Comparative Clinical Evaluation of Herbal and Allopathic Medicine in Acute Tonsillitis

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Abstract

Tonsillitis is usually caused by a viral infection or less commonly, a bacterial infection. Symptoms may include sore throat, fever, enlargement of the tonsils, pain in swallowing, and enlarged lymph nodes around the neck. Herbal remedies are popularly used due to its potential action to relieve early tonsillitis, cost-effectiveness and with fewer adverse effects. This research aimed to determine the efficacy of herbal medicine for the management of acute tonsillitis. Study was conducted at Shifa-ul-Mulk Memorial Hospital for Eastern Medicine, Madinat-ul-Hikmah, Hamdard University. Patients (n=78) were randomly assigned to receive test drug lozin (500 mg) thrice a day and control drug cephradine (250 mg) thrice a day or 500 mg twice a day for 5-12 days with a follow-up visit of 2-12 days. Both medications after a 10-day treatment period caused a significant improve-ment in all the signs and symptoms. The herbal formulation lozin demonstrated similar efficacy compared to allopathic medicine cephradine for the treatment of acute tonsillitis.

Keywords

Acute tonsillitis; Lozin herbal formulation; Cephradine.

1. INTRODUCTION

Tonsils are the two lymph nodes located on each side of the back of throat. They are involved in defense mechanism and hence prevent various infections. Upon bacterial and/ or viral infection followed by inflammation the condition is referred to as tonsillitis (Windfuhr *et al,* 2016). Most cases of tonsillitis are caused by viral infections that also causes other diseases for example, rhinoviruses (common cold), influenza virus and para influenza virus (laryngitis) and croup entero viruses (hand, foot and mouth disease), adenovirus (diarrhoea) and rubella virus (measles).

Bacterial tonsillitis are caused by a number of different types of bacterias, mainly *Streptococcus* group. In the past, serious bacterial infections, such as diphtheria and rheumatic fever, have also been linked with tonsillitis. However, due to vaccination against them and availability of other treatments these are rarely reported.

Herbal remedies are most commonly used medication for tonsillitis due to its potential action to relieve its sign and symptoms. Literature search using NAPALERT data (Natural Product Alert Database, University of Illinois at Chicago) revealed that many plant drugs are used for the treatment of tonsillitis such as,

Glycyrrhiza glabra L., *Trigonella foenum-graecum* L., *Solanum nigrum* L., *Alpinia galangal* L., *Cordia dichotoma* L. and *Morus nigra* L. and hence were selected to produce a coded herbal formulation referred to as Lozin. Among them, *Glycyrrhiza glabra* L. has a long history of usage to treat illnesses such as peptic ulcer, colds and other viral infections (stimulate interferon production and expectorant/cough suppressant properties); microbial and parasitic infections (stimulate the immune system) and cancers (Nutrasanus, 2004). The essence of *Trigonella foenum-graecum* L. used as an effective herbal drug for tonsillitis (Usmanghani *et al.,* 1997). *Solanum nigrum* L. is prescribed for the treatment of hepatomegaly, splenomegaly, gastritis, sore throat and glossitis (Zakaria *et al.,* 2006). *Alpinia galangal* L. contains enzymes, polysaccharides and nutrients exhibiting antibacterial effects against *Streptococci, Staphylococci* and coliform bacteria. It is a useful treatment for sore throat and catarrhal infections (Awan, 1956).The dried fruit of *Cordia dichotoma* L. is valued on account of its mucilaginous nature and demulcent properties for the treatment of coughs and chest infections (Vohora, 1986). Extracts of the plant *Morus nigra* L. possesses antibacterial and fungicidal activities (Butt *et al.*, 2008).

Cephradine, is a semisynthetic cephalosporin antibiotic clinically used as a short-term treatment against tonsillitis by inhibiting bacterial cell-wall synthesis, however, is ineffective for long-term therapy due to its multiple side effects.

2. MATERIALS AND METHODS

2.1. *Study Design*

A monocentric, prospective, randomized, open-label and active-controlled study was undertaken. Patients were randomly assigned to one of two treatment groups: those receiving the coded herbal formulation lozin (Test group) and those given cephradine sodium (Control group). This study was conducted according to the principles of good clinical practice i.e., informed consent was obtained from the patients before enrollment, a proper history was taken and a clinical examination was carried out at each follow up visit. The study period was 3 years from November 2003 to February 2007. Patients of both genders (>15 years and <70 years) with a clinical diagnosis of acute tonsillitis were selected. The total sample size of this study was 78 subjects and comprised lozin group (n=45) and cephradine group (n=33).

The clinical protocol was approved by the appropriate Independent Ethics Committee of the Faculty of Eastern Medicine, according to principles based on the Declaration of Helsinki. The objective was to prove that herbal medicine is effective in acute tonsilitis and has fewer side effects.

2.2. *Setting*

On the basis of a preliminary clinical examination, the patients suffering from sore throat were selected from the out-patients enrolled at Shifa-ul-Mulk Memorial Hospital. They were referred to the project physician and included in the study based on the inclusion and exclusion criteria as described below:

Inclusion Criteria

The consent for clinical trial using either herbal or allopathic medicine was undertaken from all the patients. The clinical diagnosis of acute tonsillitis was based on: A sore and scratchy throat and/or pain on swallowing (odynophagia) accompanied by at least two of the clinical signs: a) Pharyngeal erythema and/ or exudate, cervical adenopathy and b) Uvular edema and fever.

Exclusion Criteria

The major exclusion criteria for this trial were: *a*) Patients with hepatic impairment, *b*) Patients non-resident of Karachi because of the inherent difficulty in conducting follow-up visit, *c*) Having a history of adverse reactions to any of the study drugs or contraindications for their use, *d*) Suffering from complicated and serious conditions like coma, meningitis, and encephalitis or head injury, *e*) Hospitalized for serious diseases, *f*) Symptoms that collectively suggest pharyngitis (laryngitis, coryza, conjunctivitis, diarrhea and cough), *g*) Infection of the deep tissues of the upper respiratory tract (epiglottitis, retropharyngeal or buccal cellulitis) or of the suprapharyngeal respiratory tract and its connecting structures (sinusitis, otitis media, or orbital/periorbital cellulitis), *h*) History of rheumatic heart disease, *i*) Known impaired renal function, as shown by a creatinine clearance $\leq$ 25 ml/min, *j*) Myasthenia gravis, patients currently being treated with systemic anti-bacterials or treated with systemic anti-bacterials within 14 days prior to enrollment. Moreover, patients were excluded from the study if they had: *a*) temperature >38.5°C (oral temperature) or >39.0°C (axillary temperature), *b*) Pharyngitis was exudative and/or ulcerative, *c*) Active gastrointestinal ulcers, *d*) Gastro-intestinal disease, or *e*) Presumed infectious mononucleosis.

2.3. *Clinical Assessment*

The main outcome measures were:

1. Clinical response of signs and symptoms of tonsillitis determined at the end of therapy.

2. Number of cases in which a change in medicine was needed (herbal or allopathic)

3. Microbiological eradication.

4. Physician global evaluation of the patient condition (using a 5-point arbitrary scale): Complete = 1, Marked = 2, Moderate = 3, Mild = 4 and None = 5 were employed.

Clinical outcome was defined as: Clinical cure (Complete resolution of signs and symptoms); Improved (Clinical signs and symptoms are reduced but not completely resolved) and failure (Signs and symptoms worsened, persisted or reappeared).

2.4. *Statistical Analysis*

Statistical analysis were performed with SPSS, using excel software, the Chi Squared Test. All differences were considered statistically significant if the '*p*-value' was less than 0.05. A two-sided *t* test for two independent samples was used to compare the mean ages of males and females, and both sexes combined of the two treatment groups.

3. RESULTS

The therapeutic effectiveness of formulated herbal medicine lozin was compared with the allopathic medicine cephradine sodium as a treatment for acute tonsillitis.

3.1. *Patient Demographic Characteristics*

There were 45 subjects in the test group and 33 in the control group were selected that complied with the inclusion/exclusion criteria. The mean age of the subjects participating in the test group (group 1) was 32 years (range 15-68), compared with the control group (group 2) which had a mean age of 33 years (range 18-50); the gender ratio is shown in Table 1.

3.2. *Baseline Complaint History*

The patients (84%) suffering from infections were categorized into mild, moderate and severe. The demographic and baseline characteristics of the patients included in the groups evaluable for efficacy were similar in

Table 1: Age Intervals for Lozin and Cephradine Groups

Age (Years)	Lozin (Test group)	Cephradine (Control group)	Number of patients (n)
15-20	7	5	12
21-26	11	8	19
27-32	15	9	24
33-38	5	6	11
39-44	5	4	9
45-50	2	1	3
Total	45	33	78

both lozin and cephradine groups (P>0.05). The disease-related demographic and baseline characteristics of the patients enlisted (Tables 2 and 3) were age, presenting symptoms, local examination of throat and oral cavity.

The patients with acute tonsillitis were diagnosed and grouped into classes with a) Throat pain, b) Difficulty in swallowing and c) Rhinitis representing baseline complaints, Test group (Lozin) and Control (Cephradine sulphate).

The test *versus* control populations in each category were equally balanced as shown in Tables 2 and 3 (P>0.05). All patients had one or more pretreatment symptoms of tonsillitis which were almost identical in both treatment groups (P>0.05) except for difficulty in swallowing. The most frequent symptom was throat pain (100%) in both treatment groups.

3.3. *Overall Clinical Response*

The total duration of treatment (test and control) were similar; the mean duration of treatment was 13.4±5.4 days and 13.4±6.0 days in the test and control groups, respectively. Among the clinically evaluable patients, the total durations of treatment in both groups were also similar, with a mean duration of 14.3±4.6 days and 14.1± 4.6 days in the test and control groups, respectively.

Both medications caused a significant improvement in all the signs and symptoms noted at baseline after a 10-day post-treatment period. There was also a significant decline in systemic symptoms like cough, difficulty in swallowing and fever. Clinically, 96.6% *vs* 94.2% (Test *vs* Control group) patients were cured, 2.4% showed improvement while 1% *vs* 3% of the patients did not respond to the therapy and needed rescue medication.

3.4. *Microbiological Response*

Clinically relevant pathogens isolated at baseline were similar in both groups (P>0.05) as listed in Table 4. *Streptococcus pyogenes* was the most commonly isolated bacterial pathogen in both treatment groups isolated from 78 evaluable patients. The microbiological success rate at the final visit was similar for the two groups, with a diagnosis of acute tonsillitis (P>0.05). Sub-group analysis of the microbiological outcome by gender, age, and

Table 2: Clinical Symptoms at Baseline for Acute Tonsillitis

Presenting complaint		Lozin (Test group)	Cephradine (Control group)	Total (n)	*p* value
Throat Pain	Yes	45	33	78	
	No	0	0	0	
	Total	45	33	78	
Difficulty in swallowing	Yes	44	29	73	
	No	1	4	5	0.078
	Total	45	33	78	
Rhinitis	Yes	4	4	8	0.716
	No	41	29	70	
	Total	45	33	78	

Table 3: Local Examination of Throat and Oral Cavity at Baseline in Acute Tonsilitis

Presenting complaint		Lozin (Test group)	Cephradine (Control group)	Total (n)	*p* value
Soft palate	Normal	13	6	19	
	Congested	32	27	59	0.276
	Total	45	33	78	
Uvula	Inflamed	30	19	49	
	Normal	15	14	29	0.412
	Total	45	33	78	
Post tonsillar pillar	Congested	29	31	60	
	Normal	15	2	17	0.009
	Nodular	1	0	1	
	Total	45	33	78	
Anti tonsillar pillar	Congested	33	27	60	
	Normal	12	6	18	0.38
	Total	45	33	78	
Post pharyngeal wall	Inflamed	27	19	46	
	Normal	18	14	32	0.83
	Total	45	33	78	
Regional lymph nodes	Palpable	15	13	28	
	Not Palpable	30	20	50	0.581
	Total	45	33	78	

race demonstrated comparable results between the groups. There were also some co-pathogens, like *Chlamydia pneumoniae* and *Mycoplasma pneumonia,* in acute tonsillitis, whereas *Staph* spp., *H. influenzae, Streptococcus pneumoniae, Bacteroides fragilis* and *Corynebacterium diphtheria* were the co- pathogens as presented in Table 4.

After therapy, pathogens decreased dramatically in both treatment groups (Table 4). The rates of complete elimination of throat pathogens were equal in both treatment group at all times (P>0.05). In the microbiologically rates of the selected baseline pathogens (*S. aureus*, *S. pyogenes*, *Corynebacterium diphtheria, Bacteroides fragilis* and others) at the final visit are summarized for the microbiologically evaluable patients in Table 4. Eradication rates generally were similar between the two treatment groups for these pathogens. The cure rates in both treatment groups decreased with advanced age. However,

Table 4: Status of Throat Culture Before and After Treatment in Acute Tonsilitis

Treatment	Micro-organisms	Lozin (Test group)	Cephradine (Control group)	Total (n)	*p* value
Before	*Streptococcus pyogenes*	37	24	61	0.955
	Staph aureus	3	4	7	
	Haemophilus influenza	1	1	2	
	Streptococcus pneumoniae	2	2	4	
	Cornybacterium diphtheria	1	1	2	
	Bacteroides fragilis	1	1	2	
	Streptococcus pyogenes	3	2	5	
After	*Staph aureus*	1	2	3	0.709
	Haemophilus influenza	0	0	0	
	Streptococcus pneumoniae	1	0	1	
	Cornybacterium diphtheria	1	1	2	
	Bacteroides fragilis	0	1	1	
Micro-organism growth status	No growth	39	27	27	

the overall clinical success or efficacy of the test medication was similar in acute tonsillitis (P>0.709).

4. DISCUSSION

The pesent study demonstrates that lozin is as effective as cepharadine in the management of patients with acute tonsillitis. The results were similar in microbiologically evaluable patients, for which, again, the test treatment eradication response was higher than that of the control. However, both the clinical success rate and microbiological eradication rate were higher in the lozin group.

Treatment of patients with tonsillitis is often empirical. Therefore, selection of an appropriate antibacterial agent should be, to a great extent, based on its anti-microbiological activity. In this study, the most frequently isolated pyogenic throat pathogens were *Streptococcus pyogenes* and *S. pneumoniae* while *H. influenzae; H. parainfluenzae, Staphylococcus aureus, Moraxella catarrhalis* were less common. Epidemiological data from Western countries on sore throat in general and specifically Group A beta-hemolytic streptococcal infections (GABHS), both community and hospital-based, are more readily available. However, there is considerable variation in the prevalence of GABHS sore throats from one country to another. For example, in Dhaka 22% of 601 children had a positive culture but only 2.2% is due to GABHS (Faruq *et al.*, 1995). Recurrent tonsillitis was reported in 11.7% of Norwegian children in one study and estimated in another study to affect 12.1% of Turkish children (Kvestad *et al.*, 2005).

This study demonstrates that both medications have predictable activity against both typical and atypical throat tract pathogens. In the microbiologically evaluable patients, test therapy provided an overall eradication rate by pathogen which was higher in comparison with that observed in the cephardine group because of higher antimicrobial effect of the lozin.

The broad-spectrum coverage of the lozin offers a potential advantage over both cepharadine and newer macrolide therapies. All isolates from microbiologically evaluable patients were successfully eradicated by its use in acute tonsillitis and the eradication rate was higher compared to cepharadine. In selecting antimicrobial agents for the treatment of tonsillitis the practitioner must consider not only the documented efficacy but also the adverse-event profile of the agent and its cost.

This important trial is the first to provide data demonstrating that lozin therapy is an effective and safe polyherbal therapy for the empirical treatment of patients with tonsillitis. The herbs present in it has a documented clinical efficacy against all common typical and atypical throat pathogens. If bacteria are not the cause of infection, then the treatment is usually directed more at cause. Antibiotics will not help to treat viral sore throat. The cephalosporins are also resistant to beta-lactamase enzymes although this is generation-dependent. The inappropriate use of antibiotics can have a significant negative impact both on individual patients and public health in general.

Lozin has antimicrobial, anti-inflammatory, immunomodulatory, and antioxidant actions due to the presence of active phytoconstituents. For example: Glycyrrhizin from *Glycyrrhiza glabra* exhibits potent antimicrobial activity and also potentiates the reticulo endothelial system and enhances immunostimulation. It acts on macrophage function, leading to stimulation of macrophages de-novo, and beta-glycyrrhetinic acid from *G. glabra* which is a potent inhibitor of the classical complement pathway (Nose

et al., 1998). Trigonelline from *Trignella foenum-graecum* effective in treating fever, cough (Srinivasan, 2006). Alpha-solanine from *Solanum nigrum* used for the treatment of hepatomegaly, splenomegaly, inflammation of the stomach and sore throat (Keeler *et al.,* 1983). Galangin from *Alpinia galangal* show antibacterial effects against *streptococci, staphylococci* and coliform bacteria also useful for treatment of sore throat, bronchitis and catarrhal infections (Usmanghani *et al.*, 1997). Salicyl aldehyde from *Cordia dichtoma* posses demulcent properties for the treatment of coughs and chest infections (Rastogi *et al*, 1993). Anthocyanin from *Morus nigra* have antibacterial activity, used in treatment of cold, influenza, cough. (Dharrmananda, 2003).

5. CONCLUSION

The herbal formulation lozin based on a complex mixture of chemical compounds present in different herbs represent a compound formulation. It emerged as on effective pharmacological agent similar to cepharadine against tonsillitis. There were no untoward manifestations associated with the use of this medication and it was acceptable by all treated patient and found to be safe.

6. REFERENCES

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