INTESTINAL TRANSPLANTATION

Essay

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in ***General surgery***

by

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علم الرب كل عِلم، واطلع على علامة الدهر؛ مُخبِرًا بالماضي والمستقبل، وكاشِفا عن آثار الخفايا، لا يفوته فِكرٌ ولا يخفى عليه كلام.

(يشوع بن سيراخ 42:19)

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List of Abbreviations:	
Anti-IL-2	Anti-interleukin-2
APCs	Antigen presenting cells
CMV	Cytomegalovirus
CT	Computerised tomography
DD	Deceased Donor
EBV	Epstein-Barr viras
ERCP	Endoscopic retrograde cholangiopancreatography
GALT	Gut associated lymphoid tissues
GIT	Gastrointestinal tract
GVHD	Graft Versus Host Disease
HIV	Human immunodeficiency virus
HLA	Human leucocytic antigen
HPN	Home parentral nutration
IF	Intestinal failure
ITx	intestinal transplantation
LD	Living donor
MID	Microvillus inclusion disease
MRA	Magnetic resonance angiography
NEC	Necrotizing enterocolitis
PCR	polymerase chain reaction
PSRs	program-specific reports
PTLPD	Post-transplant lymphoproliferative disease
rATG	(rabbit Anti-thymocyte globulin)
SBS	Short bowel syndrome
SMA	Superior mesenteric artery
STEP	serial transverse enteroplasty
TPN	Total parenteral nutrition
UNOS	United Network for Organ Sharing
UW solution	University of Wisconsin solution

List of contents

Aim of the work:

In our study we will throw lights on the following questions ;

- ✓ What is the historical background of intestinal transplantation?
- ✓ What is the definition of intestinal failure and what are the various indications for intestinal transplantations?
- ✓ What are the different types of intestinal transplants?
- ✓ What are the criteria of donor, graft and recipient selection?
- ✓ What are the complications of intestinal transplantation?
- ✓ What is the operative technique of intestinal transplantation?
- ✓ What is the postoperative management and outcome?

INTRODUCTION

Intestinal transplantation, either alone or combined with the liver or other organs, may become necessary in patients with short bowel syndrome (SBS) who fail intestinal rehabilitation. The first successful isolated and combined small bowel transplantation occurred almost 25 years ago, between 1990 and 2008, 1041 pediatric small bowel transplantation were performed in the United States . Annually, 100–120 pediatric intestinal-containing transplants are performed worldwide. **(Mazariegos et al., 2009), (Nayyar et al., 2010).**

Indications for pediatric intestinal transplantation include failure to achieve more than half of caloric requirements enterally with either growth failure, worsening liver function, loss of central venous access, or recurrent sepsis. Most children requiring intestinal transplantation (68%) have Short bowel syndrome due to anatomic loss with the most common etiologies as gastroschisis (24%), NEC (16%), volvulus (15%), and small bowel atresia (9%). **(Avitzur & Grant 2010).**

Intestinal transplantation can occur in isolation or in combination with other organs. Many children will have advanced liver disease at the time of referral and will undergo combined liver-small bowel transplantation. **(Fishbein 2009),(Mazariegos et al. ,2009) .**

Intestinal transplantation poses a significant immunologic challenge because 80% of immune cell normally reside in gut and they are re-populated with recipient cells after transplantation. Acute rejection can limit long term survival; it occurs in 60% of pediatric intestinal recipients with a third of cases being severe. **(Fishbein 2009) , (Abu-Elmagd et al., 2009).**

Considerable progress in immunosuppression has decreased rates of Acute rejection leading to improvement of early allograft survival while minimizing toxicity. **(Abu-Elmagd et al.,2009)**

Acute cellular rejection may be asymptomatic or present with diarrhea, abdominal pain, distention, nausea, vomiting, or a sudden increase or decrease in stoma output. **(Mazariegos et al. ,2009) .**

Early diagnosis and treatment of Acute rejection is critical for successful reversal, therefore scheduled surveillance biopsies of the graft are performed through the ileostomy opening created at the time of transplantation. A typical early surveillance biopsy schedule includes twice per week in the first month, weekly during the second month, then twice per month for the third month and then monthly . Improved detection and treatment of Acute rejection have led to a marked improvement in early graft survival. **(Nayyar et al., 2010),(Fishbein 2009).**

Chronic rejection is the major cause of late graft loss. Patients can present with abdominal pain with chronic diarrhea, bowel obstruction or gastrointestinal bleeding,

weight loss or failure to thrive. In recent series, chronic rejection rates are 10–15% with liability to occur in isolated intestinal transplants compared to combined liver-intestinal transplants. (21% vs. 5%). .

(Nayyar et al., 2010),(Mazariegos et al.,2009) .

History of intestinal transplantation

The technical feasibility of the procedure has been established for a century**,** but immunological feasibility was far more difficult to establish. The high density of lymphoid tissue and the large mucosal surface area of the small intestine expressing class 2 major histocompatability antigens fuels the mutual intolerance between graft and host. As a hollow organ whose lumen is colonised by a multitude of bacteria and other micro-organisms, it behaves as a potent vector of infection to the host, a problem that is made worse by the precarious barrier from the lumen provided by the thin and vulnerable monolayer of mucosal epithelium. Here then is the fine balance between immunosuppression and infection that led to transplantation failure in so many early attempts. **(Okumura&Mester,1992).**

I. Pre Cyclosporine Era:

Following early transplantation attempts, deaths were most commonly a consequence of acute graft rejection and subsequent sepsis associated multiorgan failure. **(Okumura et al., 1969).**

This scenario was not improved even with the introduction of combination therapy with azathioprine, prednisolone and antilymphocyte globulin. **(Grant et al., 1997).** .

II. Cyclosporine Era:

The introduction of cyclosporine in 1978 by Calne and colleagues accelerated progress in solid organ transplantation and rekindled interest in intestinal grafts. .
(Calne et al. , 1978),(Calne et al. , 1979).

Success in this new cyclosporine era led to the transition from success in animals to the first long term success in humans. In 1988 Grant and colleaguesreported a patient with short gut syndrome following mesenteric infarction who had undergone combined liver and small intestine transplantation and remained alive one year after the procedure. Other groups soon reported similar experiences. **(Grant et al. , 1997).**

III. Tacrolimus Era

With the introduction of tacrolimus in the 1990s, a new chapter in intestinal transplantation began .Just as cyclosporine in the 1980s had significantly increased the survival rates of kidney, liver, pancreas, and heart transplants, tacrolimus propelled intestinal transplantation to clinical acceptance.Initial work at the University of Pittsburgh demonstrated that tacrolimus significantly decreased the incidence of rejection and increased graft and patient survival rates after intestinal transplantation. **(Todo et al., 1992),(Todo et al., 1995).**

The first Living Donor (LD) intestinal transplant in the tacrolimus era was reported by Morris et al. in 1995**(Morris et al. , 1995)** ,A 31-year-old man with a desmoid tumor underwent excision of the tumor, and in the same session, a small bowel

transplant from his monozygotic twin. The technical aspects of LD intestinal transplantation were studied in a pig model; the results of this experimental work became the basis of the first LD intestinal transplant at the University of Minnesota. After the University of Minnesota's first two technically successful LD intestinal transplants, the university of Illinois group published guidelines for a standardized technique for intestinal transplants from living donors in 1997. **(Starzl et al., 2004).**

Since then, at least 25 more LD intestinal transplants have been performed worldwide .Initially, LD intestinal transplants were performed in North America and Europe. Over time, LD intestinal transplants have also been reported in Asian countries, such as Japan, China, and Korea. **(Lee et al., 2004), (Uemoto et al., 1998).**

The first Japanese case was performed in Kyoto in a 2-year 6-month-old boy who received 100cm of distal donor ileum. **(Uemoto et al., 1998).**

LD intestinal transplants have been reported worldwide between January 1985 and March 2005. Ofnote, with the exception of the identical twin transplants, there appears to be no significant (graft and patient) survival advantage compared with the results of Deceased Donor(DD) intestinal transplants, this finding has been critically documented in the literature and has stirred a debate about whether the use of LDs for segmental intestinal transplants is justified. .
(Tzakis & Gruessner 1998),(Fryer & Angelos 2004).

However, what is frequently overlooked is thatshort bowel syndrome is not a static process and that serious TPN-associated