

## Short Communication

# Early initiation of enteral nutrition improves outcomes in burn disease

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Background: Burned patients have increased level of mortality, possibly due to late introduction of enteral feeding. The aim of this study was to compare the benefits and safety of very early enteral nutrition introduction compared to the normal diet among burns patients in an intensive care unit. Participants and Methods: Participants consisted of 101 patients, aged 20-76 years (mean age 48 years), 49 men and 52 women, with burns that covered more than 20% of the body. The intervention group consisted of 52 subjects fed via introduced nasojunal probe that started within four hours after admission to the hospital. The control group consisted of fifty patients fed in standard manner *per os* (three standard hospital meals) immediately after the first wound dressing. Results: The average decline BMI in control group was  $2.27 \pm 0.56 \text{ kg/m}^2$ , while the average reduction in BMI in the intervention group was  $1.77 \pm 0.38 \text{ kg/m}^2$  ( $p < 0.001$ ). The largest drop of albumin concentration in the control group was 28.5%, whereas in the intervention group was 23.8%. ( $p < 0.001$ ). The greatest decrease of transferrin concentration in the control group was 31.1%, while the average reduction in the intervention group was 18.3%. ( $p < 0.001$ ). C-reactive protein values were statistically higher in control group ( $p < 0.001$ ). Intervention group had lower rate of complications and infection rates. Conclusion: Enteral nutrition in burned patients should begin within few hours of burn onset. Such approach leads to better outcomes, reduces complications, and improves nutritional profile.

**Key Words:** burn, enteral nutrition, inflammation, albumins, infections

## INTRODUCTION

Consequence of serious burns is strong stressful metabolic response of the inflammatory system, with higher intensity of the stress compared to the response that occurs with injury or other kind of systemic inflammation.<sup>1</sup> Sepsis and systemic inflammatory response in burns is specific and different than in any other surgical or non-surgical patients.<sup>2,3</sup>

Multiorgan failure is the most serious complication of burn disease with high mortality rate of 45%.<sup>4</sup> Burned patients have increased level of mortality, possibly due to late introduction of enteral feeding. Namely, the absence of food in the intestinal lumen leads to impaired function of the immune system and the development of the inflammatory response, the state described with expression endogenous sepsis or gut derived sepsis.<sup>5</sup> This kind of nutrition is called trophic intestinal feeding (feeding the gut).<sup>6</sup>

Despite clear advantages of enteral nutrition in burned patients, in many intensive care units burned patients are nourished via total or partial parenteral nutrition.<sup>7</sup> The timing of enteral nutrition is crucial. Over the past decade, a few studies investigated optimal timing of enteral nutrition introduction.<sup>8</sup>

The aim of this study was to compare the benefits and safety of the introduction of very early enteral nutrition

compared to the normal diet among a group of burned patients in an intensive care unit.

## PARTICIPANTS AND METHODS

Patients treated in the Burn Department of Traumatology Clinic in Zagreb, Croatia, in the period of two years, were included in the study. Including criteria were age  $> 18$  years and burns covered more than 20% of the body surface, such burns according American Burn Association are considered as heavy.<sup>9</sup> Study participants consisted of 101 patients, aged 20-76 years (mean age 48 years), 49 men and 52 women. Burns were mainly thermal injuries from flame, hot liquid or steam (99 patients), while two patients had electrical burns from an electric shock. The patients were informed about the purpose and nature of the study and gave written consent.

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The study protocol was accepted by the local and University's Hospital Ethics Committee.

### Clinical assessment of the subjects

To determine the size of the burned area, the "Wallace rule of nines" was used.<sup>10</sup> According to this method, the size of the burned area was 18% in the 20 subjects (burns of the head, neck and one arm), 36% in 35 subjects (burns the front and rear of the trunk), 50% in 15 subjects (burns the front side of the trunk, both hands and one leg) and 46% in 30 subjects (burns the back of the fuselage, both legs, one arm and genitals). In our study 62 subjects had II degree burns (20 subjects had grade IIA, and 42 subjects stage IIB), and III degree burns had 38 subjects.

Immediately after admission to hospital, and after that in weekly intervals, laboratory blood examination were performed: complete blood count, plasma electrolytes, plasma glucose, urea (mmol/L), creatinine (micromol/L), albumin (g/L), C-reactive protein (CRP) and transferrin (mg/L) was determined. Body mass index (BMI) in both groups was obtained twice, immediately after admission and before discharge from the hospital.

### Study design

Subjects were divided into two groups using computer randomization process. The intervention group consisted of 52 subjects fed via introduced nasogastric probe equipped with enteral feeding. Feeding process in this group started within four hours after admission to the hospital with enteral preparations given through nasogastric probe. Intermittent infusion was used for feeding, and through the pump enteral food was introduced into the digestive system of the subject during the 12-16 daytime hours, with pump stopped during the nighttime. Basal feeding dose was 25 ml of liquid enteral preparation per hour over 3-5 days. The control group consisted of fifty patients fed in standard manner *per os* (three standard hospital meals) immediately after the first wound dressing. This mode of nutrition was in-hospital standard procedure for this group of patients.

### Statistical analysis

The results were expressed as arithmetic mean±SD. Normality of distribution was tested with the Shapiro-Wilk's W test. Differences between two groups were tested by Student's t-tests for independent data. The chi-square test was used to determine statistical significance of differences in the distribution of qualitative characteristics. A *p* value of less than 0.05 was considered statistically significant.

## RESULTS

Between the intervention and control groups there were no significant differences in age (53.8±12.5 vs.48.7±14.0 years, *p*=0.059) and baseline BMI.

Comparison of baseline and final BMI between the two groups demonstrated more significant decline of BMI in the control group from 24.4 kg/m<sup>2</sup> at baseline to 22.1 kg/m<sup>2</sup> at the end of treatment (decrease of 9.43%), than in the intervention group: from 24.6 kg/m<sup>2</sup> to 22.8 kg/m<sup>2</sup> (decrease of 7.3%). The average decline in BMI in control group was 2.27±0.56 kg/m<sup>2</sup>, while the average reduc-

tion in BMI in the intervention group was 1.77±0.38 kg/m<sup>2</sup>. This difference was statistically significant (*p*<0.001). In control group, the difference was more pronounced in III degree burns compared with II degree burns (3.12±0.84 vs 2.09±0.48 kg/m<sup>2</sup>, *p*=0.041).

At the baseline there was no difference in albumin plasma concentration between the intervention and control groups (29.32±1.99 vs 35.08±2.84 g/L, *p*=0.058). Analysis of plasma albumin concentration indicated a permanent decline in albumin concentration in both groups, most pronounced in the fourth and fifth week of hospital treatment (Table 1). Comparison of the groups indicated the presence of a more pronounced decline in albumin concentration values in the control group compared to the intervention group. The largest drop in the control group was 28.5%, whereas in the intervention group was 23.8%. (*p*<0.001). We could not demonstrate difference in largest albumin concentration drops between III degree burns and II degree burns subgroups (31.8 vs 27.9%, *p*=0.081). Values of transferrin concentration changed in a similar manner as albumin: the lowest average values were recorded during the fifth week of hospital treatment. The drop in average values was greater in the control group. The greatest decrease in the control group was 31.1%, while the average reduction in the intervention group was 18.3% (*p*<0.001).

At the baseline we could not find difference in plasma CRP concentration between the intervention and control groups (17.10±3.92 vs 21.70±4.33 g/L, *p*=0.087). Plasma concentration of CRP, one of the main indicators of the inflammatory process, strongly differed during hospitalization. There was significantly increase in CRP values in the control group, especially in the fourth and fifth weeks of hospital treatment. Comparisons of groups demonstrated statistically significant difference (*p*<0.001) for each week comparison (Table 2). The largest average increase of CRP in the intervention group was 109.4%, whereas in the control group the largest average increase of CRP was 147.6% (*p*<0.001). We demonstrated difference in largest

**Table 1.** The trends of plasma albumin concentration (g/L) during hospitalization

Week	Intervention group		Control group	
	mean±SD	range	mean±SD	range
1	29.3±1.99	26-34	35.1±2.84	29-40
2	26.5±1.85	23-29	30.5±1.96	27-37
3	23.8±2.22	20-28	27.4±1.50	24-30
4	22.3±2.34	19-28	25.1±1.95	22-29
5	24.5±2.27	20-29	25.6±3.03	20-31
6	26.2±2.21	22-30	28.4±2.81	22-39

**Table 2.** The trends of plasma C-reactive protein (mg/L) concentration during hospitalization

Week	Intervention group		Control group	
	mean±SD	range	mean±SD	range
1	17.1±3.92	11-29	21.7±4.33	12-28
2	22.0±3.97	17-31	28.4±5.93	17-39
3	27.7±5.21	21-48	42.1±17.7	21-84
4	35.8±7.59	24-57	53.7±25.2	18-98
5	32.0±7.10	16-48	45.5±20.1	16-84
6	20.8±6.02	9-32	26.1±9.31	11-48

**Table 3.** Differences in clinical outcomes between two groups of subjects

	Intervention group	Control group	Chi-square ( <i>p</i> -value)
All complications	11	15	3.87 (0.048)
Pneumonia	3	1	4.43 (0.035)
Sepsis	2	6	5.91 (0.022)
Renal failure	1	1	-
Wound infection	3	4	3.89 (0.432)
Multiorgan failure	2	3	2.68 (0.663)
Pathogens etiology			
Gram- negative bacteria	2	12	9.34 (0.012)
Gram- positive bacteria	8	2	6.24 (0.044)
Fungi	1	1	-
Death	5	10	4.91 (0.030)

average increase of CRP between III degree burns and II degree burns subgroups (118 vs 164%,  $p < 0.001$ ). On average there were no statistically significant differences in terms of hemoglobin levels and blood urea concentration between the two groups of subjects.

Table 3 demonstrates clinical outcomes and infection rates with specific pathogens in two groups of subjects.

## DISCUSSION

This study demonstrated that early introduction of enteral nutrition was beneficial for clinical outcomes of burned patients. Early enteral feeding of burned patients in the intensive care unit led to better nutritional and metabolic parameters, less body mass index decreases, and less inflammatory response.

Over the past decade, numerous studies have been conducted to clarify the role of the gastrointestinal system as an immune organ.<sup>11</sup> In this context, bacterial translocation is declared as a major factor that causes multi-organ failure and sepsis in burned patients.<sup>12</sup> It was clearly established that all states contribute to the disturbance of the intestinal wall (hypoalbuminemia, stress ulcers, empty gut) finally resulting in the release of inflammatory mediators, cytokines, bacteria and their endotoxins from intestine into the bloodstream. From the above-mentioned factors, in particular importance is the role attributed to the empty intestine.<sup>13</sup> The presence of food in the gut is important for intestinal cells nutrition by diffusion from the lumen: 50% enterocytes and 70% cells in colon meet energy needs from the lumen. Additionally, the food in intestine is a stimulus for the secretion of digestive enzymes, for the establishment of intestinal motility, and for satisfactory intestinal circulation.<sup>14</sup>

Many authors have pointed to the fact that the infection is the leading cause of mortality in burn disease.<sup>15</sup> In our study, among the fifty patients fed by mouth, fifteen developed infection. The most common causes of infections in this group were gram-negative bacteria (*Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Klebsiella species*) originated from gastrointestinal endogenous flora or hospital environment. In the group of fifty patients enterally fed, eleven has developed an infection. The most common cause of infection in the majority of these patients were gram-positive bacteria, mostly *Staphylococcus aureus* methicillin resistant (MRSA) and *Enterococcus faecalis*.

Finally, it may be concluded that introduction of early enteral nutrition in patients with burn injury could brought to lower incidence of inflammatory response, lower infection and mortality rates. Gudaviciene *et al*<sup>16</sup> in a retrospective study confirmed that incidence of inflammatory complications of burn disease is lower when introducing enteral nutrition within 24 hours of the occurrence of burns. In our study, enteral nutrition was started very early (within four hours). Lam and colleagues,<sup>17</sup> in a prospective randomized study, demonstrated that early enteral nutrition contributed to increased cellular and humoral immunity in burned patients.

## Conclusion

Enteral nutrition in burned patients should begin within few hours of burn onset. Such approach leads to better clinical outcomes for patients, reduces infections, and improves nutritional profile. As burn disease needs many interventions other than nutrition, the outcomes of this study have to be interpreted with respect to the complexity of such injuries.

## AUTHOR DISCLOSURES

No author declare any conflict of interest.

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背景：燒傷病人死亡風險的增加，可能是因為腸道進食較晚開始。本研究目的為比較加護病房的燒傷病人，在很早期採用腸道營養比起常規飲食者的益處及安全性。參與者與方法：參與者為 101 名年齡 20-76 歲(平均年齡 48 歲)的病人，有 49 名男性和 52 名女性，其身體燒傷面積都超過 20%。介入組有 52 名，在入院後的四小時內透過鼻空腸導管餵食。控制組有 50 名病人，在第一次換藥後立即以標準程序經口進食(三餐標準醫院餐點)。結果：控制組平均 BMI 下降  $2.27 \pm 0.56 \text{ kg/m}^2$ ，而介入組平均減少  $1.77 \pm 0.38 \text{ kg/m}^2$  ( $p < 0.001$ )。控制組的白蛋白濃度最大跌幅為 28.5%，但在介入組為 23.8% ( $p < 0.001$ )。控制組的運鐵蛋白濃度最大降幅為 31.1%，而介入組則平均下降 18.3% ( $p < 0.001$ )。控制組的 C-反應蛋白高於介入組，並達統計顯著性( $p < 0.001$ )。介入組有較低的併發症及感染率。總結：腸道營養應該開始於燒傷發生後數小時內。該項做法可導致較好的預後、降低併發症及改善營養狀況。

**關鍵字：燒傷、腸道營養、發炎、白蛋白、感染**