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Intestinal Transplantation and Bacterial Overgrowth in Humans

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Human gastrointestinal flora is part of a complex ecosystem regulated by host mechanisms, environmental factors, and bacterial interactions. Alterations in the symbiotic relationship between small bowel recipients and their gut microflora can tilt this balance and lead to serious infectious complications. This study is the first to demonstrate the occurrence of microbial overgrowth among small bowel transplant recipients.

MATERIALS AND METHODS

Over a 3-year period (May 1990 to April 1993), 43 patients received intestinal transplantation at our center. Of these, 31 were given small bowel without colon either alone (n = 10), in combination with liver (n = 17), or as part of a multivisceral graft (n = 4). These 31 recipients were included in the study because of the presence of temporary vent chimney or terminal ileostomy that facilitated sampling of the ileal contents. The principles and technical details of the vascular reconstruction and restoration of gastrointestinal continuity are described elsewhere.[1,2] The basic immunosuppressive drug therapy was FK 506 and steroids.3

Selective gut decontamination was attempted in all donors and for the first 4 weeks after transplantation in all recipients. It was also resumed during moderate to severe rejection episodes. The drugs used were aminoglycosides, Amphotericin B or nystatin, and polymyxin E. The contents of the intestinal lumen were not mechanically washed during or after the donor operation. Systemic antibiotics (cefotaxime and ampicillin) were also administered to donors as a single dose and to recipients during the first 5 postoperative days and when indicated subsequently based upon the results of blood and body fluid cultures. All patients received H_2 antagonists immediately following transplantation that were maintained during the study period.

Quantitative microbiological cultures of the terminal ileal contents were frequently performed for all patients to monitor changes in distal small bowel flora. Blood cultures were also obtained when infection was clinically suspected and the results compared for similarity and dissimilarity of the intestinal flora to obtain direct evidence of distant translocation. Anaerobic cultures were not routinely performed in this study.

All patients continued to receive total parenteral nutrition (TPN) after transplantation for a mean postoperative period of 59 ± 49 (SD) days. Enteral feeding with Peptamen was commenced during the first 3 weeks after surgery and gradually decreased with a reciprocal increase in oral intake (unrestricted diet). Peptamen is an isotonic elemental diet that contains peptide-based protein, medium-chain triglycerides, and glutamine.

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Surveillance endoscopic intestinal allograft biopsies were performed for all recipients and liver biopsies were done at the time of abnormal liver functions or when translocation was clinically and microbiologically suspected.

RESULTS

With a mean follow-up of 17 ± 11 (SD) months, quantitative microbial cultures of the terminal ileal contents showed, on at least one occasion, a bacterial count $>10^9$ colony-forming units (CFU)/mL for all but four patients (1 isolated intestine, 3 combined liver-intestine) with an overall incidence of 87%. Of 532 total cultures (17/patient), 34% showed bacterial count > 10^9 CFU/mL, 45% were between 10^5 to 10^9 CFU/mL, and the remaining 21% were $<10^5$ CFU/mL. The identified microorganisms were either gram-negatives, (6%), gram-positives (28%), or both (58%). The remaining 8% showed fungal organisms. The composition and concentration of the bacterial colonies were similar among the three types of intestinal recipients. Interestingly, none of the multivisceral recipients showed fungal colonization of the terminal ileum.

The ecology of the small bowel graft flora was influenced by gut decontamination, rejection episodes, and cytomegaloviral enteritis. During the first 30 postoperative days, the bacterial count was $>10^9$ CFU/mL in 19% of the cultures (n = 113) and the populations were 67% gram-positives and 33% gram-negatives. With discontinuation of gut decontamination and during the remaining study period, the percentage of $>10^9$ CFU/mL counts gradually increased up to 38%. Meanwhile, the concentration of gram-positives was decreased with simultaneous increase in gram-negative counts. During significant rejection episodes and CMV enteritis, the total count increased for both gram-positive and gram-negative bacteria.

Bacterial and/or fungal infections developed in 28 (90%) patients. The bacteria were mostly enteric and the fungi were *Candida albicans, Torulopsis glabrata, Trichoderma koningii,* and *Coccidioides immitis.*

The diagnosis of translocation was made in patients who had the same microorganisms in the terminal ileum and blood simultaneously with a quantitative microbial count of $>10^9$ CFU/mL with no other obvious sources of infection. Thirteen episodes of translocation occurred in 11 recipients. Four (2 adults, 2 children) of these were isolated intestinal recipients and seven (2 adults, 5 children) were combined liver-intestinal recipients. The median onset was 98 days (range 2 to 303), The isolated microorganisms were mostly enteric bacteria, *C albicans, Torulopsis glabrata,* and in different combinations. Ten (77%) of these episodes were associated with histopathological evidence of intestinal allograft rejection, including pseudomembraries and submucosal microabscesses. Distant translocation was not lethal in any of these 11 morbid cases.

DISCUSSION

Bacterial overgrowth is a common finding in the terminal ileum of intestinal allograft recipients. This could be attributed to surgical manipulation of the transplanted bowel, absence of the ileocecal valve, lymphatic disruption, high steroid doses, abnormal gastrointestinal motility, suppression of gastric acid secretion, and postoperative need for temporary intravenous nutrition and an enteral-defined formula diet.[4–6] Our surgical technique is currently modified to preserve the ileocecal valve in an attempt to reduce such morbid event.

The loss of an effective mucosal barrier due to rejection or preservation injury and the impaired host defenses due to heavy immunosuppression may potentiate the deleterious effects of bacterial overgrowth in this unique population. Although it was not always

technically feasible to prove, the high incidence of systemic infections among these recipients could be partly due to the development of translocation.

References

1. Starzl TE, Todo S, Tzakis A, et al. Surg Gynecol Obstet 1991;172:335. [PubMed: 2028370]
2. Todo S, Tzakis A, Abu-Elmagd K, et al. Ann Surg 1992;216:223. [PubMed: 1384443]
3. Abu-Elmagd K, Fung J, Reyes J, et al. Transplant Proc 1992;24:1243. [PubMed: 1376523]
4. Kirsch M. Am J Gastroenterology 1990;85:231.
5. Berg RD, Womaek E, Deitch EA. Arch Surg 1988;123:1359. [PubMed: 3178484]
6. Browne BJ, Johnson CP, Edmiston CE, et al. J Surg Res 1991;51:512. [PubMed: 1943089]