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ORIGINAL RESEARCH

Probiotics an Adjuvant in The Management of Recurrent Aphthous Ulcer: A Randomized Clinical Trial

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ABSTRACT

Background: Recurrent Aphthous Stomatitis (RAS) is a kind of benign mouth ulceration. RAS is one of the most prevalent ulcers, affecting around 20% of the population. The goal of this study was to assess the effectiveness of probiotics on RAS.

Materials and Procedures: A total of forty people were divided into two groups. For 7 days, 20 patients in Group 1 were given Bacillus coagulans (Sporolac) and Tetracycline capsules 250 mg (Resteclin) twice daily. For 7 days, Group 2 patients were given just Tetracycline capsules 250 mg (Resteclin) twice daily. At the baseline, 4th, and 7th days, pain, size, and average duration of the ulcer were assessed. For statistical Analysis, The Mann Whitney U test was used to compare the parameters between the two groups.

Results: In just four days, the Probiotic group saw a substantial drop in all of the metrics.

Conclusion: Probiotics are used in the treatment and management of RAS as an adjuvant therapy.

Keywords:Aphthous ulcers, probiotics, tetracyclines

INTRODUCTION

The most common lesion of the oral mucosa, popularly known as canker sores, is recurrent aphthous stomatitis (RAS). Ulcers are shallow and painful, with a serous discharge on the ulcer floor and a halo of inflammation surrounding them. Clinically, the disease is divided into three types: minor, major, and herpetiform. The most prevalent kind of RAU is minor RAU (MiRAU), which affects 75–80% of individuals.[1] Minor RAS is characterised by painful, recurring, tiny, spherical, well defined with confined edges, erythematous halos, and

yellow or grey pseudomembrane measuring 5 mm in diameter (2–3 mm on average) that heal between 7 and 14 days without scarring.[2] Major aphthae are healed by scarring.

The disease's genesis is unknown and contentious, although many causes have been identified, including immunologic issues, environmental and psychological stress, and viral infections.[1] Probiotics are living microorganisms that provide a health benefit to the host when given in sufficient concentrations. Probiotics interact with and enhance the immune system, which helps to avoid illnesses.[3] Organic acids, bacteriocins, and peptides are all produced by probiotics. As a result, the chance of harmful bacteria colonization is reduced.[4]Tetracyclines relieve pain by reducing prostaglandin synthesis, suppressing leukocyte activity, inhibiting collagenase and gelatinase activities, and inhibiting oxidative activation. The goal of this trial was to see if probiotics might be used as an adjuvant therapy to treat RAS.

MATERIALS AND METHODS

Patients with recurrent aphthous ulcers who presented to the Department of Oral Medicine and Radiology were enrolled in the research, which was arandomised clinical trial. RAS was diagnosed based on its clinical presentation and the individuals' medical histories. The trial enrols RAS patients who have one or more aphthous ulcers that have been present for less than 48 hours and have a diameter of 1 cm or more. This research includes nine major aphthous ulcers. Based on the parallel randomization procedure, thirteen individuals were enrolled and randomly assigned to two groups. Controls of the same age and sex were used. Before receiving therapy, all patients got written and verbal information about the research and completed an informed consent form.

INCLUSION CRITERIA

a) Patients must be willing to participate in the trial
b) Minimum age between the ages of 18 and 50
c) Patients who aren't on any other drugs.

CRITERIA TO BE EXCLUDED

a) Oral mucosal ulcers other than RAS
b) Patients with systemic disorders or syndromes
c) Women who are pregnant or nursing
d) Minors under the age of eighteen.

Bacillus was given to Group 1's 10 subjects (6 men and 4 females). For 7 days, take coagulans (Sporlac) and tetracycline 250 mg (Resteclin) twice daily. Sporlac should be given one hour after receiving antibiotics. The probiotics were combined in 10 mL of water, swished in the mouth for 1–3 minutes, then swallowed. The contents of a tetracycline capsule were similarly combined with 10 mL of water, swished for 1–3 minutes, and ingested. Only tetracyclines capsules 250 mg (Resteclin) twice day were given to Group 2's 10 participants (6 males and 4females) for 7 days. The contents of the capsules were combined in 10 mL of water and swished in the oral cavity for 1–3 minutes before being consumed.

The number, place, size with divider and scale, and pain were all assessed using the Visual Analog Scale (VAS) from 1 to 10, with 0 being nonexistent, 1 being light, 5 being moderate, and 10 being severe. Yes/no was used to indicate how tough it was to eat. In patients who had more than one ulcer, the most recent ulcer was picked. On the fourth and seventh days, patients were asked back to check ulcer healing, discomfort, and feeding difficulties. The treatment's success was determined by a decrease in all metrics in both groups. Telephone talks were held on a regular basis to monitor medicine administration.

IBM SPSS statistics (Statistical Package for Social Science) version 22 was used to examine the data (Armonk, NY: IBM Corp). For categorical variables, descriptive data was given as frequency and percentage; for continuous variables, mean, median, standard deviation, and quartiles were used. The Chi square test and the fishers' test were used to compare categorical variables between the research groups. The Mann Whitney U test was used to compare the parameters between the two groups at each time period. A statistically significant P value of <0.05 was used.

RESULT

A total of 20 individuals aged 19 to 40 years old were initially included in the trial. In this study, the average age of onset of aphthous ulcers was 28.67±9.68 years. Because of noncompliance with the research protocol, three patients from Group 1 and four patients from Group 2 had to be removed from the trial. A total of 7 patients from Group 1 and 6 patients from Group 2 were included in the final research population. On the first day of reporting, baseline values were collected for each patient, including a history of trouble eating, the number of ulcers, the size of the ulcers in both groups, and the pain severity as VAS ratings. On the 4th and 7th days, patients in the study and control groups were recalled to record their history of trouble eating, the number of ulcers, the size of the ulcers, and the pain severity as VAS ratings. These were compared to the baseline levels and statistically assessed.

Between the first and fourth days, there was no significant difference in ulcer size reduction in both groups [Table 1]. On the seventh day, the results were substantial, demonstrating that group 1 had a total reduction in ulcer size compared to group 2. At the initial visit, group 1 had 5 (71.43%) and group 2 had 4 (66.67%) ulcers with a diameter of less than 1cm, respectively. In groups 1 and 2, the proportion of patients with ulcers larger than 1cm was 2 (28.57%) and 2 (33.33%), respectively. On the fourth day, the ulcer size was zero in 4 (57.14%) and 2 (33.33%) of group 1 and 2, and 1 cm in 3 (42.86%) and 4 (66.67%) of group 2 (p = 0.11). The ulcer size was zero in 12 patients in group 1 7 (100.0 percent) and 5 patients in group 2 (83.33 percent) on the seventh day, and 1cm in 1 patients in group 2 (16.67 percent). On the seventh day, there was a statistically significant reduction in ulcer size (p = 0.05). In comparison to group 2, the number of ulcers in group 1 decreased considerably from day 1 to day 7. [Table 1].

Table 1:Ulcer Size Comparison Between Groups 1 and 2 at Different Time Intervals

Visit	size	Group		Total	Chi Square Test	
		1	2		Chi Square value	P value
First visit	1	5 (71.43 %)	4 (66.67%)	9 (69.24%)	-	0.08
	2	2 (28.57 %)	2 (33.33%)	4 (30.77%)		
Second visit	0	4 (57.14 %)	2 (33.33%)	6 (46.15%)	2.63	0.11
	1	3 (42.86 %)	4 (66.67%)	7 (53.85%)		
Third visit	0	7 (100 %)	5 (83.33%)	12 (92.31%)	-	0.05*

	1	0 (0 %)	1 (16.67%)	1 (7.69%)		

#(size: 1 =<1cm, 2=>1cm, 0=0). *p<0.05 statistically significant

At the initial visit, light pain was found in 2 (15.38%) patients, moderate pain in 4 (30.77%) patients, and severe pain in 7 (53.85%) patients in both groups. The pain level at the second visit was zero in 8 (61.54%) patients, light in 3 (23.08%), and moderate in 2 (15.38%) patients, respectively. In 13 patients (100.0%), the pain score was zero at the third visit. At the second visit, there was a statistically significant difference in pain reduction (p = 0.01) [Table 2].

Table 2:The Mann Whitney U Test was used to compare the size, number, and pain of ulcers in Group 1 and Group 2 at different time intervals

	Group	**n**	**Mean±SD**	**U statistic**	**P**
Size in 1st visit	1	7	1.23 ±0.33	103.5	0.44
	2	6	1.37±0.49		
Size in 2nd visit	1	7	0.34±0.43	85	0.17
	2	6	0.64±0.50		
Size in 3rd visit	1	7	0.0±0.0	77	0.05*
	2	6	0.38±0.47		
No. of ulcers in 1st visit	1	7	1.11±0.30	106.5	0.57
	2	6	1.19±0.45		
No. of ulcers in 2nd visit	1	7	0.54±0.50	106.5	0.60
	2	6	0.47±0.44		
No. of ulcers in 3rd visit	1	7	0.0±0.0	84.5	0.04*
	2	6	0.23±0.48		
VAS in 1st visit	1	7	2.51±0.75	116.5	0.08
	2	6	2.55±0.62		
VAS in 1st visit	1	7	0.23±0.55	56	0.01*
	2	6	0.97±0.72		
VAS in 1st visit	1	7	0.0±0.0	118	1
	2	6	0.0±0.0		

DISCUSSION

Because of the wide prevalence of RAS, there has been a lot of study into effective treatments. RAS is a painful inflammatory condition marked by necrotizing ulcers of the oral mucosa that can occur at any moment and can persist, remit, or reoccur.[5]Nonkeratinized mucosa is the most common kind of RAS. Major aphthae account for 10% to 15% of RAS cases, with ulcerations that are bigger, last longer, and can leave a scar. Herpetiformaphthae account for 5–10% of all RAS cases, and they are characterised by numerous 1–3 mm painful

ulcers that resemble herpes simplex outbreaks but include nonkeratinized mucosa and last up to 14 days.[6]Following antibiotic resistance, the World Health Organization (WHO) ranked probiotics as the second most important component of the immune defence system in 1994.[7] Probiotics can form a biofilm, which acts as a barrier between the oral mucosa and oral illnesses.[8] Using probiotics in combination with antibiotics can decrease the consequences of antibiotic-induced dysbiosis while also maximising the advantages of immunological activation on the gut.[9] Probiotics will reduce inflammation through affecting epithelial cells and mucosal immune system malfunction, both of which are at the root of inflammation.[10] Probiotics have a positive impact on the immune system by increasing nonspecific immunity and regulating the humoral and cellular immune responses.[11] Both groups showed substantial reductions in ulcer size in our research, although Group 1 showed a considerable reduction in ulcer size on the seventh day compared to Group 2 ($p = 0.05$). Probiotics coupled with tetracyclines were found to be clinically effective in speeding ulcer healing.

Within 3 - 4 days, both groups had a significant reduction in discomfort. At the second visit, there was a statistically significant difference in pain reduction between the two groups ($p = 0.05$). On the seventh day, both groups saw a reduction in the amount of ulcers and difficulty eating. Reduced production of Nitric Oxide (NO), a strong mediator of inflammation that may control the production of inflammatory cytokines such as PGE2, IFN, MMPs, and TNF, is linked to pain relief. On day 5 of treatment, our findings are similar to those of Nirmala M et al., who found that when Bacillus Clausii was given to the patients, the mean number of ulcers and ulcer size decreased equally in both groups, whereas erythema and degree of pain decreased significantly in group A patients compared to group B ($p = 0.001$ and 0.0001, respectively).[8] Furthermore, our findings correspond with those of Nalini et al., who found that utilising probiotic lozenges reduced the size of ulcers in patients. Patients in both groups improved their symptoms on day 10 of their study, with no significant difference between them.[12]

CONCLUSION

The efficiency and quickness of response to probiotic as an adjuvant in the treatment of aphthous ulcer were proven in this study. The study found that probiotics and tetracyclines reduced the number, size, and discomfort associated with ulcers while having no negative side effects. As a result, probiotics in combination with tetracyclines can be an effective adjuvant therapy for RAS.

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