Original Article

Clinical study on primary open-angle glaucoma with *Ashchyotana*, *Tarpana* and oral medication

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Abstract

Introduction: Glaucoma is the second leading cause of irreversible blindness worldwide and third leading cause in India. The disease progresses even intraocular pressure (IOP) is well under control; hence, now modern medicine is looking for strategies that are neuroprotective in glaucomatous optic neuropathy (GON) management. **Aim:** This study aimed to propound the concept of *Chakshushya Rasayana* and diuretic therapies and also evaluate the neuroprotective and IOP-lowering effects of Ayurvedic line of management in primary open-angle glaucoma (POAG). **Materials and Methods:** In this randomized parallel-group trial, patients having POAG were randomized with equal probability to one of the two treatment groups. Participants were assessed on the basis of subjective parameters such as blurred vision, frequent changes of presbyopic glasses (FCPG), delayed dark adaptation (DDA), visual field defect (VFD) and headache; objective parameters such as best-corrected visual acuity (BCVA), IOP and optic nerve head changes and perimetry findings such as mean deviation (MD) and Glaucoma Hemifield Test. In Group A, after *Koshtha Shodhana* and *Nasya, Tarpana* and *Ashchyotana* with *Shigru Pallava Arka* were done locally and *Punarnavashtaka Kwatha* and *Gokshuradi Guggulu* were given internally for 52 days along with modern antiglaucoma eye drop and in Group B, patients already taking antiglaucoma eye drop were kept under observation for 2 months. **Results:** Patients in Group A showed better results in blurred vision, FCPG, DDA, VFD, headache, BCVA, IOP and MD. Patients in Group B showed better results in blurred vision and FCPG. A comparison of both groups showed significant results in blurred vision, DDA, VFD, BCVA, IOP and MD. **Conclusion:** The clinical study concludes that Ayurvedic treatment protocol along with antiglaucoma eye drop in Group A patients was found to be more effective in reducing the IOP and controlling the progression of GON along with modern anti-glaucoma eye drop. Early diagnosis and proper management can prevent, arrest, or delay progression of POAG.

Keywords: *Gokshuradi Guggulu*, primary open-angle glaucoma, *Punarnavashtaka Kwatha*, *Shigru Pallava Arka*

Introduction

Glaucoma is the second leading cause of irreversible blindness worldwide and third leading cause in India. It is widely termed as "sneak thief of sight" and "silent killer of vision" because of its asymptomatic progression. Globally, primary open-angle glaucoma (POAG) affects more than angle-closure glaucoma (ACG) with a ratio of 3:1.[1] Glaucoma was estimated to affect 60.5 million individuals worldwide by the year 2010.[2] In India, an estimated approximately 11.2 million people aged 40 years will have glaucoma and among them 6.48 million individuals are affected with POAG.[3] According to the NPCB-WHO survey (1986–1989), glaucoma accounts for 5.80% of total blindness in India.[4]

POAG is a multifactorial disease which is affected by multiple factors such as mechanical, vascular and cellular factors; hence, the treatment should also be multilane which includes diuretic for lowering the intraocular pressure (IOP), *Rasayana* which delays the senile changes and *Chakshushya* which helps protect the vision, etc. Previous research works have been done on *Punarnavashtaka Kwatha* and *Gokshura Choorna* individually at two centers to control the IOP.[5]

Tarpana and *Ashchyotana* are powerful ocular administration methods used in Ayurveda for effective topical delivery and desired therapeutic action of drug. *Shigru Pallava Arka* for *Tarpana* and *Ashchyotana* (eye drops) are being used by ophthalmic practitioners on glaucoma patients and they report good results but relevant scientific data are not available.

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Hence, the study was planned to evaluate the efficacy of *Ashchyotana* and *Tarpana* with *Shigru Pallava Arka,* oral *Chakshushya* and diuretic medication with *Punarnavashtaka Kwatha* and *Gokshuradi Guggulu* in the management of POAG along with modern antiglaucoma eye drop.

Materials and Methods

A total of 30 patients, from the Department of *Shalakya Tantra*, Institute for Postgraduate Teaching and Research in Ayurveda (IPGT and RA), Jamnagar, Gujarat, were registered in this randomized parallel-group clinical trial. A prior written informed consent was taken from each and every patient. The clinical study was started after getting clearance from the institutional ethics committee (No. PGT/7/-A/Ethics/2014-15/1538 dated 2/9/14) and the study was also registered under the Clinical Trials Registry-India (CTRI/2016/02/006582).

Inclusion criteria

Patients aged 30–70 years diagnosed with POAG having IOP <21 mmHg (normotensive glaucoma) or IOP >21 mmHg and visual acuity >6/60 with clear media of male and female both sexes were included in the study.

Exclusion criteria

Patients with all types of primary ACG, cataract, secondary and developmental glaucoma including exfoliative glaucoma, pigmentary glaucoma, trauma-induced inflammatory glaucoma, end-stage (advanced) glaucomatous optic neuropathy or ophthalmic artery and visual acuity <6/60 were excluded from the study.

Grouping and Posology

A total of 30 participants were registered in this randomized parallel-group clinical trial. All the patients were randomly assigned into two groups, Group A and Group B ($n = 15$ each), by adopting lottery method for randomization.

Group A (trial group)

First, *Erandabhrishta Haritaki* 5–10 g HS was given for *Koshtha Shodhana* for 3 days.

After that, *Nasya Karma* with *Anu Taila* was carried out for 7 days; after *Nasya*, 7 days gap was given. Then, *Tarpana* with *Shigru Pallava Arka* was done for 7 days in 3 courses with an interval of 7 days.

Punarnavashtak Kwatha, Gokshuradi Guggulu orally and *Ashchyotana* with *Shigru Pallava Arka* were started from the 1st day of *Nasya Karma* and continued up to the completion of therapy. With this, the additional management was adopted, which included brimonidine (0.2%) and timolol (0.5%) topical antiglaucoma (IOP lowering) treatment.

Group B (control group)

In this group, patients already taking brimonidine 0.2% and timolol 0.5% topical antiglaucoma (IOP lowering) treatment were kept under observation for 2 months as a control group.

Total duration of treatment was: 52 days

Follow up: 1 month for both groups.

Raw drugs were collected and formulation prepared in the Pharmacy, IPGT and RA, Gujarat Ayurveda University (GAU), Jamnagar. *Shigru* leaves for *Ashchyotana* and *Tarpana* were collected from the premises of the institute campus and *Arka* was prepared in the *Rasa Shastra* Department, IPGT and RA, GAU, Jamnagar. The details of *Punarnavashtaka Kwatha* and *Gokshuradi Guggulu* are summarized in Tables 1 and 2.

All these drugs were identified and authenticated in the Pharmacognosy Laboratory, IPGT and RA, Gujarat Ayurved University, Jamnagar.

Criteria for assessment

1. Subjective parameters such as blurred vision, delayed dark adaptation (DDA), frequent changes in presbyopic glasses, visual field defect (VFD) and headache were assessed with the help of grading in clinical research proforma
2. Objective parameters such as visual acuity using Snellen chart, IOP using Schiotz tonometry, direct and indirect ophthalmoscopic examination for optic nerve head (ONH) evaluation, and visual field evaluation by automated perimetry were used to obtain their values.

Statistical analysis

Wilcoxon matched-pair signed-rank test and paired *t*-test were used to assess the results for individual groups.

Table 1: Ingredients of *Punarnavashtaka Kwatha*

Ingredients	Botanical name	Parts used	Ratio
Punarnava	*Boerrhavia diffusa* Linn.	Whole plant	1 Part
Nimba	*Azadirahcta indica* A. Juss.	Stem bark	1 Part
Patola	*Trichosanthes dioica* Roxb.	Leaves	1 Part
Shunthi	*Zinziber officinale* Roscoe.	Rhizome	1 Part
Kutki	*Picrorhiza kurroa* Royle ex Benth.	Rhizome	1 Part
Guduchi	*Tinospora cordifolia* (*wild.*) Mires ex Hook.f & Jhoms	Stem	1 Part
Daruharidra	*Berberis aristata* Roxb.Loud.	Heart wood	1 Part
Haritaki	*Terminalia chebula* Retz.	Pericarp	1 Part
Jala	Water		16 Part

Table 2: Ingredients of *Gokshuradi Guggulu* (*Sharangdhara Samhita Madhyamkhanda*)

Ingredients	Botanical name	Parts used	Ratio
Trikatu-		Rhizome	3 part
Shunthi	*Zinziber officinale* Roscoe.	Fruit	(1-1-1
Maricha	*Piper niegrum* Linn.	Fruit	part each)
Pippali	*Piper longum* Linn.		
Triphala-		Pericarp of	3 part
Haritaki	*Terminalia chebula* Retz.	each drug	(1-1-1
Vibhitaka	*Terminalia bellerica* Roxb.		part each)
Amalaki	*Emblica officinalis* Gaertn.		
Guggulu	*Commiphora mukul* Engl.	Oleoresin	7 part
Musta	*Cyperus rotundus*	Rhizome	1 part
Gokshura	*Tribulus terrestris* Linn.	Fruit	28 part

Unpaired *t*-test and Chi-square tests were used for comparison of results between the groups using SigmaStat software (version 3.1). 2005 developed by Jandel Scientific Software.

Results

Out of total registered patients, 2 participants discontinued the study (i.e., 6.67% discontinued the treatment), 1 in Group A and 1 in Group B and the remaining 28 patients, 14 in Group A and 14 in Group B, completed the treatment.

For the evaluation of results of symptoms within the group, Wilcoxon matched-pair signed-rank test was applied (paired data). In both the groups, there was a statistically significant improvement in blurred vision, frequent changes of presbyopic glasses (FCPG), DDA, VFD and headache in Group A and significant results were observed in blurred vision and FCPG in Group B [Table 3].

For the evaluation of results for objective parameters within the groups (paired data), paired *t*-test was used. In Group A, a statistically significant improvement was found in best-corrected visual acuity (BCVA), IOP and mean deviation (MD) [Table 4].

Comparison of difference of results between Group A and Group B

A statistically significant change was assessed on comparison (unpaired data) of difference between Group A and Group B with Chi-square test on symptoms such as blurred vision, DDA and VFD [Table 5].

A statistically significant change was assessed on comparison (unpaired data) between Group A and Group B with unpaired *t*-test on objective parameters such as BCVA, IOP and MD [Table 6].

In Group A, 57.14% patients showed moderate relief, 28.57% showed mild relief, 7.14% showed no relief, 7.14% showed marked relief and no patient was completely cured, i.e., 0%. In Group B, 78.57% patients showed no relief, 14.28% showed mild relief, 7.14% showed moderate relief and no patient showed marked relief and completely cured, i.e., 0% [Table 7].

Discussion

Out of total registered patients, 2 (6.67%) discontinued the treatment, 1 in Group A and 1 in Group B and the remaining 28 patients, 14 in Group A and 14 in Group B, completed the treatment. One patient had his/her busy working schedule so

Table 3: Effect of treatment on symptoms of primary open-angle glaucoma (Wilcoxon matched-pairs signed-ranks test)

Group	Eye	*n*	Mean		Different of mean	Difference of SD	Difference of SE	Percentage	*W*	*t*		*P*
			BT	AT						Positive	Negative	
Effect of treatment on blurred vision												
Group A	Right	13	1.307	0.076	1.230	0.438	0.121	94.11	−91	0.0	−91	<0.001
	Left	13	1.076	0.153	0.923	0.277	0.076	85.71	−78	0.0	−78	<0.001
Group B	Right	14	1.357	0.5	0.857	0.662	0.177	63.15	−78	6.5	−84.5	0.003
	Left	14	1.285	0.428	0.857	0.662	0.177	66.67	−78	6.5	84.5	0.003
Effect of treatment on frequent changes of presbyopic glasses												
Group A	Right	8	1.125	0.125	1.00	0.00	0.00	88.89	−36	0.0	−36	0.008
	Left	8	1.125	0.125	1.00	0.00	0.00	88.89	−36	0.0	−36	0.008
Group B	Right	8	1.125	0.375	0.875	0.640	0.226	70.00	−21	0.0	−21	0.031
	Left	8	1.125	0.375	0.875	0.640	0.226	70.00	−21	0.0	−21	0.031
Effect of treatment on delayed dark adaptation												
Group A	Right	7	1.00	0.00	1.00	0.00	0.00	100	−28	0.0	−28	0.016
	Left	7	1.00	0.00	1.00	0.00	0.00	100	−28	0.0	−28	0.016
Group B	Right	12	1.00	0.583	0.416	0.514	0.148	41.67	−15	0.0	−15	0.063
	Left	12	1.00	0.583	0.416	0.514	0.148	41.67	−15	0.0	−15	0.063
Effect of treatment on visual field defect												
Group A	Right	7	1.00	0.142	0.857	0.377	0.142	85.71	−21	0.0	−21	0.031
	Left	8	0.857	0.25	0.625	0.744	0.263	71.42	−20	4.0	−24	0.109
Group B	Right	12	0.916	0.75	0.166	0.577	0.166	18.18	−5	2.5	−7.5	0.375
	Left	12	0.833	0.75	0.083	0.668	0.192	10.00	−3	6.0	−9	0.813
Effect of treatment on headache												
Group A		8	1.125	0.00	1.125	0.353	0.125	100	−36	0.0	−36	0.008
Group B		7	1.00	0.285	0.714	0.487	0.184	71.42	−15	0.0	−15	0.063

W: Wilcoxon matched-pairs signed-ranks test constant, *n*: Number of eyes presented with this complaint, *t*: Constant, SD: Standard deviation, SE: Standard error, BT: beforer treatment, AT: After treatment

Table 4: Effect of treatment on objective parameters of primary open-angle glaucoma (paired' test)

Group	Eye	*n*	Mean		Different of mean	Percentage	Paired *t*-test				
			BT	AT			Different of SD	Different of SE	*t*	df	*P*
Effect of treatment on best-corrected vision											
Group A	Right	12	1.500	0.583	0.916	61.11	0.514	0.148	6.166	11	<0.001
	Left	12	1.833	0.916	0.916	50.00	0.514	0.148	6.166	11	<0.001
Group B	Right	14	2.285	2.214	0.071	3.12	0.615	0.164	0.434	13	0.671
	Left	14	2.785	2.642	0.142	5.12	0.770	0.205	0.693	13	0.500
Effect of treatment on IOP											
Group A	Right	14	4.00	2.071	1.928	48.21	0.997	0.266	7.235	13	<0.001
	Left	14	4.214	2.142	2.071	49.15	0.997	0.266	7.771	13	<0.001
Group B	Right	14	3.142	3.00	0.142	4.54	0.949	0.253	0.563	13	0.583
	Left	14	3.428	3.142	0.285	8.33	0.913	0.244	1.169	13	0.263
Effect of treatment on mean deviation											
Group A	Right	9	2.666	1.666	1.000	37.50	1.000	0.333	3.000	8	0.017
	Left	11	2.545	1.363	1.181	46.42	1.662	0.501	2.357	10	0.040
Group B	Right	12	2.833	3.000	−0.166	−5.88	1.466	0.423	−0.394	11	0.701
	Left	12	2.750	3.000	−0.250	−9.09	1.484	0.428	−0.583	11	0.571
Effect of treatment on GHD											
Group A	Right	12	2.250	1.583	0.666	29.62	1.154	0.333	2.000	11	0.071
	Left	13	1.692	1.769	−0.076	−4.54	1.037	0.287	−0.267	12	0.794
Group B	Right	14	1.785	2.142	−0.387	−20.0	0.841	0.225	−1.587	13	0.136
	Left	13	2.000	2.153	−0.153	−7.69	0.987	0.273	−0.561	12	0.584

t: Constant, df: Degree of freedom, *n*: Number of eyes presented with this complaint, IOP: Intraocular pressure, GHD: Glaucoma hemifield defect, SD: Standard deviation, SE: Standard error, BT: Before treatment, AT: After treatment

Table 5: Comparison of difference of symptoms between Group A and Group B (Chi-square test)

Symptom	Group	Number of eyes	<50%, *n* (%)	>50%, *n* (%)	χ^2	*P*
Blurred vision	Group A	26	3 (5.56)	23 (42.59)	4.056	0.044
	Group B	28	11 (20.37)	17 (31.48)		
Frequent changes of presbyopic glasses	Group A	16	4 (12.5)	12 (37.5)	0.205	0.651
	Group B	16	2 (6.25)	14 (43.75)		
Delayed dark adaptation	Group A	14	0	14 (36.84)	10.545	0.001
	Group B	24	14 (36.84)	10 (26.31)		
Visual field defect	Group A	15	3 (7.69)	12 (30.76)	9.132	0.003
	Group B	24	18 (46.15)	6 (15.38)		
Headache	Group A	8	0	8 (53.33)	0.744	0.388
	Group B	7	2 (13.33)	5 (33.33)		

n: Number of eyes having given symptom of glaucoma

he/she was having the treatment regularly and another patient was transferred from Jamnagar and hence discontinued the study.

Maximum numbers of patients, i.e., 40%, were in the age group of 51–60 years. As the age advances, risk factors such as DM and HTN increases along with the occurrence of neurodegenerative disorders which may trigger the glaucoma pathogenesis.[6-8] About 56.67% patients were males. Maximum numbers of patients, i.e., 33.33%, were homemakers. Almost 84.61% of 13 female patients of both groups were in menopausal stage. Recent researches have shown that menopause, especially early menopause, is associated with high-risk POAG.[9] Patients with a negative family history of POAG were 66.67% and with a positive family history of POAG were 33.33%. Out of total registered patients, 53.33% patients were under medical management for glaucoma.

Findings of both the groups suggests that selected drugs are effective, but better results were observed in Group A where both the drugs were given to the participants. This can be because of administration of local IOP-reducing eye drop alone is not sufficient to stop the progression of POAG. Hence, *Chakshushya, Rasayana*, diuretic and neuroprotection strategy along with IOP-lowering effect of Ayurvedic management, is important to stop the progression of primary open-angle glaucomatous optic atrophy.

Table 6: Comparison of difference of signs between Group A and Group B (unpaired *t*-test)

Signs	Group	Mean	*n*	SD	SE	*P*	*t*	df
Best-corrected visual acuity	Group A	0.917	24	0.504	0.103	<0.001	4.783	50
	Group B	0.107	28	0.685	0.130			
Intraocular pressure	Group A	2.00	28	0.981	0.185	<0.001	7.035	54
	Group B	0.214	28	0.917	0.173			
Mean deviation	Group A	1.100	20	1.373	0.307	0.004	3.060	42
	Group B	−0.208	24	1.444	0.295			
GHD	Group A	0.280	25	1.137	0.227	0.063	1.901	50
	Group B	−0.259	27	0.903	0.174			

n: Number of eyes having given signs ofglaucoma, SD: Standard deviation, SE: Standard error, *t*: Constant, df: Degree of freedom

Table 7: Overall assessment of therapy

Result	Group A, number of patients (%)	Group B, number of patients (%)
No relief (below 25%)	1 (7.14)	11 (78.57)
Mild relief (26%-50%)	4 (28.57)	2 (14.28)
Moderate relief (51%-75%)	8 (57.14)	1 (7.14)
Marked relief (above 75%)	1 (7.14)	0
Complete relief (100%)	0	0
Total	14 (100)	14 (100)

Punarnavashtaka Kwatha contains drugs, namely *Punarnava, Nimba, Patola, Sunthi, Kutaki, Guduchi, Daruharidra and Haritaki*; all drugs have *Mootrala, Shothahara, Rasayana*, and immunomodulatory effect.[10]

Gokshuradi Guggulu contains nine drugs which are *Gokshura, Guggulu, Triphala, Trikatu* and *Musta*. *Triphala*[11] is a well-known *Chakshushya* and *Rasayana* drug and among them. *Amalaki* is rich in antioxidant vitamins.[12] *Trikatu* has *Ushna,* and *Teeksna Guna* and *Ushna Virya* act as *Srotoshodhaka* and *Amapachaka. Musta* has anti-inflammatory and antioxidant activity. It has superoxide anion scavenging, hydroxyl radical scavenging, nitric oxide scavenging, metal-chelating activity and lipid peroxidation inhibition activity.[13] *Gokshura* is *Srotovishodhaka*, immunostimulant, *Mootrala* (diuretic), and *Shothahara*. *Guggulu* is *Shothahara, Vednasthapana* drug; all these drugs through its their properties are useful to relieve the signs and symptoms of POAG.

Multi centric studies with larger sample size on the same drugs should be carried out to bring authenticity to our science. Photo-documented studies are required to demonstrate the improvement in signs. Higher investigation for evaluation of ONH and retinal nerve fiber layer analysis should be done, as optical coherence tomography, pachymetry etc.

Conclusion

Group A (trial group) patients showed better results in blurred vision, FCPG, DDA, VFD, headache, BCVA, IOP and MD. Group B (control group) patients showed better results in blurred vision and FCPG. None of the groups had a significant effect on GHD and laboratory investigations. No changes were found in ONH analysis in both groups.

A comparison of both groups showed significant results in blurred vision, DDA, VFD, BCVA, IOP, and MD.

The clinical study establishes that Ayurvedic treatment protocol along with antiglaucoma eye drop in Group A patients was found to be more effective. The test drugs can reduce the IOP and control the progression of glaucomatous optic atrophy along with modern antiglaucoma eye drop. An early diagnosis and proper management on *Doshika* lines can prevent, arrest, or delay the progression of POAG.

Limitations of study

- Due to time constraints in postgraduation, it was not possible to give a long time for the study
- Due to time constraints, it was not possible to observe the changes on nerve fiber layer and ONH
- Fundus photographs were not included in this study.

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Conflicts of interest

There are no conflicts of interest.

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