Research Article

EFFECT OF *NIRGUNDI* (*VITEX NEGUNDO* LINN.) *PATRA ARKA* AS *ASCHOTHANA* (EYE DROPS) IN CATARACT-A CLINICAL STUDY

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ABSTRACT

Purpose: Age-related cataract is one of the leading causes of blindness and avoidable visual impairment in the world. There is no time-tested, FDA-approved, or clinically proven medical treatment exists till date to delay, prevent, or reverse the progression of senile cataract. *Nirgundi* (*Vitex negundo*) is a *Chakshushya* single drug mentioned in Ayurvedic classics. Various animal experimental study and invitro studies in recent years using flavonoids extracted from leaves of *Vitex negundo* on selenite induced cataract models proved to be beneficial in arresting the progression of cataract. Hence a clinical study with *Vitex negundo* eye drops in the form of *Arka* was planned with primary objective to assess the effect of *Nirgundi patra arka* as *Aschotana* (eye drops) in pre senile cataract. **Methods:** The study design was interventional pre and post evaluation without control. Patients were advised to instill *Nirgundi patra arka* two drops thrice daily i.e. 6 am, 12 pm and 6pm for a period of 6months. Log mar visual acuity score and contrast sensitivity score were recorded before treatment, 3rd month of treatment, after treatment, 9th month (1st follow up) and 12th month (2nd follow up). Slit lamp photographs were recorded before treatment and 12th month. Study and follow up were done in 31 eyes. **Result:** The intervention is statistically significant while considering visual acuity and contrast sensitivity. All the 27 cases of nuclear cataract responded to the intervention, while only 83.3% of posterior sub capsular cataract and 60% of cortical cataract showed response. But the change was not significant statistically. **Conclusion:** The intervention was effective in improving visual acuity and contrast sensitivity in all types of pre senile cataract. Clinical assessment revealed the study was effective in preventing the progression of pathogenesis in early stage of nuclear cataract.

KEYWORDS: *Arka, Salakyatantra, Nirgundi, Aschothana,* Eye Drops, Cataract.

INTRODUCTION

Globally 285 million people are affected by visual impairment, of which 80% of visual impairment is avoidable. Cataract (33%) and uncorrected refractive errors (42%) are the leading causes of avoidable visual impairment. Unoperated Cataract (51% i.e. about 20 million people) and Glaucoma (8%) are the leading causes of avoidable blindness (2010). The WHO estimates that cataract blindness will reach 40 million by 2020[1]. Aging is the most common aetiological factor contributing to the disease cataract. There is no single universally accepted pharmacological agent that can either inhibit or reverse the progression of cataract.

At present, the most effective conventional treatment of cataract is the surgical extirpation of opacified lens and IOL implantation. In spite of the progress made in surgical techniques during the last ten years, cataract remains the leading cause of visual impairment in all areas of the world, except for developed countries. The WHO proposes that between 2000 and 2020, number of cataract surgeries performed worldwide have to be tripled to keep pace with the need of population.[1]

Department of Biochemistry of Kerala University, Karyavattom campus conducted various invivo and invitro studies, using flavonoids extracted from leaves of *Vitex negundo* on selenite induced cataract models in the recent years, considering the role of free radical mediated oxidative stress in pathogenesis of cataract[2-6]. Luteolin is a bioactive flavonoid isolated and characterized from the leaves

of Vitex negundo. Studies were conducted to prove the role of luteolin in preventing selenite induced oxidative stress and cataract. This was done by extraction of lens from Sprague Dawley strain rats and was organ cultured in DMEM medium.

After experimental study period, lenses were taken out and various parameters were studied. It was found that luteolin treatment abated selenite induced oxidative stress and cataractogenesis by maintaining antioxidant status, reducing Reactive Oxygen Species Generation and lipid peroxidation in the lens. This firmly demonstrated the anticataracto-genic effect of luteolin by virtue of its antioxidant property. [2]

On the basis of the above studies this clinical study is attempted as the next phase. The main intention of the study was to assess the effect of drug in preventing or reversing the progression of cataract at the pre senile stage. So the age group of the study was pre fixed as 40-50.

Acharyas explained various diseases affecting eye and visual function in Ayurveda Samhithas. The progressive nature of blindness in *Thimira-kacha-linganasa* has clinical similarity with progressing nature of senile cataract. The similarity in surgery done in *Kaphaja linganasa* points the condition to be that of mature cataract. So the disease cataract may be compared to *Thimira-kacha-linganasa.*

Among all *Kalpana, Arka kalpana* is mentioned as the most potent form of drug preparation by Lord Ravana in *Arkaprakasa[7].* It is user friendly and has long shelf life of 6 months to 1 year. It does not require any preservatives; frequent dose of medicines can be easily administered. Above all various *Arka* preparations in the form of eye drops have been using in our department for long, which are proved to be beneficial in various ocular diseases.

The disease cataract requires long period of medication and long duration of follow up. Considering all these factors *Arka* prepared from *Nirgundi* leaves (blue flowered variety) in the form of *Aschothana* was planned in the study as intervention drug. The pilot study conducted in the Out Patient Department is found to be relatively safe, user friendly and beneficial.

In this clinical trial, 51 eyes of patients between the age group 40-50 years having the features of cataract, based on slit lamp photographs were selected. Visual acuity was assessed by the log Mar visual acuity chart and contrast sensitivity was assessed by the Pelli Robson contrast sensitivity chart. These patients were given *Nirgundi patra arka* in sterile glass dropper bottles and was advised to instill two drops of *Arka* three times daily (6am, 12noon, and 6pm) for a period of 6 months.

Out of these 51 eyes, only 31 eyes came regularly to collect medicines and for follow up. Remaining 20 cases were considered as dropouts of the study. Assessment of visual acuity and contrast sensitivity were done in 3rd month during medication, 6th month after treatment and in 9th and 12th month as the follow up.

Slit lamp photographs were taken from the Regional Institute of Ophthalmology prior to the treatment and 12th month during last follow up period. Study was supervised and monitored by the co-guide from Regional Institute of Ophthalmology during the selection of patients, throughout the study period and during grading of cataract. Grading of cataract was done before treatment and during last follow up (12th month) based on LOCS III and was analyzed.

AIM AND OBJECTIVE OF THE STUDY

To evaluate the effect of *Nirgundi patra arka* as *Aschothana* (eye drops) in cataract.

Methodology

Study Design

Interventional study with pre and post evaluation without control.

Study Setting

Department of *Salakyatantra*, Govt. Ayurveda College, Trivandrum.

Study Population

Patients diagnosed as having cataract from OPD of *Salakyatantra*, Govt: Ayurveda College, Trivandrum, fulfilling the inclusion and exclusion criteria.

Inclusion Criteria

Patients having cataract aged 40-50 irrespective of sex.

Exclusion Criteria

1. Patients suffering from inflammatory and infective disease of eyeball and its appendages
2. Patients on local and systemic steroid medication.
3. Patients with history of steroid intake.
4. Patients having Diabetes Mellitus
5. Traumatic cataract

Sample Size

The proposed sample size was 40 eyes, considering the long duration of study and follow up 51 eyes were selected. Among them only 31 cases came regularly to collect medicine and for follow up. Remaining 20 cases were considered as drop outs of the study.

Study Tool
Case proforma
A structured questionnaire
Investigations

- LogMar Chart
- Pelli-Robson Contrast Sensitivity Chart
- Slit lamp photography

Procedure

The patients diagnosed as having cataract and registered in OPD of Salakyatantra, Govt. Ayurveda College Hospital, Trivandrum, are selected as per inclusion and exclusion criteria.

Preparation of medicines

Fresh leaves of *Nirgundi* (blue variety) were collected in the morning and were washed properly with water. Equal amount of distilled water was added to it and kept in sunlight for 1 *Gadi*, i.e. 24 minutes.[8] Then immediately transferred into the *Arka yantra* (distillation unit) and subjected to distillation process. The distillate obtained was filtered under sterile conditions collected to glass bottle. This was kept in medicinal shelf under hygienic conditions away from light and heat.

Analytical study of *Nirgundi patra arka*
Organoleptic Characters

Colour	:	Transparent.
Odour	:	Smell of *Nirgundi.*
Touch	:	Cold
Taste	:	As that of *Nirgundi*
Consistency	:	Liquid

Analytical Values

Specific gravity	:	1.0001
Refractive index	:	1.30
Solid content	:	0.14 %
Volatile oil content	:	0.5 %
PH	:	5.81

T.L.C

T.L.C of Ethyl acetate extract of *Nirgundi patra arka* on silica gel plate using solvent system Toluene: Ethyl acetate: Formic acid in the ratio 20:5:1 under U.V (366nm) one fluorescent zone at R_f:.5

Interventions

After all clinical examination and investigations they were given *Nirgundi patra arka* as eye drop and the procedure of administration was demonstrated to them. The patients were directed to instil eye drops for a period of 6 months two drops thrice daily (6am, 12noon, 6pm).

Assessment of the patients and follow up

Clinical evaluation and investigations was done prior to the commencement of intervention, i.e., before study and consecutive assessments was made on the 3rd month medication, 6th month after medication and subsequent every third month till one year as follow up to assess the outcome.

Outcome Variable

1. Change in contrast sensitivity by Pelli - Robson contrast sensitivity chart
2. Change in vision by Log Mar visual acuity chart
3. Grading of cataract using slit lamp photography

Statistical Analysis

Quantitative variables were described by mean, standard deviation, minimum and maximum. Paired comparison of quantitative variables were analysed by paired 't' test or 'Wilcoxon Signed Rank' test according to the nature of data. 'P' value of 0.05 was taken as the level of significance.

Ethical Considerations

- Consent from the patient.
- Consent from Head of institute.
- Consent from Regional Institute of Ophthalmology was obtained prior to study.

RESULTS

Out of 51 eyes selected for study 70.59% of eye were having nuclear cataract, 21.57% were with mixed type of cataract, 5.88% were with posterior sub capsular cataract and 1.96 % were having cortical type of cataract. This is because nuclear opacities are the most commonly seen type of age related cataract.
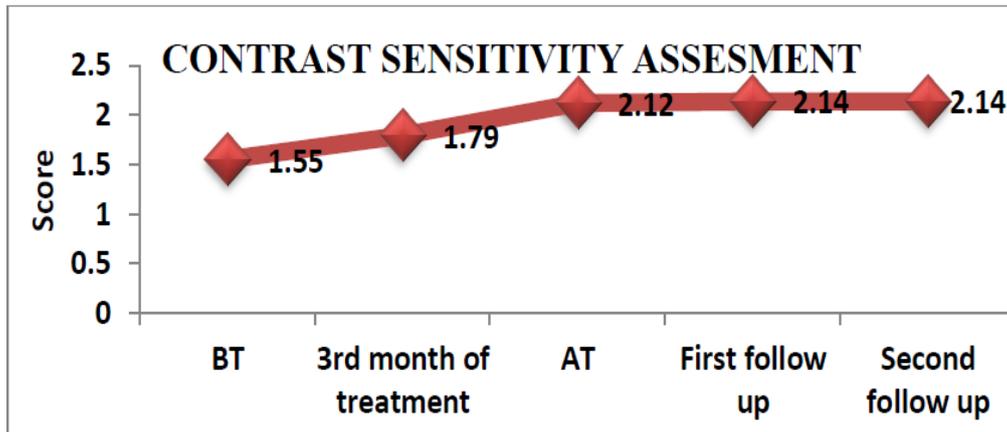
Table No: 1 Contrast Sensitivity Analysis

Assessment period	N	Contrast Sensitivity Assesment	
		MEAN	SD
Before treatment-BT	31	1.55	0.36
During treatment-DT	31	1.79	0.24
After treatment-AT	31	2.12	0.11
1st follow up-AF1	31	2.14	0.11
2nd follow up-AF2	31	2.14	0.11

Graph No: 1

CONTRAST SENSITIVITY ASSESMENT

Table No: 2 Contrast Sensitivity Comparison

Paired comparison using paired 't' test	Paired Differences		Paired t test	
	MEAN	SD	t	P
BT- DT	.240	.283	4.734	<0.001
BT- AT	.573	.325	9.816	<0.001
BT-AF$_1$	.592	.330	9.974	<0.001
BT- AF$_2$	.592	.333	9.906	<0.001
AT- AF$_2$	.019	.051	2.108	.043

 Average change in contrast sensitivity between BT & DT, BT & AT, BT & AF1, BT & AF $_2$ and AT & AF$_2$ is given. The p value obtained shows that difference is statistically significant.

Table No: 3 Logmar Visual Acuity Analyses

Assessment period	N	Logmar Visual Acuity Assessment	
		MEAN	SD
Before treatment-BT	31	0.56	0.25
During treatment-DT	31	0.49	0.23
After treatment-AT	31	0.40	0.20
1st follow up-AF$_1$	31	0.39	0.19
2nd follow up-AF$_2$	31	0.40	0.20

Graph No: 2

LOGMAR VISUAL ACUITY ASSESMENT
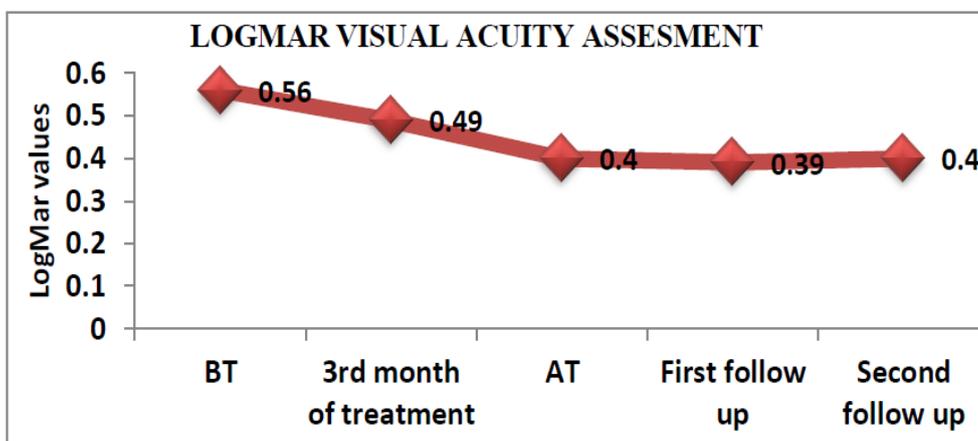
Table No: 4 Log Mar Visual Acuity Comparison

Paired comparison	Paired Differences		Paired t test	
	MEAN	SD	t	P
BT- DT	.071	.101	3.926	<0.001
BT- AT	.155	.155	5.577	<0.001
BT-AF1	.165	.156	5.868	<0.001
BT- AF2	.161	.154	5.823	<0.001
AT- AF2	.006	.025	1.438	.161

Average change in log Mar visual acuity between BT & DT, BT & AT, BT & AF1, and BT & AF $_2$ given. The p value obtained shows that difference is statistically significant. While comparing AT $-AF_2$,, the p value obtained is .161 which shows no significant improvement in visual acuity.

Assessment of Nuclear Cataract

Table No: 5 Analysis of data related to nuclear cataract

Nuclear Cataract	BT		AF2	
	N	%	N	%
Grade 1	9	33.3	12	44.4
Grade 2	18	66.7	15	55.6
Total	27	100.0	27	100.0
Wilcoxon signed rank test Z=1.732: P=0.083				

In the case of 27 nuclear cataract eyes, before treatment assessment revealed 33.3% (9 eyes) of grade I cataract and 66.7 % (18 eyes) of grade II cataract. During 12th month assessment 44.4 % (12 eyes) of grade I and 55.6 % (15 eyes) of grade II cataract were reported.

Graph No: 3
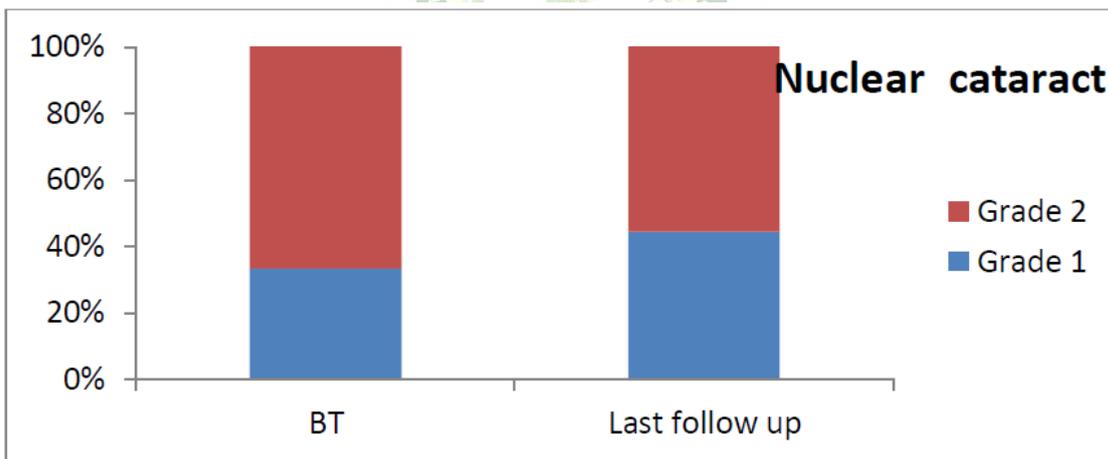
Here the calculated p value (0.083) is greater than 0.05.hence the test is statistically not significant, that means the change in grade of cataract with the intervention is not significant statistically.
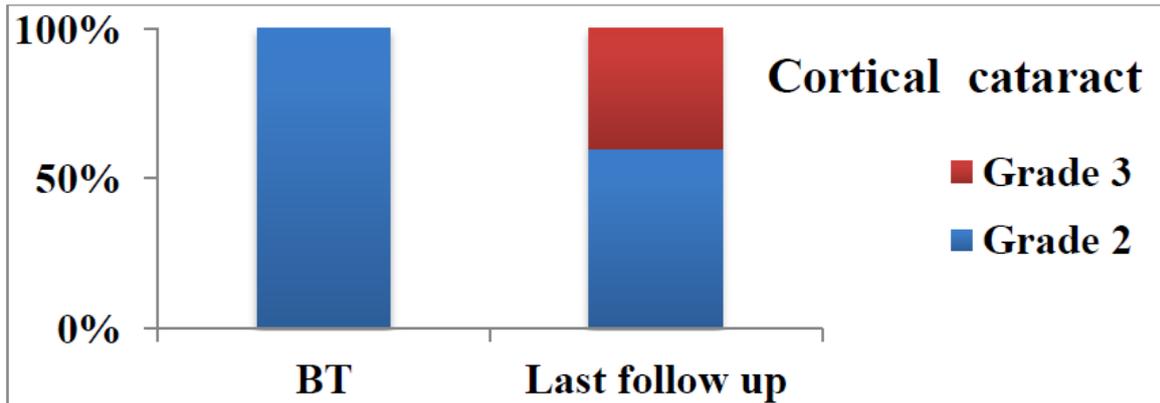
Assessment of Cortical Cataract

Table No: 6 Analysis of data related to cortical cataract

Cortical Cataract	BT		AF$_2$	
	N	%	N	%
Grade 2	5	100.0	3	60.0
Grade 3	0	0	2	40.0
Total	5	100.0	5	100.0
Wilcoxon signed rank test Z= 1.414: P=0.157				

In the case of 5 cortical cataract eyes, before treatment assessment revealed 100% (5 eyes) of grade II cataract and during 12th month assessment 60 % (3 eyes) of grade II and 40% (2 eyes) of grade III cataract were reported.

Graph No: 4

Here the calculated p value (0.157) is greater than 0.05.Hence the test is statistically not significant, that means the change in grade of cataract with the intervention is not significant statistically.

Assessment of Posterior Sub Capsular Cataract

Table No: 7: Analysis of data related to PSCC

	BT		AF$_2$	
PSCC	N	%	N	%
Grade 1	1	16.7	1	16.7
Grade 2	1	16.7	0	0
Grade 3	4	66.7	5	83.3
Total	6	100.0	6	100.0
Wilcoxon signed rank test z= 1.000 p=0.317				

In the case of 6 PSCC eyes, before treatment assessment revealed 16.17% (1 eye) of grade I cataract, 16.7 % (1 eye) of grade II and 66.7% of grade III. During 12th month assessment 16.7 % (1 eye) of grade I and 83.3 % (5 eyes) of grade III cataract were reported.

Graph No: 5
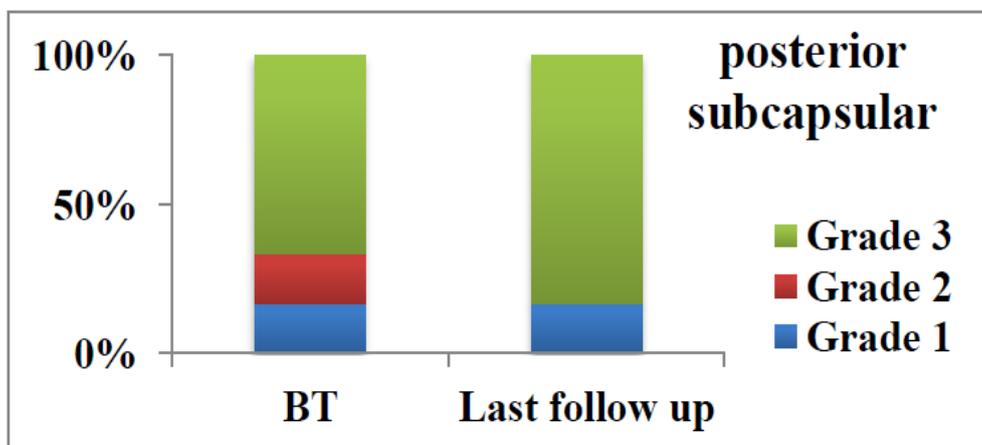
Images of Some Photographs Obtained [BT-AF$_2$]

Nuclear Cataract

Fig: 1 BT-grade II Fig: 2 AF2-grade I

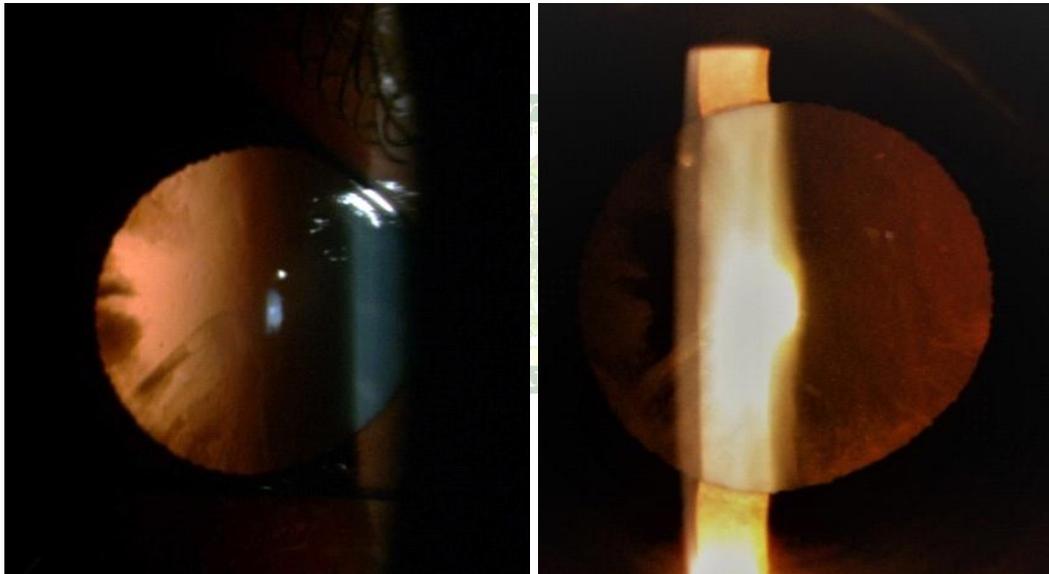**Cortical Cataracts**

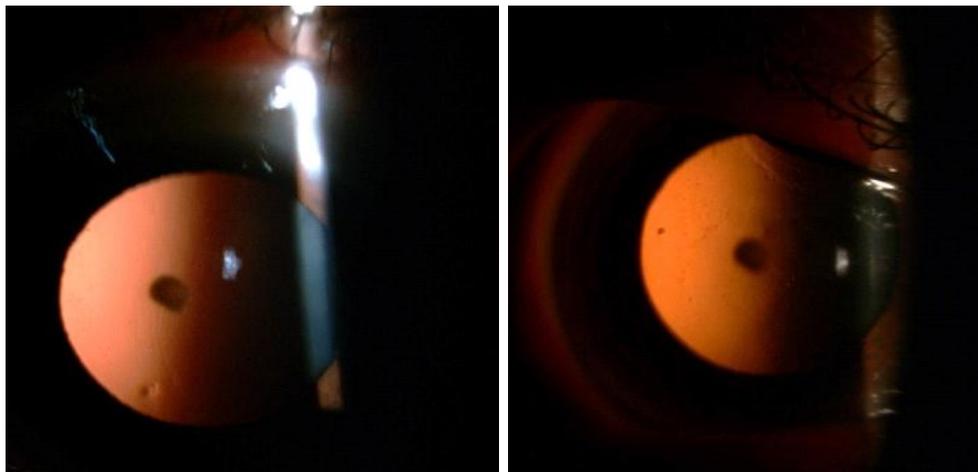**Fig: 5 BT Grade II Fig: 6 AT Grade III**

PSCC

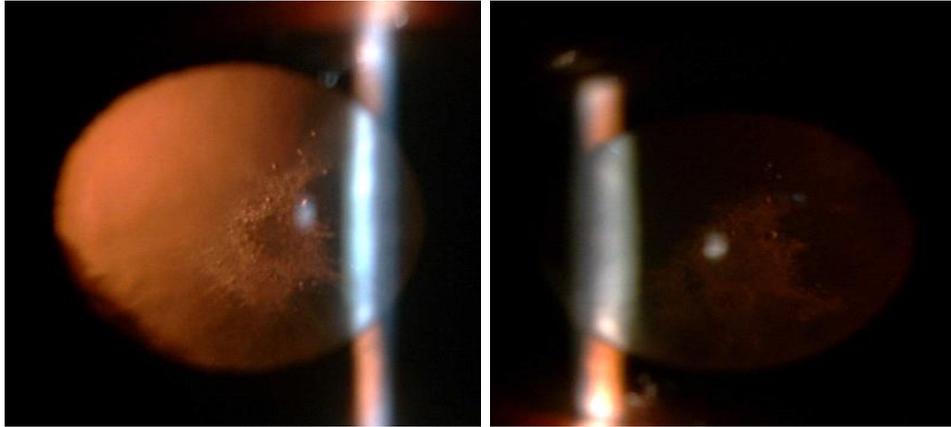**Fig: 7 BT Grade I   Fig: 8 AF2 –Grade I**

PSCC

Fig: 11 BT Grade III Fig: 12 AF2 Grade III

Here the calculated p value (0.317) is greater than 0.05. Hence the test is statistically not significant, that means the change in grade of cataract with the intervention is not significant statistically.

Summary

Statistically analyzed comparison results between BT-DT, BT-AT, BT–AF_1 and AT-AF_2 suggested there was significant improvement in contrast sensitivity. In the case of visual acuity there was significant improvement while comparing BT-DT, BT-AT, BT–AF_1 and BT-AF_2. There was no significant improvement in visual acuity on comparing AT –AF_2, but the improved visual acuity sustained and there was no deterioration of vision noted throughout follow up period.

Slit lamp photographs obtained shows that:

In case of nuclear cataract,

- The whole 33.3% of grade I cataract was responded with intervention and persisted in the state of grade I.
- Among 66.7% of grade II cataract, 55.6% remained in grade II and 11.12% improved to grade I. That means in the case of nuclear cataract the intervention is effective.

In the case of cortical cataract,

- Even though the sample size is small, 60% of grade 2 type responded with the intervention but the remaining were not.

In the case of posterior sub capsular cataract,

- Even though the sample size is small, 16.7% of grade 1 and 66.7% of grade 3 responded to the treatment but 16.7% were not responded.

The clinical study revealed that the intervention is effective in improving visual acuity and contrast sensitivity in all forms of cataract. That means the study is statistically significant while considering visual acuity and contrast sensitivity assessment. The intervention was more effective in nuclear cataract when compared with cortical and posterior sub capsular cataract in preventing the progress of pathogenesis. Here the study is not statistically significant but it can arrest the progression of cataract in the initial stage.

Probable Mode of Action of Drug

Nuclear Cataract

Vata vaigunya cause *Soshana* of *Drava guna* and *Kshaya* of *Snigdha guna* of *Kapha, which* increases *Sthira guna* of *Kapha* (*Kapha sanchaya* in lens). *Rooksha guna* of *Vata* leads to sclerotic changes in lens, and *Pitta vikrithi* cause accumulation of metabolic by-product *(Mala sanchaya). Nirgundi* is a drug having *Vata kaphahara* property[9] which normalize *Vikrutha gunas* of *vata* and *Kapha*. The *Thiktha kashaya rasa* of drug pacifies *Pitta dosha*. It posses deepana and *Chakshushya karma*[10], which help in maintaining function of *Pitta*. Thus help in maintaining the anti-oxidant state & prevent progression of cataract.

Cortical Cataract

Stage of hydration: Relative *Kapha vridhi* occurs in lens. The normal *Sthairya sangatha* property of the lens fibre is lost and *Vishyandhana, kledana* and *Gourava* occurs in the cortex of lens.

Denaturation of proteins: This stage may be inferred as loss of *Drava guna* and *Sneha guna* of normal soluble crystalline protein thereby increasing *Sthira* and *Rooksha guna*, transforming it into an insoluble form. *Vata kapha samanatwa* of *Nirgundi* normalize the *Vikritha gunas* of *Vata* and *Kapha* in cataract. Along with this *Sopha hara* property[10] also help in reversal of the stage of hydration

Posterior sub capsular cataract

Vikrithi of *Vata* occurs in old age to those who are resort to *Vatika ahara vihara*. *Gathi*, the property of *Vayu* is getting hampered and abnormal migration of lens epithelium occurs. Abnormal *Vibajana* by this

Vikrutha vayu results in the formation of aberrant lens fibres. *Vatahara* and *Chakshushya* nature of *Nirgundi* balancing *Vata* to its equilibrium stage.

Functional impairment in cataract

The *Chala* (accommodation, refraction, transport), *Visada* (transparency), *Sookshma* (permeation of light) *Gunas* of *Vata* and *Ushma guna (Alochaka agni)* of *Pitta* are impaired in cataract. *Vata kapha hara* property, *Ushna veerya,* and *Lagu guna* of *Nirgundi* helps in normalizing *Vikrutha gunas* of *Dosha* to a great extent. This improves transparency of lens and makes it permeable to light rays to pass through. *Deepana, Sophahara, Chakshushya karma* of *Nirgundi* also helps in maintaining normal function of lens. Thus contrast sensitivity and visual acuity improved in patients to a great extent.

CONCLUSION

Age related cataract is most common among all types of cataract. Nuclear cataract is the commonest form of age related cataract. The intervention was effective in improving visual acuity and contrast sensitivity in all types of age related cataract in the early stage. Clinical assessment revealed the study was significant in preventing the progression of pathogenesis of nuclear cataract in the presenile stage. The study drug was found to be safe and user friendly Sample size was not adequate to minimize the sampling and systematic error. Long duration follow up was excused for the attrition of cases from the sample. Study has to be conducted by employing large sample size. Evaluation of biochemical changes on administration of medicine have to be studied incorporating the advanced technologies.

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