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# Microbial cell preparation in enteral feeding in critically ill patients: A randomized, double-blind, placebo-controlled clinical trial☆

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ABSTRACT

Gut failure is a common condition in critically ill patients in the intensive care unit (ICU). Enteral feeding is usually the first line of choice for nutrition support in critically ill patients. However, enteral feeding has its own set of complications such as alterations in gut transit time and composition of gut eco-culture. The primary aim of this study was to investigate the effect of microbial cell preparation on the return of gut function, white blood cell count, C-reactive protein levels, number of days on mechanical ventilation, and length of stay in ICU. A consecutive cohort of 60 patients admitted to the ICU in University Malaya Medical Centre requiring enteral feeding were prospectively randomized to receive either treatment (n = 30) or placebo (n = 30). Patients receiving enteral feeding supplemented with a course of treatment achieved a faster return of gut function and required shorter duration of mechanical ventilation and shorter length of stay in the ICU. However, inflammatory markers did not show any significant change in the pretreatment and posttreatment groups. Overall, it can be concluded that microbial cell preparation enhances gut function and the overall clinical outcome of critically ill patients receiving enteral feeding in the ICU.



## 1. Introduction

Gastrointestinal dysfunction is a major complication encountered in the critically ill, especially in the intensive care unit (ICU) setting, whereby patients commonly experience dysmotility of the gastrointestinal system [1]. An approximate 50% of mechanically ventilated patients exhibit antral hypomotility-reduced gastric emptying, lesser migrating motor complexes, and higher risks to infections, usually leading to infectious diarrhea [2]. Enteral feeding is a major factor that contributes to the clinical outcome and duration of stay of critically ill patients in the ICU, and in that sense, tolerance to enteral feeding is of great importance [2]. A functional gastrointestinal tract has now been recognized as an important factor in the clinical outcome of ICU patients [1].

Nutritional support in critically ill patients is one of the major aspects of patient care in the ICU. Because of the nature of their illnesses, critically ill patients are usually under physiologic and psychosocial stress, thus placing them in a hypercatabolic state; thus, the provision of adequate nutrition is of utmost importance for their recovery [3]. Enteral feeding is the first-line and commonly used nutritional support system in critically ill patients as an adjunct therapy with the primary goal of achieving the caloric requirement of the patient and preventing the patient from developing malnutrition. However, enteral diets are known to affect the physiologic state of the gut due to modification in gut transit time and alteration of the secretory and absorptive capacity of the intestines, as well as modification to the gut ecosystem. However, delivery of calories could be limited by the set pump itself, mainly due to nursing protocols and frequent cessation of feed due to medical reasons or surgical procedures [4]. This reduced tolerance would result in high gastric residual volumes (GRV) [4]. In 2008, Gatt [5] defined the *return of normal gut function* as at least 80% tolerance of an individual's daily caloric requirement for a consecutive period of 48 hours or more. Tolerance of less than this value may be associated with poor clinical outcome and may indicate the lack of gut function [5]. Thus, in this study, the return of normal gut function would be defined as being able to achieve at least 80% of caloric requirement for a consecutive period of 48 hours.

Furthermore, bacterial strains, such as *Lactobacillus* and *Bifidobacterium*, are defined as preparations of microorganisms that exert therapeutic effects when administered in specific recommended

*Abbreviations:* AIDS, acquired immune deficiency syndrome; APACHE, Acute Physiology and Chronic Health Evaluation; BALT, bronchus-associated lymphoid tissue; CFU, colony-forming unit; CRP, C-reactive protein; GALT, gut-associated lymphoid tissue; GCP, Good Clinical Practice; GRV, gastric residual volume; GSN, gut-specific nutrients; ICU, intensive care unit; IRB, institutional review board; MALT, mucosa-associated lymphoid tissue; MCP, microbial cell preparation; MEC, Medical Ethics Committee; MODS, multiple-organ dysfunction syndrome; UMMC, University Malaya Medical Centre; WBC, white blood cell.

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dosages [6]. They can colonize the human intestine and modulate the gut ecosystem, which serves as a defense mechanism hindering the growth and colonization of pathogenic bacteria. The term "probiotic" was coined in 1965 by Lilly and Stillwell [7]. In light with current scientific progresses, probiotics are more specifically referred to as microbial cell preparation (MCP) or components of microbial cells that exert beneficial effects on the health and overall well-being of the host [8]. Henceforth, we would refer to probiotics as MCP in the context of this study. Current scientific research has not fully tapped and elucidated the various mechanisms of action of MCP and its role in improving gut function. Diarrhea is commonly seen in ICU patients on enteral feeding, with almost 15% to 50% of patients reported to be affected [9]. Replenishing the altered ecosystem of the gut with MCP may prove beneficial to reestablish the favorable homeostatic environment in the gastrointestinal tract [6,10]. Slow bowel movements are common in ICU patients, with an estimated 80% of patients having no bowel movements in the first 72 hours of admission [9]. Several hypotheses exist to explain the delayed gastric motility of patients in the ICU, namely, sepsis and shock, elevated levels of endotoxins, inflammatory mediators, nitric oxide production, and lastly, drugs such as sedatives, opiates, and vasoactive drugs [9]. It is believed that the acidic environment induced by MCP may stimulate the motility of the intestines, as shown in patients with chronic constipation [11].

We hypothesize that enteral feeding supplemented with MCP improves the time required for the return of normal gut function in critically ill patients in the ICU.

## 2. Materials and methods

This study protocol was approved by the institutional review board of University Malaya Medical Centre (Reference No. 835.1) prior to the commencement of the study. This study was conducted in accordance to Good Clinical Practice Guidelines and was registered at the US National Institutes of Health Web site (http://www.clinicaltrials.gov; Reference No. NCT01792401). The data obtained from the patients were with prior consent either by the patient themselves or their respective next of kin. No ethical restraints were noted in regard to the execution of this study or in the treatment modalities used.

The primary end point for this study was the duration to return to normal gut function, which is defined as the time (in hours) taken to achieve a minimum of 80% of calculated caloric requirement for a consecutive 48-hour period.

The sample size was calculated based on published data [12], which showed that a minimum number of 24 patients in each group was required to demonstrate a difference in hours in the return of normal gut function at a level of 5% significance with a power of 95% according to Altman's formula. This study was a prospective, randomized, double-blind, placebo-controlled trial. The random allocation sequence was generated by a computerized system to randomly allocate 30 subjects in each group. All researchers and subjects remained blinded to the allocation until the end of the study.

### 2.1. Subject recruitment criteria

The inclusion criteria were as follows: critically ill patients 18 years and older; admitted to the ICU of University Malaya Medical Centre, Kuala Lumpur, for more than 48 hours; requiring enteral feeding via nasogastric tube feeding alone; and not taking any forms of MCP prior to commencement of the study.

The exclusion criteria were as follows: patients admitted to the ICU for monitoring purposes, patients on immunosuppressive treatment, patients with hematological diseases, patients with AIDS, pregnant patients, patients who were known to have allergy to MCP, contraindication to placement of nasogastric feeding tube, on parenteral feeding alone or combined with enteral feeding, and enrolled in other studies and on other forms of MCP prior to commencement of the study.

### 2.2. Product, dosage, and administration

The random allocation was generated by a computer model, and both researcher and participants remained blinded to the contents of the sachets throughout the study procedure and statistical analysis. Un-blinding was performed after completion of analysis.

The treatment sample is an orange-flavored granule, containing 30 billion colony-forming units of highly compatible, acid- and bile-resistant strains of *Lactobacillus acidophilus*, *Lactobacillus casei*, *Lactobacillus lactis*, *Bifidobacterium bifidum*, *Bifidobacterium longum*, and *Bifidobacterium infantis*. The placebo mixture samples have similar appearance and taste, but without fermentation. Both preparations were prepared in sealed aluminum foil of 3 g labeled A (placebo) and B (treatment). These were administered twice daily at 0800 and 2000 hours for a consecutive 7 days [11] once the patient was started on enteral feeding. The trial product (treatment or placebo) was diluted in 5 mL of water and was administered to the patient via the nasogastric tube. After administration, flushing of the tube with 5-10 mL of water was done to make sure that the test sample passes through the tube completely.

### 2.3. Enteral feeding regimen

Enteral feeding regimen in the ICU was as follows: Osmolite 1 cal (standard formula), Glucerna (glucose intolerance formula), Peptamen (semielemental formula), and Novasource Renal (electrolyte and fluid restriction). The feeding regimen was in accordance to the Enteral Feeding Flowsheet (Fig. 1). Feeding was started within the first 24 to 48 hours after admission to ICU. Feeding was administered continuously using a feeding pump for 24 hours. The energy requirements for all subjects were calculated based on a weight-based formula (weight obtained from weighing bed in ICU) at the time of patient recruitment, which is 25 kcal $kg^{-1}$ $d^{-1}$ [13]. Moreover, complications of feeding such as feeding intolerance in terms of abdominal distension/discomfort, lack of bowel activity and any subjective symptoms reported by patients, vomiting, GRV, diarrhea, refeeding syndrome, and suspected aspiration of feed were monitored. Return of gut function was monitored through records of input output chart, and the tolerance and absorption of the enteral feed was measured based on GRV. The GRV was checked every 6 hours for continuous feeding. A GRV less than 200 mL would result in readministration of the GRV to the patient and continuation of the enteral feeding protocol. A GRV more than 200 to 500 mL would be based on 2 episodes, whereby the first episode would be to continue enteral feeding and start the patient on prokinetic agent, whereas the second consecutive episode would require notification of medical staff and dietitian. A GRV more than 500 mL would result in cessation of enteral feeding.

## 3. Results

Data were collected between March 2011 and December 2011, from the time of enrollment of the patient into the trial to the time of completion of treatment. It included demographic data, diagnosis on admission to ICU, Acute Physiology and Chronic Health Evaluation (APACHE) II score, and anthropometric measures included weight that was the adjusted body weight [14], caloric requirement calculated based on Cerra et al [13], inflammatory markers, ventilation days, and days of ICU stay. SPSS 17 for Mac (Chicago, Ill) was used for the statistical analysis. *P* value less than .05 was considered statistically significant.

### 3.1. Demographic data

Fig. 2 shows the flowchart of patient recruitment and analysis. Although 70 patients were screened, only 60 patients were recruited to participate in the study due to failure to obtain consent. These 60 patients were randomly allocated to either treatment or placebo group in equal number, via sealed envelope method. During the trial period,

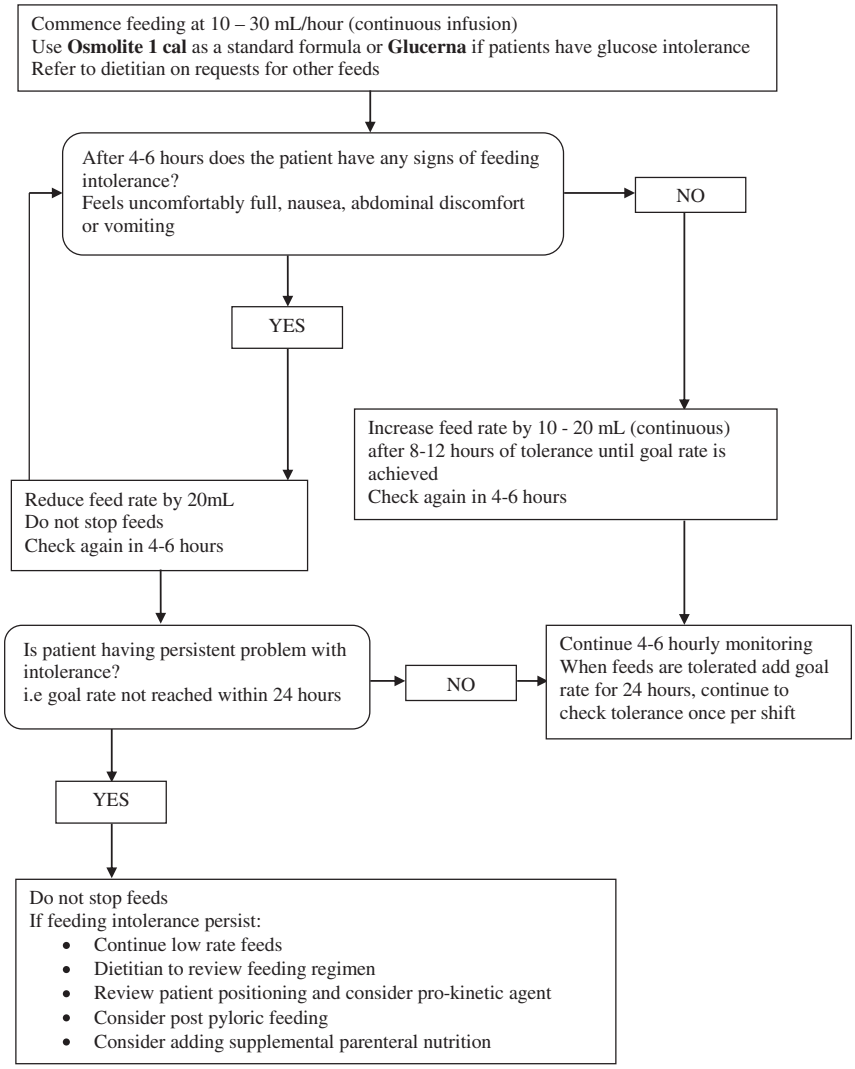


**Fig. 1.** Enteral feeding flow diagram.

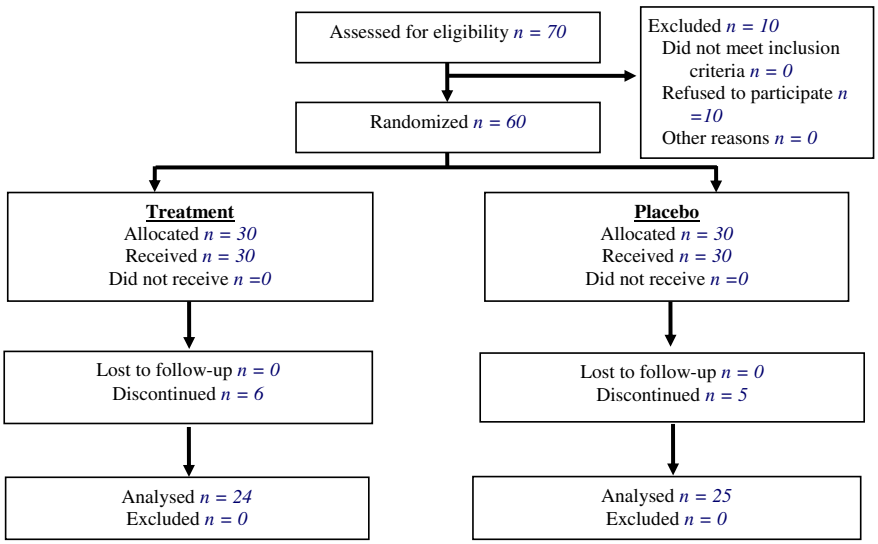


**Fig. 2.** Consort diagram of patient recruitment and analysis.

**Table 1**
Baseline characteristic and demographic profile of patients in treatment and placebo groups

| Parameter | Treatment | Placebo | *P* |
|---|---|---|---|
| Age (y), mean (SD) | 60 (14.4) | 55 (17.7) | .278 |
| Sex, n (%) | | | .419 |
| – Male | 16 (64) | 17 (70) | |
| – Female | 9 (36) | 7 (30) | |
| Ethnicity, n (%) | | | .214 |
| – Malay | 6 (24) | 11 (45) | |
| – Chinese | 9 (36) | 7 (30) | |
| – Indian | 10 (40) | 6 (25) | |
| Weight (kg), mean (SD) | 60 (6.3) | 60 (6.0) | .712 |
| Height (cm), mean (SD) | 165 (7.6) | 166 (7.1) | .907 |
| Caloric requirement (kcal), mean (SD) | 1730 (231) | 1778 (237) | .433 |

All *P* values obtained using $\chi^2$ test.

11 patients dropped out, and the remaining 49 patients underwent the final analysis.

Table 1 shows the demographic profile of the 2 groups of patients, 33 were men (67.3%) and 16 were women (32.7%). This table demonstrated that the 2 groups were equally matched in terms of age, ethnicity, weight, height, caloric requirement, and underlying primary diseases.

Fig. 3 demonstrates the box-plot graph of the hours taken to tolerate enteral feeding between the 2 groups of patients, based on the definition of normal gut function. Patients in the treatment arm achieved their caloric goal in 72 hours, compared with those patients in the placebo arm who achieved in 168 hours (Table 2). The median difference of 96 hours was statistically significant with a *P* value less than .001 (Mann-Whitney *U* test).

Table 2 demonstrates postintervention results in both groups of patients. The time to return of normal gut function was 2 times higher in the placebo group compared with the treatment group. This enhanced recovery of gut function was associated with a reduction of mechanical ventilation duration by 40% and the length of stay in the ICU by 31%. There were no significant differences between both groups in levels of inflammatory markers (Table 3).

## 4. Discussion

In this study, we set out to investigate the effect of MCP on the return of normal gut function. In the context of this study, we defined the return of normal gut function as achieving 80% of the caloric requirement for a minimum expected duration (48 hours) for the patient [15]. However, the time to achieve this is not constant due to variable gut function in different disease states. Hence, if there is gut failure, tolerance may be delayed or not achievable at all. This was demonstrated by the ability of the patient's gut to accept and tolerate feeding of 80% of the required calories for a consecutive 48 hours. Reports of intolerance to enteral feeding is seen in up to 60% of patients in the ICU, including symptoms such as vomiting, nausea, abdominal pain or distension, constipation, and diarrhea [16]. However, diarrhea was the most common symptoms in these patients. The causes may include depletion or alteration of the numbers of intestinal microbiota, antibiotic therapy [17], infections due to enteropathogens, colonization by the bacterium *Clostridium difficile*, contaminated preparations of enteral feeds, the route of enteral feeding [18,19], osmotically active medications [20], low serum levels of albumin [21], and impaired colonic water and electrolyte secretion [22].

Results of this study suggest that the use of MCP is associated with more rapid return of gut function reported to be 72 ± 42 hours in the treatment group and 168 ± 41 hours in the placebo group. A study by Gatt and MacFie [12] investigated the effect of gut-specific nutrients (GSNs) on the return of gut function. The GSN given in that trial included MCP as well as prebiotic in addition to multivitamins and glutamine. Patients in that study were mainly surgical patients, whom he had determined that gut failure was evident to begin with. In that study, the investigators found similar result to those we have produced. In fact, patients on GSN did have their gut function returned in a shorter period [12]. Although there are differences in design between this study and that of Gatt and MacFie [12], the findings concur and consolidate the idea of the benefits of the MCP in enteral feeding among critically ill patients. A study done by Majid et al [19] suggested that manipulation of the colonic microbial ecosystem may exert protective effects against diarrhea during enteral feeding. They may exert their effects via immunomodulation [23], by suppressing the growth of enteropathogens

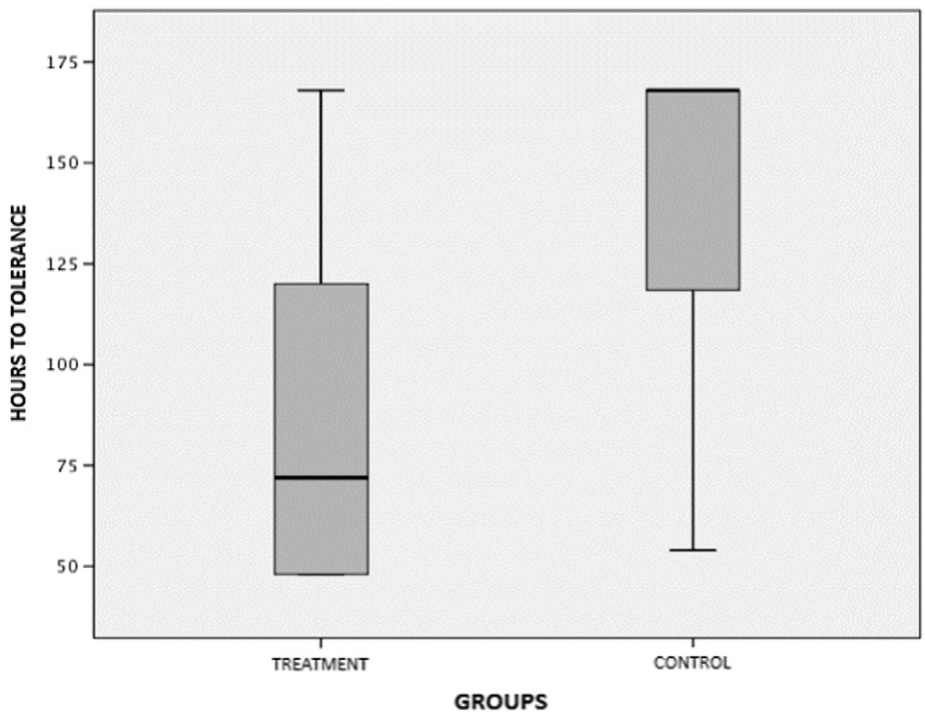


**Fig. 3.** Box-plot graph of time to return of normal gut function. Box-plot shows 25th and 75th percentile, and median and range; $P = .00$. $P < .001$.

**Table 2**
Clinical data of patients in treatment and placebo groups

| Parameter | Treatment | Placebo | *P* |
|---|---|---|---|
| Diagnosis, n (%) | | | .310 |
| – Medical | 5 (25) | 12 (50) | |
| – Surgical | 20 (75) | 12 (50) | |
| • Gastrointestinal | 10 (50) | 4 (30) | |
| • Nongastrointestinal | 10 (50) | 8 (60) | |
| Pathology, n (%) | | | .404 |
| – acute coronary syndrome | 0 (0) | 1 (4.2) | |
| – Acute kidney injury with sepsis | 0 (0) | 2 (8.3) | |
| – Acute pulmonary edema | 1 (4) | 0 (0) | |
| – Appendicular mass | 1 (4) | 0 (0) | |
| – Cellulitis | 0 (0) | 1 (4.2) | |
| – Cerebrovascular accident | 1 (4) | 0 (0) | |
| – Colon cancer | 1 (4) | 1 (4.2) | |
| – Colitis | 0 (0) | 1 (4.2) | |
| – Diabetic ketoacidosis with sepsis | 0 (0) | 2 (8.3) | |
| – Esophageal Cancer | 1 (4) | 0 (0) | |
| – Intestinal obstruction | 1 (4) | 0 (0) | |
| – Intra-abdominal sepsis | 1 (4) | 0 (0) | |
| – Left thigh abscess | 0 (0) | 1 (4.2) | |
| – Leukemia | 0 (0) | 1 (4.2) | |
| – Leptospirosis | 0 (0) | 1 (4.2) | |
| – Lung cancer | 1 (4) | 0 (0) | |
| – Myasthenia gravis | 0 (0) | 1 (4.2) | |
| – Non–ST-segment elevation myocardial infarction | 1 (4) | 0 (0) | |
| – Ovarian cancer | 1 (4) | 0 (0) | |
| – Pancreatitis | 2 (8) | 0 (0) | |
| – Perforated appendicitis | 0 (0) | 1 (4.2) | |
| – Pneumoniae | 1 (4) | 1 (4.2) | |
| – Postgonococcal urethritis | 1 (4) | 1 (4.2) | |
| – Pulmonary hemorrhage | 0 (0) | 1 (4.2) | |
| – Rectal cancer | 0 (0) | 1 (4.2) | |
| – Septic arthritis | 0 (0) | 1 (4.2) | |
| – Sepsis with diabetes mellitus | 0 (0) | 1 (4.2) | |
| – Stomach cancer | 1 (4) | 0 (0) | |
| – Trauma | 7 (28) | 2 (8.3) | |
| – Upper gastrointestinal bleeding | 2 (8) | 2 (8.3) | |
| – Urosepsis | 1 (4) | 0 (0) | |
| – Uterine perforation | 0 (0) | 1 (4.2) | |
| APACHE score, mean (SD) | 22.12 (6.0) | 23.00 (8.9) | .200 |

All *P* values obtained using $\chi^2$ test.

via the production of bacteriocins [6], competing for nutrients and adhesion sites on the intestinal wall [24,25], preventing translocation of bacteria out from the intestinal lumen via its action on tight junctions [26].

In a study of tolerance, safety of formula supplemented with prebiotics and MCP in critically ill children found that although there was good tolerance of the formula with probiotic, it did not show any difference in terms of achieving the caloric requirement [27]. This study did not agree with our findings and this was because of the different baseline characteristics of the patients included in the study. In other words, their "critically ill" children did not refer to populations that were homogenous. As a matter of fact, subjects in original trials as well as those in review articles differ widely in their diagnosis, disease severity, metabolic derangements, therapeutic procedures, and gastrointestinal functions [28].

**Table 3**
Preintervention and postintervention results in treatment and placebo groups

| Criteria(s) | Treatment | Placebo | *P* |
|---|---|---|---|
| Time to return of gut function (h), mean (SD) | 72 (42) | 168 (41) | .000 |
| White blood cell count (billion cells/L), mean (SD) | | | |
| – Pretreatment | 15.88 (7.7) | 15.06 (6.5) | .952 |
| – Posttreatment | 13.44 (4.9) | 16.29 (6.2) | 0.090 |
| CRP (mg/L), mean (SD) | | | |
| – Pretreatment | 14.75 (8.6) | 15.17 (10.6) | .944 |
| – posttreatment | 9.64 (10.4) | 9.75 (9.76) | .090 |
| Albumin (g/L), mean (SD) | | | |
| – Pretreatment | 23.17 (8.6) | 21.72 (5.9) | .090 |
| – Posttreatment | 19.88 (5.9) | 21.16 (6.1) | .090 |
| Duration of ICU stay (d), mean (SD) | 10.9 (3.9) | 15.8 (7.8) | .014 |
| Duration on ventilator (d), mean (SD) | 8.4 (3.5) | 14.0 (8.0) | .004 |

All *P* values obtained from Mann-Whitney *U* test; $P < .05$, statistically significant.

Microbial cell preparation has been studied extensively in terms of their ability to modulate the immune response [28]. Although predominantly used by healthy individuals, the use of MCP in the prevention and treatment of intestinal inflammatory diseases and many other disease conditions is on the rise [6,29,30]. Scientific studies have reported the significance of a balance gut microbiota and the pivotal role it plays in the development and sustenance of gut-associated lymphoid tissue, which is an essential part of the human immune response [31].

Microbial cell preparation has been reported to be as effective as conventional antimicrobials in suppressing pneumonia-causing bacteria commonly found in the oral cavity of critically ill patients [32]. Other examples include their effect in improving lactose digestion presenting a possible usefulness in lactose intolerance [33]. A study by Whelan et al [34] reported significant variability from norm in the intestinal microbiota of patients with diarrhea during enteral feeding [34]. Patients with diarrhea had higher counts of Clostridia and lower counts of Bifidobacteria in comparison to those with no diarrhea. Maintenance of normal gut flora in patients who are on enteral feeding might increase the antimicrobial [34] and immunological activity of the patient, suppress the colonization of the gut by enteropathogens [35], and assist in colonic water reabsorption due to presence of short-chain fatty acids [36]. Gut flora also improve mucosal immune response [37] and positively influence intestinal barrier function [23]. Gordon et al [38] demonstrated the anti-inflammatory effects of gut flora involving the epithelium. In this article, we have consolidated additional clinical indication of MCP with a positive clinical outcome in terms of improvement on the tolerance of enteral feeding and return of normal gut function. Safety of MCP in critically ill patients is always a concern. The breakdown of gut barrier function and immune dysfunction is associated with the onset of multiple-organ dysfunction syndrome, which is a major cause of mortality in ICUs. Microbial cell preparation has been shown to modulate intestinal barrier and immune function, thus probably lowering the risk of developing multiple-organ dysfunction syndrome [39]. Several strains of *Lactobacillus* and *Bifidobacterium* were able to stimulate epithelial cell signaling pathways, and *L acidophilus* in particular have been shown to be able to alter the expression of tight junction proteins, thus playing an important role in barrier functions [31]. In vitro studies have indicated the potential of MCP in preventing the translocation of pathogenic organisms and its adherence to enterocytes [14]. It has been shown that feeding MCP to patients with predicted severe acute pancreatitis did not reduce the risk of infectious complications and was associated with an increased risk of mortality. Hence, they advocated that MCP should not be recommended to patients with acute pancreatitis [40]. In contrast, a study reported that supplementation of early enteral feeding with probiotic in patients with acute pancreatitis was reported to be effective in reducing pancreatitis-related sepsis and the number of surgical interventions [41].

The inflammatory markers that were studied in this study were white blood cell count and C-reactive protein (CRP) levels. Both markers are known to be elevated in inflammatory conditions and sepsis. However, they are not very specific. We hypothesize that adding MCP in enteral feeds will not only modulate the gut microbiota, but may enhance the gut immune system which will prevent bacterial translocation, and initiation and propagation of sepsis. As such, the inflammatory markers would therefore show a decline in their levels. However, the differences in posttreatment of these 2 markers in this study were not statistically significant. This could be due to the fact that the sample size is too small to show the statistical difference or that some patients in this study were already diagnosed of having sepsis on admission.

A study by Alberda et al [39] investigated the effects of MCP on inflammatory markers, CRP, and immunoglobulins and found that the immunoglobulins of patients supplemented with MCP showed significant

improvements, but not CRP levels. These findings have shown that although the immune response appeared to enhance as indicated by the changes in the level of immunoglobulins, the white blood cell and CRP levels may not be sensitive or specific enough to highlight this immunological response. In fact, changes in these markers may only reflect the general septic condition of the patient. Critically ill patients are usually in a state of heightened and perhaps altered immune response. The inflammatory response is occurring at a systemic level as well as at the organ level. For such high levels to show improvements may require a lengthier time and a delayed follow-up [42]. Nonetheless, the matched levels of inflammatory markers between the 2 groups of patients indicated that they had the same level of septic response, and the tolerance of feeding or regain of gut function was not due to an initial lesser level of sepsis in the treatment group.

This study also demonstrated that those patients who received MCP had a shorter mechanical ventilation duration in days and a shorter length of stay in ICU in days when compared with those patients who received placebo ($P = .04$ and $P = .014$, respectively). Scientific data have reported that MCP may exert similar processes in the respiratory tract to that in the digestive tract [43]. Microbial cell preparation has also been hypothesized to decrease the colonization of pathogenic bacteria at the oropharyngeal and gastric level in mechanical ventilated patients with ability to modulate the immune system through its effects on mucosa-associated lymphoid tissue, bronchus-associated lymphoid tissue, and gut-associated lymphoid tissue [43]. This may indicate the correlation between return of gut function and shorter mechanical ventilation day. Studies have shown that the occurrence of gastrointestinal complications and intolerance to enteral feeding results in decreased provision of enteral feeding to the patient and often leads to longer duration of ICU stay [16]. As mentioned above, diarrhea and other complications of feeding such as abdominal distension/discomfort, vomiting, GRV, refeeding syndrome, and suspected aspiration of feed are an important indicator of tolerance to enteral nutrition; however, in this study, incidences of diarrhea and other complications of feeding were a general observation and were not recorded unless it translated into a more serious complication. Therefore, it would be interesting to investigate this in future studies. The APACHE II is a severity of disease classification system, commonly used to provide a general measure of disease severity in acutely ill patients [44]. The APACHE II is one of several ICU scoring systems based on 12 physiologic measurements, age, and previous health status [44]. Patients in both the treatment and placebo groups had similar mean APACHE II scores at baseline with no significant difference between groups. Thus, at baseline, patients in both groups had similar disease severity based on their APACHE II scores.

Besides, further investigation into the role of MCP in modulating the immune response and gut barrier function in critically ill patients and its relationship to length of mechanical ventilation and length of hospital stay among a homogenous group of patients is required.

## 5. Conclusion

The results of this study suggest that the concomitant use of MCP during enteral feeding in critically ill patients is associated with improved tolerance and earlier return of gut function. This may prove beneficial to the overall clinical outcome and enhance recovery of the patient.

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