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Probiotics in Diabetic Wound Care

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Abstract: *Diabetic foot is a leading cause of DALY with both physical and economic cost to the patient. With increasing cost of healthcare and antibiotic resistance, there is a need for new and innovative methods for management of the diabetic foot ulcers. Ourresearch studied the effect of local application of probiotics on the healing of diabetic foot ulcers by comparing the changes in wound bed score and wound swab culture results in the test and control population. The control group was managed by the current regimen of sharp and chemical debridement at ward, cleaning and dressing, glycemic management and antibiotic therapy. In the intervention group, in addition to the above, probiotic solution was applied daily during dressing. Wound swab cultures were taken at Day 0, Day 5 and Day 10. Both the groups were compared with respect to the wound bed score at day 1, day 7 and day 14 and the wound swab cultures and outcomes identified. A total study population of 36 was analyzedand it was found that all the patients had improvement in the wound status and the mean wound bed score of the intervention group was better than the control group. Also the wound swab culture report in the intervention group reported more number of 'no growth'. However it was not statistically significant. In conclusion, probiotics can be safely utilized in therapy of infected diabetic wounds by hastening the wound healing process as evidenced by the significant difference in the day 7 wound bed score*
Keywords: *Probiotics, diabetic foot ulcer, lactobacillus, gangrene*

I. Introduction

The diabetic foot is an important cause of mortality and morbidity. It ranges from an uninfected chronic ulcer to frank gangrene of the limb [1]. It causes great physical handicap, and psychosocial disability. Also the economic cost with respect to health care expenditure, loss of work days, indirect costs to the patient are high. Moreover, with the indiscriminate use of antibiotics, the problem of antibiotic resistance is a rapidly rising one. So novel therapies and interventions is the need of the hour to reduce both the cost, time and deal with the problem of antibiotic resistance [2]. There were only 36 papers dealing specifically with diabetic foot in the Pubmed database for the past 5 years, as compared to other complications of diabetes like nephropathy which has 8000 papers [3, 4]. One of the novel technology is the application of probiotics [5,6]. The research in probiotics is at a nascent stage. Few studies in mice, rats and even one study on burns patients have given positive evidence regarding the probiotics. Hence, further research in this field is need of the hour.

Aims And Objectives

- To study the effect of local application of probiotics on the healing of Diabetic foot ulcers
- To compare the change in wound bed score in the test and control population
- To compare the wound swab culture results in the test and control population

II. Materials And Methods

Study Centre
Institute of General Surgery, Madras Medical College and Rajiv Gandhi Government General Hospital
Study Type
Prospective study
Study Duration
December 2015 to June 2016
Sample Size
40 patients
Patient Inclusion Criteria
Patients admitted with clinically infected diabetic foot to RGGGH Chennai with the following characteristics:

- Age > 18 years , Age < 70 years
- Diabetics with average RBS < 250
- Ulcers involving the foot
- Wound size more than 10 cm^2 and less than 60 cm^2

Exclusion Criteria

- Unstable vital signs.
- Peripheral Arterial Disease
- Peripheral neuropathy
- Diabetic Ketoacidosis
- Osteomyelitis

Probiotic suspension

The probiotic solution is prepared by dissolving 5 billion CFU of probiotic bacteria (lactobacillus plantarum manufactured by Pharmagenica Healthcare Inc.) in 10ml of sterile water. This solution was applied to the wound at a volume of 1ml/cm^2 and dressed using cotton gauze and pad.

Assessment Of Wound Characteristics

The patients were assessed daily for wound progression. Wound bed scoring system developed by Falanga was utilised to monitor the wound in an objective manner. Both the groups were compared with respect to the wound bed score at day 1, day 7 and day 14 and the wound swab cultures and outcomes identified. Wound swab was checked for pathogenic bacteria. As per the policy of our microbiology department, swabs with normal commensal bacteria such a gram positive rods were reported as 'no growth'. The results were then checked for statistical significance.

Wound bed score			
Characteristics	0	1	2
Healing edges	None	25%-75%	>75%
Black eschar	>25% of wound surface area	0%-25%	None
Greatest wound depth	Severely depressed	Moderate	Flushed
Exudate amount	Severe	Moderate	None/mild
Edema	Severe	Moderate	None/mild
Peri-wound dermatitis	Severe	Moderate	None or minimal
Peri-wound callus fibrosis	Severe	Moderate	None or minimal
Pink wound bed	None	50%-75%	>75%
Total WBS adds each individual score for each characteristic to give a total score			
The maximum possible score is 16			
The minimum possible score is 0			

Wound Swab C&S

Wound swab cultures were taken at Day 0, Day 5 and Day 10 using a sterile swab and sent for microbiological analysis. They were grown on nonselective media. As per the existing policy of our microbiology department, only pathogenic bacteria was reported whereas commensal bacteria like bacillus, were reported as commensals.

III. Methods

Diabetic patients presenting with acute infected ulcers of the foot (below ankle) were taken up for surgical debridement on the day of presentation. The size of their wounds were assessed by wound tracing and planimetrymethod. A household plastic wrap was placed over the wound. A transparency marking pen was used to mark the wound. The wrap was placed over a graph paper and the number of squares counted. Those with an area less than 60 cm^2 were included in the study. The patients were screened for peripheral vascular disease by using ankle brachial pressure index. Only patients with ABPI >0.9 measured using Doppler method were taken up for the study [7]. The patients were also screened for peripheral neuropathy at the medial malleolus using 128Hz tuning fork vibratory sense testing to exclude those with severe neuropathy [8, 13]. Severely ill patients and those with diabetic ketoacidosis were excluded from this study. The patients who consented to participate in the study were allocated into two groups based on the use of sequentially numbered, opaque sealed envelopes (SNOSE) [9]. The control group were managed by the current regimen of sharp and chemical debridement at ward, cleaning and dressing, glycemic management and antibiotic therapy was given.

In the intervention group, in addition to the above, probiotic solution was applied daily during dressing. The probiotic solution was prepared by dissolving 5 billion CFU of probiotic bacteria in 10ml of sterile water [10]. This solution was applied to the wound at a volume of 1ml/cm^2 and dressed using cotton gauze and pad [11, 12].

(This was based on the concentration used by Peral MC et al in their study on Burns patients using Lactobacillus plantarum) [14, 15]. The patients were assessed for glycemic control by taking RBS every 3 days and taking the average of the value. Patients whose average RBS was above 250 were removed from the study. The patients were assessed daily for wound progression. Wound bed scoring system developed by Falanga [16] was utilised to monitor the wound in an objective manner. Wound swab cultures were taken at Day 0, Day 5 and Day 10. Both the groups were compared with respect to the wound bed score at day 1, day 7 and day 14 and the wound swab cultures and outcomes identified. The results were checked for statistical significance.

Analysis

The collected data was analysed for improvement in wound status between the study groups and the change in swab status. The software used to analyse the data was SPSS software version 19.

Age Distribution

Statistics

Age

N	Valid	36
	Missing	0
Mean		53.47
Median		53.50
Std. Deviation		7.930
Range		45
Minimum		25
Maximum		69

The majority of the subjects were in the 40-60 age group. The youngest was 25 and the oldest patient was 69

Sex Distribution

	Frequency	Percent	Valid Percent	Cumulative Percent
ValidFM	17	47.2	47.2	47.2
Total	19	52.8	52.8	100.0
	36	100.0	100.0	

The study population had an almost equal distribution of male and female subjects, with 17 females and 19 males

Group Statistics

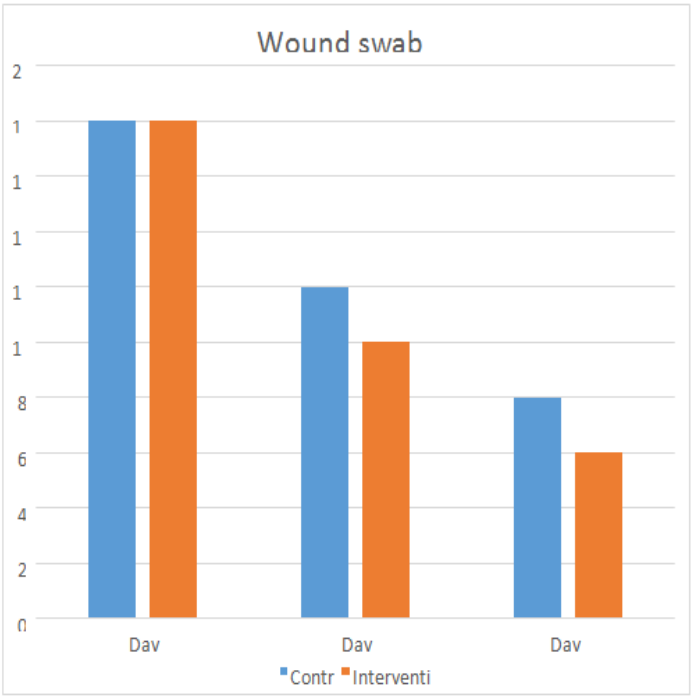
	Group	N	Mean	Std. Deviation	Std. Error Mean
Wound bed score	Intervention	18	8.22	.878	.207
	Control Group	18	8.11	.758	.179
WBS Day 7	Intervention	18	11.11	.963	.227
	Control Group	18	10.33	.907	.214
Wound bed score	Intervention	18	13.56	1.199	.283
	Control Group	18	12.72	1.320	.311

Wound Bed Score Analysis

The wound bed score at day1, day 7 and day 14 between control and test groups were recorded.

There were a total of 18 subjects in either group. The mean wound bed score on day 1 was 8.11 with a standard deviation of 0.758 for the control and 8.22 with standard deviation of 0.878 for the intervention group. The mean wound bed score on day 7 was 10.33 for the control group with a standard deviation of 0.907 and 11.11 with a standard deviation of 0.963 for the intervention group. On day 14 the mean value was 12.72 for the

control group with a standard deviation of 1.320 and 13.56 with a standard deviation of 1.199 for the intervention group.

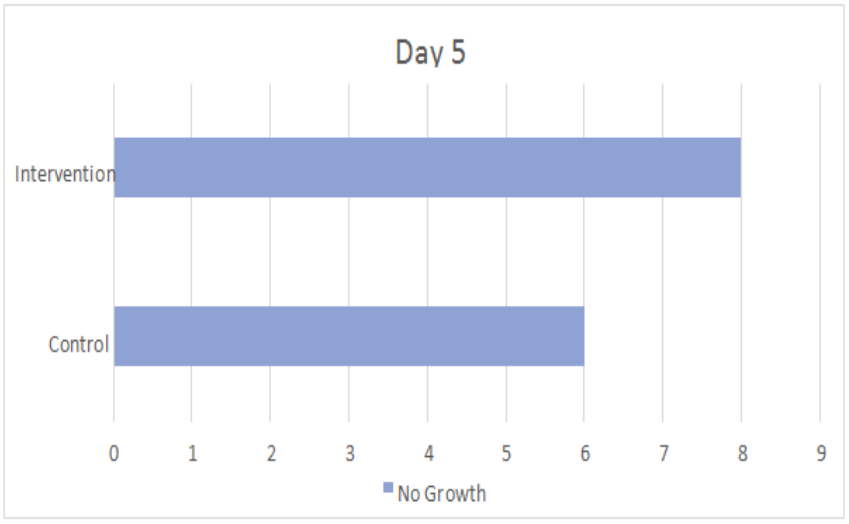


The mean wound bed score of control group on day 1 was 8.11 which improved to 10.33 on day 7 and 12.72 in day 14. In the intervention group the mean wound bed score was 8.22 on day one which increased to 11.11 on day 7 and finally to 13.56 on day 14. The Improvement on wound bed score on Day 7 over Day 1 was 2.22 in the control group and 2.89 in the intervention group. The wound bed score on day 14 improved by 4.61 in control group and 5.34 in the intervention group over the day 1 bed score. The mean WBS on Day 1 for Intervention group and control group were similar around 8. There were differences in the mean of day 7 (intervention 11.11 vs control 10.33) and in the mean of day 14 (intervention 13.56 vs control 12.72). The difference on WBS on day 7 attained statistical significance (0.018). The difference on WBS on day 14 did not attain statistical significance but was close to significant (0.056, p value 0.05).

Wound Swab C&S Analysis

The wound swab was sent for analysis on day 1, day 5 and day 10. Those with positive results were grouped as one and with no growth as another. The number of patients testing positive for wound swab progressively decreased over the course of treatment.

Day 5



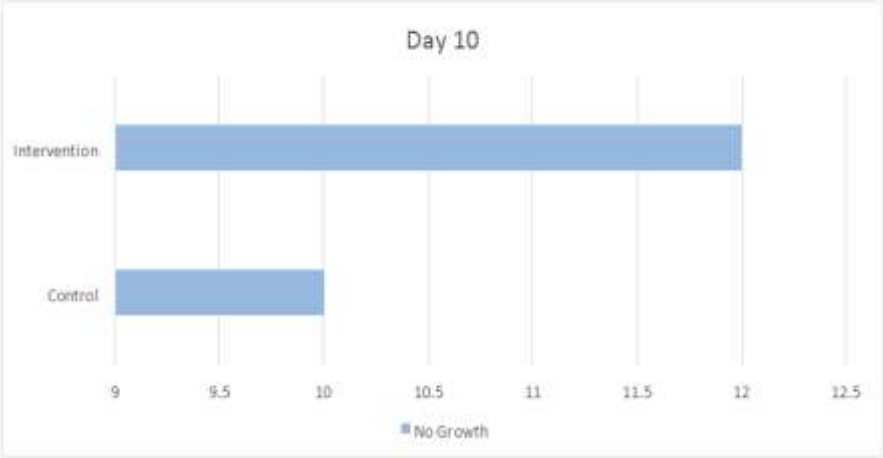
Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.468[b]	1	.494		
Continuity Correction[a]	.117	1	.732		
Likelihood Ratio	.469	1	.494		
Fisher's Exact Test				.733	.367
Linear-by-Linear Association	.455	1	.500		
N of Valid Cases	36				

a. Computed only for a 2x2 table

b. 0 cells (.0%) have expected count less than 5. The minimum expected count is 7. 00.

Day 10



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N of Valid Cases	36				

a. Computed only for a 2x2 table

b. 0 cells (.0%) have expected count less than 5. The minimum expected count is 7. 00.

We used a chi square analysis to identify any statistical significance in the wound swab cultures. But no significant association could be found.

IV. Conclusion

In our study, a total of 40 patients enrolled. However 4 of them (2 from each group) could not complete the study as they had to leave the hospital for personal reasons. Patients were debrided on the same day and insulin started for everyone with diabetes mellitus. Wound swab was taken on first day. The wound size was measured using tracing method. They were assessed for peripheral artery disease using handheld Doppler, and screened for peripheral neuropathy. These patients were included in the study after checking the inclusion and exclusion criteria and obtaining consent. They were allotted into their group based on sequentially numbered, opaque sealed envelopes.

There were 18 subjects in either group. Majority of them were in 40-60 age group and almost equally distributed between male and female. At the start of the study post debridement, either group had similar mean wound bed score, 8.11 in the control group and 8.22 in the intervention group. The difference was just 0.11. On day 7 however, the difference in the mean was 0.78. Independent samples test (t test for equality of means) showed a significant difference (p value 0.018). On day 14 the difference in mean was 0.84 and was not significant.

The wound swab culture of the wounds were studied on day 0 day 5 and day 10. The number of wounds with a positive status came down as the course progressed in either group. At the end of day 5, 8 subjects in the intervention had negative wound swab cultures while in the control group only 6 had negative wound swab cultures.

On day 10, 12 subjects in the intervention group had negative wound cultures while the control group had 10. Chi square analysis was done and no significance could be attributed to the difference.

In conclusion,

- Probiotics can be safely utilized in therapy of infected diabetic wounds
- They do hasten the wound healing process as evidenced by the significant difference in the day 7 wound bed score
- More studies are needed in this field to give better evidence for the support of probiotic use

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