Safety of Saccharomyces boulardii (Florastor) in Solid Organ Transplant Patients

Nicole Marie Dores
Butler University

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Applicant: Nicole Marie Dores
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Thesis title: Safety of Saccharomyces boulardii (Florastor®) in Solid Organ Transplant Patients

Intended date of commencement: May 12, 2012

Thesis adviser(s)

Reader(s)

Certified by

Read, approved, and signed by:

Date

Date

Date

For Honors Program use:

Level of Honors conferred: University

Departmental

Magna Cum Laude

Pharmacy with Highest Honors

University Honors Program
Safety of *Saccharomyces boulardii* (Florastor®) in Solid Organ Transplant Patients

A Thesis
Presented to the Department of Pharmacy Practice
College of Pharmacy and Health Sciences
and
The Honors Program
of
Butler University

In Partial Fulfillment
of the Requirements for Graduation Honors

Nicole Marie Dores
May 4, 2012
Abstract

Introduction:

Probiotics have been promoted for use in many gastrointestinal ailments. Most studies find probiotics safe for human use, reporting no severe adverse effects. However, probiotics are live microorganisms and thus have the potential to cause infection. Transplant recipients are considered at high risk for infectious complications from probiotics due to the immunosuppressive medications used to prevent organ rejection. Nonetheless, clinicians are currently utilizing probiotics in the transplant population, due to their benefit in gastrointestinal disorders, particularly recurrent Clostridium difficile. Limited knowledge and paucity of prospective trials in this patient population demands the need for completion of studies to identify the safety of probiotics in transplant patients.

Objective:

The primary objective of this study was to investigate the safety of utilizing Saccharomyces boulardii for the prevention of antibiotic-associated diarrhea in kidney, pancreas, and liver transplant recipients. A secondary objective of this study was to evaluate the efficacy of the use of Saccharomyces boulardii to prevent antibiotic-associated diarrhea.

Methods:

A prospective chart review was performed to assess the safety of Saccharomyces boulardii in transplant patients. All kidney, pancreas, and liver transplant patients who received Saccharomyces boulardii were included in the safety analysis. Only those who meet criteria for the prevention of antibiotic-associated diarrhea with Saccharomyces boulardii were included in the efficacy analysis.
Results:
No infections due to the probiotic, *Saccharomyces boulardii*, in 16 solid organ transplant patients treated were observed.

Conclusion:
There are multiple of case reports regarding infectious complications of probiotics, particularly in groups at high risk for infection. However, some studies have shown probiotics given immediately after transplantation may help restore normal gut flora and prevent the translocation of bacteria across the gut wall thereby preventing infections in these immunosuppressed patients. This study found no infectious complications of probiotics in solid organ transplant recipients.
**Introduction:**

The World Health Organization and the Food and Agriculture Organization of the United Nations define probiotics as “live microorganisms which when administered in adequate amounts confer a health benefit to the host.” ¹ In recent years, probiotics have been promoted for use in many disease states. In the hospital setting, probiotics are mainly used to replenish the colon microflora in patients with diarrhea due to antibiotics or to prevent recurrence of disease following treatment of *Clostridium difficile* colitis.²

Most studies have found probiotics safe for human use, reporting no severe adverse effects. However, probiotics are live microorganisms and have the potential to cause infection. Patients at a higher risk of developing infection from probiotic therapy include those with immunosuppressed states, critical or terminal illness, prosthetic heart valves, bowel surgery, history of rheumatic heart disease or infective endocarditis, or use of proton pump inhibitors or histamine H₂ antagonists. These higher risk patients are often excluded from probiotic studies limiting knowledge concerning the safety of probiotic therapy in these populations.³,⁴,⁵

Organ transplant recipients are considered a high risk group for infectious complications from probiotic therapy due to the administration of immunosuppressive medications used to prevent organ rejection.⁶ Conversely, some studies have shown probiotics beneficial in restoring normal gut flora and preventing the translocation of bacteria across the gut wall and thereby preventing infections in these immunosuppressed patients.⁷,⁸

There are no previous prospective trials regarding the use of a *Saccharomyces* probiotic in the solid organ transplant population. The primary objective of this study was to investigate the safety of using *Saccharomyces boulardii* for the prevention of antibiotic-
associated diarrhea in solid organ transplant recipients. A secondary objective of this study was to evaluate the efficacy of the use of *Saccharomyces boulardii* to prevent antibiotic-associated diarrhea.

**Methods**

All patients > 18 years of age who were recipients of a simultaneous kidney/pancreas, pancreas after kidney, isolated pancreas or liver transplant and were initiated on *Saccharomyces boulardii* therapy while admitted to the organ transplant unit at Indiana University Hospital from July 1, 2011 to March 1, 2012 were eligible for this prospective study. Patients who were pregnant, had a known hypersensitivity to *Saccharomyces* spp., or received other probiotics prior to admission were excluded. Following approval from the Indiana University School of Medicine Institutional Review Board, data was collected from the electronic medical record including age, sex, admission diagnosis, medical history, concomitant illness, documented infection via culture results, probiotic administration information, and results of tests for *Clostridium difficile*. Clinical outcomes data was also collected which included incidence of diarrhea or constipation, infectious complications, and other serious adverse effects associated with the probiotic therapy. Data was assessed using descriptive statistics. All patients were included in the safety analysis to determine the incidence of infectious complications due to *Saccharomyces boulardii*. Those patients who received antibiotic therapy as well as *Saccharomyces boulardii* and no other probiotic were included in the efficacy analysis to determine the benefit of *Saccharomyces boulardii* for the prevention of antibiotic associated diarrhea.
**Results:**

Sixteen patients received probiotics with no documented infections or other serious complications. The demographics of the patient population are shown in Table 1. Five of these patients met the criteria for efficacy analysis of prevention of antibiotic-associated diarrhea with *Saccharomyces boulardii*. Three of these patients experienced diarrhea. Two had been admitted with diarrhea and found to have *Clostridium difficile* colitis and were treated with either the standard of care for *Clostridium difficile* colitis (metronidazole or vancomycin) in addition to the *Saccharomyces boulardii*. Both patients had resolution of their diarrhea with this treatment. The other patient experienced diarrhea after 5 days of probiotic therapy. The probiotic was continued and due to improvement of diarrhea the patient was discharged on the probiotic.

**Discussion:**

In this study, *Saccharomyces boulardii* therapy was well tolerated in pancreas, kidney, and liver transplant patients with no serious adverse effects. Although this was a small study, it contradicts literature showing infectious complications of probiotics particularly in patients who are immunosuppressed. Current guidelines for the prevention and treatment of *Clostridium difficile* infection from the Society for Healthcare Epidemiology of America and the Infectious Diseases Society of America state “administration of currently available probiotics is not recommended to prevent primary *Clostridium difficile* infection, as there are limited data to support this approach and there is a potential risk of bloodstream infection.” These guidelines also discourage the use of *Saccharomyces* spp. therapy; “administration of *Saccharomyces boulardii* has, however, been associated with fungemia in
immunocompromised patients and in patients with central venous lines, and should be avoided in critically ill patients.  

These recommendations are based on case reports that describe infectious complications of probiotics in groups at risk for infection. In a review of 92 cases of invasive infections due to *Saccharomyces* spp., *Saccharomyces boulardii* was responsible for 37 fungemias. Of these patients, 32 had taken a probiotic that contained *Saccharomyces boulardii*. Those who had a *Saccharomyces boulardii* infection were more likely to have a digestive tract disease, a central venous catheter, and be hospitalized in an intensive care unit.

Muñoz, and colleagues, investigated an outbreak of *Saccharomyces cerevisiae* fungemias in an intensive care unit. The investigators revealed the commonality between the three patients with fungemia was treatment with a *Saccharomyces boulardii* probiotic, brand name Ultralevura®. Both the probiotic strain of yeast and the blood cultures isolated from the three patients were identified by the hospital microbiology laboratory as *Saccharomyces cerevisiae* with identical DNA fingerprinting. Discontinuation of the probiotic product ended further infections in the unit.

Like critically ill patients, organ transplant recipients are considered high risk for infectious complications of probiotics. The purported reason suggested for this increased risk of infectious complications in transplant recipients is the immune compromised state induced from the transplant medications required to prevent rejection of the transplanted organ.

Luong and colleagues report their experience in which a 56-year-old male with human immunodeficiency virus underwent a double-lung transplant and developed an empyema which cultured positive for *Lactobacillus rhamnosus GG*, the strain of bacteria
identical to the probiotic administered as part of the standard post-transplant *Clostridium difficile* prophylaxis regime. Riquelme and colleagues report a case of a 42-year-old woman, having received a kidney-pancreas transplant developed *Saccharomyces cerevisiae* fungemia after treatment with *Saccharomyces boulardii* for *Clostridium difficile*. Though the strain of *Saccharomyces* spp. was *S. cerevisiae* and not *S. boulardii*, the investigators concluded the fungemia was a result of the administration of the probiotic as it is very difficult for most laboratories to distinguish *Saccharomyces boulardii* from *Saccharomyces cerevisiae.*

In our study, conclusions regarding efficacy cannot be made due to the limited number of patients meeting the inclusion criteria at this time. Trials have shown benefit with the use of probiotics for diarrhea. In a study conducted by Hickson and colleagues, older adults taking antibiotics were randomized to receive either a probiotic drink containing *Lactobacillus casei, Lactobacillus bulgaricus,* and *Streptococcus thermophilus* or a sterile milkshake. The incidence of both antibiotic-associated and *Clostridium difficile* diarrhea was decreased in the probiotic group.

In a review of probiotics by Imhoff and Karpa, a tendency towards benefits from probiotics was observed. Clinical trials of probiotics containing multiple strains were shown to be most favorable for primary prevention of *Clostridium difficile* associated disease. However, clinical trials and case reports of the probiotic *Saccharomyces boulardii* in combination with high-dose vancomycin were most advantageous for the prevention of recurrence disease.

Current guidelines for the use of nutritional support in critical ill patients from the Society of Critical Care Medicine and the American Society for Parenteral and Enteral
Nutrition state, “administration of probiotic agents has been shown to improve outcome (most consistently by decreasing infection) in specific critically ill patient populations involving transplantation, major abdominal surgery, and severe trauma.” However, the guidelines do not recommend one probiotic strain or combination over another. “It seems that each species may have different effects and variable impact on patient outcome, making it difficult to make broad categorical recommendations.”

Rayes and colleagues have shown the administration of probiotics immediately after transplantation may help restore normal gut flora and prevent translocation of bacteria across the gut wall thus preventing infections in these immunosuppressed patients. In a group of 66 adult liver transplant patients, those patients treated with a probiotic containing *Pediococcus pentosaceus, Leuconostoc mesenteroides, Lactobacillus paracasei, and Lactobacillus plantarum* twice daily for 14 days immediately post-transplantation showed a significant decrease in post-operative infections. Post-operative infections were seen in 48% of patients who did not receive probiotic therapy and 3% of patients who received probiotic therapy.

**Conclusion:**

Although the use of probiotics in solid organ transplant recipients and other immunocompromised individuals is controversial, they are still utilized in these populations. This prospective trial found no infectious complications with the administration of the probiotic *Saccharomyces boulardii* in sixteen solid organ transplant patients. Further research is required to determine the safety of probiotics, including *Saccharomyces boulardii*, in the solid organ transplant population.
References:


