

## Role of Probiotics in the Management of Burns Patients

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**Abstract:** Burn wound infection delay the grafting, prolongs hospital stay and responsible for septicemia. Burn wound infection is due to immunosuppression in burns patients, colonization of burn wound, translocation of microbes from gastrointestinal tract and over growth of the resistant organism due to prolong use of topical and systemic antibiotics. Objective: To find alternate, effective method to reduce burn wound infection, predictable grafts take and minimize hospital stay. This study investigated 64 patients having deep dermal and full thickness burns during May 2012 to June 2014. Patients of either sex having up to 50% BSA affected having either deep dermal, full thickness burn; expected to need grafting; were enrolled. The treatment group of this study, after taking informed consent, was given probiotics supplementation during entire period of hospitalization. The difference(s) in variables of interest between two groups were compared using student t test/ Chi Square test. Results revealed that in the 22 patients received probiotics supplementation (Treatment Group) and 42 considered Control Group. The mean age of treatment group was  $28.2 \pm SD 10.2$  years while for control groups it was  $30.2 \pm SD 13.80$  ( $p = 0.6004$ ). On admission mean BSA affected for treatment group was  $40.2\% \pm SD 13.80$ , for control it was  $38.2\% \pm SD 14.2$  ( $p = 0.5909$ ). The leukocytosis was seen in 68.96% of CBC for control and 67.64% CBC in treatment group. On average for each patients of control group, 9.75% body surface area was grafted as compared to treatment group where it was 10.81% for each patient. The graft loss was 29.26% in control group and 20.14% in treatment group. The mortality was 26% and 22% for control and treatment group respectively. In Conclusion: The use of probiotics does not prevent septic complications in burn patients; however for undiscovered reason(s) graft takes is more predictable.

**Key words:** Probiotics • Burn Patients • Management

### INTRODUCTION

Burns is 4<sup>th</sup> leading cause of traumatic injury, after road traffic accidents, fall from height and interpersonal violence [1]. Those commonly affected are poor, 300 000 people die every year after burns and 95% of death occurs in low and middle-income countries [2]. Soon after the incidence the burn wound is almost sterile for 24-48 hours, soon migration of gram-positive organisms from sweat glands and appendages colonize the burn wound. These gram positive organisms are replaced by more virulent gram negative organism derived from hospital Environment, translocation from gastrointestinal tract of the patient

or emerged as resistant organism due to prolong use of topical silver sulphadiazine [3]. These infectious complication delays the separation of eschar and growth of healthy granulation tissue, resulting in prolong hospital stay with all its attended threats. Even colonized burn wound when grafted under umbrella of appropriate antibiotics, the ratio of lost graft is significant necessitating repeat surgery with consequently increased burden on the already exhausted resources. To address the issue, various natural medicines, like honey, caria papaya fruit and aromatherapy with aromatic oils have been used with variable results [3]. The probiotics are currently the focus of the research.

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As define by WHO probiotic is "live microorganisms which, when administered in adequate amounts, confer a health benefit on the host" [4]. The beneficial effects of fermented diary product are known since the ancient time of Greek and Roman [5], essentially fermentation is the process to preserve the dairy products [6]. Probiotics naturally live within human body to maintain our health [7]. The probiotic are considered "good bacteria" as they help in digestion, immune function, absorption of nutrients and other bowl functions [8]. They naturally occur in many diary products like yogurt, which is commonly used in diarrhea and other gastrointestinal disorders. Fukushima *et al* in a double blind study showed that diet supplemented with lactobacillus, reduces incidence of wound infection and increases HB% and serum albumin in elderly patients [9]. It has been shown in experimental models that *lactobacillus plantarum* has beneficial role in healing of incised cutaneous wound [10] and diet supplemented with mixture of probiotics prevents bacterial translocation and maintain mucosal integrity of gut [11]. Maria C Peral *et al* performed bacteriotherapy with *lactobacillus plantarum* in 2nd and 3<sup>rd</sup> degree burn and shown that it reduces bacterial load and graft take is more predictable [3].

We at our unit, after appropriate resuscitation in deep major burn wait for natural separation of the slough; meanwhile silver sulphadiazine is used topically after surgical toilet of the wound with povodine iodine and normal saline. Once slough separated the development of healthy granulation is inversely dependent upon severity of wound infection, while directly proportional to the nutritional status of the patients. In most cases when granulated wound grafted under cover of appropriate systemic antibiotic, a significant loss of graft is observed necessitating repeat procedure. This comparative study designed to analyze beneficial effect of probiotics, if any, in the management of burn patients. The objective is to find some alternate, effective method to reduce burn wound infection, predictable graft take and minimize hospital stay.

## MATERIALS AND METHODS

This study investigated 64 adult patients having deep dermal and full thickness burns admitted to Burn Emergency Unit, Liaquat University of Medical and Health Sciences Jamshoro, during period of 26 months from May 2012 to June 2104. The informed consent taken, those consented enrolled as treatment group and those

refused were followed as control group. Patients of either sex having up to 50% BSA affected having either deep dermal, full thickness burn; expected to need grafting; were enrolled. Patients needed diverse management like those pregnant, Diabetic, Hypertensive, aged more than 50 years, sustained associated trauma with incidence of burn, needed ICU support for any reason, presented with superficial burn, chemical burns and electric burns were excluded. Patients who presented after 48 hours of the incidence were also excluded.

**General Procedure:** All patients at our unit are resuscitated with crystalloid according to parkland formula with monitoring of urine output. Prophylactic antibiotic is given to all patients during 2<sup>nd</sup> to 5<sup>th</sup> day of the admission and then according to the results of swab sensitivity. We offered 1<sup>st</sup> dressing at 3<sup>rd</sup> day of admission and then on alternated day basis. The affected area is washed with normal saline, povidone iodine and pat dry. About 2 mm thick layer of 1% silver sulphadiazine applied and affected area covered with two layer of gauze with cotton wool in between as absorbent and finally wrapped with crepe bandage. The swab for culture is taken weekly in all patients. High protein diet with adequate calories is encouraged to all patients.

Those who consented to have diet supplemented with probiotics constitute treatment group of this study, in addition to the above protocol, were given probiotics supplementation during entire period of hospitalization. Matching of the age, sex, BSA and etiology of the burn chose the controls from our record. The outcome variables considered includes factors indicative of sepsis, time taken from admission to the surgery, graft loss after surgery and total hospital stay. Sepsis considered when patient having any one of the following; continuous fever more than 101 for 4 days a week, leukocytosis, Positive swab cultures. Post operatively graft loss of up to 5% of the total body surface area grafted is considered insignificant, between 6-20 minimum loss, 21-30% as significant loss, 31-50% near total loss, while more than 50% loss is considered as failure; because all such cases needs revision graft.

The probiotics supplementation was given twice a day in the form of Sachet ECOTEC®, manufactured by Searle Pakistan. This oral probiotics was started at 2<sup>nd</sup> day of admission and continue during entire period of hospitalization in addition to the generally recommended diet for burn patients. Each sachet of ECOTEC contain each sachet of ECOTEC contain s2.0 g of (>8 billion CFU) standardized freeze-dried cultures of

- *Lactobacillus acidophilus*, LA-5
- *Bifidobacterium*, BB-12
- *Streptococcus thermophilus*, STY-31
- *Lactobacillus delbrueckii ssp. Bulgaricus*, LBY-27

**Analysis:** Demographic variables presented as mean  $\pm$ SD, frequency/percentage. The difference(s) in variables' of interest between two groups were compared using student t test/ Chi Square test. The level of significance was considered  $>0.05$ . MedCalc® version 12 was used for statistical calculation.

## RESULTS

The 22 patients received probiotics supplementation (Treatment Group) and 42 were considered as Control Group as they do not received probiotics. Except probiotics supplementations all patients managed identically as per above protocol. As treatment and control groups were matched with respect to affected age, sex and BSA, therefore differences were statistically insignificant as shown in Table 1. The mean age of treatment group was  $28.2 \pm SD 10.2$  years while for control groups it was  $30.2 \pm SD 13.80$  ( $p = 0.6004$ ). On admission mean BSA affected for treatment group was  $40.2 \% \pm SD 13.80$ , for control it was  $38.2\% \pm SD 14.2$  ( $p = 0.5909$ ). In control group females' were 22 and 12 in treatment group, while male were 20 in control group and 10 in treatment group.

The features suggestive of sepsis were observed in treatment group with almost same frequency as seen in control group, results are shown in Table no 2. The fever in treatment group was present for 38% of the days before surgery while for control it was 29.166%. Complete blood count was done in 116 for control group and 68 for treatment group. The leukocytosis was seen in 68.96% of CBC for control and 67.64% CBC in treatment group. The 85% swabs for culture and sensitivity turn out positive in controls subjects while turn out rate for treatment group was 80%. With dressing superficial burns heals and area remaining after 2-3 weeks of the incidence needs graft. On average for each patients of control group, 9.75% body surface area was grafted as compared to treatment group where it was 10.81% for each patient. The graft loss was 29.26% in control group and 20.14% in treatment group. The mortality was 26% and 22% for control and treatment group respectively. These results with their p values are shown in table 2.

Table 1: Comparison of Differences

Variable	Control Group	Treatment Group	P Value
AGE	30.2 ( $\pm$ SD 13.80)	28.2 ( $\pm$ SD 10.2)	0.6004*
BSA	38.2% ( $\pm$ SD 14.2)	40.2 % ( $\pm$ SD 13.80)	0.5909*
Male	12	10	0.8933†
Female	22	20	0.8950†

\*= Student t test, †= Chi Square Test.

Table 2: Comparison of Sepsis Features with Control in Treatment Group

Variabales of Interest	Control		P value
	Control	Treatment	
Mean days with more than 1001°F fever	16	14	0.3601†
Leucocytosis /CBC	80/116	46/68	0.9685†
Positive Swab (aerobic )	102/120	48/60	0.8893†
Mean preparatory time in days from admission to surgery	42	48	0.7088†
Mean BSA grafted for each patient	9.75%	10.81%	0.0917*
Total BSA grafted in all patients in %	410	238	
% Mean Graft Loss (29.26%)	120/410.		
(20.14%)	56/278		
Morbidity	11	5	0.9529†

†= Chi Square Test, \*= comparison of proportion

The cause of death in all cases was multiple organ failure except in one case from treatment group where it was liver failure due to hepatitis C. This female patient was found to be carrier of HCV on routine serological screening on admission, Liver function were within normal limit except for mild SGPT elevation. She was grafted under general anesthesia. On 4<sup>th</sup> post-operative day she developed features suggestive of fulminate liver failure that prove fatal.

## DISCUSSION

The resurgence to use probiotics for different indication in health sciences is comparatively new, however its health promoting effects is documented in Persian bible [12]. The credit of 1<sup>st</sup> scientific work goes to Metchnikoff (1845-1916)[13], a Russian biologist known for his theory of phagocytosis, who linked longevity with the consumption of fermented milk by lactic acid. In recent past probiotics has been investigated in many specialties' with variable results, this may be attributed to the different types of the probiotics used in different studies [12]. The translocation of microorganism from gastrointestinal tract is major factor for nosocomial infection and colonization of burn wound. The meta-analysis of randomized controlled trials has recently showed that use of probiotics reduces the incidence of nosocomial infection in trauma patients [14]. In burns we found conflicting results; work done by Olguin F *et al* showed that probiotics does not normalize permeability of

gastrointestinal tract [15]; it therefore can be assumed that it remains major source of nosocomial infection. In contrast Feryal Gun *et al* showed in experimental animals that probiotics' prevent translocation of the microbes [16] and ultimately nosocomial infection. The results of the current study favors study of Olguin, as we did not found statistically significant ( $p=0.889$ ) difference in the incidence of positive swab between control and the treatment group. Consequently control and treatment groups did not showed much difference in clinical features indicative of sepsis including fever and leukocytosis. Infectious complications are major factor for delay in the surgery and therefore we did not find much difference ( $p=0.7088$ ) in mean preparatory time from admission to surgery between groups. The mortality between two groups in this study was also statistically insignificant and this favors other studies, which showed that use of probiotics does not reduce mortality [11,16]. The most striking finding of this study is the improved graft takes in treatment group ( $p=0.0093$ ) as compared to control, which is difficult to explain in the presence of insignificant difference in infectious complications between control and treatment group. A probable explanation may be that the probiotics improves systemic immune functions [17], that may be inadequate to prevent surface colonization but sufficient to provide healthy granulation tissues that accepted graft much more reliably in treatment group then in control group. Similar evidence is provided from the study Tan *et al* [18], conducted in patients having traumatic brain injury, which showed that use of probiotics leads to increase in serum concentration of IL-12p70 and interferon gamma (IFN $\gamma$ ) levels with dramatic decrease in IL-4 and IL-10 concentrations making immune system more stable. We ourselves do not have any documented evidence of this finding and therefore further studies are needed to elaborate this finding.

### CONCLUSION

The use of probiotics does not prevent septic complications in burn patients; however for undiscovered reason(s) graft takes is more predictable.

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