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The effect of *Lactobacillus* bacteria supplement on sepsis and its complications in patients with acute burns

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ABSTRACT

Sepsis as a result of bacterial translocation from the gastrointestinal tract (GIT) is a known associate of morbidity and mortality in patients with severe burns. This translocation is influenced by the GIT flora. Oral consumption of Lactobacillus bacteria was previously shown to reduce translocation.

We conducted a retrospective cohort study on a series of 56 patients with burns admitted to Soroka University Medical Center in Beer-Sheva, Israel. Those 56 patients included 28 who were given lactobacillus supplements and 28 who were not. The parameters that were compared between the groups evaluated the level of sepsis and its complications. The parameters of morbidity during hospitalization were significantly higher in the treatment group; however, their mortality was lower. That difference in mortality between the groups was not significant as a whole ($p = 0.071$), but it was significant in the subgroup analysis of 41–70% total body surface area burned. In that subgroup there were zero cases of death in the treatment group versus five cases in the control group ($p = 0.005$). Our findings suggest that in acute burns, lactobacillus bacteria food additives may be clinically beneficial in patients with total burned body surface area of 41–70%.

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1. Introduction

The etiology of sepsis after burn has changed in recent decades. In the past, wound infection was the main reason for systemic infection. This cause has been minimized with the advances in wound treatment that include early surgical care, appropriate antibiotics, and better dressing techniques. A less investigated mechanism that seems to contribute to sepsis in burns is bacterial translocation—the passage of microorganisms and/or their products from the gastrointestinal tract (GIT) lumen. The presumed mechanism for the translocation is a diminished mesenteric blood supply during the severe burn and the following stress period [1]. Physiological stress and trauma influence the incidence of translocation from the GIT. Stress alone does not seem to evoke translocation, but once it is accompanied by trauma, especially one that involves extensive tissue damage (such as that in burns) translocation ensues [2]. Moreover, hypovolemic or anemic shock (states quite prevalent in burns) are directly connected to bacterial translocation in a mechanism of reduced mesenteric blood flow [3]. GIT flora composition also contributes to the degree of translocation. The greater the concentration of pathogenic

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bacteria, the greater the incidence of translocation [4]. Maintaining normal flora in the GIT decreases the level of the translocation [5].

Antibiotic therapy, also very common in burn care, further contributes to the translocation through alteration of the GIT flora [6]. Finally, burn itself was shown in animal models to evoke translocation. It was found that the severity of the burn is directly related to translocation [7].

Several treatment options were investigated to decrease bacterial translocation, among them a *per os* supplement of lactobacillus bacteria. Those bacteria may decrease translocation by improving host defenses in several ways [8]—some are non-immunological in nature, such as production of antimicrobial agents [9], competition with the pathogens on adhesion to GIT cells [10], stabilization of the GIT epithelial barrier [11], and promotion of the GIT motility and by that reducing the number of anaerobic GIT bacteria [12].

Lactobacillus bacteria also influence the immunological defense system by the production of diverse cytokines that enhance the reaction of the immunological system to pathogens [13], enhancement of the phagocytic capabilities of polymorphonuclears [14], augmentation of natural killer cell activity [15], and amplification of production of specific antibodies against pathogenic bacteria [16].

The benefit of oral administration of lactobacillus bacteria was shown in animal models suffering stress situations similar to burns such as acute liver injury [17], and liver resection and colonic anastomosis [18]. In humans, a benefit was shown in patients after major abdominal surgery [19], elective surgery [20], liver transplantation [21], and acute pancreatitis [22]. In acute burn itself, the benefit of lactobacillus bacteria supplements has previously been shown only in rat models [23].

Our study aimed to assess benefits of lactobacillus bacteria supplements in acute burn injury in a clinical, retrospective, cohort study.

2. Materials and methods

Our study investigated a retrospective cohort and utilized data collected from the files of 56 patients with acute burns who were admitted to Soroka University Medical Center from May 1999 to June 2003.

The lactobacillus supplement was recommended by the dietitian to all the burned patients admitted. Twenty-eight patients who agreed to take the supplement were singled out as the treatment group. Matched to them as the control group, were 28 patients with similar demographic characteristics and similar acute burns who decided not to take the supplement. The lactobacillus supplement was given in two ways:

1. Capsules containing *Lactobacillus acidophilus* manufactured by the Solgar Company. Two capsules a day were given to patients under the age of 18 years and 3 capsules a day were given for patients above 18 (300 million bacteria per capsule).
2. ''Actimel'' yogurt made by the Tnuva Company containing *Lactobacillus casei*. Two cups a day were given (1.5 billion bacteria per cup).

Twenty-five of the 28 patients of the treatment group received capsules and 3 received the yogurt.

The mean time for starting the food supplement was 8.25 days after-injury (range 1–21 days). The mean time of treatment was 23.9 days (range 3–119 days).

The inclusion criteria for the study were: (1) Hospitalization in Soroka hospital within 24 h of injury, in order to obtain a uniform standard of treatment for all the patients, (2) Total burn surface area (TBSA) of less than 70% to exclude patients whose cause of morbidity and mortality was mainly shock and not sepsis, (3) Only deep second or third degree burns to exclude those with first degree burns, who are not likely to suffer bacterial translocation (those with fourth degree burns were all above 70% TBSA), and (4) No other kind of trauma to exclude multiple trauma patients with several probable morbidity etiologies.

The control patients were chosen by matching age, TBSA, and whether they were first admitted to the intensive care unit (ICU). The patients were also divided into three subgroups by TBSA: up to 20%, 21–40%, and 41–70%.

The parameters evaluated were those that aimed at estimating the severity of the sepsis and its complications: (1) number of days with body temperature above 38.5 or below 36 °C; (2) number of positive bacterial cultures; (3) number of days in which antibiotics were given; (4) time from injury to hospital discharge; (5) mortality.

The study data were gathered from patients' files and were incorporated into SPSS for Windows Version 11 (SPSS, Chicago, IL). The data were analyzed using Paired *t*-test and χ^2, Fisher's exact test, and Mann–Whitney *U*.

3. Results

3.1. *Demographics and admission condition*

The treatment and control groups were similar with regard to demographics and initial clinical status (Table 1). The two groups were similar in age, first hospitalization to the ICU, and mean TBSA. As a result of the retrospective nature of this study and matching difficulty, there was a higher incidence of women and inhalation injury in the treatment group. In the 41–70% TBSA subgroup there were no significant differences between the subgroups in all the parameters except for the mean TBSA that was higher in the control group (51.6% in the treatment group versus 60.0% in the control group; Table 2).

3.2. *Outcome parameters*

The following infection morbidity parameters (Table 3) were measured: mean number of days in which body temperature above 38.5 or below 36 °C was measured, mean number of positive bacterial cultures, mean number of days in which antibiotics were given, and mean time from injury to hospital discharge (days); all were higher in the treatment group. Those parameters were also higher in the treatment subgroup of 41–70% TBSA (Table 4). Mortality – in all cases reviewed – was a result of severe sepsis with intractable shock and multi-organ failure. Mortality, unlike the morbidity parameters, was higher

Table 1 – Comparison of demographic and primary clinical status

	Control group ($n = 28$)	Treatment group ($n = 28$)	p
Age[a]	27.5 ± 22.0	26.7 ± 20.3	NS
Gender (M:F)	20:8	17:11	NS
TBSA[a,b]	31.1 ± 19.3	31.2 ± 15.9	NS
Subgroups of TBSA (<20%, 21–40%, 41–70%)	10:11:7	9:11:8	NS
First hospitalization in the ICU	16	16	NS
Inhalation injury	8	12	NS
Third degree burns	5	5	NS

[a] Mean ± S.D.
[b] Total burn surface area.

Table 2 – Comparison of demographics and primary clinical status in the subgroup of 41–70% TBSA

	Control group ($n = 7$)	Treatment group ($n = 8$)	p
Age[a]	24.0 ± 18.9	25.0 ± 11.6	NS
Gender (M:F)	1:6	4:4	NS
TBSA[a,b]	60.0 ± 7.6	51.6 ± 5.2	<0.05
First hospitalization in the ICU	7	8	NS
Inhalation injury	4	5	NS
Third degree burns	3	2	NS

[a] Mean ± S.D.
[b] Total burn surface area.

Table 3 – Infection morbidity and mortality

	Control group ($n = 28$)	Treatment group ($n = 28$)	p
Mean number of days with body temperature above 38.5 or below 36 °C	8.4	14.8	<0.05
Mean number of positive bacterial cultures	1.0	3.0	<0.01
Mean number of days in which antibiotics were given	6.8	16.6	<0.01
Mean time from injury to hospital discharge (days)	17.2	41.6	<0.01
Mortality	7	2	NS

Table 4 – Infection morbidity and mortality in the subgroup of 41–70% TBSA

TBSA 41–70% subgroup	Control group ($n = 7$)	Treatment group ($n = 8$)	p
Mean number of days with body temperature above 38.5 or below 36 °C	15.1	30.8	NS
Mean number of positive bacterial cultures	2.3	5.8	NS
Mean number of days in which antibiotics were given	10.3	33.0	<0.01
Mean time from injury to hospital discharge (days)	22.9	71.0	<0.05
Mortality	5	0	<0.01

in the control group (Table 3). However, that dissimilarity was insignificant ($p = 0.071$). In the subgroup of 41–70% TBSA (Table 4), there was a significantly higher mortality than in the control subgroup ($p < 0.01$).

4. Discussion

In the treatment group there was less mortality than in the control group (2 versus 7). This difference between the two arms was not significant ($p = 0.071$). In the subgroup of 41–70% TBSA, that difference was augmented (0 versus 5 deaths) and was statistically significant ($p < 0.01$).

That subgroup of extensive TBSA is especially important, because a greater degree of bacterial translocation can be expected here, due mainly to the elevated physiological stress and trauma typical of such injuries.

It should be noted that in the 41–70% TBSA subgroup, there was an average lower TBSA of 8.4% in the treatment group (Table 2). Notwithstanding this, the striking difference in mortality in those subgroups is still significant in our view because of the similarity between the subgroups in mean age, inhalation injury, gender, and the third degree thickness of the burn injury.

Our research was a retrospective cohort study. Due to nature of the study, the lactobacillus bacteria supplement was not given in ideal conditions. The lactobacillus bacteria were given in two ways and the supplement was given, on average, 8.25 days after the injury and thus covering only the stress phases that followed that period. These constraints may have reduced the gains of the supplement.

Morbidity compared to mortality showed an inverse trend. There was a higher morbidity in the treatment group. Several reasons for that trend are proposed. It may have been caused

by the higher ratio of inhalation injury patients (12 versus 8) and women (11 versus 8) in the treatment group. Female gender and inhalation injury were shown to be risk factors for higher morbidity and mortality in burns. O'Keefe et al. [24] found that the risk factors for morbidity and mortality are high TBSA, deeper degree of the burn, inhalation injury, advanced age, and female gender. Moreover, Tobiasen and colleagues abbreviated burn severity index [25] points to inhalation injury and female gender as important risk factors. Thus, higher inhalation rate and more women in the treatment group may have been the reason for its higher morbidity.

It could be hypothesized that the greater morbidity in the treatment group might have been caused by the administration of the lactobacillus bacteria themselves. A different type of probiotic – *Saccharomyces cerevisae* – was found to be a cause of fungemia in immunosuppressed patients who were given that supplement [26].

Notwithstanding, bacterial cultures were taken for each patient every few days, none with Lactobacillus bacteria. Moreover, lactobacillus bacteria and their safety as food additives were investigated more than *S. cerevisae*. It is known that bacteremia caused by lactobacillus bacteria is extremely rare, and data on its clinical significance are based only on case reports [27].

Another explanation for the inverse trend between mortality and morbidity can be found in the increased mortality rate in the control group compared to the treatment group (7 versus 2). This higher mortality rate meant that there were fewer patients in the control group who had numerous fever days, positive bacterial cultures, days of treatment with antibiotics, and hospitalization days, and that they did not survive long enough to develop these complications.

The difference in trends in morbidity and mortality between the groups points to a beneficial effect of the lactobacillus bacteria supplement, since there was reduced mortality even in the face of higher morbidity.

In conclusion, our findings suggest that in acute burns, lactobacillus bacteria food additives may be clinically beneficial in patients with a total burned body surface area of 41–70%. Comprehensive, prospective, controlled, and blinded studies are needed to clarify this issue further.

It is our impression that lactobacillus bacteria supplement may become an addition to the routine regimen for reducing sepsis and mortality in acute extensively burned patients.

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