International Journal of Herbal Medicine
Available online at www.florajournal.com

IJHM International Journal of Herbal Medicine

E-ISSN: 2321-2187
P-ISSN: 2394-0514
IJHM 2015; 3(2): 51-54
Received: 15-04-2015
Accepted: 21-05-2015

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Randomized clinical study to assess the efficacy of Gilo (*Tinospora cordifolia*) in allergic rhinitis

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Abstract
Aim: This study was planned to scientifically validate the efficacy of TC in allergic rhinitis patients.
Methods: Fifty patients were randomly given either TC or placebo for 8 weeks. They were clinically examined and Hb %, TLC, DLC and nasal smear was done.
Results: It was seen that allergic rhinitis was more common in the age group 20–30 years (68%). There were 7 patients in the age group of 31–40 (14%), 6 in 41–50 (12%) and 3 in 51–60 age group (6%). Women were more affected than men (32:18). On analyses of the effect of TC and placebo after 8 weeks of administration on the symptoms of allergic rhinitis, it was seen that there was total relief from sneezing in nearly 82% patients who received TC while in placebo group 80% had no relief at all. In case of nasal discharge, TC showed 100% improvement in nearly 68% while in placebo group only one patient (3%) had such relief. Nasal obstruction was totally cleared in nearly 60% patients who had received TC while nearly 82% patients on placebo had no relief from it. In nasal pruritus, 70% patients of TC group had 100% improvement whereas in placebo group 88% had no relief from this symptom.
Conclusion: TC significantly decreased all symptoms of allergic rhinitis. Nasal smear cytology and leukocyte count correlated with clinical findings. TC was well tolerated.

Keywords: Herbal extract, Immunostimulation. Rhinitis, *Tinospora cordifolia*

1. Introduction

Tinospora cordifolia is a plant prescribed in Ayurveda[1], the Indian traditional system of Medicine as a 'Rasayana' or general tonic [2]. It belongs to the family Menispermaceae and is a large, glabrous climber with succulent, corky grooved stems. The stem is the most commonly used part and has been shown to contain a glycoside giolin, a non glycoside bitter gilenin as well as gliosterol. *Tinospora cordifolia* has been found to protect rats against mixed bacterial abdominal sepsis [3] and mice against E.co/iinduced peritonitis [4], Further, cyclophosphamide myelosuppression was also prevented by *Tinospora cordifolia* (TC) in mice [5, 6].

Tinospora cordifolia (T.C.) known as "Culwel" in loc al dialect is reported to have several useful therapeutic properties in the ayurvedic system of Medicine [7]. The aqueous extract of the roots of the plants have been traditionally used to treat diabetes [8]. Pendse et. al., (1981) have studied the anti inflammatory activity of T.C. They observed that the aqueous extract of the roots of T.C. inhibited carrageenan induced oedmea in rats and interfered with the release of 5 HT and histamine, the mediator of inflammation [9].

Allergic rhinitis is the commonest atopic disease with prevalence of 5–22% [10]. It is the sixth most prevalent condition in the US, outranking cardiac disease [11]. It is characterized by sneezing, rhinorrhea, nasal congestion and pruritus of nose and eyes. The disease and its complications like sinusitis, eustachian tube dysfunction, sleep disturbance and the consequences of chronic mouth breathing are responsible for morbidity and absenteeism. Allergic rhinitis begins at any age but peak incidence is during the childhood–adolescence. The incidence is higher in those whose parents have positive history of the disease.

Allergic rhinitis implies hypersensitive response following exposure to allergens including pollens of grass, weeds, trees, animal danders, house dust and food. Rhinitis symptoms impair patients' quality of life [12]. *Tinospora cordifolia* (Willd) Miers is a deciduous climbing shrub indigenous to tropical Indian subcontinent, belonging to the family Menispermaceae. In Indian vernacular the plant is known as Giloya, meaning heavenly elixir, which saved celestial beings from old age and kept them eternally young. It is widely used in veterinary medicine and in Ayurveda for its general tonic, antispasmodic, anti-inflammatory, antiarthritic, antiallergic and antidiabetic effects [13]. This study was planned to scientifically validate the efficacy of TC in allergic rhinitis patients.

Methods

This was a randomized, double blind, placebo-controlled trial. The trial procedure was in accordance with the guidelines of the Declaration of Helsinki and Tokyo. Ethical permission was obtained from Institutional Ethics Committee. Patients diagnosed to be suffering from allergic rhinitis in the ENT out-patient department of the hospital, were approached with request to participate in the trial. Those who showed interest were supplied with detailed information sheet about the trial, in language understood by them. From those who volunteered to participate, informed witnessed written consent was taken.

Inclusion criteria

- Subjects diagnosed to be suffering from allergic rhinitis.
- Volunteering to participate and give signed informed consent.
- Of either gender.
- In age range of 18–60 years.

Exclusion criteria

- Pregnant and lactating women.
- Clinical evidence of bacterial sinusitis.
- Associated chronic diseases like hypertension, ischemic heart disease, diabetes, psychiatric and CNS disorders.
- Consuming concurrent medication for chronic diseases.
- Alcoholics and drug addicts.
- Having cyanosis, clubbing or lymphadenopathy.
- Within 6 weeks of having received antihistaminic or steroid therapy.

M/s Pharmanza (India) supplied the active drug and matching placebo. Each tablet of TC (Tinofend)® contained 300 mg of standardized extract obtained from water extract of stem of TC. It contained more than 5% bitter principles and was tested for presence of cordioside and tinosporoside by HPLC. After clinical examination by ENT surgeon, Hb %, TLC, DLC and nasal smear (Wakode *et al*., 1989) were done to get the baseline data. Pulse, respiratory rate, blood pressure and temperature were recorded. X-ray of paranasal sinuses was done to rule out sinusitis in suspected cases. Patients suffering from acute sinusitis were treated with antibiotics for 1 week followed by wash out of 1 week and later entered in the trial.

All data was logged in case record form by chief investigator. Fifty participants were randomly allocated totaling 25 to group A and 25 to group B, to either receive coded TC 300 mg one tablet thrice daily or matching placebo in the same formulation, packing, size, weight, color and dose for 8 weeks. The drug was issued to patients for duration of fortnight at a time. The patients were asked to bring the unused drugs and container during the follow-up. Eighty percent consumption was considered to be compliant. The returned drugs were discarded. After completion of the 8 weeks study period, all baseline investigations were repeated. The participants were followed up for 1 month after stoppage of the drug. At the end of the study period the drug was decoded and the results calculated by Fisher's exact test and Chi-square test. As rescue medication, initially H1 antagonist and later antibiotics were allowed. The patients were at liberty to withdraw from the trial anytime. During the trial one patient developed sinusitis requiring antral puncture. She was dropped from the trial and after decoding, was found to be on TC.

Results

Table 1: Demographic details

Age in years	N%
20-30	34 (68%)
31-40	7 (14%)
41-50	6 (12%)
51-60	3 (6%)
Gender	
Male	32 (64%)
Females	18 (36%)

It was seen that allergic rhinitis was more common in the age group 20–30 years (68%). There were 7 patients in the age group of 31–40 (14%), 6 in 41–50 (12%) and 3 in 51–60 age group (6%).Women were more affected than men (32:18).

Table 2: Percentage improvement in symptoms of allergic rhinitis

Percentage improvement in symptoms	*Tinospora cordifolia* extract (n = 25)				Placebo (n = 25)			
	100	75	50	0	100	75	50	0
Nasal discharge (TC 25, placebo 25)	68	22	6	3	3	0	12	85
Sneezing (TC 25, placebo 25)	82	15	3	0	4	7	10	80
Nasal obstruction (TC 25, placebo 25)	60	0	34	6	0	3	14	82
Nasal pruritus (TC 25, placebo 25)	70	0	25	3	0	4	8	88

Allergic rhinitis was found to be more common in the age range of 20–30 and women. On analyses of the effect of TC and placebo after 8 weeks of administration on the symptoms of allergic rhinitis, it was seen that there was total relief from sneezing in nearly 82% patients who received TC while in placebo group 80% had no relief at all. In case of nasal discharge, TC showed 100% improvement in nearly 68% while in placebo group only one patient (3%) had such relief. Nasal obstruction was totally cleared in nearly 60% patients who had received TC while nearly 82% patients on placebo had no relief from it. In nasal pruritus, 70% patients of TC group had 100% improvement whereas in placebo group 88% had no relief from this symptom. On comparison, the difference between TC and placebo treated groups in all the symptoms of allergic rhinitis viz. sneezing, nasal discharge, nasal obstruction and nasal pruritus was found to be highly significant (p<0.00001).

Table 3: Percentage change in total leukocyte count (TLC) due to intervention

Change in TLC	Tinospora (n = 25)	Placebo (n = 25)
Increase	70	12
Decrease	25	15
No change	6	75

In TC treated group, there was increase in total leukocyte count in 70% patients, while in placebo group such increase was seen in only 12%. This difference between TC and placebo group was significant (p<0.001).

Discussion

Allergy is an altered state of the host after contact with specific antigen. Individuals with allergic rhinitis have IgE antibodies that bind to high affinity receptors on mast cells and basophils, and other cells like eosinophils, monocytes and platelets [15, 17].

On nasal reexposure to antigen in allergic rhinitis, the mast cells degranulate, releasing various mediators of inflammation [18], causing itching, sneezing, nasal discharge and congestion in more than 90% of the patients. Nasal challenge induces immediate and delayed response in the form of recurrence of symptoms characterized by influx of eosinophils, neutrophils, basophils and mononuclear cells [19]. The eosinophils are reduced by treatment with topical steroids and immunotherapy [20, 21].

TC is known to have powerful immunostimulant effect [6]. Being a rasayana, it increases leukocyte count and ablates neutropenia following single or multiple doses of cyclophosphamide [14]. Pretreatment with TC affords protection against induced infections in mice [22]. The phagocytic and intercellular bactericidal capacity of polymorphs of TC treated mice is significantly greater [22]. The aqueous extract of TC stimulates peritoneal macrophage in a dose dependent manner [23], suggesting that global activation of macrophage system is essential for the non-specific effects of TC. The primary target of TC is believed to be the macrophages, which play key role in the generation of immune response.

In our study, there was a significant improvement in the allergic rhinitis symptoms of sneezing, nasal obstruction, nasal discharge and pruritus. These findings correlated well with clinical finding of change in color of nasal mucosa from bluish to pink in patients on TC. Pink coloration along with symptomatic improvement is considered to be sign of good response [24]. The patients who were on TC were satisfied with the treatment, with only one dropout from the study group due to development of sinusitis in early weeks of the trial. No patient from the TC group went for the rescue medicine. As compared to this the patients from placebo group constantly complained of no relief of symptoms and needed continuous counseling to continue with the study. In the placebo group, there were three dropouts and three patients asked for rescue medication, when the symptoms were bothersome.

The significant increase in the leukocyte count in our study is suggestive of immunostimulant action of TC. Decrease in goblet cells and eosinophils are indicative of antiallergic effect of TC. Decrease in neutrophils is suggestive of anti-inflammatory effect.

Conclusion

Immunostimulation is a known pharmaco-therapeutic intervention in disease management. *Tinospora cordifolia* extract, a plant derived immunostimulant, significantly decreased (p<0.00001) symptoms of allergic rhinitis like sneezing, nasal discharge, nasal obstruction and nasal pruritus. The nasal smear cytology, leukocyte count and clinical findings validated efficacy of TC. Because of its high efficacy, excellent tolerability and absence of serious adverse reactions *Tinospora cordifolia* could be an important constituent of the treatment of allergic rhinitis.

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