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Efficacy of Sublingual Therapeutic Bacterial Vaccine in Patients with Recurrent Sore Throat: A Randomized Controlled Trial

Abdul Shakoor[1], Abdul Malik Mujahid[2], Muhammad Junaid Ashraf[3], Izzah Islam[4], Junaid Rasul Awan[5], Waqas Aslam[6]

[1]MBBS, FCPS ENT, Department of Otolaryngology and Head and Neck Surgery, Services Institute of Medical Sciences, Lahore, Pakistan; [2]MBBS, FCPS Plastic Surgery, Burn and Plastic Surgery Department, Teaching Hospital, D.G. Khan Medical College, Pakistan; [3]MBBS, Department of Medicine, Jinnah Hospital Allama Iqbal Medical College, Lahore, Pakistan; [4]MBBS, Department of otolaryngology and Head and Neck Surgery, Services Institute of Medical Sciences, Lahore, Pakistan; [5]MBBS, MRCP1, Department of Respiratory Medicine, University, University Hospital Limerick, Limercik, Ireland; [6]MBBS, FCPS, Department of Pulmonary Medicine, Ali Fatima Hospital, Lahore, Pakistan.

ABSTRACT

Introduction: Recurrent sore throat is a significant burden on healthcare system. It is associated with significant morbidity and antimicrobial resistance due to frequent antibiotic use. Sublingual live-attenuated polyvalent bacterial vaccine has been used as an adjunct treatment in these patients for its immunomodulatory properties, increasing immune responses, and boosting the innate immune system.

Objective: To determine the efficacy of sublingual live-attenuated polyvalent bacterial vaccine in patients with recurrent sore throat.

Materials and Methods: This randomized control trial was conducted at Department of ENT, Services institute of Medical Sciences, Lahore from July, 2019 to January, 2020 A Total of 60 patients full filling the inclusion criteria were included in the study and were equally divided into two groups. Each group had 30 patients to compare the mean number of sore throat episodes in treatment and control groups. After approval from hospital ethical review committee (No.Estt/ 20980/S.H), informed consent was obtained from each patient.Group A patients received sublingual live-attenuated polyvalent bacterial vaccine and whereasgroup B were given placebo (normal saline 0.9%). Treatment response was noted for a period of 3 months.

Results: The mean number of sore throat episodes was 0.53 ± 0.63 in the sublingual polyvalent live-attenuated bacterial vaccine group compared to 1.67 ± 0.92 in the placebo group (p-value =0.0001). The mean duration of disease in Group A was 3.20 ± 1.56 years compared to 3.40 ± 1.63 years in Group B.

Conclusion: Sublingual live-attenuated polyvalent bacterial vaccine is effective in reducing the number of recurrent sore throat episodes and need for frequent antibiotic use and/or tonsillectomies.

Key Words: Recurrent sore throat, Sublingual polyvalent bacterial vaccine, Efficacy, Live attenuated, Outcome, Placebo group

INTRODUCTION

Recurrent sore throat is a one of the common health problems that is associated with significant morbidity. It is common manifestation of upper respiratory tract infection, affecting the quality of life andcontributes to antimicrobial resistance due to widespread use of antibiotics.[1] Currently, there are no formal recommendations for the prophylaxis of recurrent episodes of throat infection. Several studies have shown that the oral administration of bacterial vaccines resulted in reduction in recurrent episodes of sore throat in adults and children by decreasing the numbers of these episodes, duration and severity.[2,3,4] Although this problem is relatively more common in children but still there is a significant burden of this disease in adults[5]. Group A beta-hemolytic streptococciare one of the most common organisms to cause this problem.[6,7] The treatment is primarily based on anti-inflammatory medications and antibiotics and prophylaxis is rarely provided to these patients. Recurrent sore throat can also cause lifelong problems such as

Corresponding Author:
Dr. Abdul Malik Mujahid, Assistant Professor of Plastic Surgery, Burn and plastic surgery Department, Teaching Hospital, D.G. Khan, Medical College, Der Ghazi Khan; Email: Iqbalian_127@yahoo.com

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rheumatic fever and post-infective renal problems in children[8]

The sublingual route of bacterial preparations has been proposed as a safer and effective immunotherapy.[9]Sublingual vaccine is a polyvalent bacterial preparation. It contains strains of different inactivated bacteria which are frequently present in the UPRT. Such bacteria include *Streptococcus pneumonia*, *Staphylococcus aureus* and many others bacterias.[10]Macchiet al. evaluated the prophylactic role of an immunostimulating bacterial lysate in patients with recurrent URTI and showed promising results.[11]

As there is no local data available so result of this study will help to evaluate the role of sublingual live-attenuated bacterial vaccine in reducing recurrent episodes of sore throat.

OBJECTIVE

To determine the efficacy of sublingual live-attenuated polyvalent bacterial vaccine in patients with recurrent sore throat.

MATERIALS AND METHODS

This RCTwas conducted at Department of ENT, Services Institute of Medical Sciences (SIMS), Lahore from July, 2019 to January, 2020. A Total of 60 patients full filling the inclusion criteria (All patients with sore throat > 4 episodes during last one year, ages between 10 to 40 years and both genders) were included. Patients having acute diseases, sensitive to polyvalent vaccine, who have already taken polyvalent vaccine, Diabetic and immunocompromised patients were excluded from the study. Patients were randomlydivided into two equal groups by using ballot paper method. After the approval from institutional review board, written informed consent was obtained from the patients or guardians. The parents/guardians of the patients were fully explained about the purpose, procedure, risks and the benefits of vaccine. Group-A received sub lingual live attenuated polyvalent bacterial vaccines on daily basis for 3 months while the group B received placebo (0.9% Normal Saline) for the same duration once a day. All patients were followed up for three months at which outcome i.e., number of episodes of sore throat was noted.SPSS version 23.0 was used to analyze the collected data. The mean and standard deviations were used for quantitative variables like age, duration of disease, BMI and number of episodes. The qualitative variables like gender, place of living (rural/urban) and occupation were presented as frequency and percentage. Independent 't' test was used to compare the mean number of episodes of sore throat in both groups and p-value ≤ 0.05 was considered as significant.

RESULTS

In this study a total of sixty cases were included, out of that 19 (31.67%) were females and 41 (68.33%) were males with male to female ratio of 2.16:1. Group A patients were given sub lingual live attenuated polyvalent bacterial vaccine, while the Group B received placebo. Age range was from 10 to 40 years with mean age of 25.68 ± 7.20 years. The mean age in group A was 26.33 ± 7.70 years and in group B was 25.03 ± 6.73 years. Majority of the patients 31 (51.67%) were between twenty-six to forty years of age. Distribution of patients according to occupation and location is also shown(Table no: 1).

Mean duration of disease was 3.30 ± 1.59 years. The mean duration of disease in group A was 3.20 ± 1.56 years and in group B was 3.40 ± 1.63 years. Majority of the patients 33 (55.0%) were of>3 years duration. Mean numbers of sore throat episodes were 0.53 ± 0.63 in group A and 1.67 ± 0.92 in the placebo groupB(p-value = 0.0001) (Tableno: 2) Stratification of mean episodes of sore throat with respect to age groups showed significant difference in mean episodes of sore throat in all age groups among both groups. Similarly, statistically significant difference was found in mean episodes of sore throat among both groups in both genders. Stratification of mean episodes with respect to duration of disease also showed statistically significant difference among them. Stratification of episodes of sore throat with respect to place of living, BMI and occupation is also shown (Table no: 3)

DISCUSSION

Live vaccines have played a critical role from the beginning of vaccinology. Within the last two decades, the concept of live vaccines regained interest due to increased understanding and availabilityof molecular techniques for preparation of safer live vaccines possible. It has led to the development of new bacterial vaccines that can avoid the downsides of intravenously administered vaccine.[12,13] Furthermore, these vaccines can be designed to induce an immune response to itself or to a carried heterologous antigen. More than two thousand papers were published regarding application of live vaccines; but few of those could be registered after the licensing process.[14-17]

We have conducted this study to compare the mean episodes of sore throat after 03 months of treatment with sublingual polyvalent live attenuated bacterial vaccine versus treatment with placebo for recurrent sore throat. In this study, the mean numbers of episodes were 0.53 ± 0.63 in the sublingual polyvalent live attenuated bacterial vaccine group and 1.67 ± 0.92 in the placebo group.

In a study by Macchi A et al.[11], out of three groups, the group with sublingual bacterial vaccine had less numbers of respiratory tract infections and fewer requirements of antibiotics. Many questions regarding sublingual vaccinations still remain to be addressed. However, the different studies have demonstrated promising aspects of sublingual immunization which are highly effective and safe in generating robust immune responses. Furthermore, it provides protective immunity by simultaneously eliciting systemic IgG and mucosal IgA antibodies as well as CTL responses. The result of these research studies suggests that against respiratory and genital organisms, sublingual vaccination could be a better choice than parental vaccines[18,19,20]. In another multicenter study, there was fifty percent reduction in the number, severity, and duration of respiratory tract infections. [21]

In another study, forty-seven patients were included and were divided into two groups randomly. In Group A, twenty-four patients received one sublingual tablet of MLBL per day for 10 consecutive days per month for 3 months and Group B patients (23) received daily one sublingual tablet of taste masked placebo for 10 consecutive days per month for 3 months. During the treatment and after completion, the number of sore throats infection and their duration were statistically lower in the MLBL group than in the placebo group. The beneficial effects in vaccine treated group were maintained during the treatment and in 3 months follow-up after completion of treatment.[22]

CONCLUSION

Sublingual live-attenuated polyvalent bacterial vaccine is effective in reducing the number of recurrent sore throat episodes and need for frequent antibiotic use and/or tonsillectomies. So, we recommend that routine use of sublingual polyvalent live attenuated bacterial vaccine should be encouraged for recurrent sore throat in order to reduce the morbidity of these patients and avoid unnecessary antibiotics use and tonsillectomies.

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Authors Contribution

Dr. Abdul Shakoor

Principal contributor, conceptualization and design of research work

Dr. Abdul Malik Mujahid.

Co contributor, plagiarism correction, final approval

Dr. Muhammad Junaid Ashraf

Co contributor, data analysis,

Dr. Izzah Islam

Statistical analysis, literature search

Dr. Junaid Rasul Awan

Writing of manuscript, collection of data, drafting

Dr. Waqas Aslam

Literature search, result analysis, review of manuscript

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Table 1: Demographic characteristics of the patients included in this study.

Patient characteristics	Vaccine group (N=30)	Placebo group (N=30)
Gender		
Male	21 (70%)	20 (66.7%)
Female	9 (30%)	10 (33.3%)
Residential status		
Urban	13 (43.3%)	16 (53.3%)
Rural	17 (56.7%)	14 (46.7%)
Age		
Mean age ± SD	**26.33 ± 7.70**	**25.03 ± 6.73**
10-25 years	13 (43.3%)	16 (53.3%)
26-40 years	17 (56.7%)	14 (46.7%)
BMI (kg/m²)		
<30	22 (73.3%)	24 (80%)
>30	8 (26.7%)	6 (20%)
Occupation		
Office	10 (33.3)	13 (43.3%)
Field	6 (20%)	3 (10%)
Factory	7 (23.3%)	9 (30%)
Domestic	7 (23.3%)	5 (16.7%)

Table 2: Duration of illness and mean episodes of sore throat episodes among groups

Variables N=60	Vaccine group (n=30)	Placebo group (n=30)	Total	P-value
Duration of Illness (Years) (Mean ± SD)	**3.20 ± 1.56**	**3.40 ± 1.63**	**3.30 ± 1.59**	**0.629**
1 - 3 years	14 (46.7%)	13 (43.3%)	27 (45.0%)	
> 3 years	16 (53.3%)	17 (56.7%)	33 (55.0%)	

Table 2: *(Continued)*

Variables N=60	Vaccine group (n=30)	Placebo group (n=30)	Total	P-value
No of sore throat episodes (Years) (Mean ± SD)	**0.53 ± 0.63**	**1.67 ± 0.92**	**1.1 ± 0.78**	**<0.001**
0	16 (53.3%)	3 (10.0%)	19 (31.6%)	
1	12 (40.0%)	10 (33.3%)	22 (36.7%)	
2	2 (6.4%)	11 (36.7%)	13 (21.7%)	
3	0 (0.0%)	6 (20.0%)	6 (10.0%)	

Table 3: Comparison of mean episodes of sore throat with demographic and clinical profile of subjects among groups

Characteristics	Sore throat episodes in vaccine group (mean ± SD)	Sore throat episodes in placebo group (mean ± SD)	P-value
Age			
10-25 years	0.38 ± 0.65	1.50 ± 0.89	0.001
26-40 years	0.65 ± 0.61	1.86 ± 0.94	0.002
Gender			
Male	0.57 ± 0.60	1.70 ± 0.86	0.0001
Female	0.44 ± 0.73	1.60 ± 1.07	0.0133
Duration of Illness			
1-3 years	0.50 ± 0.65	1.23 ± 0.93	0.213
>3 years	0.56 ± 0.63	2.00 ± 0.79	0.0001
Living			
Rural	0.47 ± 0.51	1.64 ± 0.84	0.0002
Urban	0.62 ± 0.77	1.69 ± 1.01	0.0032
BMI			
>30	0.68 ± 0.65	1.54 ± 0.93	0.0487
<30	0.13 ± 0.35	2.17 ± 0.75	0.0001
Occupation			
Office	0.40 ± 0.52	1.54 ± 0.97	0.0018
Field	0.67 ± 0.82	2.33 ± 0.58	0.0138
Factory	0.57 ± 0.53	1.20 ± 0.84	0.0893
Domestic	0.57 ± 0.79	1.89 ± 0.93	0.0334