Route delivery of nutrition in patients with enterocutaneous fistula

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ABSTRACT

Malnutrition is one of the most frequent effects of an enterocutaneous fistula (ECF). There are some factors that contribute to it including inadequate intake, fluid loss via fistula and underlying disease. The role of nutrition is very important as a part of ECF therapy to give adequate nutrition, maintain fluid and electrolyte state and increase the likelihood of fistula closure spontaneously. Therefore, it is anticipated that adequate nutrition management will lower morbidity and mortality while enhancing clinical results. Nutritional requirements and nutritional route, whether oral, enteral and parenteral nutrition in ECF management, are influenced by the anatomical, physiological and aetiology of the fistula. The purpose of this review was to highlight the evidence based on nutritional therapy in ECF patients by calling attention to nutritional route selection based on the anatomy and physiology fistula to prevent malnutrition.

KEYWORDS:
Enterocutaneous fistula, malnutrition, enteral, parenteral nutrition

INTRODUCTION

Enterocutaneous fistula (ECF) is a feared complication after gastrointestinal surgery. ECF incidence is unknown but has been estimated at less than 0.5 patients per 100,000 citizens.[1] Approximately, 75% of all ECF is caused by open surgery or laparoscopy, and the rest (25%) is caused by diverticular disease, inflammatory bowel disease (IBD), malignancy and radiation therapy.[2] As cited by Teixeira et al, 1.5% of the patients developed an ECF after acute trauma laparotomies and the most common site of ECF was a colon (69%), followed by small bowel (53%), duodenum (36%) and stomach (19%). This complication exerts a significant negative impact on length of stay, longer intensive care unit utilisation and higher hospital costs.[3]

The classic triad describes the problems of ECF: sepsis, malnutrition, fluid and electrolyte imbalance.[4] Subsequently, 55–90% of patients become severely malnourished.[1] Factors that cause malnutrition in ECF are underlying disease, inadequate intake, increased protein requirements related to systemic inflammation and increased fluid loss, including nutrients through the fistula.[5]

Optimal nutritional support plays a major role in preventing malnutrition, reducing morbidity and mortality.[6] Without optimal nutrition, ECF patients can experience delayed wound closure and worse overall outcome.[7] ECF patients who received 1,500–2,000 calories per day had a lower mortality rate and a higher rate of fistula closure. Otherwise, patients who only received <1,000 calories per day had a higher mortality rate and lower fistula closure rate.[4] To provide optimal nutritional support, the selection of a nutritional route—oral, enteral or parenteral—should be considered.

Dudrick et al. reported that providing total parenteral nutrition (TPN) could treat malnutrition in patients with severe nutritional debility or complex gastrointestinal disease.[8] Although 60–70% ECF patients ultimately require TPN, it is preferred to administer enteral nutrition (EN) via a nasogastric tube or percutaneous endoscopic gastrostomy device.[7,9] Only a few studies have investigated outcomes associated with the use of enteral or parenteral nutrition in ECF patients and the discussion about which is the better nutritional route is still ongoing. A cohort study from Levy et al (1989) of 335 ECF patients with high output fistula have reported though many patients received TPN as initial stabilisation, 85% of patients were maintained exclusively with EN. In 38% of patients, the fistula closed spontaneously and the mortality rate was only 19% in 234 patients who managed conservatively.[10] A study conducted by Li et al for 30 years on 1,168 patients showed that 86.4% of patients receiving EN found it effective. Only 13.6% of patients received parenteral nutrition exclusively. The mortality rate was very low, and overall closure rates were high. EN can even be used successfully in patients with high-output fistulas when combined with elemental formulas, anti-motility drugs, and fibre-bulking agents.[11]

Given the high risk of malnutrition in ECF patients, an optimal nutritional medical therapy approach was needed to reduce morbidity and mortality. The anatomy and physiology of ECF also affect the nutritional route selection to support nutrition therapy. This review will go through the nutrition dietary aspects of ECF therapy, with a particular emphasis on the nutritional route selection.

Definition and Classification

ECF is an abnormal connection between the gastrointestinal tract and external skin.[2] ECF can be classified according to the anatomy, aetiology and physiology that contribute to morbidity, mortality and the possibility of spontaneous fistula closure.[12] Based on the anatomy, ECF is divided according to the organ of origin: type I (abdominal, esophageal, gastroduodenal fistula), type II (small intestinal fistula), type III (large intestine fistula) and type IV (entero-atmospheric fistula, regardless of origin).[12] Based on the

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Table I: Prognostic factors of ECF2

Favourable	Unfavourable
Albumin >3 g/dL	Undernutrition
	Short fistula, multiple, complex fistula
Diverticular fistula	Large enteral defect (>1 cm), visible mucosa
	High output (>500 mL/day)
Single fistula	Prior radiation
Intestinal continuity	Multiple prior operations

Table II: Pros and Cons nutritional routes in ECF

Nutritional Route	Pros	Cons
Parenteral	- Useful in high-output fistula - Ability to reduce gastrointestinal secretion 30-50%, therefore potentially decreasing mortality rate and helping spontaneous closure in 70% of patients	- Catheter-related complications - Risk of hyperglycaemia
Enteral	- Can initiate immediately if the patient is stabilised and sepsis in controlled - Lower cost - Greater availability - Fewer complications - Useless in high-output fistula	- Contraindicated if there are intestinal discontinuity, ileus, short bowel length, enteral feeding intolerance
Combination Enteral and Parenteral	- To achieve the caloric requirement - Could be applied if enteral feeding was accessible but not well tolerated (keeping 20% of the required calories achieved by enteral and 80% by parenteral)	
Oral	- Only useful when the patient enable to tolerate fluids and solid food with solid food	- May increase the output of the fistula, especially
Fistuloclysis	- Useful in patients with intact intestinal absorption ability distal to the infusion site - Beneficial in patients with complications associated to TPN (infection, venous access problem, liver failure).	- Difficult to perform - Complication can occur because the peristaltic activity of the small intestine moves the fistula catheter into the distal small intestine

etiology, ECF is classified into iatrogenic (75–85%) and spontaneous (15–25%). Spontaneous fistulas occur in patients with IBD, malignancy, appendicitis, diverticulitis, post-irradiation, tuberculosis and ischaemia.[13] Based on physiology, fistulas are classified according to the volume of fistula output, namely high output (>500 mL/day), moderate (200–500 mL/day) and low output (<200 mL/day).[14]

Prognostic Factor

Patients with a proximal fistula, high output and hypoalbuminaemia (<3g/dL) have more complications and a less likely tendency for spontaneous fistula closure. In contrast, patients without comorbidities who have fistula after surgery and are low output tend to have higher rates of spontaneous closure.[2] There are some factors that favour spontaneous closure, such as small enteric defects (<1 cm) and long fistula tracts (>2 cm). Factors influencing the failure of spontaneous fistula closure include bowel discontinuity, radiation therapy, adjacent abscess, stricture or inflammation of the bowel, distal obstruction and foreign body.5 These factors are presented in Table I.

Nutritional Route in ECF Patients

In the majority of ECF patients, adequate oral intake is not possible. As an alternative to providing an optimal nutrition, nutrients can be provided either by enteral route (via nasogastric or nasojejunal tube, or via gastrostomy or jejunostomy, or fistuloclysis into the distal small bowel) or parenterally (via a peripheral or central vein).[15] The selection of the nutritional route is influenced by several factors, namely patient tolerance, the origin of the fistula, the length of the intestine that functions well to absorb, and the volume of fistula output.[6,16] EN can be chosen if the intestine is functioning properly to perform the absorption (no sign of intra-abdominal sepsis) and the volume can be controlled. On the other hand, if the volume of the fistula is high, parenteral nutrition may be used.[6]

ASPEN recommends the use of an oral diet or EN in patients who have passed the fluid and electrolyte stabilisation phase if the ECF output is low (<500 mL/day) and there is no distal obstruction. In patients with a high-output fistula (>500 mL/day), intestinal obstruction, impaired ECF drainage that interferes with wound and skincare or impaired fluid and electrolyte balance, parenteral nutrition may be required. This aims to meet the needs of nutrition, fluids and electrolytes and support spontaneous closure of the ECF.[5]

Parenteral Nutrition

Nutrition in the resuscitation phase begins with TPN. This step is taken for a short period to avoid complications related to the use of a central route, with a caloric requirement of 30–40 kcal/kg, 1.5–2 g of protein per kg, 30–40 mL of water per kg. During nutrition administration, it is necessary to monitor blood glucose levels tightly to prevent hyperglycaemia.[6] The ratio of calories between carbohydrates, fats and proteins in TPN should be adjusted to the patient's medical history, such as a history of diabetes mellitus or lung disease. Patients with lung disease required to adjust macronutrient composition by increasing the percentage of fat and decreasing the percentage of dextrose to reduce the production of carbon dioxide by dextrose oxidation.[6]

After fluid and electrolyte resuscitation and drainage of percutaneous infection or surgery, patients with high-output fistula (>500 mL/day) are initiated with parenteral nutrition. Other indications for parenteral nutrition include intestinal obstruction or ECF drainage that would interfere the wound and skincare or disturb fluid and electrolyte balance.[5] The concept of 'bowel rest' in TPN based on the observation that providing TPN especially in high-output fistulas will reduce gastrointestinal secretions by 30–50% thereby aiding closure of the fistula, reducing the incidence of dehydration and electrolyte imbalances.[2,13,17]

Providing TPN not only reverses the catabolic state of the patient but also allows the fistula to close spontaneously. If the fistula does not close spontaneously, the patient can undergo surgery without infection and is likely to have a good outcome.[4] Parenteral nutrition is the only option in high output or bowel failure due to diffuse disease.[13] Parenteral nutrition can be used independently or in conjuction with enteral feeding to meet the nutritional requirement of the patient and to allow minimal enteric flow through fistula.[18] MacFadyen et al (1973) reported that TPN decreased the mortality rate to 6.45%, and among 70% of subjects had spontaneous fistula closure.[6] Nowadays, most centers use a combination of TPN and enteral feeding. Study by Li et al that analyse therapeutic results among 1,168 subjects with ECF showed the combination of TPN and enteral feeding had a better outcome. Only 13.6% of patients received only TPN.[11]

Patients commonly receive parenteral nutrition formulas containing intravenous lipid emulsion, representing a major source calories and essential fatty acids.[1,15] The first commercially intravenous lipid emulsion was soybean-oil based, containing high of essential and long-chain polyunsaturated fatty acids (PUFA). Its product have high content of omega-6 PUFA, which has pro-inflammatory effect.[15] Long-term use of soybean-oil based has been associated with the development of parenteral nutrition-related liver disease.[19] As an alternative, it has been developed partial replacement of soybean oil with other lipid emulsion such as medium-chain triglycerides (MCT), olive oil, and fish oil. Both MCT and olive oil-rich emulsions are less prone to lipid peroxidation than PUFA, while fish oil contains omega-3 PUFAs that have immunomodulatory and anti-inflammatory effect.[15] Patients who receive little or no EN need to receive micronutrients such as selenium and zinc via parenteral nutrition.[19]

TPN causes several other side effects, such as catheter-related bloodstream infection (BSI), hyperglycaemia, central venous thrombosis and refeeding syndrome.[4] Marra et al reported that 80.9% of patients who received long-term TPN developed BSI and 78.9% of patients had more than one episode of BSI.[20] Refeeding syndrome could occur when TPN is administered rapidly and characterised by metabolic and electrolyte abnormalities induced by rapid repletion of elements that the body has adapted to be scarce.[21] Parenteral nutrition is contraindicated in cases of liver dysfunction or failure, difficulty in vascular access or infection in the vascular access device.[13]

Enteral Nutrition

Enteral nutrition (EN) has been identified as an independent factor associated with fistula closure.[4] Although initial bowel rest may be useful for early control and minimisation output of the fistula, if the patient is stabilised and sepsis is under control, EN is recommended to be initiated immediately.[4,21] EN has a number of benefits including lowering infection incidence, lowering costs and improving immune function compared to parenteral nutrition.[2] Achieving a caloric requirement of at least 20% via the enteral route can help to maintain intestinal flora, mucosal barrier integrity, hormonal signaling and reduce bacterial translocation.[2,13] To achieve moderate success using EN, ECF patients should have at least 4 feet (1.2 meters) of healthy bowel from the ligament of Treitz to the external fistula opening.[13] However, in multiple organ dysfunction syndrome, gut function may be compromised and EN is not always tolerated.[1] If nutritional requirements cannot be achieved via enteral or if the fistula output is high, then parenteral nutrition is given.[6]

EN is contraindicated in conditions such as short bowel (small bowel length less than 75 cm), bowel discontinuity, ileus, perforation, inaccessible enteral access, intolerance to enteral feeding and high fistula output.[6,15] When gastrointestinal blood flow is compromised during haemodynamic instability phases, EN also will be contraindicated.[15] Complications associated with EN include aspiration, nasogastric tube misplacement, diarrhoea, nausea, vomiting and obstruction (ileus).[1]

Total calorie requirement can be met on the first day by enteral feeding. However, in some cases, enteral feeding takes 5–10 days to meet the total daily requirement. To provide optimal nutritional support, a combination of EN and parenteral nutrition is required. This combination may also be given when access to EN is available but is not well tolerated. Therefore, 20% of the total calories required are fulfilled by enteral and 80% by TPN. This combination can protect mucosal integrity as well as maintain immune and hormonal function.[6]

In proximal duodenal fistulas, a percutaneous jejunostomy tube (PEJ) can be used, while in distal ileal or colonic fistula, patients may be able to obtain nutrition via mouth or gastric tube.[7] In the acute phase, continuous EN via nasogastric, gastrostomy or jejunostomy tube may be better tolerated than bolus feeds, although there are benefits in bolus feeds after the patients have stabilised.[19] Feeding tube volumes and concentrations are usually low at the start of the administration, then increased gradually to achieve a tolerable target.6 EN can be started at a rate of 20 mL/hour in the first 24–48 hours then gradually increased based on the patient's ability to tolerate feeding. If tolerable, the maximum rate of EN is 120 mL/hour per day.[4]

Administration of EN in ECF patients has shown good results. A cohort study by Levy et al (1989) of 335 ECF patients with high output fistula reported that, though many patients received TPN as initial stabilisation, 85% of patients were maintained exclusively with EN. 38% of patients had spontaneous fistula closure, and the mortality rate was only 19% in 234 patients who were managed conservatively.[10] A study conducted by Li et al for 30 years on 1168 patients showed that 86.4% of patients receiving EN found it effective. EN can even be used successfully in patients with high-output fistulas when combined with elemental formulas, anti-motility drugs and fibre-bulking agents.11 Yuan et al in their 10-year retrospective studied the benefit of early EN on the fistula outcome. They reported that patients who received early EN within 14 days of hospital admission had earlier fistula closure and fewer complications compared to patients who received EN more than 14 days after hospital admission.[22]

The polymeric formula is the most frequently used formula for patients requiring EN support. This formula is designed to resemble the general diet by providing carbohydrates, proteins and fats in a non-hydrolysed form. The source of carbohydrates in this formula comes from maltodextrin and solid corn syrup. The protein source comes from protein isolate, sodium and calcium caseinate while the fat source comes from canola, soybean or safflower oil. The use of this polymeric formula requires a normal digestive function.[23]

In patients who have malabsorption disorders and/or have difficulty digesting and absorbing standard polymeric formulas, elemental and semi-elemental formulas are used more often. The composition of hydrolysed macronutrients in these formulas is useful for increasing absorption. The carbohydrate source comes from hydrolysed cornstarch, maltodextrin or fructose. Sources of protein are amino acids and dipeptides or tripeptides (hydrolysed casein, whey or soy protein isolate) and fat sources are fatty acid esters or MCTs.[23]

The majority of ECF patients can typically receive adequate nutrition by administering standard polymeric enteral formulas. However, elemental or semi-elemental formulas should be available in patients with a very short bowel or patients who cannot tolerate polymeric formulas or if polymeric feeds cause diarrhea. In addition, in high-output fistula, the elemental formulas should be considered as they have been shown to be related with an 80% reduction in fistula effluent.[24]

Based on the location of the fistula, the elemental formula can be applied to a distal fistula that provides pre-digested nutrients (glucose, amino acid, MCTs).[25] This will result in decreased output fistula, but it should be noted that drainage around the fistula should be in good condition.[4,25] Otherwise, in very proximal ECF, EN can be administered distally to the fistula using the remaining bowel. If all pancreatic secretions exit through the fistula, elemental formulas are required unless the fistula output itself is reintroduced distally. This approach will minimise the loss of electrolyte, calorie and bile salt/cholesterol even though it is impractical.[25] The enteral formula is generally initiated at a rate of 30–50 mL/hr, increased over 24–48 hours as gastric aspiration decreases and tolerance increases until the target is reached.[25]

Hafejee et al conducted a prospective study by providing nutritional therapy to 63 patients with high-output fistula. In this study, the nutritional regimen was divided into three categories, namely TPN, a combination of TPN and EN, and EN only. The formula used in EN is an elemental low-residue formula. The results of this study suggested that a low-residue elemental diet is beneficial in ECF without the risk of sepsis and other complications associated with TPN.[26] Enteral immuno-nutrition supplementation such as arginine, omega-3 fatty acids and nucleotides in critically ill patients and infants has been shown to reduce infection and length of stay but not mortality.[1]

Oral Nutrition

Oral feeding is started when the patient can tolerate fluids and solid food. The selection of a diet that is high in calories, high in sodium, low in fibre and high in residue is explained to patients.[6,9] Regular meals as well as oral nutritional supplements should be considered.[15] In some cases, even if the patient has normal intestinal absorption, the administration of oral feedings especially with solid foods may increase fistula output. If the fistula output is increased, then providing food orally is not beneficial.6 Datta et al reported that oral nutrition could be made in high output fistula with the following modification: (1) limit intake of low sodium fluids to 500 mL/day, (2) provide oral solution with high sodium (90–120 mmo/L sodium content), (3) small volume fluid intake with solid foods and (4) administration of protein pump inhibitor, octreotide and anti-motility drugs.[27]

Fistuloclysis

Fistuloclysis (distal feeding) is a method that allows the administration of nutritional formula into the normal intestine distal to the ECF.15 Nutrition can be given as the formulas, fluid, or chyme (effluent refed distally from a proximal fistula).[28] Fistuloclysis is indicated when the fistula is located in the small intestine and is not distal enough to allow adequate enteral absorption or in patients where TPN is contraindicated.[6] Before initiating fistuloclysis, anatomy of the bowel and fistula must be established to ensure that there are no distal enterotomies or obstruction. This technique has been for centuries and even though it is difficult, it is considered efficient, efficacious and successful.[28] ASPEN recommends the use of fistuloclysis in patients with intact intestinal absorption ability distal to the infusion site and when the ECF is not expected to close spontaneously.[5]

Fistuloclysis has been demonstrated in some trials to preserve nutritional status, water and electrolyte balance, which can reduce and replace parenteral nutrition requirements. As cited from Teubner et al, fistuloclysis can provide effective nutritional support by successfully replacing TPN in 11 of 12 ECF patients and showed no complication associated with fistula.[29] Coetzee et al reported that about half of patients with enteric fistula by fistuloclysis is feasible and can eliminate the need for parenteral nutrition.[30]

Fistuloclysis is helpful in patients with complications associated with TPN including infection, venous access problems or liver failure. In high-output ECF with distal mucocutaneous limb, fistuloclysis may be an adjunct to standard EN.[2] Administration of nutrition begins with a polymeric formula, but if the patient is intolerable, it can be changed to an oligomeric formula (semi-elemental). Polymeric nutrition was started at a rate of 30 mL/day and increased by 20 mL/hour daily until the target was reached. If EN reaches a rate of 90 mL/hour then parenteral nutrition can be discontinued.[5] Complications such as obstruction can occur as peristaltic activity of the small intestine moves the fistula catheter into the distal small intestine.[2]

Monitoring and Evaluation

During nutritional therapy, it is necessary to monitor and evaluate the patient. Assessment of nutrition tolerance and the ability to provide targeted nutrition should be done routinely.[5] Assessment of nutrition intake is very important in ECF patients by calculating calories and protein requirements, assessing feeding tolerance, modifying feeding methods, adjusting needs with changing clinical conditions and observing complications during nutritional therapy.6 In intensive care patients, investigations and procedures may cause interruption in feeding, especially in the case of EN, resulting in a clinically relevant difference between prescribed and delivered nutrients.[15]

Fluid status in ECF patients should be assessed daily, and all sources of intake and output should be monitored.[13] To adjust the initial target caloric intake and follow the patient's progress, laboratory tests such as albumin, prealbumin, transferrin and CRP in stable patients are required at least weekly during hospitalisation.[13] Transferrin levels greater than 140 are associated with an increased rate of spontaneous fistula closure and reduced mortality.[2]

Hypertriglyceridaemia is often found in ECF patients. Therefore, lipid profile examination should be done especially in patients who received parenteral nutrition. A study by Visschers et al showed that high triglyceride levels in ECF patient were associated with sepsis, small bowel fistula with high output, use of the parenteral route and underlying disease with inflammation as the etiology.[31]

Serum electrolytes, glucose, urea nitrogen, creatinine, calcium, magnesium and zinc levels are taken during the first week to resolve the deficiency quickly and to maintain metabolism.[32] Nitrogen balance calculations with correction for enteric loss should be performed to ensure and maintain a positive nitrogen balance. A positive nitrogen balance indicates a negative transient anabolic state, inadequate caloric intake, unresolved sepsis and excessive gastrointestinal fluid loss. The examination is carried out with urine levels for 24 hours to measure urea nitrogen levels. However, it should be noted that these nitrogen balance calculations are significantly meaningful in patients who have recovered from sepsis.[13] If the nitrogen balance result is negative, nutritional therapy needs to be modified. Monitoring the fistula is also required to see if there is a possibility of spontaneous closure of the fistulas. Generally, 90% of fistulas are resolved without surgery within 5 weeks with medical management.[33] If medical management does not result in spontaneous fistula closure within 4–6 weeks, then surgical treatment may be considered.[4,33]

CONCLUSIONS

To prevent medical problems, especially malnutrition, in ECF patients, nutritional route selection should be considered based on the anatomy and physiology of fistula. Nutrients can be provided either by enteral route (via nasogastric or nasojejunal tube, or via gastrostomy or jejunostomy, or through fistuloclysis into the distal small bowel) or parenterally (via a peripheral or central vein). The selection of the nutritional route is influenced by patient tolerance, the origin of the fistula, the length of the healthy intestine to absorb the nutrients and the volume of fistula output.

EN is a preferable route compared to parenteral nutrition unless there is a clear contraindication. It enhances the functional and structural integrity of the gastrointestinal tract, prevents bacterial invasion into intestinal epithelial cells, stimulates the secretion of immunoglobulin A and supports the mass of gut-associated lymphoid tissue (GALT).[4] However, EN is contraindicated in short bowel (small bowel length less than 75 cm), bowel discontinuity, ileus, perforation, inaccessible enteral access, intolerance to enteral feeding, high fistula output and during hemodynamic instability phases. High-output fistula is contraindicated because EN may increase gastrointestinal secretion and increase fistula output, which will delay the fistula's closure. If enteral feeding is available but cannot be well tolerated, or unable to meet the nutritional requirement, a combination of EN and parenteral nutrition is required. This combination can protect mucosal integrity, maintain immune and hormonal function, increase the rate of spontaneous fistula closure and decrease mortality rate. To lower the risk of catheter-related infection while utilising parenteral nutrition, the infusion line must be carefully managed and treated.

Monitoring and evaluation, including assessment of food intake and EN tolerance, are necessary during nutritional therapy. Furthermore, laboratory tests such as albumin, prealbumin, transferrin, CRP, serum electrolytes, glucose, urea nitrogen and creatinin are required to adjust the initial target caloric intake and follow the patient's progress. Monitoring the fistula is also required to see if there is a possibility of spontaneous closure of the fistulas.

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