Available online through
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ISSN 2321 - 6328

Research Article

ROLE OF TOPICAL APPLICATION OF SHRINGVERADI EYE DROPS IN NETRABHISYANDA WITH SPECIAL REFERENCE TO ALLERGIC CONJUNCTIVITIS

Kanaujia Sakshi [1]*, Kumar Manoj [2]
[1]PG Department of Shalakya Tantra, Junior Resident, Banaras Hindu University, Varanasi, India
[2]Associate Professor, PG Department of Shalakya Tantra Banaras Hindu University, Varanasi, India
*Corresponding Author Email: sakshi.kanaujia@gmail.com

Article Received on: 21/06/15 Accepted on: 13/08/15

DOI: 10.7897/2321-6328.03437

ABSTRACT

Ocular allergy manifests as a number of distinct disease entities, ranging from allergic conjunctivitis, a relatively mild condition, to keratoconjunctivitis, which may be sight-threatening condition affecting the cornea. Underlying immune mechanism behind this has not yet been fully understood, but it is known that IgE related mast cell and eosinophil mediated inflammation leads to the release of mast cell mediators and toxic eosinophil granule protein and enzymes. Patients suffering from ocular allergy might experience such symptoms such as redness, itching, burning, swelling or dryness in eyes in differing degrees of severity and duration. Based on clinical features Allergic conjunctivitis can be correlated with Abhisyanda *o*f predominantly a Kaphaja etiology. The features like itching, edema of conjunctiva and lid, heaviness of eyelid indicate Kaphaja etiology of allergic conjunctivitis. Features like burning sensation indicate vitiation of Pitta. Dryness of eye indicates vitiation of Vata. Redness suggests vitiation of Rakta. Hence, features of allergic conjunctivitis are mainly linked with Kaphaja activity with subsidiary action of other doshas .To search a safe, potent and cost-effective Ayurvedic treatment for Netrabhisyanda a randomized control clinical trial was conducted on 67 patients. Patients were divided in three groups 25 in Group I (Control Group i.e. Ketotifen 0.025%), 27 in group II (trial Group i.e. Shringveradi Drops) and 15 in Group II I (Placebo i.e. Normal saline) treated topically four times per day for 14days.The effect of Ayurvedic management was found to be equivalent to the standard therapy and more effective than placebo, although the trial drug showed more effect in blepharitis and follicles in lower palpebral conjunctiva. Study shows that Shringveradi eye drops can be used as potent, safe and cost-effective treatment to ameliorate the symptoms of allergic conjunctivitis.

Keywords: Allergic conjunctivitis, Kaphaja Abhisyanda, Shringveradi eye drops

INTRODUCTION

Ocular allergy manifests as a number of distinct disease entites, ranging from allergic conjunctivitis, a relatively mild condition to Keratoconjunctivitis, a sight threatening condition affecting the cornea[1]. It is a group of disease which includes Seasonal allergic conjunctivitis (SAC), Perennial allergic conjunctivitis (PAC), Vernal allergic conjunctivitis (VKC), Atopic Allergic conjunctivitis (AKC) and Giant papillary allergic conjunctivitis (GPC). All there forms of allergic conjunctivitis, for many years, were considered as the results of classical type 1 IgE-mediated hypersensitivity reaction of conjunctival tissue. More recent studies, however suggest that whole of ocular surface including lids, conjunctiva, cornea and tear film is involved in pathological process.

The cellular components and pro-inflammatory mediators are responsible for development of inflammation in ocular surface tissue. The inflammation clinical manifests in the form of symptoms of itching, watering, photophobia etc., and signs of redness, papillary response, lid swelling etc[2].

Allergic conjunctivitis is correlated with Netrabhisyanda of kapha predominance with varying degree of involvement of other doshas viz. vata and pitta. There are numbers of formulations described in Ayurveda to control this condition. These formulations are though new no or fewer side effects and well tolerated by patients.

The purpose of this study is to find out the clinical efficacy of ophthalmic drops based on a formulation described in Suhsruta Samhita Uttaratantra Chapter 11 Verse 18 for the treatment of Kaphaja Abhisyanda. The constituents herbs i.e. Shringvera (*Ginger officinale*). Mustaka, (*Cyperus rotundus*), Surdaru (*Cedrus deodara*), Jati Mukul (*Jasminum officinale*) and Saindhava *lavana* have shown anti-allergic anti-inflammatory, anti-microbial and wound healing activity in various experimental studies.

Study Design

This is a short-term, randomized placebo (Normal saline) and controlled clinical trial (Ketotifen 0.025% as a control drug) to evaluate the efficacy of "Shringveradi eye drops*"* on the course of Allergic conjunctivitis.

MATERIAL AND METHODS

Preparation of Drugs

The formulation was prepared in laboratory of Department of Shalakya Tantra, Faculty of Ayurveda, Institute of Medical Science, BHU and Varanasi.

Procedure

Shringveradi eye drops were prepared by preparing decoction of above ingredient and filtered with help of fine cloth and residue was discarded. Then this filtrate was centrifuged at 2500 rpm for

20 min. The supernatant portion was taken, purified Saindhava lavana (7.2 gm or 0.9% of solution) was added to this and make it an isotonic solution.

After this solution were autoclaved at 120^0C temperature for 15 minutes. The autoclaved solution was filled in 10ml pre-autoclaved dispensing bottles under sterile conditions. PH range of this solution was in between 6.8 – 7.4 in different batches of preparation.
Microbial culture was done on the day of preparation, 10 days after preparation and after 60 days of preparation which was negative, indicating that at least for 2 months the preparation remained sterile without necessity to add preservatives.

Experimental study

Shringveradi eye drops were instilled in eyes of rats to see any adverse effects. There were no adverse effects observed after 1, 6 and 24 hours of instillation of first dose.

Sample size

A total 134 eyes of 67 patients were recruited for this study as bilateral nature of disease. Groups and randomization – 67 patient were randomly divided into 3 groups –
Groups 1 (Control Group) :
50 eyes were kept in this group.
Group 2 (Trial Group) :
54 eyes were kept in this group
Group 3 (placebo) :
30 eyes were kept in this group.

Selection of patients

The present clinical study was carried out in Department of Shalakya Tantra and upgraded Department of ophthalmology, Sir Sunder Lal Hospital, Institute of Medical Science, Banaras Hindu University, Varanasi from 1 Aug. 2012 to 1 Dec. 2013. Ethical clearance number: Dean/2011-2012/399 (date: 12-12-2011)

Dose and Dosage

In each group patient received eye drops 4 times / day in dose of 2 drops per instillation for 14 days.

Inclusion criteria

Male and female subjects aged 5 years or older were randomly assigned who were suffering from allergic conjunctivitis which was diagnosed on the basis of their history, bilateral signs and symptoms.

Exclusion criteria
Patients without any concomitant disease of eye which can interfere outcome of therapy were excluded. Patients with ocular surgery within 3 months of study or taking systemic or ocular corticosteroids or mast cell stabilizers within 2 weeks were excluded from study.

Assessment criteria

Assessment was done on already standardized grading scale of symptoms and signs with score of severity 0 to 4[3]. Other criteria are evaluation of novel scoring system named 5-5-5 exacerbations grading scale for Allergic conjunctivitis disease[4].

Table 1: Assessment of individual symptom and signs

Score	Description
Itching	
0	Absent
1	An intermittent tickle sensation involving more than just the inner corner of the eye.
2	A mild continuous itch (can be localized) not requiring eye rubbing.
3	A definite itch, the subject would like to able to rub eye
4	An incapacitating itch which would require significant eye rubbing
Tearing	
0	Absent
1	Mild (eyes feel slightly watery)
2	Moderate (occasional need to wipe eyes)
3	Severe (tears rolling down cheeks)
Redness	
0	Absent (vessels normal)
1	Mild (some vessels definitely injected above normal)
2	Moderate (diffusely red eye with individual vessels dilated but still discernible)
3	Severe (intensely red eye with intensive dilatation of conjunctival vessels which are still but not easily visible)
Eyelid swelling	
0	Absent
1	Mild (lids are a little puffy)
2	Moderate (frank swelling of upper and lower lids)
3	Severe (eyelids are swollen)

Table 2: Exacerbation grading scale

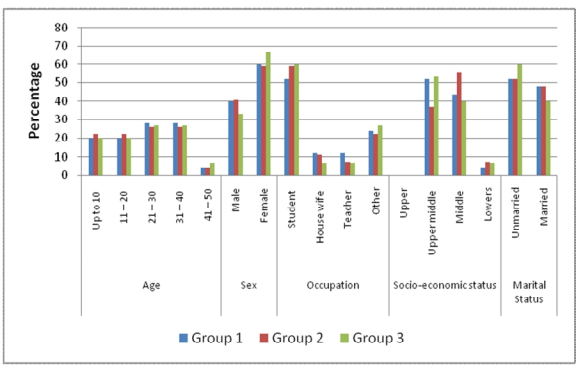
Grade of clinical sign	100-point-grade	10-point-grade	1-point-grade
Clinical signs	• Active giant papillae • Gelatinous infiltrates of the limbus • Exfoliative epithelial keratopathy • Shield Ulcer • Papillary proliferation at lower palpebral conjunctiva	• Blepharitis • Papillary proliferation with velvety appearance • Horner-Trantas spots • Edema of bulbar conjunctiva • Superficial punctate keratopathy	• Papillae at upper palpebral conjunctiva • Follicular lesion at lower palpebral conjunctiva • Hyperemia of palpebral conjunctiva • Hyperemia of bulbar conjunctiva • Lacrimal effusion
Score	100 points × number of positive signs	10 points × number of positive signs	1 point × number of positive signs
Rang	0-500 point	0-50 point	0-5 point

Statistical Methods

The group was statistically analyzed by applying **"chi-square test" (**between group comparisons) and "**Wilcoxon Singed Rank test"** (within group comparison)

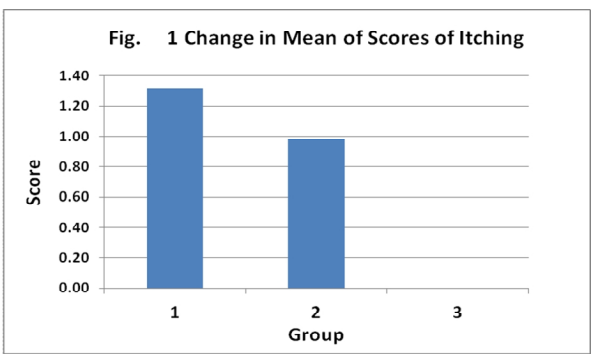
Demographic Profile

Data show that all three groups are comparable with each other in terms of age, sex, occupation, socio-economic and marital status of the patient.

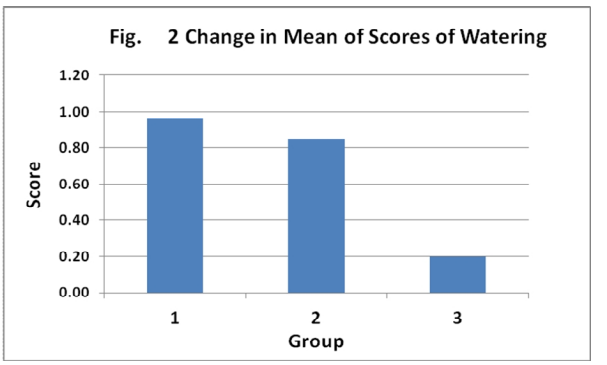


CLINICAL PROFILE

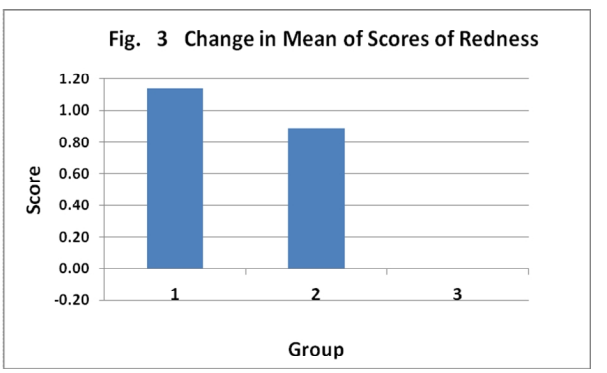
Itching : Clinically and statistically, the effect of trial group on itching was better than placebo but not better than control groups (Figure 1).



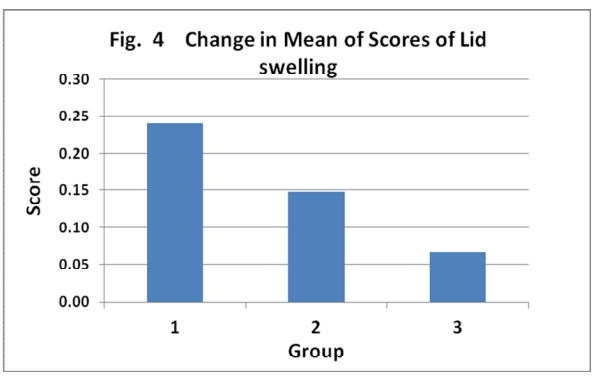
Watering: Clinically and statistically, the effect of trial drug on watering was slightly less than control group and better than placebo group (Figure 2).



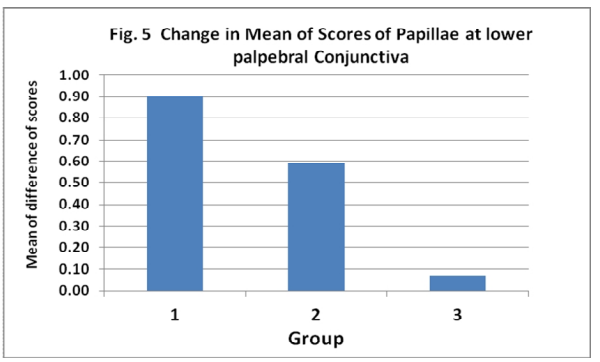
Redness : The effect of trial drug on redness was slightly less than control but no any effect on redness of placebo group(Figure 3).



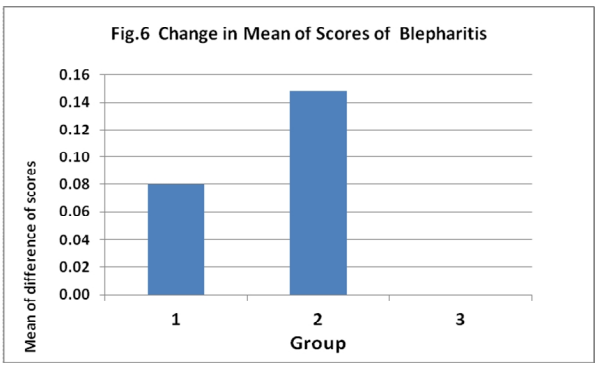
Lid swelling : The effect of trial drug on lid swelling was not better than control but much better than placebo group (Figure 4).



Papillae at lower palpebral conjunctiva : The effect of trial drug on papillae at lower palpebral conjunctiva was less than control group but much better than placebo group(Figure 5).

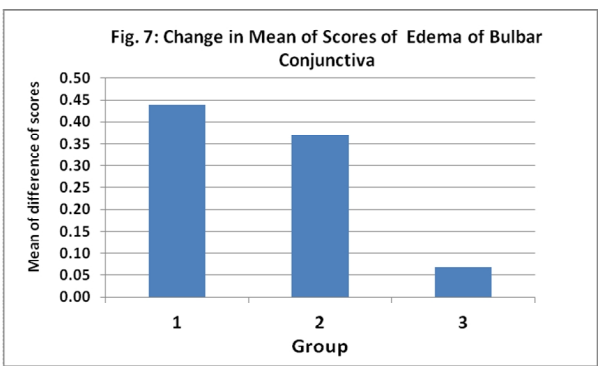


Blephritis : The effect of trial gorup on blephritis was much better than control and placebo group (Figure 6)

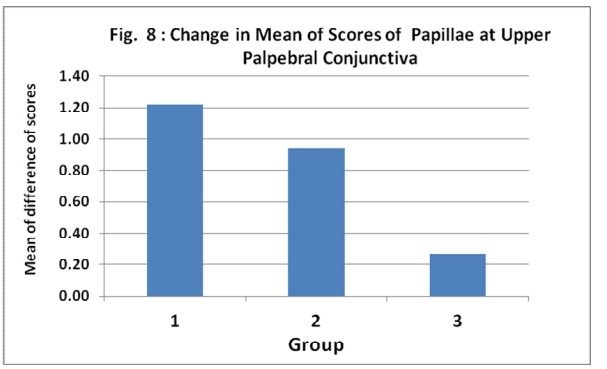


Edema of bilbar conjunctiva

The effect of trial drug on edema of bulbar conjunctiva was slightly less than control group (Figure 7).

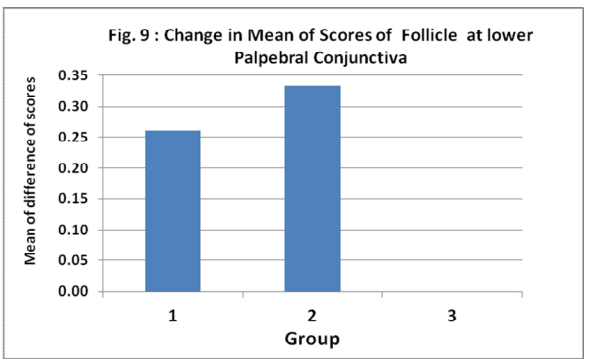


Upper palpebral conjunctiva -The effect of trial drug on papillae at upper palpebral conjunctiva was slight less than control group but better than placebo group (Figure 8).

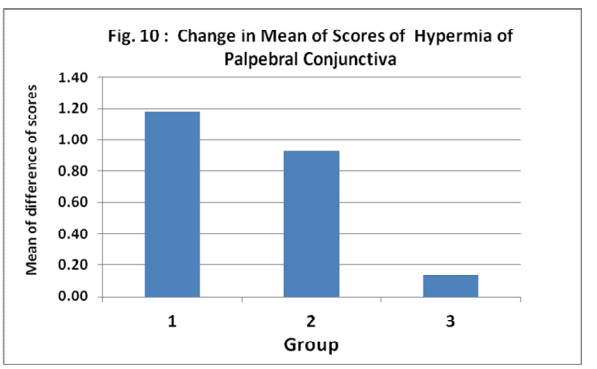


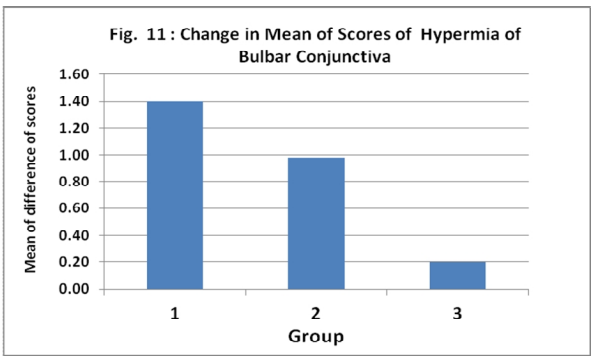
Follicle at lower palpebral conjuctiva

The effect of trial drug on follicle was slightly better than control group and much better than placebo group (Figure 9).

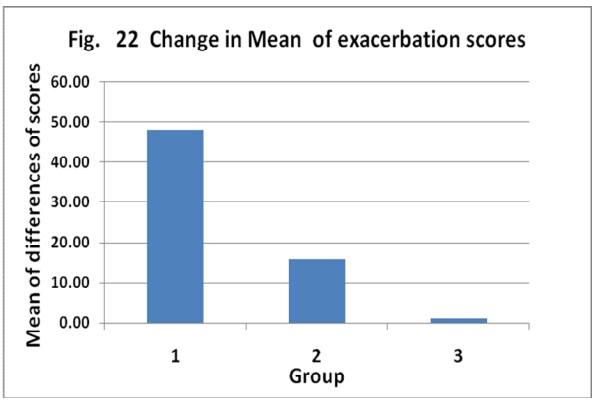


Hyperemia of palpebral conjuctiva and bulbar conjunctiva : The effect and lacrimation of trial drug on Hyperemia of palpebral(Fig:10) and bulbar conjunctiva (Figure 11). was less than control group, but much better than placebo.





Result on Novel scoring system of 5-5-5 excerbation grading scale of allergic conjuctivitis. The effect of trial group was better than placebo but not better than control group. Figure 22).



DISCUSSION

Allergic conunctivitis can be correlated with "Abhisyanda" it has been mentioned in review that various etiological factors of eye disease seasonal changes, atmosphere changes and habitual factors of the patient, immunological status of patient etc. contribute in occurrence of Abhisyanda.[5]

Based on clinical features Allergic conjuctivitis can be correlated with Abhisyanda of predominantly kaphaja etiology.

The features like itching edema of conjunctiva and lid, heaviness of eyelid indicate kaphaja etiology of Allergic conjuctivitis. Features like burning sensation indicate vitiation of pitta. Dryness of eye indicates vitiation of vata. Redness suggests vitiation of rakta. Hence features of Allergic conjuctivitis are mainly linked with kaphaja activity with subsidiary action of other doshas.

Probable mechnaism of drug action

The "Shringveradi eye drops" contains four drugs namely Shunti, Mustak, Devdaru Jati-Mukul and Saindhava. Shunti, Mustak and Devdaru have katu guna and katu vipaka which causes kaphanashak, kandunashaka, krimighna which alleviates itching lid and conjunctival swelling.[6]

Tikta rasa is also present in most of content of Shringveradi eye drop. Tikta rasa has vishaghna, krimighana and dahashamak properties alleviates abhisyanda and itching[7]. Lagu guna is shrotas shodhaka which is present in all herbs of trial drug which alleviates kapha[8].

Properties of Saindhava are lagu, Snigdha and sheeta which cause agnidipana, pachana shrotoshodhaka and kaphavishyandana[9]. By there properties Shringveradi eye drop has capacity to alleviate he disease originating from kapha causes.

According to pathogenesis of Allergic conjunctivitis, Shunti *(Zingiber officinale)* has anti-inflammatory property and analgesic property[10]. It has also anti-oxidant properties[11].

Some constituent of ginger also inhibit growth of bacteria like staphylococcus[12]. . Mustak *(Cyperus rotundus*) possess anti-inflammatory and analgesic property[13].Devdaru *(Cedrus deodara)* also shows anti-inflammatory properties[14].

Jati *(Jasminum officinale*) again shows anti-inflammatory anti-microbial and analgesic activity[15-16-17].

CONCLUSION

"Shringveradi eye drop" has a combinaitn of ingredient which possess different properties which may be acting at various level to control the disease. The drug may not have strong anti-inflammatory, anti-allergic and anti-microbial activities but the over-all effect of all properties acting in combination on disease is significant and comparable with ketotifen (0.025%). It can be concluded that trial drug is though less effetive as compared to control drug in providing symptomatic relief and altering the course of disease but it is a good condidate for further studies to be conducted on individual phytochemicals present in the formulation or higher concentration of same combination. It is recommended that this study may be considered as a lead for future studies which can be taken up to carry out standardization of shringveradi eye drop and determine the effect of individual.

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Cite this article as:

Kanaujia Sakshi, Kumar Manoj. Role of topical application of shringveradi eye drops in netrabhisyanda with special reference to allergic conjunctivitis. J Biol Sci Opin 2015;3(4):170-175 http://dx.doi.org/10.7897/2321-6328.03437

Source of support: Nil; Conflict of interest: None Declared