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Probiotics in Surgical and Critically Ill Patients

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Despite advances in surgical technique and intensive-care medicine, nosocomial bacterial infections frequently occur in patients after major abdominal surgery and have a negative impact on operative outcome and hospital costs. In parallel, the routine use of antibiotics led to the development of resistance. Some probiotics (living bacteria) and prebiotics (fibers) are able to stabilize the intestinal barrier and to prevent bacterial infections.

Increased mucosal permeability has been suggested to be the cause of bacterial translocation and subsequent infection, sepsis and multiple organ failure. More recent views are that increased permeability is just a symptom of mucosal inflammation induced by a multitude of factors in the critically ill patient. One of these consists of a distorted balance between bacteria, which can downregulate inflammation, and pathogenic bacteria that upregulate inflammation. These pathogenic strains have been found to be able to sense the stressed state of their host and to upregulate their virulence when they are sufficiently numerous. The effect of probiotics may consist of preventing these pathogenic bacteria to reach this quorum and to become virulent, and thereby prevent infection, sepsis and multiple organ failure.

To date, 10 clinical trials in patients following abdominal surgery and 2 trials in trauma patients have been published. In addition, 3 trials have been performed in critically ill patients with acute severe pancreatitis. The primary endpoint of all reported studies was the occurrence of bacterial infections. The type and concentration of the probiotics, duration of therapy and route of administration were not comparable in most of the trials.

In 8 of the 12 studies in surgical patients, probiotics led to a significant reduction in bacterial infection rates compared to the control groups. In 2 studies there was a positive trend in the groups with probiotics, but the results were not statistically significant. Two studies showed no effect.

The results in acute pancreatitis patients were conflicting: in 2 of the trials, probiotics had a beneficial effect, whereas in the third study, the probiotic group had a significantly higher mortality, largely related to bowel ischemia.

All 3 trials were flawed in some respect, but the most likely conclusion of the combined data is that most patients with multiple organ failure are not able to tolerate full enteral feeding with high-fiber formulas. In addition, bacterial strains used in the trial in which probiotics were harmful had not been shown to confer a health benefit in humans. In critically ill patients with organ failure the amounts and types of probiotics, the addition of prebiotics, the amount of enteral feeding and the site of administration should be carefully adapted to prevent bowel ischemia and further deterioration of organ function (table 1).

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Table 1. Results of the published studies in patients following abdominal surgery and critically ill patients

First author/ reference	Patients	Study design	Kind of operation	Probiotics	Controls	Length of therapy days	Infection rates %	Other findings
McNaught [1]	129	prosp. rand.	mixed (mainly colon)	10^7 *L. plantarum* 299v + oat fiber (Proviva)	no treatment	9 pre 5 post	13 vs. 15 (n.s.)	
Anderson [2]	137	prosp. rand.	mixed (mainly colon)	10^9 *L. acidophilus, L. bulgaricus, Bifidob. lactis, Strept. thermophilus* + oligofructose (Trevis)	placebo	12 pre 4 post	32 vs. 31 (n.s.)	
Reddy [3]	88	prosp. rand.	colon	Trevis	1 = MBP 2 = neomycin + MBP 3 = symbiotic + neomycin + MBP 4 = synbiotics + neomycin	n.s.	21 vs. 18 vs. 15 vs. 14 (n.s.)	less BT in group 3
Rayes [4]	90	prosp. rand.	mixed (liver, gastric, pancreas, colon)	10^9 *L. plantarum* 299 + oat fiber	1 = parenteral 2 = enteral + synbiotics 3 = enteral + prebiotic	5 post	30 vs. 10 vs. 10 (n.s.)	fewer antibiotics in synbiotic group, best effects in pancreas and gastric resection
Nomura [5]	70	prosp. rand.	pancreas (PPPD)	*E. faecalis, Clostridium butyricum, Bacillus mesentericus* (Bio-Three)	no treatment	3–15 pre 10 post	23 vs. 53	less DGE in synbiotic group
Rayes [6]	80	prosp. rand. double-blind	pancreas (PPPD)	10^{10} *L. plantarum* 2362, *L. paracasei*, leuconostoc mesenteroides, pediacoccus pentosaceus + inulin, pectin, starch, β-glucan (Synbiotic 2000)	prebiotics	1 pre 8 post	12.5 vs. 40	fewer antibiotics in synbiotic group
Kanazawa [7]	44	prosp. rand.	liver resection	10^8 *Bifidob. breve, L. casei* + galacto-oligosaccharides (Yakult BL Seichoyaku)	no treatment	14 post	19 vs. 52	fewer pathogenic bacteria and higher organic acid concentrations in the feces
Sugawara [8]	81	prosp. rand.	liver resection	10^{10} *Bifidob. breve, L. casei* (Yakult 400)	treatment only postop.	14 pre 14 post	12 vs. 30	fewer fecal pathogenic bacteria, enhanced immune response
Rayes [9]	95	prosp. rand.	liver transplantation	10^9 *L. plantarum* 299 + oat fiber	1 = SBD 2 = synbiotics 3 = prebiotics	12 post	48 vs. 13 vs. 34	
Rayes [10]	66	prosp. rand. double-blind	liver transplantation	Synbiotic 2000	prebiotics	14 post	3 vs. 48	fewer antibiotics in synbiotic group
Kotzampassi [11]	65	prosp. rand.	trauma	Synbiotic 2000	prebiotics	15	49 vs. 77	less severe sepsis, days of stay on ICU and on mechanical ventilation
Spindler-Vesel [12]	113	prosp. rand.	trauma	Synbiotic 2000	1 = glutamine 2 = prebiotics 3 = peptide diet 4 = synbiotics	n.s.	50 vs. 59 vs. 50 vs. 19	decreased intestinal permeability
Olah [13]	45	prosp. rand.	pancreatitis	10^9 *L. plantarum* 299 + oat fiber	prebiotics	7	5 vs. 30	
Olah [14]	62	prosp. rand. double-blind	pancreatitis	Synbiotic 2000	prebiotics	7	27 vs. 52 (n.s.)	fewer SIRS + MOF

Table 1 (continued)

First author/ reference	Patients	Study design	Kind of operation	Probiotics	Controls	Length of therapy days	Infection rates %	Other findings
Besselink [15]	296	prosp. rand. double-blind multicenter	pancreatitis	10^{10} *L. acidophilus, L. casei, L. salivarius, L. lactis, Bifidob. bifidum, Bifidob. lactis* + cornstarch and maltodextrin (Ecologic 641)	prebiotics	28	30 vs. 28 (n.s.)	higher mortality

prosp. rand. = Prospective randomised; *L.* = *Lactobacillus*; *Bifidob.* = *Bifidobacterium*; *Strept.* = *Streptococcus*; *E.* = *Enterococcus*; BT = bacterial translocation; DGE = delayed gastric emptying; ICU = intensive care unit; MBP = mechanical bowel preparation; pre = preoperatively; post = postoperatively; SIRS = systemic inflammatory response syndrome; MOF = multiorgan failure; PPPD = Pylorus preserving pancreaticoduodenectomy.

Conclusion

The existing randomized controlled trials have demonstrated a beneficial effect of probiotics in surgical patients with high-risk abdominal operations and multiple trauma patients.

In critically ill patients, insufficient data exist to draw firm conclusions. However, bacterial strains and their mode of administration should be extensively tested before using them in clinical trials, especially in patients with acute necrotizing pancreatitis and multiple organ failure.

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N.R. does not have any relationship to disclose.
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