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Original research

Preoperative oral immunonutrition versus standard preoperative oral diet in well nourished patients undergoing pancreaticoduodenectomy

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HIGHLIGHTS

- Immunonutrition in surgical patients.
- Preoperative oral immunonutrition and pancreatic surgery.
- Perioperative Nutrition in well nourished patients undergoing pancreatic surgery.
- Postoperative complications after pancreatic surgery.

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ABSTRACT

Background: Pancreaticoduodenectomy is still associated to high morbility, especially due to pancreatic surgery related and infectious complications: many risk factors have already been advocated. Aim of this study is to evaluate the role of preoperative oral immunonutrition in well nourished patients scheduled for pancreaticoduodenectomy.

Methods: From February 2014 to June 2015, 54 well nourished patients undergoing pancreaticoduodenectomy were enrolled for 5 days preoperative oral immunonutrition. A series of consecutive patients submitted to the same intervention in the same department, with preoperative standard oral diet, was matched 1:1. For analysis demographic, pathological and surgical variables were considered. Mortality rate, overall postoperative morbility, pancreatic fistula, post pancreatectomy haemorrhage, delayed gastric emptying, infectious complications and length of hospital stay were described for each groups. Chi squared test, Fisher's Exact test and Student's T test were used for comparison. Differences were considered statistically significant at $p < 0.05$. Statistics was performed using a freeware Microsoft Excel ® based program and SPSS v 10.00.

Results: No statistical differences in term of mortality (2.1% in each groups) and overall morbility rate (41.6% vs 47.9%) occurred between the groups as well as for pancreatic surgery related complications. Conversely, statistical differences were found for infectious complications (22.9% vs 43.7%, $p = 0.034$) and length of hospital stay (18.3 ± 6.8 days vs 21.7 ± 8.3, $p = 0.035$) in immunonutrition group.

Conclusion: Preoperative oral immunonutrition is effective for well nourished patients scheduled for pancreaticoduodenectomy; it helps to reduce the risk of postoperative infectious complications and length of hospital stays.

1. Introduction

Improvements in surgical technique, perioperative management and experience of high volume centers lead to a dramatical reduction of mortality rate after pancreaticoduodenectomy (PD), currently ranging from 3% to 5% [1]. However, the postoperative

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morbidity still elevated remains between 40% and 60% [2–5]. Postoperative complications include pancreatic fistula (POPF), delayed gastric emptying (DGE) and infectious complications (wound infections, Surgical Site Infections – SSI, pneumonia, urinary tract infections) among others [1,6]. POPF and DGE affect from 2% to 30% of patients submitted to PD [7,8]; their occurrence leads to an increase of other postoperative complications, such as infectious complications, with delayed recovery and metabolic alterations.

Reduction of the host response and of the immunity, which are facilitated by low caloric intake and by intestinal bacterial translocation, characterize patients undergoing PD; alteration of postoperative intestinal motility and loss of mucosal barrier function are certainly contributing factors [9,10]. This impaired immunological activity leads to a greater risk of infection and a prolonged hospital stay with increased health care costs.

Preoperative careful evaluation of patients is crucial to set a planned strategy to reduce morbidity [11,12]. Among strategies proposed to reduce complications, artificial enteral diets supplemented with arginine, omega-3 fatty and ribonucleics acids have been suggested to improve immune response, inflammatory pathway and wound healing trough the provision of key nutrients involved in T – lymphocyte activity and other immune functions [13–17]. As a matter of fact Immune-nutrition (IN), and especially arginine, promotes T cell activities, reduces production of IL 1, IL 6 and alpha-TNF and helps tissue regeneration. Furthermore, omega 3 fatty acids are useful to modulate inflammatory status trough reduction of prostacyclin and thromboxane (TX-A2), reduction of prostaglandin G2 and leukotrienes and consequent modulation of cell mediated immunity [18–21]. Finally, RNA supplementation plays a key role for proliferation of cells involved in wound healing [22].

In patients undergoing gastrointestinal cancer surgery, positive effects of perioperative IN in terms of reduction of postoperative local (SSI) and general infectious complications as well as length of hospital stays (LOS) have been postulated [15,23,24]. Some authors have recently indicated that preoperative exclusive IN support might be as effective as the perioperative one and might be useful to optimize patient without surgical stress [15,25]. To the best of our knowledge, only few reports of oral preoperative IN in patients scheduled for pancreatic surgery have been proposed [18,25,26] and most of which assess the benefits in malnourished patients [27]. Actually it remains poorly codified the role of immunonutrition in well-nourished patients proposed to undergo major pancreatic surgery [25,28].

The aim of this study was to determine whether preoperative IN alone is efficacious in improving outcomes in patients undergoing pancreatic surgery in well nourished patients. To determine this, we report on overall postoperative and infectious complications after PD as well as on LOS.

2. Material and methods

From February 2014 to June 2015, 54 well nourished patients were scheduled for PD at 4th Division of General Surgery of AOU City of Health and Science, Turin – Italy. Indications to surgery were for pancreatic primary or metastatic malignancy, ampullary or biliary carcinoma and chronic pancreatitis. Patients submitted to neo-adiuvant chemotherapy were excluded from the protocol.

During preoperative period and after the signature of an informed consent, patients were included in a prospective study of preoperative immunonutrients supplemental liquid diet (Oral Impact®, Nestlè Italia) for at least 5 days before pancreatic surgery, in addition to oral standard diet at a dose of 750 ml/day (3 packs). All patients kept a written record of the daily amount of supplemented diet consumed. Nutritional value of this dietary supplement is summarized in Table 1. Exclusion criteria are listed in Table 2. Demographic and surgical data were collected for each patient in a prospective database.

This series of patients submitted to preoperative immunonutrition (IN) was compared with a homogenous cohort of consecutive patients well nourished submitted to PD without preoperative IN and with a standard oral preoperative diet at 4th Division of General Surgery of AOU City of Health and Science, Turin – Italy from October 2012 to January 2014. Data of non IN patients were retrospectively reviewed from a prospectively maintained database. Exclusion criteria were the same as for IN group, listed in Table 2.

Patients were matched 1:1 for age, gender, ASA score, comorbidities, preoperative biliary drainage (endoscopic or percutaneous trans-hepatic drainage), performance status, hemoglobin (g/L), BMI (k/m2), degree of weight loss (with respect to usual body weight in the previous 6 months), mean albumin level (g/dl), plasma levels of total proteins (g/L), pancreatic texture, Wirsung's diameter and type of pancreatic anastomosis.

The following clinical variables were noted for each patients: age, gender, ASA score, comorbidities, preoperative biliary drainage (endoscopic or percutaneous transhepatic drainage), performance status, hemoglobin (g/L), BMI (k/m2), degree of weight loss (with respect to usual body weight in the previous 6 months), mean albumin level (g/dl), plasma levels of total proteins (g/L), pancreatic texture (soft or hard), Wirsung's diameter, histology, type of pancreatic anastomosis, operative time, overall postoperative morbidity, need for a second laparotomy, mortality, pancreatic fistula (POPF), post pancreatectomy haemorrhage (PPH), delayed gastric emptying (DGE), infectious complications and hospital length of stay.

2.1. Surgical technique

All PD considered were performed by the same team of high experienced pancreatic surgeons. All patients underwent standard Whipple procedure with regional lymphadenectomy and subtotal stomach preserving gastrectomy In each case a pancreato-enteric reconstruction was done: pancreato-jejunal anastomosis or pancreato-gastro anastomosis, depending on intraoperative local conditions and features of pancreatic parenchyma. Pancreato-jejunal anastomosis was typically done as an end to side with a double layer of interrupted sutures of polydioxanone 5/0 (PDS II®,

Table 1
IN Composition.

Oral impact® composition	Amount
Proteins	7.6 g
L-arginine	1.8 g
RNA[b]	0.2 g
Fats (total)	3.9 g
Saturated fatty acids	1.8 g
MCT[a]	1.12 g
Monounsaturated	0.73 g
Polyunsaturated	1.3 g
Linoleic Acid	0.6 g
Ω-3 fatty acids	0.6 g
Carbohydrates	18.9 g
Maltodestrines	7.6 g
Sucrose	10.5 g
Lactose	<0.02 g
Soluber Fibers	1.4 g
Energy	141 g
Water	77 g

[a] MCT, Medium Chain Triglycerides.
[b] RNA, Ribo-Nucleics Acid.