Centre for Clinical Effectiveness
Enhancing patient outcomes through clinical application of the best available evidence

CRITICAL APPRAISAL
Series 2003: Therapy

Assessing the effectiveness of total parenteral nutrition for simultaneous renal and pancreatic transplant patients

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SUMMARY STATEMENT

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REQUEST

Does total parenteral nutrition (TPN), if commenced immediately following combined renal-pancreas transplantation improve recovery time and reduce subsequent morbidity in these patients, compared with patients not given TPN after renal-pancreas tranplantation?

REQUESTED BY

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METHODOLOGY

Search Strategy

The Centre for Clinical Effectiveness defines the 'best available evidence' as that research we can identify that is least susceptible to bias. We determine this according to pre-defined National Health and Medical Research Council (NHMRC, 2000) criteria (see Appendix 1).

First, we search for systematic reviews, evidence based clinical practice guidelines, health technology assessments and randomised controlled trials. If we identify sound, relevant material of this type, the search stops. Otherwise, our search strategy broadens to include studies that are more prone to bias, less generalisable or have other methodological difficulties. We include case-control and longitudinal cohort studies in our critical appraisal reports. While observational studies, case series studies, narrative reviews and consensus statements are cited in our reports we do not critically appraise these studies. Such studies can produce accurate results but are generally too prone to bias to allow determination of their validity beyond their immediate setting.

Details of Evidence Request

Patients (Subjects):	adult patients (18 years and over) undergoing simultaneous renal-pancreas transplantation
Intervention:	total parenteral nutrition initiated at time of transplant (TPN)
Comparisons:	no TPN
Outcomes:	faster recovery from transplant surgery (faster discharge, fewer readmissions, lower rates of mortality and morbidity arising from surgery)

Search terms

(see Appendix 2 for exact search strategy)

Patient:	kidney transplant, renal transplant
Intervention:	total parenteral nutrition, perioperative, postoperative

Resources Searched

We searched the following databases and internet websites:

Resource	Issue or Access Date
The Cochrane Library (Online)	Issue 3, 2003
Medline (OVID)	1966 to May Week 3, 2003
EBM Reviews (OVID) -	
Cochrane Database of Systematic Reviews	Issue 3, 2003
Database of Abstracts of Reviews of Effectiveness	Issue 3, 2003
Cochrane Controlled Trials Register	Issue 3, 2003
CINAHL (OVID)	1982 to May Week 3 2003
PREMEDLINE (OVID)	May 27 2003
Australasian Medical Index	February 2003
PubMed (National Library of Medicine)	May 27 2003
National Guideline Clearinghouse	May 27 2003

Other guidelines sites (Australian and International)- September 2003

Various other internet sites, including Dietetics associations and practice guidelines sites were also searched.

Refinements, Searching & Reporting Constraints

Only articles published from 1995 onwards and published in English were considered eligible for the current review.

Inclusion criteria

- Studies conducted in adult patients undergoing simultaneous renal-pancreatic transplant.
- Studies conducted in adult patients undergoing major surgery, particularly gastrointestinal surgery.
- Papers published 1995 onwards.

Exclusion criteria

- Studies conducted in children.
- Studies examining critically ill patients or patients with medical conditions such as pancreatitis.
- Studies published in a language other than English.

RESULTS

No studies were found which examined patients undergoing simultaneous pancreatic-renal transplant.

ADDITIONAL INFORMATION

Searching was therefore broadened to include studies examining TPN among renal transplant patients. No studies assessing TPN versus other nutritional support were identified for renal transplant patients.

One set of evidence-based guidelines from the American Dietetic Association were identified ("Guidelines for Nutrition Care of Renal Patients", 2002). While these may be a useful additional resource they address renal transplantation patients and nutritional requirements separately.

Searching was again broadened to include TPN in more general surgical patients. Evidence-based guidelines from the American Gastroenterological Association (2001), assessing parenteral nutrition in a variety of medical conditions states that for renal disease "There are no RCTs comparing parenteral nutrition to standard therapy. The decision to use it or not must be made by the responsible physician without the benefit of such data."

A number of possible papers of interest concerning nutrition in general surgical patients or general medical illness were identified and the abstracts, where available, are included below only as articles of possible interest. Articles are cited in alphabetical order by first author's name.

References of possible interest:

Anonymous (2001). American Gastroenterological Association medical position statement: parenteral nutrition. *Gastroenterology* **121:** 966-969.
This document presents the official recommendations of the American Gastroenterological Association (AGA) on Parenteral Nutrition. It was approved by the Clinical Practice and Practice Committee on April 13, 2001 and by the AGA Governing Board on May 18, 2001.

Braunschweig CL, Levy P, Sheean PM & Wang X (2001). Enteral compared with parenteral nutrition: a meta-analysis. *American Journal of Clinical Nutrition* **74:** 534-542.
BACKGROUND: The difference in outcomes in patients is unclear when 2 types of enteral nutrition, ie, tube feeding and conventional oral diets with intravenous dextrose (standard care), are compared with parenteral nutrition. OBJECTIVE: We reviewed systematically and aggregated statistically the results of prospective randomized clinical trials (PRCTs) to examine the relations among the nutrition interventions, complications, and mortality rates. DESIGN: We conducted a MEDLINE search for PRCTs comparing the effects of enteral and parenteral nutrition in adults. Two different people abstracted data for the method and outcomes separately. We used fixed-effects meta-analysis technique to combine the relative risks (RRs) of the outcomes of infection, nutrition support complications, other complications, and mortality. RESULTS: Twenty-seven studies in 1828 patients met the study criteria. Aggregated results showed a significantly lower RR of infection with tube feeding (0.64; 95% CI: 0.54, 0.76) and standard care (0.77; 95% CI: 0.65, 0.91). A priori hypotheses showed a lower RR of infection with tube feeding than with parenteral nutrition, regardless of nutritional status, presence of cancer, year of study publication, or quality of the study method. In studies in which participants had high rates of protein-energy malnutrition, there was a significantly higher risk of mortality (3.0; 95% CI: 10.9, 8.56) and a trend toward a higher risk of infection with standard care than with parenteral nutrition (1.17; 95% CI: 0.88, 1.56). CONCLUSIONS: Tube feeding and standard care are associated with a lower risk of infection than is parenteral nutrition; however, mortality is higher and the risk of infection tends to be higher with standard care than with parenteral nutrition in malnourished populations.

Dominguez-Cherit G, Borunda D & Rivero-Sigarroa E (2002). Total parenteral nutrition. *Current Opinions in Critical Care* **8:** 285-289.
In recent months, numerous reports concerning total parenteral nutrition in critically ill patients have been published, including the guidelines and recommendations of the American Society for Parenteral and Enteral Nutrition. The old controversy regarding the use of the enteral versus parenteral route still exists. Although the enteral route is indicated in those patients with normal gastrointestinal function, the parenteral route is obviously beneficial in several clinical conditions and appears to be associated with few procedure-related complications when performed by experienced clinicians. There is also continued interest in the supplementation of parenteral formulas with nutrients that were previously considered nonessential, such as arginine, glutamine, and omega-3 fatty acids, but that may become essential in the setting of critical illness.

Hasse JM (1998). Recovery after organ transplantation in adults: the role of postoperative nutrition therapy. *Topics in Clinical Nutrition* **13:** 15-26.
Appropriate nutrition therapy is vital during the acute posttransplant period to promote healing, fight infection, provide energy for activity, and replenish depleted nutrient stores. Energy, protein, fluid, vitamin, mineral, and electrolyte requirements reflect a patient's pretransplant status and perioperative complications. Altered graft function, drug-nutrient interactions, and complications involving neurological, psychological, cardiac, pulmonary, gastrointestinal, renal, and endocrine systems influence modes of feeding and nutrient requirements. If transplant recipients are unable to eat during the postoperative period, nutrition support may be required; tube feeding is preferred over total parenteral nutrition. Objective and subjective assessment parameters are used to measure the effectiveness of nutrition therapy.

Hasse JM (2001). Nutrition assessment and support of organ transplant recipients. *JPEN: Journal of Parenteral & Enteral Nutrition.* **25:** 120-131.
Timely nutrition assessment and intervention in organ transplant recipients may improve outcomes surrounding transplantation. A pretransplant nutrition assessment should include a variety of parameters including physical assessment, history, anthropometric measurements, and laboratory tests. Malnutrition compromises posttransplant survival; prolonged waiting times worsen outcomes when patients are already malnourished. Severe obesity may decrease graft function and survival in kidney transplant recipients. In the pretransplant phase, nutritional goals include optimization of nutritional status and treatment of nutrition-related symptoms induced by organ failure. Enteral tube feeding is indicated for patients with functional gastrointestinal tracts who are not eating adequately. Parenteral nutrition is rarely needed pretransplant except in cases of intestinal failure. When determining pretransplant nutrient requirements, nutritional status, weight, age, gender, metabolic state, stage and type of organ failure, malabsorption, induced losses, goals, and comorbid conditions must be considered. During the acute posttransplant phase, adequate nutrition is required to help prevent infection, promote wound healing, support metabolic demands, replenish lost stores, and perhaps mediate the immune response. Nutrient recommendations reflect posttransplant metabolic changes. The appropriateness of posttransplant nutrition support depends on the prevalence of malnutrition among patients with a specific type of organ failure and the benefits when nutrition support is given. Organ transplantation complications including rejection, infection, wound healing, renal insufficiency, hyperglycemia, and surgical complications require specific nutritional requirements and therapies. Many potential applications of nutrition in the pre- and posttransplant phases exist and require further study.

Heyland DK, MacDonald S, Keefe L & Drover JW (1998). Total parenteral nutrition in the critically ill patient: a meta-analysis. *Journal of the American Medical Association* **280:** 2013-2019.
CONTEXT: Nutritional support has become a standard of care for hospitalized patients, but whether total parenteral nutrition (TPN) affects morbidity and mortality is unclear. OBJECTIVE: To examine the relationship between TPN and complication and mortality rates in critically ill patients. DATA SOURCES: Computerized search of published research on MEDLINE from 1980 to 1998, personal files, and review of relevant reference lists. STUDY SELECTION: We reviewed 210 titles, abstracts, and papers. Primary studies were included if they were randomized clinical trials of critically ill or surgical patients that evaluated the effect of TPN (compared with standard care) on complication and mortality rates. We excluded studies comparing TPN with enteral nutrition. DATA EXTRACTION: Relevant data were abstracted on the methodology and outcomes of primary studies. Data were abstracted in duplicate, independently. DATA SYNTHESIS: There were 26 randomized trials of 2211 patients comparing the use of TPN with standard care (usual oral diet plus intravenous dextrose) in surgical and critically ill patients. When the results of these trials were aggregated, TPN had no effect on mortality (risk ratio [RR], 1.03; 95% confidence interval [CI], 0.81-1.31). Patients who received TPN tended to have a lower complication rate, but this result was not statistically significant (RR, 0.84; 95% CI, 0.64-1.09). We examined several a priori hypotheses and found that studies including only malnourished patients were associated with lower complication rates but no difference in mortality when compared with studies of nonmalnourished patients. Studies published since 1989 and studies with a higher methods score showed no treatment effect, while studies published in 1988 or before and studies with a lower methods score demonstrated a significant treatment effect. Complication rates were lower in studies that did not use lipids; however, there was no difference in mortality rates between studies that did not use lipids and those studies that did. Studies limited to critically ill patients demonstrated a significant increase in complication and mortality rates compared with studies of surgical patients. CONCLUSIONS: Total parenteral nutrition does not influence the overall mortality rate of surgical or critically ill patients. It may reduce the complication rate, especially in malnourished patients, but study results are influenced by patient population, use of lipids, methodological quality, and year of publication.

Heyland DK, Montalvo M, MacDonald S, Keefe L, Su XY & Drover JW (2001). Total parenteral nutrition in the surgical patient: a meta-analysis. *Canadian Journal of Surgery* **44:** 102-111.
OBJECTIVE: To examine the relationship between total parenteral nutrition(TPN) and complication and death rates in surgical patients. DATA SOURCES: A computer search of published research on MEDLINE, personal files and a review of relevant reference lists. STUDY SELECTION: A review of 237 titles, abstracts or papers. Primary studies were included if they were randomized clinical trials of

surgical patients that evaluated the effect of TPN (compared to no TPN or standard care) on complication and death rates. Studies comparing TPN to enteral nutrition (EN) were excluded. DATA EXTRACTION: Relevant data were abstracted on the methodology and outcomes of primary studies. Data were independently abstracted in duplicate. DATA SYNTHESIS: There were 27 randomized trials in surgical patients that compared the use of TPN to standard care (usual oral diet plus intravenous dextrose). When the results of these trials were aggregated, there was no effect on mortality (risk ratio = 0.97, 95% confidence intervals, 0.76 to 1.24). There were fewer major complications in patients who received TPN, although there was significant heterogeneity in the overall estimate (risk ratio = 0.81, 95% CI, 0.65 to 1.01). Because of this significant heterogeneity, several a priori hypotheses were examined. Studies that included only malnourished patients demonstrated a trend to a reduction in complication rates but no difference in death rate when compared with studies of patients who were not malnourished. Studies published in 1988 or earlier and studies with a lower methods score were associated with a significant reduction in complication rates and a trend to a reduction in death rate when compared with studies published after 1988 and studies with a higher methods score. There was no difference in studies that provided lipids as a component of TPN when compared with studies that did not. Studies that initiated TPN preoperatively demonstrated a trend to a reduction in complication rates but no difference in death rate when compared with studies that initiated TPN postoperatively. CONCLUSIONS: TPN does not influence the death rate of surgical patients. It may reduce the complication rate, especially in malnourished patients, but study results are influenced by methodologic quality and year of publication.

Satyanarayana R & Klein S (1998). Clinical efficacy of perioperative nutrition support. *Current Opinion in Clinical Nutrition & Metabolic Care.* **1:** 51-58.
Despite a large number of published randomized prospective controlled clinical trials the indications for perioperative parenteral and enteral nutrition support remain controversial. This article reviews the reports of several recently published consensus conference reports and prospective randomized controlled trials evaluating nutritional therapy in surgical patients.

APPENDIX 1

Copyright

Disclaimer

The information in this report is a summary of that available and is primarily designed to give readers a starting point to consider currently available research evidence. Whilst appreciable care has been taken in the preparation of the materials included in this publication, the authors and Southern Health do not warrant the accuracy of this document and deny any representation, implied or expressed, concerning the efficacy, appropriateness or suitability of any treatment or product. In view of the possibility of human error or advances of medical knowledge the authors and Southern Health cannot and do not warrant that the information contained in these pages is in every aspect accurate or complete. Accordingly, they are not and will not be held responsible or liable for any errors of omissions that may be found in this publication. You are therefore encouraged to consult other sources in order to confirm the information contained in this publication and, in the event that medical treatment is required, to take professional expert advice from a legally qualified and appropriately experienced medical practitioner.

Levels Of Evidence

Based on "How to use the evidence: assessment and application of scientific evidence" (National Health & Medical Research Council, Canberra, 2000):

Level I		Evidence obtained from a systematic review (or meta-analysis) of all relevant randomised controlled trials.
Level II		Evidence obtained from at least one randomised controlled trial.
Level III	-1	Evidence obtained from pseudo-randomised controlled trials (alternate allocation or some other method).
	-2	Evidence obtained from comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomised, cohort studies, case control studies or interrupted time series with a control group.
	-3	Evidence obtained from comparative studies with historical control, two or more single-arm studies or interrupted time series without a parallel control group.
Level IV		Evidence obtained from case series, either post-test or pretest/post-test.

APPENDIX 2

Search strategy

	Search terms for MEDLINE
1	exp Parenteral nutrition, total/
2	total parenteral nutr$.tw
3	(parenteral$ adj5 nutrition$).mp
4	or/1-3
5	exp Kidney transplantation/
6	(kidney adj5 transplant$).tw
7	(renal adj5 transplant$).tw
8	perioperative$.tw
9	postoperative$.tw
10	or/5-9
11	4 and 10
12	limit 11 to year=1995-2003

Similar terms, appropriately translated, were used in other databases searched.