

## **Comparative prospective randomized open label trial of synbiotic (bifilac) as an add on therapy with standard treatment in patients with aphthous ulcer**

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### **ABSTRACT**

**Background:** To trial the safety, efficacy and rapidity of response to a lozenges containing synbiotic in patients with minor aphthous ulcer.

**Methods:** A total of 60 patients were enrolled for the trial after obtaining IEC approval and randomly allocated into two groups. Control “Group A” was administered with conventional treatment i.e., zytee and B complex for 2 weeks and trial “Group B” was administered with Bifilac along with conventional treatment for 2 weeks. The results of this trial were analyzed both subjectively and objectively.

**Results:** Comparing with control group, where standard treatment was used with analgesics and B-complex, the trial group showed a quick relief of pain and helped in reducing mean size of ulcer.

**Conclusions:** This trial was done with synbiotic lozenges in minor aphthous ulcers and it proved to be better alternative for them. Moreover, synbiotics have no adverse effects.

**Keywords:** Analgesics, Aphthous ulcer, Synbiotic, Lozenges

### **INTRODUCTION**

Synbiotic are the products that contain both probiotic and prebiotic.<sup>1</sup> The term probiotic was introduced in 1965 by Lilly and Stillwell. In contrast to antibiotics probiotic are defined as microbial derived factors that stimulate growth of other useful organisms.<sup>2</sup> Normal microbial flora is disturbed in infectious conditions like aphthous ulcer. Probiotics produce organic acids, bacteriocins and peptide.<sup>3</sup> Thereby they reduce the risk of colonization by pathogenic microorganisms.

Prebiotic is a non-digestible food ingredient that confers benefits on the host by selectively stimulating one bacterium or a group of bacteria with probiotic properties. Various bacterial genera most commonly used in probiotic preparations are Lactobacillus, Bifidobacterium, Escherichia, Enterococcus, Bacillus and Streptococcus. Some fungal stains belonging to Saccharomyces have also been used.

Aphthous ulcers or recurrent aphthous stomatitis (RAS) commonly referred to as canker sores are inflammatory lesions of the mucous lining of the mouth which may

involve the cheeks, gums, tongue, lips and floor of the mouth.<sup>4</sup> Aphthous minor is amongst the most common form of oral ulcerative disease and affects an estimated 80% of the population worldwide. Aphthae is derived from Greek word “aphthai” which means “burn”. Although the exact etiology is unknown, the probable causes proposed include immunodeficiency, nutritional deficiency, and psychological factors.<sup>5</sup> Clinical features comprises of recurrent bouts of one or several rounded, shallow, painful oral ulcers. RAS usually presents in either of three forms; minor, major, and herpetiform ulcers.<sup>1</sup>

The aim of the following trial is to determine the efficacy and rapidity of response to synbiotic lozenges in patients with minor aphthous ulcers. The objective being to evaluate safety, efficacy of synbiotic lozenges in patients with aphthous ulcer on conventional therapy in tertiary care hospital.

## METHODS

**Trial design** Comparative prospective randomized open label trial.

**Trial centre** Govt. Kilpauk Medical College, Dental OP Department, Chennai.

**Trial population** 30 patients in each of the 2 groups namely “Group A” and “Group B” attending dental out patient department for newly diagnosed minor aphthous ulcers.

**Trial period** was 3 weeks and trial duration was 3 months.

### Inclusion criteria

- 18 -65 years
- Both sexes
- Newly diagnosed minor form of aphthous ulcer

### Exclusion criteria

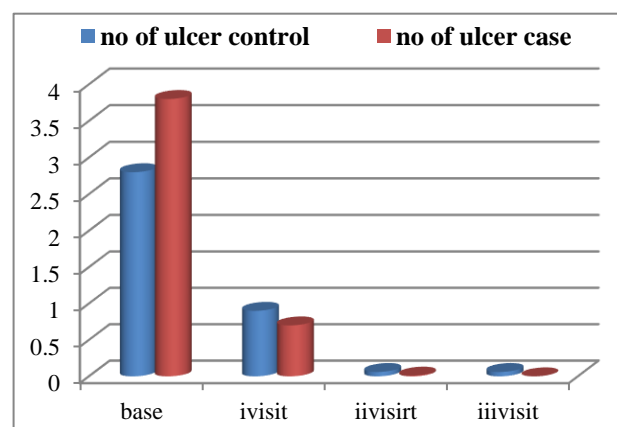
- Age below 18 and above 65 years
- Pregnant and lactating women
- Patient with major and herpetiform type of aphthous ulcer
- Patient with systemic diseases like ulcerative colitis, crohns disease, bechets syndrome
- Immuno compromised and HIV /AIDS patients
- Diabetics, smokers, beetle nut chewers
- Malignancy or any end organ damaged patients
- Synbiotic administration in the past one month
- Known hypersensitivity to synbiotic

The trial was conducted after obtaining approval from institutional ethics committee of Govt. Kilpauk Medical College and Hospital. Patients who are attending the outpatient department, Department of dental surgery in Govt. Kilpauk Medical College, Chennai, with history of minor aphthous ulcer were explained about the trial

purpose and the treatment to be given. Written informed consent in local language was obtained from those who were willing to participate in this trial. Sample size calculation was done on the basis of previous studies and it was concluded to have a total of 60 patients (30 in each group) in order to achieve appropriate power of the study. Hence, a total of 60 patients were enrolled for the trial. Patients were randomly allocated with the help of a computerized randomization chart into two groups having 30 patients each. Participants were enrolled to the trial “Group A” which received analgesics with B complex or the control “Group B” which received analgesics with B complex and Bifilac lozenges. Analgesics and B complex were given once a day for 15 days and followed up at the end of first week, second week and third week for a total of 3 weeks. Synbiotic lozenges were given thrice a day along with conventional therapy. The results of this trial were analyzed both subjectively and objectively by using SPSS software. The clinical parameters that were assessed in the trial were number of ulcers present, size of ulcer (1mm/2mm/3mm/4mm/5mm), duration of ulcer in days and degree of pain (no pain/moderate pain/severe pain).

## RESULTS

According to Table 1, the number and size of ulcer along with pain reduced considerably in subsequent follow ups for the trial group when compared to control group.



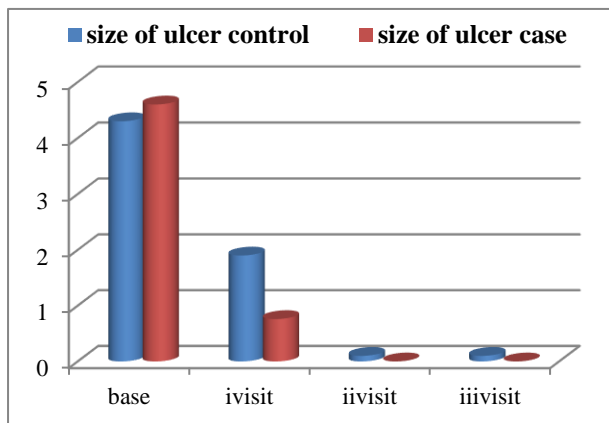
**Figure 1: Case vs control variation in number of ulcers in subsequent follow ups.**

As per Figure 1, comparing the mean value of the control and the trial group, the mean number of ulcer in control group was reduced from 2.833 at the beginning of the trial to 0.966 at the end of first week, 0.06 at the end of second week and 0.06 at the end of third week i.e. at the follow up week.

Whereas in trial group the mean number of ulcer reduced from the basal value of 3.866 to 0.76 at the end of first week, 0.1 at the end of the second week and 0 at the end of follow up at the third week with p value of 0.05, which is significant.

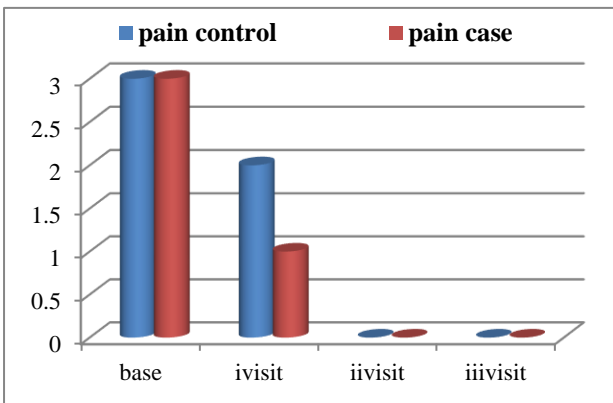
**Table 1: Statistical analysis of various parameters in the study.**

Visit	Parameter	Control Group B		Trial Group A	
		Mean	SD	Mean	SD
Base	No of ulcer	2.833	0.985	3.866	1.195
	Size of ulcer	4.3	1.10	4.6	1.22
	Pain	3	0	3	0
I visit	No of ulcer	0.966	0.764	0.7666	0.858
	Size of ulcer	1.9	0.66	0.766	0.6260
	Pain	2	0	1	0
II visit	No of ulcer	0.06	0.253	0.01	0.3051
	Size of ulcer	0.1	0.305	0	0
	Pain	0	0	0	0
III visit	No of ulcer	0.0666	0.253	0	0
	Size of ulcer	0.1333	0.345	0	0
	Pain	0	0	0	0



**Figure 2: Case vs control variation in size of ulcers in subsequent follow ups.**

As per Figure 2, comparing the mean value of the control and the trial group, the mean size of the ulcer in control group was reduced from 4.3 at the beginning of the trial to 1.9 at the end of first week, 0.1 at the end of second week and 0.1 at the end of third week.



**Figure 3: Case vs control reduction in pain control in subsequent follow ups.**



**Figure 4: Before treatment in a patient in Group B- presence of aphthous ulcer can be noted.**



**Figure 5: After treatment in a patient in Group B- the aphthous ulcer has healed.**

As per Figure 3, comparing the mean value of the control and the trial group, the mean pain perception in control group was reduced from 3 at the beginning of the trial to 2 at the end of first week and 0 at the end of second week and 0 at the end of third week. Whereas in trial group the mean pain perception was reduced from 3 at the beginning of the study to 1 at the end of first week, 0 at the end of second week and 0 at the end of third week. Whereas in trial group the mean size of the ulcer in control group was

reduced from 4.6 at the beginning of the trial to 0.76 at the end of first week, 0 at the end of second week and 0 at the end of third week.

Further, pictorially distinct reduction in the size and number of ulcers could be noticed while comparing the Figure 4 (before treatment) and Figure 5 (after treatment).

## DISCUSSION

Aphthous ulcers or recurrent aphthous stomatitis (RAS), commonly referred to as canker sores, are inflammatory lesions of the mucous lining of the mouth which may involve the cheeks, gums, tongue, lips, and floor of the mouth.<sup>6</sup> Minor aphthous ulcer is amongst the most common form of oral ulcerative diseases and affects an estimated 15-20% of the population worldwide.<sup>7</sup> It is less than 5mm in diameter. It is characterized by round or oval shallow ulcers with grey white pseudomembrane enveloped by a thin erythematous halo. Usually minor aphthous ulcer occurs at labial and buccal mucosa and floor of the mouth and it is uncommon on the gingival, palate or dorsum of the tongue.<sup>8</sup> Probiotics are live microorganisms which confers health benefit in the host. They are indicated and widely recommended in infective diarrhoea, antibiotic induced diarrhoea, lactose intolerance, inflammatory bowel disease, traveller's diarrhea and irritable bowel syndrome. Prebiotics are non digestible substances that provide physiological benefit to the host by providing favourable environment for the growth of limited number of indigenous bacteria. Most prebiotic are used in food ingredient chocolate, cakes, biscuits. Commonly known prebiotics are oligofructose inulin, lactulose, and galactooligosaccharides.<sup>9</sup>

Synbiotics are products that contain both prebiotic and probiotic<sup>9</sup>. Although various studies about treatment of aphthous ulcer have been done, in this trial effectiveness of synbiotic lozenges in minor aphthous ulcers were studied. Comparing with control group, where standard treatment was used with analgesics and B-complex, the trial group showed a quick relief of pain and helped in reducing mean size of ulcer.

## CONCLUSION

This trial done with synbiotic lozenges in minor aphthous ulcer has proved to be better alternative in patient suffering from it. Moreover, synbiotics have no adverse effects.

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*Conflict of interest: None declared*

*Ethical approval: The study was approved by the Institutional Ethics Committee of Kilpauk Medical College and Hospital, Chennai, India*

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