PROBIOTICS IN SURGERY

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It has been a century since Elie Metchnikoff, regarded as the father of probiotics, published the textbook “The Prolongation of Life: Optimistic Studies” (1), describing the potential benefits of dietary supplementation with lactic acid bacteria. Ever since, a significant number of publications have been elaborated concerning the problem where analysis comprised the different varieties of bacteria, possible configurations, preparations, and clinical applications. In many fields of medicine there still is lack of clear guidelines considering the use of pro-, syn-, and prebiotics. The presented article attempted to review literature data considering the use of probiotics in surgery.

Nomenclature

According to the FAO/WHO (2) definition probiotics are considered as live organisms, which administered in adequate doses exert a beneficial health effect. Scientific data also mentions the following terminology: prebiotic – nutritional content subject to selective fermentation leading towards specific changes of the content and activity of gastrointestinal microorganism, which are beneficial to the well-being and health of the host (inulin, fructooligosacharide). Synbiotics are the combination of pre- and probiotics.

Probiotics available in Poland

The number of preparations containing probiotics, available on the market is continuously growing at an enormous pace. They are most commonly sold as dietary supplements. Milk products enriched with bacteria (yogurts, milk drinks) and advertised as probiotics have also gained significant popularity. One should bear in mind that not all mentioned above products are beneficial, and not all bacterial strains meet the requirements of the term - probiotics. Table 1 presented available products containing strains with proven efficacy.

The mechanism of action of probiotics

The past years, bringing sustainable development and the emergence of new molecular study technologies enabled to increase knowledge concerning the properties and functioning of the gastrointestinal flora. Analysis of various bacterial strains constituting the ecosystem of the gastrointestinal tract can enable the scientists to select bacteria potentially useful for clinical application (3). Several mechanisms of probiotic activity exist rendering the development of alimentary tract pathogens impossible (4). Some bacterial strains adhering to the intestinal epithelial cells prevent the access of potential harmful strains. Sarem-Damerdji et al. (5) proved the above-mentioned, considering Lactobacillus GG. Individual bacteria in various preparations produce different specific substances inhibiting growth of pathogenic bacteria in alimentary tract. In 1987, M. Silva et al. (6) described a substance produced by Lactobacillus GG inhibiting the following bacterial strains: Clostridium, Bacteroides, Bifidobacterium, Pseudomonas Staphylococcus, Streptococcus, and Enterobacteriaceae. The experimental study elaborated by scientists from Helsinki described Lactobacillus casei LC-10 and L. Casei.
Table 1. Available probiotics on the Polish market

<table>
<thead>
<tr>
<th>Preparation</th>
<th>Probiotic strain</th>
<th>Manufacturer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dicoflor 30 i 60</td>
<td><em>Lactobacillus rhamnosus</em> GG (LGG)</td>
<td>VitisPharma</td>
</tr>
</tbody>
</table>
| Trilacc         | *Lactobacillus acidophilus*  
*Lactobacillus delbrueckii subsp. bulgaricus*  
*Bifidobacterium bifidum*               | Krotex                   |
| Lactoral        | *Lactobacillus rhamnosus* KL 53A  
*Lactobacillus plantarum* PL 02  
*Bifidobacterium longum* PL 03         | IBSS Biomed              |
| Lakcid          | *Lactobacillus rhamnosus*                                                      | Biomed Lublin            |
| Lakcid forte    | *Lactobacillus rhamnosus*                                                      | Biomed Lublin            |
| Dietavit        | *Lactobacillus acidophilus*                                                     | Slab                     |
| BioGaia         | *Lactobacillus reuteri* Protectis                                               | Ewopharma AG             |
| Prolactiv       | *Lactobacillus acidophilus* Rosell  
*Bifidobacterium longum* Rosell  
*Lactobacillus rhamnosus* Rosell  
*Bifidobacterium breve* Rosell  
*Bifidobacterium bifidum* Rosell       | Naturell                  |
| Quartum         | *Lactobacillus acidophilus*  
*Bifidobacterium*  
*Streptococcus thermophilus*  
*Lactobacillus delbrueckii ssp. bulgaricus* | PSM                      |
| Acidolac        | *Lactobacillus acidophilus* i *Bifidobacterium*                                | Medana                   |
| Enterol         | *Saccharomyces boulardii*                                                       | Biocodex                 |
| Ido Form Kid    | *Lactobacillus rhamnosus* GG (LGG)  
*Bifidobacterium animalis subsp. lactis* Bb12                                  | Ferrosan                 |

pseudoplantarum LB1931 bacteria from tissue cultures, which produced Pyroglutamic acid (PCA) inhibiting the development of selected Gram (-) and Gram (+) bacteria (7). Bacteriocins are considered to be a special group of substances with specified microbiological properties produced by gastrointestinal bacteria (8). Practically each group of bacteria has characteristic bacteriocines able to inactivate or even kill pathogenic organisms (8). Another mechanism of competition between probiotics and gastrointestinal pathogens is that probiotic bacteria use the substances that the pathogens need to carry out basic metabolic processes such as monosaccharides (essential for Clostridium difficile’s metabolism) (9). Gastrointestinal environment acidification by probiotics also creates unfavorable conditions for bacterial development (10).

Literature data widely described the influence of probiotics on the local (intestinal) and systemic immunological system. Probiotics activate and increase the number of lymphocytes (11), as well as increase the activity of macrophages (12). On the other hand, they can induce apoptosis of the lymphocytes programmed to kill the host’s own microflora. This particular mechanism was observed among patients suffering from nonspecific bowel inflammation receiving probiotics (13). Rigby et al. (14) described the stimulating effect of probiotic bacteria on the production of anti-inflammatory cytokines (IL10), with the simultaneous increase of pro-inflammatory cytokines (IL2) caused by pathogenic bacteria. Lactobacillus GG strains are responsible for the increased expression of genes involved in mucin synthesis, which are considered protective from of gastrointestinal infections (15, 16). Encouraging results were obtained from experimental studies describing the decrease in bacterial translocation in rats receiving Lactobacillus strains (17, 18, 19). McNaught et al. (19) investigated the gut barrier function in patients subject to major surgical procedures. The Authors determined the bacterial translocation in case of patients receiving perioperative Lactobacillus plantarum 299v, as compared to the control group. Statistically significant differences were not observed. The problem of bacterial translocation requires further investigations, as well as the role of
probiotics in the control of the above-mentioned process.

Probiotics in gastroenterology

The section dedicated to research on probiotics in the World Gastroenterology Organisation, published guidelines considering the use of probiotics in gastroenterology, based on EBM (20). The use of probiotics is recommended in the management of diarrhea (especially post-antibiotic). The meta-analysis undertaken by Sazawal et al. (21, 22) concerning the efficacy of probiotics in the prevention of diarrhea of various etiology (post-antibiotic and travelers’ diarrhea), demonstrated benefits connected with the use of probiotics. Another confirmed indication is the treatment of pouchitis after reconstructive proctocolectomy. The Authors described not only the favorable effect of pouchitis treatment results, but also improved quality of life after surgical treatment of colitis ulcerosa (23). Therapy of irritable bowel syndrome (IBS) should also be supplemented by probiotic administration. Nikfar et al. (24) demonstrated in a meta-analysis the efficacy of probiotics in the management of IBS. The beneficial effect of probiotics was also mentioned, considering the eradication of H. pylori (25, 26). Probiotics not only reduce the adverse effects of antibiotic therapy on the gastrointestinal tract, but also increase the efficacy of eradication. The use of probiotics in patients with colitis ulcerosa and Crohn’s disease has no proven effectiveness.

Probiotics in surgery

Most investigations concerning the use of probiotics in gastroenterological surgery, focuses on their influence on perioperative infectious complications.

Rayes et al. (27) investigated patients after pancreateodudodenectomy, who received a mixture of probiotics during the perioperative period consisting of Pediacoccus pentosaceus, Leuconostoc Mesenteroides, Lactobacillus paracasei subspecies paracasei F19, and Lactobacillus plantarum 2362 strains. In comparison to the control group the Authors observed a reduction in the amount of infectious complications (12% in the probiotic group and 40% in the control group), as well as reduction in the duration of antibiotic therapy (27) (tab. 2).

<table>
<thead>
<tr>
<th>Study author/year</th>
<th>Probiotic /Synbiotic</th>
<th>Description of the group</th>
<th>Number of patients (n)</th>
<th>Infectious complications: N: control group, P: probiotic group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rayes/2002 (28)</td>
<td>L. plantarum 299</td>
<td>elective laparotomy</td>
<td>90</td>
<td>N:30% do P:10%</td>
</tr>
<tr>
<td>Rayes/2002 (29)</td>
<td>L. plantarum 300</td>
<td>liver transplant</td>
<td>105</td>
<td>N:48% do P:13%</td>
</tr>
<tr>
<td>McNaught/2002 (30)</td>
<td>L. plantarum 299v</td>
<td>elective laparotomy</td>
<td>129</td>
<td>N:13% do P:15%</td>
</tr>
<tr>
<td>Anderson/2004 (31)</td>
<td>L. acidophilus La5,</td>
<td>elective laparotomy</td>
<td>144</td>
<td>N:32 do P:31%</td>
</tr>
<tr>
<td></td>
<td>L. bulgaris,</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>B. lactis Bb-12,</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kanazawa/2005 (32)</td>
<td>L. casei, Bifidob. Breve</td>
<td>liver transplant</td>
<td>54</td>
<td>P:19% do N: 52%</td>
</tr>
<tr>
<td>Rayes/2005 (33)</td>
<td>P. pentosaceus,</td>
<td>liver transplant</td>
<td>95</td>
<td>P:3% do N:48%</td>
</tr>
<tr>
<td></td>
<td>Leuconostoc mesenteroides,</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>L. paracasei,</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>L. plantarum 2362</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Kotzampassi/2006 (34)</td>
<td>Pediacoccus pentosaceus 5:33:3,</td>
<td>severe injuries treated</td>
<td>77</td>
<td>P:63% do N:90%</td>
</tr>
<tr>
<td></td>
<td>Leuconostoc mesenteroides 92-77:1,</td>
<td>at the ICU</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>L. paracasei ssp. paracasei 19</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>L. plantarum 2,362</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sugawara/2006 (35)</td>
<td>Lactobacillus casei,</td>
<td>liver and biliary duct</td>
<td>101</td>
<td>P:12% do N:30%</td>
</tr>
<tr>
<td></td>
<td>Bifidobacterium breve</td>
<td>operations</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
The meta-analysis of 9 randomized trials undertaken by Pitsouni et al. (38) comprising 733 patients subject to abdominal cavity surgery, demonstrated a reduction in the number of patients diagnosed with pneumonia and cholangitis, as well as shorter antibiotic therapy and hospitalization in patients receiving probiotics, as compared to the control group. The Authors observed no statistically significant differences in the occurrence of postoperative wound infections, urinary tract infections, intra-abdominal abscesses and mortality, considering both groups. It is important to notice that analysis comprised patients subject to various surgical procedures (colorectal surgery, pancreatoduodenectomy, liver transplantations, and bile duct surgery). Additionally, the activity of different probiotic strains was evaluated (L. acidophilus, L. bulgaricus, B. lactis BB-12, S. thermophilus, L. paracasei F19, L. plantarum 2362+ prebiotyki).

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<th>Infectious complications: N: control group, P: pro- or symbiotic</th>
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The use of probiotics in the treatment of acute pancreatitis remains a controversial issue. The most recent results pose many questions and doubts. The Hungarian study which was performed in 2007 comprised 62 patients with acute pancreatitis (39). The Authors compared the control group with patients receiving Synbiotic 2000. In case of patients’ that received the above-mentioned probiotic, the Authors’ observed a reduction in the inflammatory response and multiorgan failure, as well as in the mortality rate (statistically insignificant difference). The multicenter Dutch trial (40) comprised 296 patients with severe acute pancreatitis. The control group was compared to patients additionally receiving a mixture of strains: L. acidophilus, L. casei, Lactobacillus salivarius, Lactococcus lactis, Bifidobacterium bifidum, and B. lactis with maltodextrins. In case of infectious complications, results were similar, while a significant increase of mortality rate was observed in the group receiving probiotics (6% vs16%). Literature data concerning probiotics previously described no such severe complications. The unfavorable effect of probiotics in the investigated group was attributed to intestinal ischemia. Due to major increase in mortality rate caused by probiotics authors concluded that the usage of probiotics to treat severe acute pancreatitis needs more studies and this particular bacterial mixture should not be applied for this indication.

Another issue is the use of probiotics in case of liver surgery. Kanazawa et al. (32) performed a study comprising 44 patients with liver cancer subject to surgical resection. The control group was compared to patients receiving the symbiotic containing *Bifidobacterium breve* and *Lactobacillus casei* strains. The Authors observed a reduction in the number of postoperative infectious complications (12 (52.2%) control group patients and 4 (19%) symbiotic group patients). The hospitalization period and duration of antibiotic therapy showed no statistically significant differences, considering both groups. Rayes et al. (33) ob-
served a reduction in the number of infectious complications after liver transplantation (13% vs 48%), considering patients who received L. plantarum 299 bacteria during the perioperative period.

In case of patients with severe multi-organ injuries hospitalized in the intensive care unit, Kotzampassi et al. (34) compared treatment results considering patients receiving Synbiotic 2000 Forte, which comprised the following bacterial strains: Pediococcus pentosaceus 5–33: 3, Leuconostoc mesenteroides 32–77:1, L. paracasei ssp. paracasei 19, and L. plantarum 2.362 with the control group. A significant reduction in the number of infectious complications was observed in the control group (from 90% to 63%). One observed the reduction of SIRS from 77% to 49%, while mortality from 30% to 14.3% (34).

Interesting conclusions arose from the study concerning the role of probiotics in the surgical management of obesity. Woodard et al. (41) applied probiotics (Lactobacillus) in case of patients subject to bariatric surgery. These patients underwent procedures requiring Roux-en Y anastomosis. The Authors observed improved quality of life after the above-mentioned procedures, and greater weight reduction in patients receiving probiotics (after 3 months of observation: weight reduction in the control group – 38.55%, while in case of patients on probiotics – 47.68%).

Perspectives

The role of probiotics in the treatment and prevention of neoplasms remains unclear, although the results of analysis provide interesting conclusions and perspectives for the future. Experimental studies provide hope and show the need for further analyses on human beings (42-52). In vitro analysis demonstrated the influence of the supernatant derived from the fermentation of pre- and probiotics, on cultured cancer cell lines (41, 43). Results showed suppression and inhibition of the neoplasmatic cells by probiotics through their impact on the genetic and enzymatic components of carcinogenesis. In the cancer cells treated with SFS (supernatant from the fermentation of prebiotics and probiotics) the mitochondrial activity was increased with simultaneous increase of their mortality rate (45). Other investigations performed on rats demonstrated a reduction in the occurrence of colorectal cancer in cases of rodents receiving synbiotics, as well as the reduction in the level of the cancer markers among rodents, treated with synbiotics, with induced colorectal cancer (Bifidobacterium lactis Bb12 and Lactobacillus rhamnosus) (47-50). Human studies, although with initial promising effects, require long-lasting observations.

Conclusions

Pre-, pro- or synbiotics in most cases reduce the frequency of infections and help in the management of antibiotic therapy complications. In case of economy, probiotics exert a beneficial effect on the cost-effectiveness relationship.

The fundamental problem considering study analysis of probiotics and elaboration of guidelines for their application, concerns the multiplicity and heterogeneity of bacterial strains. Each type of bacteria has a specific and unique configuration of properties. Thus, based on the analysis of one strain of bacteria conclusions considering the features of another bacterial strain cannot be inferred. Initial literature data showed that a specific preparation can be used in selected clinical conditions. This is especially true in case of gastroenterological surgery, where procedures performed on the gastrointestinal tract, and antibiotic therapy can significantly influence the inhibition of local bacterial flora, development of pathogens, and ensuing immunological disturbances and infectious complications.

REFERENCES


