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COMPARATIVE STUDY BETWEEN ANJANA AND GHRITAPAAN IN THE MANAGEMENT OF SUSHKAKSHIPAKA (DRY EYE SYNDROME)

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ABSTRACT

Objective: Compare the clinical efficacy of Haridradi anjana and Vibhitakadi ghrita in the management of Sushkakshipaka (Dry Eye Syndrome). **Methods:** Ayurvedic formulations (Haridradi anjana and Vibhitakadi ghrita) were evaluated in a randomized, open lable pre and post trial study. four-arm, multicentre equivalence drug trial of 15 days dur- ation. A total of 40 eligible patients suffering from symptomatic Sushkakshipaka were enrolled and divided into 2 groups and monitored as per protocol. **Results:** Differences between the intervention arms for mean changes in primary efficacy variables were within the equivalence range by intent-to-treat and per protocol analysis. Statistically Extremely Significant relief were found in FBS, Burning sensation, Mucoid discharge, Dryness, Conjunctival congestion, Schirmer -1 test, TBUT ect in Group I and Statistically Extreamly Significant relief were found in FBS, Mucoid discharge, Dryness, Conjunctival congestion, TBUT and Tear Meniscus in Group II. Other adverse events were mild and did not differ by intervention. **Conclusion:** In this 45 days trial study of Sushkakshipaka, Ayurvedic formulations (Haridradi anjana and Vibhitakadi ghrita) sig nificantly reduced Dryness and improved Tear production. The unexpected itching rise requires further safety assessment.

KEYWORDS: Haridradi anjana, Vibhitakadi ghrita, Sushkakshipaka.

INTRODUCTION

Vision is unarguably the most important of the five senses, as mentioned in our Ayurvedic texts. Hence, all sincere efforts should be made by all to protect the eyes. Without eyes the day and night are equal, so eyes must be protected with extreme care. Sushkashipaka[1] is a Sarvagat akshiroga which can be correlated to Dry Eye Syndrome in modern ophthalmology.

Dry eye disease is a common yet frequently under-recognized clinical condition whose etiology and management challenge clinicians and researchers alike. Dry Eye Syndrome is a highly prevalent 3.5-33% across different population (Am J Opthalmol Aug 2003) yet largely undiagnosed condition that can substantially affect the quality of life. Though underestimated by many just as an ocular irritation the discomfort related to Dry Eye Syndrome is grave; as patients of severe DES[2] willing to trade 1.6 years of their expected 10-year longevity to be free of the condition that is comparable with Angina patients. If left untreated Dry Eye Syndrome can lead to visual morbidity. It may compromise the result of corneal, cataract and refractive surgery and successful contact lens fitting. The economic burden is reflected in loss of productivity, number of physician's office visits and the multibillion dry-eye therapeutic industry. Despite the magnitude of problem no definitive cure is available for Dry Eye Syndrome and palliative measures are inadequate too with symptoms often improving without achievement of cure causing frustration on the part of patient and physician.

While modern ophthalmology is struggling to find a definite cure for Dry Eye Syndrome Ayurvedic texts have given an elaborate account of Sushkakshipaka management. In lieu of above facts it was tempting to evaluate the effectiveness of formulations mentioned in classical Ayurvedic texts for the treatment of Sushkakshipaka; thus re-establishing the ancient therapy by means of through and intensive research. Thus the present study was undertaken entitled on **"**Comparative study between Anjana and Ghritapaan in the management of Sushkakshipaka w.s.r. to Dry Eye Syndrome".

AIMS AND OBJECTIVE

1. Conceptual and clinical study on Sushkakshipaka w.s.r. to Dry Eye Syndrome & its management with Ayurvedic principles.
2. Clinical evaluation of the efficacy of Haridradi Anjana in the management of Sushkakshipaka on various scientific parameters.
3. Clinical evaluation of the combined efficacy of Haridradi Anjan and Vibhitakadi Ghrita internally in the management of Sushkakshipaka on various scientific parameters.

MATERIAL AND METHODS

In the present study, 40 clinically diagnosed patients of Sushkakshipaka (Dry eye syndrome) were selected and randomly divided into two groups. Randomization was done on the basis of random number table. Patients attending the O.P.D. and I.P.D. of N.I.A. were screened having the signs and symptoms of Sushkakshipaka.

Inclusion criteria

- Age: 20 to 70 years
- Patient having specific symptoms of Sushkakshipaka (Dry eye syndrome).
- Patients of either sex were selected randomly.

Exclusion criteria

- Individuals above 70 years and below 20 yrs of age of either sex.
- Patient with impaired eyelid function as in Bell's palsy etc.
- Patients with lid globe apposition.
- Patients with infective pathologies of eye.
- Patients with severe systemic illness.

Investigations: ESR and RA factor tests were carried out to rule out other systemic diseases associated with Dry Eye in the patients.

Design of the study: This study is designed with an open label pre and post study evaluation method.

Intervention methods: Topical administrations of Haridradi Anjana 1 Vidangphal (1 drop) once daily and Haridradi anjana with oral administration of Vibhitakadi Ghrita (12 gm) twice a day for 15 days.

Duration of Trial- 15 days.

Follow up – Follow up was done once in 15 days for a period of one month.

Method of preparation of the Drugs

In Haridradi raskriya anjana[3], Haridra and Daruharidra were taken in equal quantity in churna form and kwath was prepared by adding 16 times water to the total weight of drugs and then reduced it to one fourth by boiling over heat. Then the kwath was filtered and it

mixed into Goghrita and add little amount of Sandhav lavan and paka was done in mandagni till it attained Raskriya form.

In Vibhitakadi ghrita[4], Amalaki, Vibhitak, Haritaki, Vasa, Nimba and Patola were taken in equal quantity in churna form and kalka was prepared by adding some amount of water. One part of kalka of all dravayas was mixed into 4 part morchita ghrita and then mixed with 16 part of jala and subjected to ghritapaka in mandagni. They both drug are prepared in NIA pharmacy.

Assessment criteria- It was done on the basis of symptoms and signs of Sushkakshipaka. (Table No I. showing Assessment criteria of Sushkakshipaka).

OBSERVATION AND RESULTS

Statistical analysis

The scoring criteria of assessment were analyzed statistically in terms of mean values of B.T. (Before Treatment), A.T (After treatment), S.D (Standard Deviation) and S.E (Standard Error). Various observations were made and results obtained were computed statistically using Student t- test and Wilcoxon matched pairs signed ranks test on Graph Pad Instat III software. Finally result were shown in terms of probability (p value) as $p>0.05$-Not Significant, $p<0.01$-Significant, $p<0.001$- Highly Significant $P<0.0001$- Extremely significant. Student paired t-test for parametric data and Wilcoxon matched pair signed ranks test for nonparametric data were used.

RESULTS

Group I

The effect of treatment on different symptoms and investigations studied in this clinical study on dry eye were analyzed statistically. Effect of treatment on foreign body sensation (FBS) was observed statistically extremely significant (ES) with p value <0.0001 with 70.37% relief. On all the subjective symptoms except asthenopia and Tear meniscus the effect of treatment shows statistically extremely significant results with significant relief on percentage basis which are shown in Table No. II. Effect of treatment on reduction of mucin strands or debris on tear film was statistically extremely significant with 66.67% of relief. On conjuctival congestion the treatment was observed extremely significant with 75% of relief. Not significant result was observed on Rose Bengal Staining with 50% of relief. Treatment was observed extremely significant on objective parameters like Schimer-I and Tear film

break up time (T-BUT) with 80.33% and 12.33% of relief respectively. These results are shown in Table No. III and IV.

Group II

Effect of treatment on foreign body sensation (FBS) was observed statistically extremely significant (ES) with p value <0.0001 with 82.60% relief. On all the subjective symptoms except crusting and matting of eye lashes the effect of treatment shows statistically extremely significant results with significant relief on percentage basis which are shown in Table No. V. 83.33% of relief was observed on objective criteria like Tear Meniscus stabilization. Effect of treatment on reduction of mucin strands or debris on tear film was statistically extremely significant with 81.25% of relief. On conjuctival congestion the treatment was observed extremely significant with 80% of relief. Significant result was observed on Rose Bengal Staining with 60% of relief. Treatment was observed extremely significant on objective parameters like Schimer-I and Tear film break up time (T-BUT) with 85.62% and 15.08% of relief respectively. These results are shown in Table No. VI and VII.

INTER GROUP COMPARISON OF EFFECT OF THERAPY ON INDIVIDUAL CRITERIAS

In comparative study on criteria of assessment no statistically significant difference was observed between two therapies except in Asthenopia, Dryness and photophobia. Statistically Highly significant result were found in Redness. Group II showed better result than Group I which was admimistered combined therapy. These results are shown in Table No.VIII and IX.

Table No I. Showing Assessment criteria of Sushkakshipaka

Symptoms	BT							
	RE				LE			
	0	1	2	3	0	1	2	3
Garsh (foreign body sensation)	Abst	Occ.	Freq	Cont	Abst	Occ	Freq	Cont
Ushnadaha(Burning sensation)	Abst	Mild	Mod	Severe	Abst	Mild	Mod	Severe
Updeha(Mucous discharge)	Abst	Mild	Mod	Severe	Abst	Mild	Mod	Severe
Vishushkatva(Dryness)	Abst	Occ	Int.	Cont	Abst	Occ	Int	Cont
Toda(Anesthopia)	Abst	Mild	Mod	Severe	Abst	Mild	Mod	Severe
Kunita Vartma (Photophobia)	Absts	Mild	Mod	Severe	Abst	Mild	Mod	Severe
Kandu (Itching)	Abst	Occ	Int.	Cont	Abst	Occ	Int	Cont.
Rag (Redness)	Abst	Bul. Conj	Pal. Conj	Pal+ Bul	Abst	Bul. Conj	Pal. Conj	Pal+ Bul
Darun Vartma (Crusting of lid)	Abst	Occ	Int	Cont.	Abst	Occ	Int	Cont.
Krachonmeelnmilan (Matting of lashes)	Abst	Stuck on waking	Freq	Cont.	Abst	Stuck on waking	Freq	Cont.
Mucin Strants	Abst	Spotting on S/L Examination	Spotting on diffuse illumination		Abst	Spotting on S/L Examination	Spotting on diffuse illumination	
Conjuctival Congestion	Abst	Mild	Mod	Severe	Abst	Mild	Mod	Severe
Tear Meniscus	Convex >1 mm	Convex < 0.5 mm	Abst		Convex >1 mm	Convex < 0.5 mm	Abst	
Schirmer – 1 Test	>15-30 mm	11-15 mm	6-10 mm	<5 mm	>15-30 mm	11-15 mm	6-10 mm	<5 mm
T – BUT	>15 sec	11-15 sec	6-10 sec	<5 sec	>15 sec	11-15 sec	6-10 sec	<5 sec
Rose Bengal Stain	Abst	Fine puncctate in intrapalpebral area	Moderate entire exposed part	Modera_te entire exposed part + Corneal	Abst	Fine puncctate in intrapalpebral area	Moderate entire exposed part	Modera_te entire exposed part + Corneal

Table No. II Effect of therapy in Group I on subjective criteria with Non Parametric data (Wilcoxon matched pairs signed ranks test)

SL. No.	Parameters	Mean		D	%age Relief	SD ±	SE±	W	P	R
		BT	AT							
1.	FBS	1.35	0.40	0.95	70.37	0.749	0.12	465	<0.0001	ES
2.	Burning Sensation	1.10	0.50	0.60	54.57	0.590	0.0933	139	<0.0001	ES
3.	Mucous Discharge	0.82	0.37	0.45	54.54	0.597	0.094	136	<0.0001	ES
4.	Dryness	1.65	0.55	1.10	66.66	0.778	0.12	528	<0.0001	ES
5.	Asthenopia	0.55	0.35	0.20	36.36	0.405	0.064	36	<0.01	S
6.	Photophobia	0.85	0.30	0.55	64.70	0.504	0.080	253	<0.0001	ES
7.	Itching	1.02	0.35	0.675	65.85	0.797	0.126	190	<0.0001	ES
8.	Redness	1.37	0.45	0.925	67.27	0.526	0.083	595	<0.0001	ES
9.	Crusting	0.40	0.15	0.25	62.50	0.439	0.069	55	<0.0001	ES
10.	Matting of lashes	0.60	0.20	0.40	66.66	0.496	0.078	136	<0.0001	ES

Table No. III Effect of therapy in Group I on Objective criteria with Non Parametric data (Wilcoxon matched pairs signed ranks test)

SL. No.	Parameters	Mean		D	%age Relief	SD ±	SE±	T	P	R
		BT	AT							
11.	Tear Meniscus	0.20	0.05	0.15	75.00	0.362	0.057	21	<0.01	S
12.	Mucin Debris	0.75	0.25	0.50	66.67	0.506	.080	210	<0.0001	ES
13.	Conjunctival Congestion	1.30	0.32	0.97	75	0.479	.075	630	<0.0001	ES
14.	Rose Bengal Stain	0.10	0.05	0.05	50	0.220	0.034	3.00	<0.500	NS

Table No.IV Effect of therapy in Group I on Objective criteria with Parametric data (Wilcoxon matched pairs signed ranks test)

SL. No.	Parameters	Mean		D	%age Relief	SD ±	SE±	T	P	R
		BT	AT							
15.	Schirmer- I	12.07	21.77	9.70	80.33	3.31	.524	18.51	<0.0001	ES
16.	T-BUT	11.5	12.97	1.42	12.33	0.957	.151	9.41	<0.0001	ES

Table No. V Effect of therapy in Group II on subjective criteria with Non Parametric data (Wilcoxon matched pairs signed ranks test)

SL. No	Parameters	Mean		D	%age Relief	SD ±	SE±	W	P	R
		BT	AT							
1.	FBS	1.15	0.20	0.95	82.60	0.677	0.107	465	<0.0001	ES
2.	Burning Sensation	0.85	0.20	0.65	76.47	0.662	105	253	<0.0001	ES
3.	Mucous Discharge	0.85	0.30	0.55	64.70	0.597	0.094	210	<0.0001	ES
4.	Dryness	1.90	0.45	1.45	76.32	0.749	0.118	741	<0.0001	ES
5.	Pain	0.70	0.20	0.50	71.42	0.599	0.094	171	<0.0001	ES
6.	Photophobia	0.82	0.22	0.60	72.72	0.672	0.10	210	<0.0001	ES
7.	Itching	0.85	0.30	0.55	64.70	0.597	0.094	210	<0.0001	ES
8.	Redness	1.70	0.50	1.20	70.58	0.516	0.081	741	<0.0001	ES
9.	Crusting	0.35	0.50	0.30	85.71	0.564	0.089	55	<0.01	VS
10.	Matting of lashes	0.30	0.05	0.25	83.33	0.438	0.069	55	<0.01	VS

Table No. VI Effect of therapy in Group II on Objective criteria with Non Parametric data (Wilcoxon matched pairs signed ranks test)

SL. No	Parameters	Mean		D	%age Relief	SD ±	SE±	W	P	R
		BT	AT							
1.	Tear Meniscus	0.35	0.05	0.30	85.71	0.464	0.073	78	<0.0001	ES
2.	Mucin Debris	0.80	0.15	0.65	81.25	0.483	0.076	351	<0.0001	ES
3.	Conjunctival Congestion	1.25	0.25	1.00	80.00	0.320	0.050	741	<0.0001	ES
4.	Rose Bengal Stain	0.25	0.10	0.15	60.00	0.361	0.057	21	<0.01	S

Table No. VII Effect of therapy in Group II on Objective criteria with Parametric data

(Wilcoxon matched pairs signed ranks test)

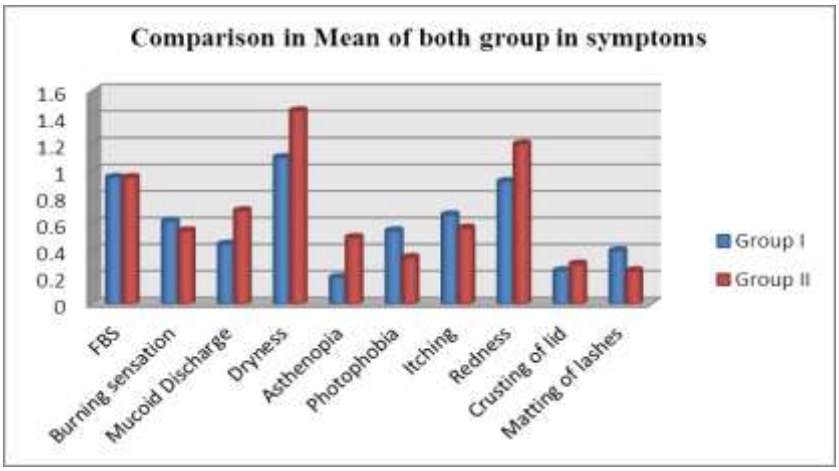
SL. No	Parameters	Mean		D	%age Relief	SD ±	SE±	"t"	P	R
		BT	AT							
1	Schirmer- I	10.95	20.32	9.37	85.62	3.184	0.542	18.62	<0.0001	ES
2	T-BUT	10.82	12.02	1.200	15.08	0.791	0.125	9.595	<0.0001	ES

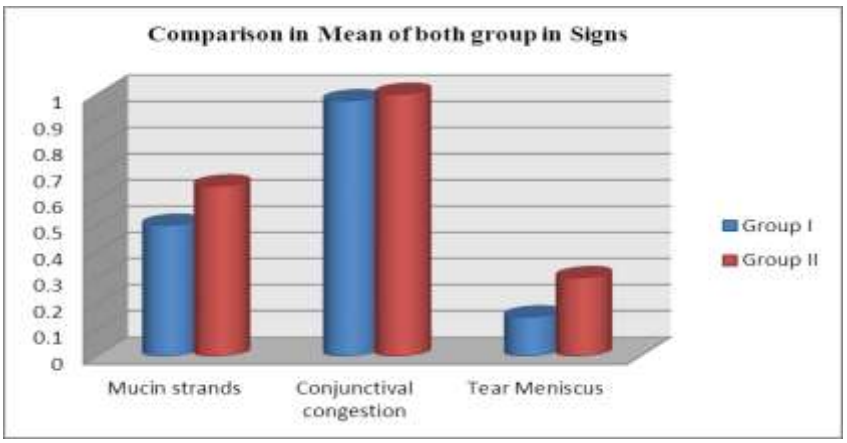
Table No. VIII: Comparison over individual criteria's of Assessment (Mann Whitney test)

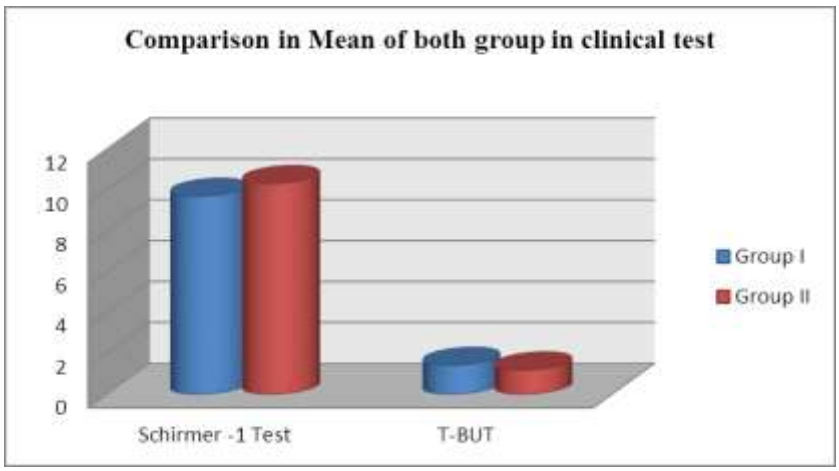
Symptom	Groups	Mean difference	SD	SE ±	T	P	Results
FBS	Group I	0.95	0.749	0.118	822	0.816	NS
	Group II	0.95	0.677	0.107			
Burning sensation	Group I	0.62	0.585	0.092	857	0.5395	NS
	Group II	0.55	0.597	0.094			
Mucoid Discharge	Group I	0.45	0.597	0.094	968	0.0712	NS
	Group II	0.70	0.648	0.102			
Dryness	Group I	1.10	0.779	0.123	990	0.043	S
	Group II	1.45	0.749	0.118			
Asthenopia	Group I	0.20	0.405	0.064	1008	0.014	S
	Group II	0.50	0.599	0.094			
Photophobia	Group I	0.55	0.503	0.079	978	0.048	S
	Group II	0.35	0.579	0.091			
Itching	Group I	0.67	0.797	0.126	831	0.741	NS
	Group II	0.57	0.636	0.100			
Redness	Group I	0.92	0.525	0.083	1007	0.008	HS
	Group II	1.20	0.516	0.081			
Crusting of lid	Group I	0.25	0.438	0.069	810	0.903	NS
	Group II	0.30	0.563	0.089			
Matting of lashes	Group I	0.40	0.496	0.078	920	0.015	NS
	Group II	0.25	0.438	0.069			
Mucin strands	Group I	0.50	0.506	0.080	920	0.179	NS
	Group II	0.65	0.483	0.076			
Conjunctival congestion	Group I	0.975	0.479	0.075	819	0.781	NS
	Group II	1.00	0.320	0.050			
Tear Meniscus	Group I	0.15	0.361	0.057	920	0.112	NS
	Group II	0.30	0.464	0.073			
Rose Bengal Stain	Group I	0.050	0.220	0.034	580	0.141	NS
	Group II	0.150	0.361	0.057			

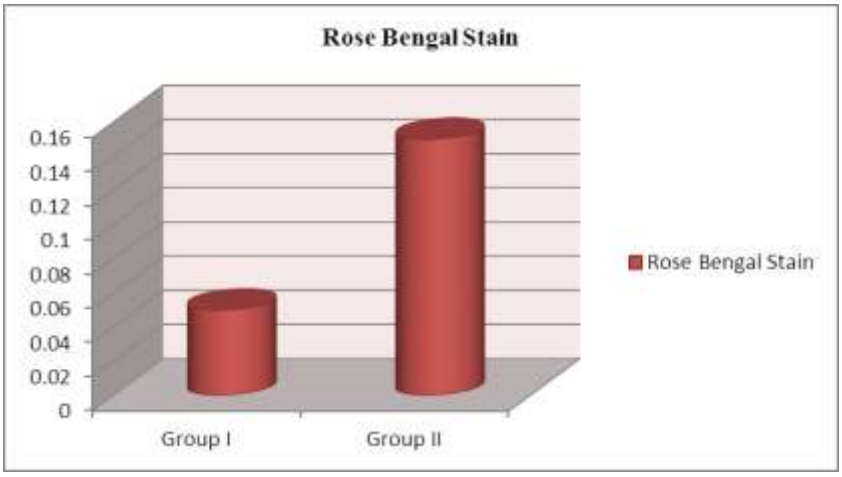
Table No. IX: Comparison over objective criteria's of assessment (Student unpair t test)

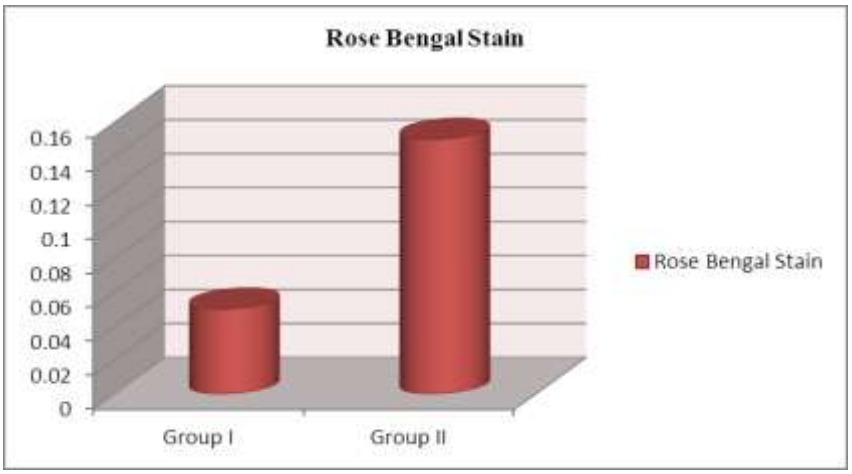
Symptom	Groups	Mean difference	SD	SE ±	T	P	Results
Schirmer -1 Test	Group I	9.70	3.314	0.524	0.447	0.655	NS
	Group II	9.37	3.184	0.503			
T-BUT	Group I	1.425	0.957	0.151	1.146	0.255	NS
	Group II	1.200	0.791	0.125			











DISCUSSION

In Dry eye syndrome Foreign body sensation, itching, asthenopia, photophobia due to irritation of cornea and conjunctiva and loss of moisture in ocular surface and in this stage effect of Haridra, Daruharidra, Goghrita, Godugdha was seen due to its vednasthapana, varnropana and anti-inflammatory[5] properties. Burning sensation due to inflammation and in this stage effect of Amalki, Vasa, Patol, Nimba was seen due to its dahashamak[6] and sheet virya properties. In other symptoms like mucous discharge, redness and conjunctival congestion due to inflammation and in this stage Haridra, Daruharidra, Sandhav, Amalki, Nimba shows great result due to its antinflamatory[7] properties. Symptom like dryness and less Tear meniscus height due to inadequate amount of aqueous tear. Schirmer test shows great result in tear secretion due to effect of Goghrita and Godugdha of its snehana property. Basal secretion of tear is activated by hypothalamus and reflex secretion of tear is activated by trigeminal nerve and in this stage effect of Godugdh and Goghrita shows great result due to its vatashamak, snehana and CNS stimulant properties. Symptoms like crusting of lids and mucin debris was less due to effect of Haridra, Daruharidra, Vibhitaka and Sandhav of its

lekhneya[8] properties. Tear flim breakup time was less due to aqueous deficiency and lipid layer abnormality by evopration of tear and in this stage drug shows less effective result.

CONCLUSION

1. The study shows that Haridradi Anjana alone were effective in alleviating symptoms of Sushkakshipaka (Dry Eye Syndrome) to lesser extent but both combined Haridradi Anjana and Vibhitakadi Ghrita drug therapy had much greater potential to ameliorate the symptoms of Sushkakshipaka (Dry Eye Syndrome).
2. There was no specific effect on Itching in both groups.
3. The study shows that local therapy combined with systemic therapy give better result in Sushkakshipaka
4. Thus it can be concluded that this formulation is effective in management of Sushkakshipaka thus providing a cost effective and preservative free Ayurvedic formulation can be developed for this condition.
5. Research showed sustained relief as evident from 30 Days follow up study. Prolongation of therapy may provide better results.
6. No adverse effects were seen in both groups.
7. A study on a large sample is required and prolonged duration is needed to ascertain the effect of drug.
8. More advanced tests like impression cytology and tear film osmolarity are to be conducted to analyze whether the formulation breaks the pathology of DES or just provide stabilizes the tear film.

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