management. The content of the handout was further modified by a professional medical illustrator and a health promotion officer. It was content validated by 10 experts in ophthalmology, health promotion, public health and representatives from the Glaucoma Association of Ghana, and face validated by 15 patients with glaucoma.[15]

Detailed account of the design, development, and validation of these interventions have been reported elsewhere.[13,14,15]

Study participants during their follow-up visit were asked few questions about the educational handout to find out if they had read the material.

The mixed intervention used both behavioural and educational interventions described earlier in the text for improving adherence to glaucoma medication. The interventions were administered by trained ophthalmic nurses. Table 1 shows the allotment of participants to the interventions.

Because of the nature of the interventions (the behavioural intervention with the use of a reminder application and a motivational counselling session at the clinic), study participants and research staff were not blinded to the intervention allocation, but clinicians and the principal investigator were blinded as to which patients were participating in the study. The principal investigator (who was the data analyst) was blinded as to which data belonged to the intervention/control group during analysis. Therefore, the study was single blinded.

Data collection and measurement of non-adherence after intervention

Data were collected using a standardised data collection form designed to capture both the demographic and clinical characteristics of participants. Demographic information included; age (young adults: ≤ 59 and older adults: ≥ 60 years),[17] sex (male or female), employment (employed or unemployed), education (low level – education from pre-school to the basic school level in Ghana or high level – education from the senior high school or vocational or technical level to the tertiary level in Ghana), marital status (married or single), religion (Christian or Islam or Traditional or Others), family history of glaucoma (yes or no), self-efficacy – able to self-instil eye drop (yes or no), knowledge about glaucoma (adequate or inadequate), forgetfulness (yes or no), affordability of medication (yes or no), health insurance (yes or no), following recommended visits (yes or no).

Knowledge about glaucoma was determined using the first five questions on the Glaucoma Treatment Compliance Assessment Tool-Short form (GTCAT-S)[18] which examined patients' personal knowledge of the symptoms of glaucoma, whether a person can have glaucoma and not know it, whether an eye pain is a common symptom of glaucoma, whether glaucoma treatments can prevent future vision loss and whether vision lost from glaucoma is permanent. Participants used a 5-point Likert scale ranging from disagree a lot (1) to agree a lot (5) to answer each question. Correct and wrong answers were scored 1 and 0, respectively. Participants who scored three out of the five questions were classified as having adequate knowledge about glaucoma and those with scores lower than three were classified as having inadequate knowledge about glaucoma.

Clinical information included; date of diagnosis of glaucoma, age at diagnosis, current IOP, cup-to-disc ratio (CDR), OCT (Optical Coherence Tomography) findings, visual fields test (VFT) findings and visual acuity measurements with the Snellen chart.

Medication and treatment given were also recorded and classified as prostaglandin analogues, beta blockers and carbonic anhydrase. These data were extracted from the records of patients after they were seen by ophthalmologists at the centres.

Participants were followed for an initial 3 months (the routine follow-up period for glaucoma patients in Ghana) and another 3 months post intervention. During the routine follow-up visit to the clinic for review, adherence was measured, and the interventions were repeated while the control group received standard care. Questions on adherence covered the past 4 weeks in order to minimise the risk of recall bias where participants may not be able to accurately remember a past event or leave out

TABLE 1: Allotment of participants to the interventions.

Study site	Control intervention							Total
	Standard care for glaucoma	GROUP B behavioural		GROUP E educational	GROUP M mixed			
		EyeApp	MI		EyeApp	MI	Educ.	
A	59	10	10	20	6	6	7	118
B	20	3	4	6	2	3	2	40
C	20	3	3	7	2	2	2	39
D	19	3	3	6	3	2	3	39
Total	**118**	**19**	**20**	**39**	**13**	**13**	**14**	**236**

Educ., educational intervention; MI, motivational interviewing.

details. Non-adherence was measured 3 and 6 months after the intervention using the GTCAT-S.[18] The GTCAT-S is a self-reported, indirect, non-invasive and subjective technique with a 27-statement questionnaire validated for measuring adherence to glaucoma medications.[18]

A 5-point Likert scale ranging from 'disagree a lot- (1)' to 'agree a lot- (5)' was used in soliciting responses from the questionnaire. Scores were analysed and converted into percentages. A score ≥ 80.0% was identified as adherent and scores < 80.0% were non-adherent. Short- and long-term durations were defined as 3 and 6-months duration respectively after administration of the designed interventions. Demographic and clinical data collected from the baseline were recorded in a Microsoft Excel software.

Missing data

Missing data were imputed using a multivariate normal imputation model after transformation to ensure that the data were normally distributed. This was followed by a sensitivity analysis to assess the effect of the missing data. Findings (not shown) show that the outcome was not sensitive to the missing data.

Adverse event

There were no adverse events resulting from the administration of the interventions.

Participants flow through the study

The flow of study participants through the study is outlined in Figure 1.

Data monitoring

A three-member safety monitoring board was constituted to ensure the safety, rights and well-being of enrolled participants. The Board ensured the accuracy and completeness of the data collected and compliance with ethical regulations.

Data management

The principal investigator ensured that appropriate archiving of data generated during the study and at the end of the study was made. All non-electronic research data were stored in a locked filing cabinet (including CD and flash drive) and the principal investigator ensured that the data were accessible only to authorised persons.

Primary outcome variable

The primary outcome measure for this study was the effectiveness of the interventions at 3 months and 6 months intervals respectively.

Secondary outcome variable

The secondary outcome was changes in prevalence of non-adherence from baseline to 6 months.

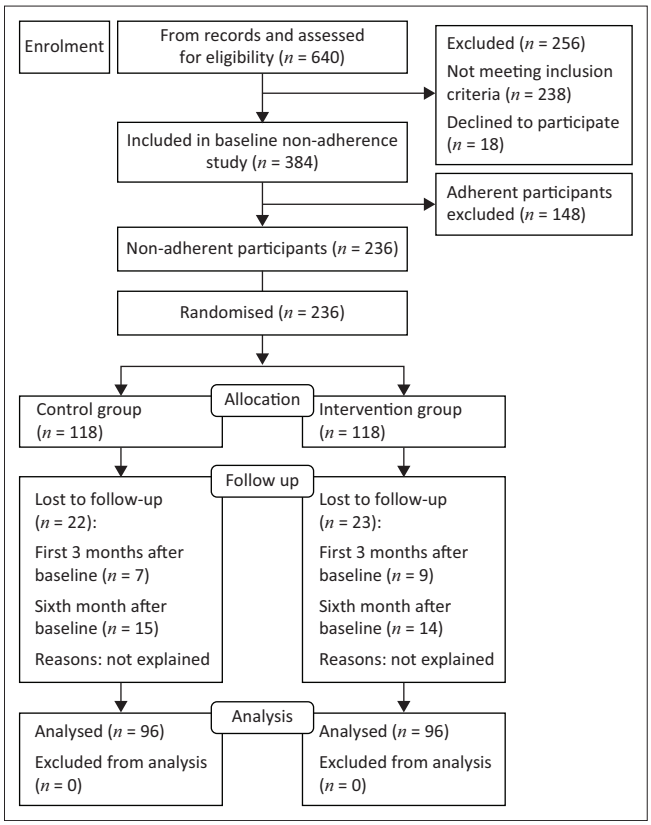

FIGURE 1: Consolidated standard of reporting trials (non-pharmacological treatments).

Statistical analysis

Statistical analysis was performed using IBM Statistical Package for the Social Sciences (SPSS) software version 25. Quantitative data were analysed descriptively and reported as mean, standard deviation, percentages and frequencies.

Mean differences in adherence between the intervention and control groups were determined at baseline, at 3 months and 6 months intervals, respectively using the Independent-Sample-*t*-test and repeated measures analysis of variance (ANOVA). The effect size (ES) or the effectiveness of the interventions overtime was calculated by dividing the difference between the mean score for the intervention and control groups by the standard error of the difference. An ES < 0.20 was described as trivial effect, ES ≥ 0.20 < 0.50 referred to small effect, ES ≥ 0.50 < 0.80 was seen as a moderate effect and ES ≥ 0.80 was classified as large effect.[19] *P*-values less than 0.05 were considered statistically significant. Analyses were based on the principle of intention-to-treat.

Results

Enrolment of study participants

Out of the 384 participants, 236 were found to be non-adherent at baseline. These participants were included in this RCT study, and were randomised into intervention (118) and control (118) groups respectively.

A total of 22 (7-were lost to follow-up after the first 3 months following the baseline study, and 15 were lost to follow-up

6 months after the baseline study) participants were lost to follow-up in the control arm of the study with reasons not explained. In all, 23 (9- were lost to follow-up after the first 3 months following baseline study and 14 were lost 6th months after baseline study) participants were lost to follow-up in the intervention arm of the study. Reasons for the loss were not given (Figure 1).

Demographic profile of the study participants

A total of 236 adult patients with glaucoma with an average age of 61.0 ± 7.9 years participated in this trial. At baseline, the intervention and control group each had 118 participants with an average age of 60.9 ± 8.9 years and 61.1 ± 6.9 years, respectively which did not demonstrate any significant difference ($P = 0.826$). There were more females (128, 54.2%) than males.

A total of 218 (92.4%) participants were able to instil their eye drops without assistance. Few (15, 6.4%) had adequate knowledge about glaucoma and more than half (163, 69.1%) admitted forgetting to take their glaucoma medication. Less than half (76, 32.2%) could afford their glaucoma medication and 174 (73.7%) had health insurance. In all, 163 (56.4%) participants followed recommended visits by their caregivers.

Less than half of the participants (101, 42.8%) have a family history of glaucoma. In all, there was no significant difference between the intervention and control groups at baseline for all the demographic characteristics ($P > 0.05$) (Table 2). Other demographic information on study participants relating to employment, education, marital status and religion is presented in Table 2.

Similarities and differences among participants across the study sites

Participants were similar in terms of age, IOP and CDR, across the study centres ($P > 0.05$). However, there was a significant difference in sex ($\chi^2 = 10.8$; $P = 0.013$) across the study centres (Table 3).

Classification of glaucoma medications used by study participants

Among the class of glaucoma medications used by the participants, the three most prescribed categories were: prostaglandin analogues (124, 28.0%), followed by beta blockers (95, 21.4%) and carbonic anhydrase (80, 18.1%).

TABLE 2: Baseline profile of study participants in the trial.

Characteristics	Total ($N = 236$)			Intervention ($n = 118$)			Control ($n = 118$)			*P*-value	
	Mean ± s.d.	*n*	%	Mean ± s.d.	*n*	%	Mean ± s.d.	*n*	%	Independent *t*-test	χ^2
Age (years)	61.0 ± 7.9	-	-	60.9 ± 8.9	-	-	61.1 ± 6.9	-	-	0.826	-
Age (years)	-	-	-	-	-	-	-	-	-	-	0.091
≤ 59 (young adults)	-	73	30.9	-	43	18.2	-	30	12.7	-	-
≥ 60 (older adults)	-	163	69.1	-	75	31.8	-	88	37.3	-	-
Gender	-	-	-	-	-	-	-	-	-	-	0.695
Male	-	108	45.8	-	56	23.7	-	-	-	-	-
Female	-	128	54.2	-	62	26.3	-	66	28.0	-	-
Employment	-	-	-	-	-	-	-	-	-	-	0.272
Employed	-	52	22.0	-	30	12.7	-	22	9.3	-	-
Unemployed	-	184	78.0	-	88	37.3	-	96	40.7	-	-
Education	-	-	-	-	-	-	-	-	-	-	0.430
High level of education	-	135	57.2	-	64	27.1	-	71	30.1	-	-
Low level of education	-	101	42.8	-	54	22.9	-	47	19.9	-	-
Marital status	-	-	-	-	-	-	-	-	-	-	0.239
Married	-	63	26.7	-	36	15.3	-	27	11.4	-	-
Single	-	173	73.3	-	82	34.7	-	91	38.6	-	-
Religion	-	-	-	-	-	-	-	-	-	-	0.391
Christianity	-	179	75.8	-	89	37.7	-	90	38.1	-	-
Islamic	-	40	16.9	-	18	7.6	-	22	9.3	-	-
Traditional	-	17	7.2	-	11	4.7	-	6	2.5	-	-
Self-efficacy	-	218	92.4	-	113	47.9	-	105	44.5	-	0.084
Knowledge about glaucoma	-	15	6.4	-	8	3.4	-	7	3.0	-	1.000
Forgetfulness	-	163	69.1	-	81	34.3	-	82	34.7	-	1.000
Affordability of medication	-	76	32.2	-	40	16.9	-	36	15.3	-	0.676
Health insurance	-	174	73.7	-	92	39.0	-	82	34.7	-	0.183
Follow recommended visits	-	133	56.4	-	59	25.0	-	74	31.4	-	0.066
Family history of glaucoma	-	101	42.8	-	56	23.7	-	45	19.1	-	0.188
Study sites	-	-	-	-	-	-	-	-	-	-	1.000
A	-	118	50.0	-	59	25.0	-	59	25.0	-	-
B	-	40	16.9	-	20	8.5	-	20	8.5	-	-
C	-	40	16.9	-	20	8.5	-	20	8.5	-	-
D	-	38	16.1	-	19	8.1	-	19	8.1	-	-

s.d., standard deviation.

Prevalence of adherence to glaucoma medication after intervention

At baseline, all the study participants were non-adherent. At 3 months following intervention, the intervention group had an adherence prevalence of 55.1% which increased to 59.3% after 6 months. Males had higher adherence prevalence compared to females at 3 months (37.0% vs 34.4%). However, at 6 months, adherence in females increased significantly compared to males (40.6% vs 38.0%). Participants on behavioural intervention had higher prevalence compared with the other interventions at three and 6 months respectively (57.9% and 65.8%) (Table 4).

Effectiveness of the interventions

There was a significant difference ($P < 0.05$) in mean score for adherence between the intervention and control groups at baseline, 3 months and 6 months respectively for all the interventions with an ES $\geq$ 0.80, signifying a large effect (Table 5).

At both short- and long-term durations, there was no significant difference in the mean score for adherence in all the interventions ($P > 0.05$) (Table 6).

In all the interventions, there was a significant difference in mean score for adherence between the short- and long-term durations and a corresponding large effect size (ES $\geq$ 0.80) (Table 6).

Discussion

This study sought to assess the effectiveness of short- and long-term behavioural, educational and mixed interventions for improving adherence to glaucoma medications. Participants who were non-adherent to glaucoma medications were recruited from a baseline study[13] to estimate the ES and the level of adherence following the interventions. Other studies that assessed the effectiveness of interventions for improving adherence to glaucoma medications adopted a similar approach.[10,11,20] Our results showed a significant

TABLE 4: Prevalence of adherence to glaucoma medication at three and six months after intervention.

Characteristics	Prevalence of adherence (%)	
	Three months (short term)	Six months (long term)
Group		
Intervention	55.1	59.3
Control	16.1	19.5
Gender		
Male	37.0	38.0
Female	34.4	40.6
Behavioural	57.9	65.8
Educational	55.0	55.0
Mixed	51.2	56.1

TABLE 6: Study duration, and mean score of adherences for the interventions.

Intervention	Duration		Effect size	*P*-value (independent *t*-test)
	Short	Long		
Behavioural				0.001
Mean score (Mean ± s.d.)	76.8 ± 5.7	79.0 ± 4.4	2.71	-
Prevalence of adherence (%)	57.9	65.8	-	-
Educational				0.001
Mean score (Mean ± s.d.)	76.5 ± 7.9	78.6 ± 6.7	1.63	-
Prevalence of adherence (%)	55.0	55.0	-	-
Mixed				0.001
Mean score (Mean ± s.d.)	76.4 ± 8.0	78.3 ± 6.8	1.52	-
Prevalence of adherence (%)	51.2	56.1	-	-
Analysis of variance (ANOVA) test				
F-statistics	0.084	0.333	-	-
P-value	0.920	0.717	-	-

TABLE 3: Similarities among participants across the study sites.

Characteristics	Study sites												*P*-value		
	A			B			C			D			χ^2	*F*†	Independent *t*-test
	Mean ± s.d.	*n*	%	Mean ± s.d.	*n*	%	Mean ± s.d.	*n*	%	Mean ± s.d.	*n*	%			
Age (years)	60.9 ± 7.6	-	-	63.2 ± 3.7	-	-	59.7 ± 11.5	-	-	60.4 ± 7.8	-	-	-	1.44	0.232
Gender													10.8	-	0.013*
Male	-	45	19.1	-	22	9.3	-	16	6.8	-	25	10.6	-	-	-
Female	-	73	30.9	-	18	7.6	-	24	10.2	-	13	5.5	-	-	-
Mean IOP right eye (mmHg)	16.7 ± 3.9	-	-	17.6 ± 5.7	-	-	17.4 ± 4.4	-	-	17.1 ± 3.9	-	-	-	0.53	0.663
Mean IOP left eye (mmHg)	16.5 ± 3.8	-	-	18.0 ± 5.6	-	-	17.1 ± 4.5	-	-	16.4 ± 3.9	-	-	-	1.4	0.257
Mean CDR right eye	0.8 ± 0.1	-	-	0.8 ± 0.1	-	-	0.8 ± 0.1	-	-	0.8 ± 0.1	-	-	-	1.205	0.309
Mean CDR left eye	0.8 ± 0.1	-	-	0.8 ± 0.1	-	-	0.8 ± 0.1	-	-	0.8 ± 0.1	-	-	-	0.701	0.553

Note: The independent *t*-test was used to calculate the *p*-values.
s.d., standard deviation; IOP, intraocular pressure; CDR, cup-to-disc ratio.
*, showing statistical significance.
†, *F*-distribution was calculated with analysis of variance (ANOVA) test.

TABLE 5: Effect of short- and long-term intervention for improving adherence to glaucoma medications.

Adherence	Baseline		Three months (short term)				Six months (long term)			
	Intervention	Control	Intervention	Control	*P*†	ES	Intervention	Control	*P*†	ES
Mean score (Mean ± s.d.)	47.2 ± 8.1	48.0 ± 4.2	76.8 ± 5.7	70.0 ± 3.4	0.001	-	79.0 ± 4.4	72.0 ± 5.5	0.001	-
Prevalence (%)	-	-	55.1	16.1	0.001	5.86	59.3	19.5	0.001	8.64

Note: Effect size (ES) interpretation: ES < 0.20 = Trivial effect; ES $\geq$ 0.20 < 0.50 = Small effect; ES $\geq$ 0.50 < 0.80 = Moderate effect; ES $\geq$ 0.80 = Large effect.
ES, effect size; s.d., standard deviation.
†, independent *t*-test was used to calculate the *P*-values.

difference in mean score and proportion of adherence between the intervention and control group at the 3rd month (76.8 ± 5.7 vs 70.0 ± 3.4; 55.1% vs 16.1%) and 6th month (79.0 ± 4.4 vs 72.0 ± 5.5; 59.3% vs 19.5%) respectively. We also recorded a significant improvement in adherence to glaucoma medication from baseline to the first 3 months which was sustained at the 6th month across all interventions. In addition, the results showed a large effect (ES $\geq$ 0.80) describing the effectiveness of the behavioural, educational and mixed interventions in improving adherence among patients with glaucoma from baseline to the 6th month.

When comparing the three interventions, although there was no statistically significant difference in mean score and prevalence of adherence among the three interventions for both short and long durations ($F = 0.084$, $P = 0.920$; $F = 0.333$, $P = 0.717$), there was a slightly higher mean score from the behavioural group compared to the educational and mixed groups respectively (76.8 ± 7.1 vs 76.1 ± 8.9 vs 76.3 ± 8.7; 78.9 ± 4.9 vs 77.6 ± 8.2 vs 78.2 ± 7.2). The same trend was observed for the prevalence of adherence across the interventions for both short and long durations (57.9% vs 55.0% vs 51.2%; 65.8% vs 55.0% vs 56.1%). This suggests that the behavioural intervention alone could yield a better adherence outcome compared to the educational and mixed interventions. The finding of a lower mean score for adherence in the mixed intervention group compared with behavioural and educational interventions requires further investigation in a larger population-based sample. There was an increase in the mean score for adherence from short to long term with a large effect for all the three interventions (ES $\geq$ 0.80) indicating that the change could be sustained over a period of time.

These findings align with the results of the Support, Educate, Empower (SEE) study which showed an improvement in adherence from 60% at baseline to over 80% after an in-person counselling and motivation session.[21] In another study done by Subhan et al.,[22] which aimed at evaluating compliance to anti-glaucoma medications before and after a structured interventional programme, non-compliance decreased from 15.7% to 7.5% among the participants after the structured programme. This reduction in non-compliance was attributed to an increase in glaucoma education, duration of treatment for more than 2 years and bilateral eye disease.[22]

In a RCT of 200 participants known as the 'Medication Adherence in Glaucoma to Improve Care' (MAGIC), findings showed that after 6 months of administering interventions made up of glaucoma education, personalised disease management suggestions and a reminder aid, the mean proportion of adherent participants was significantly higher in the intervention group compared to those in the control group (85% vs 62%; $P < 0.001$).[12] Compared to the MAGIC study, a significantly higher percentage difference in adherence was observed in this current study between the intervention and the control in the 6th month (59.3% vs 19.5%).

Although there may likely be a Hawthorne effect[23] where participants in knowing they are being monitored might have impressed their caregivers, our significant increase in adherence may be attributed to the good rapport and positive relationship created by the counsellors (nurses) during the motivational interviewing sessions. However, Ajit et al.[23] have shown that the Hawthorne effect tends to decrease after 2 months of monitoring patients.

Furthermore, although the use of subjective tools in the measurement of adherence is known to bias adherence estimates, the current study used the GT-CAT-short which is a glaucoma-disease specific and validated tool known to predict electronic adherence (an objective measure) with good psychometric properties.[19,24]

We did not perform a sub-analysis to demonstrate whether the sustained improved adherence with the behavioural and mixed approaches could be attributed to the use of the reminder application, the MI only or the educational component, as the sample size for the sub-categories of the interventions was small. A larger population sample may better explain this.

Our use of the behavioural intervention, made up of MI and the KPM reminder App significantly increased adherence in the intervention group from baseline to the 6th month, resulting in an improved mean score for adherence and a corresponding increase in adherence rate. Thus, the behavioural intervention recorded a significant improvement from baseline through to the 6th month ($P < 0.001$) with a large effect (ES $\geq$ 0.80). At the 3rd month, the mean score for the intervention group differed significantly from the control group (76.8 ± 5.7 vs 70.0 ± 3.4; $P = 0.001$), which was also evident from the outcome of the 6th month (79.0 ± 4.4 vs 72.0 ± 5.5; $P = 0.001$).

Our MI comprised of education on glaucoma and motivational support from trained ophthalmic nurses which empowers patients for self-care by enhancing their skills and dexterity positively.

Although our study did not consider a sub-analysis of the individual contributions made by the MI and KPM Eye App because of the small sample size in each group, we do appreciate the joint improvement by these two constituents of the behavioural intervention. In spite of this, the use of reminder applications has demonstrated significant improvements in adherence in other studies.[9,25,26,27] Others have also argued that the use of medication reminder applications did not produce any significant effect on adherence to medications.[27,28] However, in studies where reminder applications could not yield significant improvement in adherence, the failure was attributed to poor design, problems with importing medication information and inability to create reminders for several people on several drugs.[9]

The educational intervention demonstrated a significant improvement from baseline through to the 6th month

($P < 0.001$) with a large effect (ES ≥ 0.80). At the 3rd month, the means score for the intervention group differed significantly from the control group (76.5 ± 7.9 vs 65.8 ± 8.4; $P = 0.001$), which was also noticed at the 6th month (78.6 ± 6.7 vs 66.4 ± 8.5; $P = 0.001$). This outcome is similar to the results from Gray et al.[29] which assessed the impact of educational interventions on glaucoma medication adherence. Gray et al.[29] found adherence to be significantly better in the intervention group compared to controls (70% vs 43%; $P = 0.002$). Our educational intervention component was made up of knowledge about glaucoma, reasons for non-adherence, use of glaucoma medication, steps for proper instillation of eye drops, information on medication adherence and the role of patients in the management of glaucoma.

This study has shown that the use of multi-faceted interventions in addressing non-adherence to glaucoma medications is effective in a population known to be the second highest in glaucoma prevalence globally. Thus, most of the challenges of non-adherence to glaucoma medications may be resolved using behavioural and educational approaches.

A significant strength of this study is the use of a glaucoma-disease specific adherence tool (GTCAT-short) in measuring non-adherence. This tool is capable of measuring specific constructs related to adherence such as barriers, benefits, cues-to-action, patient–physician relationship, physical and mental health, self-reported adherence, susceptibility, severity, self-efficacy and knowledge about glaucoma.

Another strength of this study is the use of RCT design which provides the most reliable evidence on the effectiveness of interventions as it tends to reduce the risk of confounding factors that may influence the outcome. Another strength relates to the analysis of both short- and long-term outcomes to validate the sustainability of the interventions.

Our intervention was based on a behavioural change approach that incorporated behavioural theory, MI, patients' education and the use of mobile reminder application which have been identified by a Cochrane review of medication adherence interventions as a key strategy capable of promoting change in behaviour.[30]

Limitations

Despite the strength associated with this study, there were some few limitations. Firstly, the subjective nature of the tool for assessing adherence and the need to rely on participants' memory to recall information could bias the outcome. Another limitation is the inclusion of only participants who were educated at least to the grade 9 level of the US educational system or its equivalence (equivalent to the basic Junior High School in Ghana), with access to an android mobile phone which may compromise the generalisability of our findings.

Conclusion

Despite the numerous reasons associated with non-adherence and gaps in the identification and treatment of non-adherence, a multi-faceted approach appears to be ideal in resolving non-adherence. The behavioural, educational and mixed interventions significantly improved medication adherence among non-adherent patients with glaucoma. Our findings therefore support the use of multi-faceted interventions to reduce non-adherence to glaucoma medications. These interventions could further be evaluated by examining its effectiveness and scalability in a large-scale, multi-centre RCT across a larger population.

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Competing interests

The authors declare that they have no financial or personal relationships that may have inappropriately influenced them in writing this article.

Authors' contributions

B.A. contributed to the conceptualisation, methodology, formal analysis and the writing of the original draft. P.G.-P. and K.P.M. contributed to the methodology, supervision and the review and editing of the article. K.P.M. B.A. and P.G.-P. approved the final version for publication.

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Data availability

The data that support the findings of this study are available from the corresponding author, B.A., upon reasonable request.

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