Review Article

Nutritional Management in Enterocutaneous Fistula. What is the evidence?

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Abstract

The management of Enterocutaneous fistula (ECF) is challenging. It remains associated with morbidity and mortality, despite advancements in medical and surgical therapies. Early nutritional support using parenteral, enteral or fystuloclysis routs is essential to reverse catabolism and replace nutrients, fluid and electrolyte losses. This study aims to review the current literature on the management of ECF. Fistulae classifications have an impact on the calories and protein requirements. Early nutritional support with parenteral, enteral nutrition or fistuloclysis played a significant role in the management outcome. Published literature on the nutritional management of ECF is mostly retrospective and lacks experimental design. Prospective studies do not investigate nutritional assessment or management experimentally. Individualising the nutritional management protocol was recommended due to the absence of management guidelines for ECF patients.

Keywords: *enterocutaneous fistula, nutritional support, parenteral feeding, enteral feeding*

Introduction

Enterocutaneous fistula definition and causes

An Enterocutaneous fistula (ECF) is an abnormal communication between stomach, small or large bowel, and the skin allowing the gastrointestinal contents to flow onto the skin (1–3). Literature has shown that ECF occurs as a result of a set of factors: surgical misadventure is the most common cause (4,5). other factors include malignancy, inflammatory bowel disease, post radiation therapy for malignancy (5,6), distal obstruction (5); iatrogenic or spontaneous bowel injury, complicated intra abdominal infections such as tuberculosis, amoebiasis, and typhoid (2,7), or diverticular disease (8).

Enterocutaneous fistula incidence

The true incidence of ECF has not been well known (5).The iatrogenic surgical cause were influenced by surgeon's experience and skills; patient's condition, like nutritional and immunological status or factors related to the type of surgery itself and the underlying pathology (2). In 2009 Teixeira reported an incidence of 1.5% of ECF developed after laparotomy (9). A few years before, Tsuei et al. (2004) found that the incidence of fistula as a complication of laparotomy procedures (done due to various reasons as gastrointestinal sepsis, pancreatitis or trauma) for 71 patients was 16.9% (10). Incidence of spontaneous fistula formation due to inflammatory bowel disease also has not been sufficiently studied (11). Tang et al. (2006) found that fistulising among 1595 Crohn's disease (CD) patients was 22.1% (12). After iatrogenic causes, spontaneous fistula has been reported 23%–48% as a result of disease conditions like CD and diverticulitis disease (11).

ECF complications

ECF have been associated with considerable morbidity and mortality (2,3–16). The common complications of ECF were sepsis, malnutrition, electrolyte and fluid abnormalities (2,13–15). Intestinal failure is less common, but a devastating complication with significant morbidity and mortality (14). These complications were the predominant causes of death in the ECF patients (16). The mortality rates in most institutions have significantly decreased because of advanced critical care management, nutritional, and metabolic support, antimicrobial therapy, improvement in wound care, and advanced intraoperative techniques (6,13).

Nutritional implications in ECF

Nutrition played a major role in ECF fistula management and decreases the morbidity and the mortality (2,17–21). Despite this impact, malnutrition remains a major clinical problem of ECF patients (6). This was especially seen in high output fistula or those who had septic complications (22). Aggressive calories and protein replacement were required to lessen the deteriorated effect of ECF (6,17).

Methods

In this review a summary of the current evidence of the nutritional management in ECF patients in light of nutritional status assessment, calories and protein requirement and the routes of feeding were reviewed. This summary was done by conducting a comprehensive search in the literature to find the published studies related to nutritional management of ECF using the following key words: enterocutaneous fistula with nutrition management, nutrition requirement, and nutrition status assessment. The main objectives is to examine the current evidence and report study design and methodology for the reviewed publications, and then determine what was missing in the nutrition management in terms of nutritional status assessment, the rout, and duration of feeding.

Nutritional management of ECF

In ECF management a multidisciplinary team including physicians, dietitians, nurses, and pharmacists, all participated in designing and performing the management plan (1). The management plan was affected by anatomical, physiological, and etiological status of the fistula (2,18,20). It involved diagnosis and defined the anatomical classification of the fistula, drainage control, nutritional assessment, early nutrition support by using the appropriate feeding access, and decreasing the fistula output which could be achieved by keeping the patient nothing by mouth (NPO) and using pharmacological agents such as an H2 receptor antagonist, proton pump inhibitors, somatostatin, and octroide (20). The nutritional support plan was individualised according to patient condition. It provided adequate nutrients and reversal of the catabolic state (17,20). It must have been started with nutritional status assessment as any nutritional management in hospitalised patients (23).

Nutritional status assessment for ECF patients

Nutritional status assessment was very important in ECF patients because the patients were at higher risk of malnutrition. Full nutritional status assessment should have involved assessment of nutritional intake, anthropometric and body composition, signs and symptoms of nutritional deficiency, biochemical tests, and clinical assessment (23). Studies designed to assess the relation between nutritional status and clinical outcome in ECF patients were available. However, the nutritional assessment was brief and the nutritional parameters were the same of those commonly and routinely used in hospitals such as body mass index, albumin, and prealbumin. No published study was found with comprehensive nutritional status assessment using parameters specific for ECF patients such as the length of functioning bowel, citrollin and nitrogen balance.

Nutritional status parameters in ECF patients

The nutritional status assessment in ECF patients was similar to any hospitalised patients, but should include assessment of functional bowel and losses through fistula effluent (24). The anthropometric measurements for weight, height, body mass index, mid upper arm circumferences, calf circumferences, and skin fold all could be used for nutritional status assessment in ECF patients (24).

Bio impedance (BIA), a method of body composition assessment, was not validated in hospitalised patients, and it had not been sufficiently studied in all clinical situations, including ECF (25). It is important to highlight that at the time of this review, no study to validate the use of BIA in ECF patients was found.

Albumin, transferrin, prealbumin and retinol-binding protein have been recommended as indicators or markers of nutrition status (26). The human serum albumin was the most abundant plasma protein, representing about 50% of the total protein content (3.5–5 g/l). Osmolarity and oncotic pressure mainly regulated the production of albumin of the interstitial fluid in the liver extravascular space. It was also induced by hormonal factors (insulin, cortisol, and growth hormone) and inhibited by acute phase cytokines, such as interleukin (IL)-6 and tumour necrosis factor (TNF)-α by liver cells that release it directly into the blood stream without storage. Hypo albuminemia was a common problem among persons with acute and chronic medical conditions and malnutrition (27). Serum albumin level could be affected by capillary permeability, drugs, impaired liver function, inflammation, and other factors. It was of virtually no value in assessment or monitoring nutritional status (23); however, it was still an important prognostic indicator. Among hospitalised patients, lower serum albumin levels correlate with an increased risk of morbidity and mortality (27). The relatively long half life of albumin (14–20 days) has been considered as a marker of chronic nutritional status (26).

In ECF patients, serum albumin has been found to be of prognostic value in fistula closure; however, albumin level may be falsely high in ECF patients due to decreased plasma volume especially in high output fistula, as a result albumin could not be a significant predictor of fistula closure (28). Prealbumin, known as transthyretin, was a visceral protein and negative acute phase reactant (26). Its level was affected by same factors that affect the albumin level, but it was preferable over the albumin due to its relatively short half life of 2 days. Therefore, it was more sensitive to detecting the changes in protein energy status than albumin. Prealbumin concentration could be a sign of the recent dietary intake rather than overall nutritional status. The importance of prealbumin was that as it rapidly falls as a result of inflammatory response, the synthetic rate of prealbumin was decreased to give priority to the acute phase proteins such as C-reactive protein (CRP), fibrinogen to be synthesised (23). In ECF, prealbumin could predict inflammation and catabolism status. Prealbumin and CRP can provide early indication of mortality rates among ECF patients (28).

Transferrin has been identified as a marker of nutritional status with a half-life of 8–10 days. Iron deficiency, dehydration, pregnancy, medications, and chronic medical conditions increase transferring. A decreased is seen in anaemia, folate deficiency, over hydration and acute catabolic states. Pre-albumin and transferrin can be useful predictors to predict spontaneous fistula closure (29).

White blood cell count was an important index to the outcome of hospitalised patients as leukopenia was accompanied by high mortality, morbidity, and treatment costs. However, leukopenia in ECF has been associated with several conditions such as the presence of bacterial infection and hypo albuminemia (30). CRP is a positive acute phase reactant which is elevated in both acute and chronic inflammatory conditions, Its half-life is 19 hours (26). The use of CRP alone is not specific in ECF (28), but it can be used in conjunction with pre-albumin. The CRP:pre-albumin ratio has been validated to prognosticate in patients with multiple organ dysfunction (31).

Nitrogen balance (NB) has a clinical acceptable significance as a measure of anabolic status. It was important in ECF patients because it could indicate the need to modify the nutritional plan if its value was negative. In case of ECF, there was a need to include correction factors in the nitrogen balance calculation since there was a protein loss through the fistula output. An additional 1 g of nitrogen loss for each 500 ml of fistula output should be added to the nitrogen balance equation (32). The modified (NB) equation in ECF patients is as follows:

NB = [Protein intake (g) ÷ 6.25] – Urinary Urea Nitrogen (UUN) + 4 g + (2 g × liters of abdominal fluid loss) + (2 g × liters of fistula effluent) (21).

Citrollin, a non-essential amino acid produced almost by the enterocytes, had high sensitivity and specificity for prediction of permanent intestinal failure when the serum level was below (20 μmol/l) (21). Validity of citrollin, a blood marker that could assess the functional absorptive bowel length, was proven in more than one study (33,34). In ECF management, measurement of bowel length could be done by tomography or magnetic resonance enterography and fistulography. But serum citrollin measurement could be used to provide an estimation of functional residual bowel length (21).

Clinical assessment

For the clinical assessment of nutritional status, it could be conducted by using validated scales; for instance, the Subjective Global Assessment (SGA). It was simple, and widely used with other methods to assess the risk of malnutrition and to identify patients who required nutritional support. It has been used in a variety of conditions including surgery, cancer, and critically ill patients (35). SGA assessed the nutritional status based on features of the history and physical examination (36). Assessment of diet intake was very essential in ECF patients. It started with calculating calories and protein requirement, assessing tolerance of feeding regimen, modifying feeding methods, adjusting requirements with the changes in the clinical conditions, and finally observing feeding complications (17).

Nutritional requirement of ECF patients

The Harris-Benedict equation for basal energy expenditure was often used to determine calories requirement. Additional calories and protein were required due to increases in metabolic demands caused by protein loss in the effluent and sepsis (21). More advanced methods could also be used to determine the calories requirement by using indirect calorimetry in certain complicated cases. When using any of the methods mentioned above most of the recent references highlighted the importance of the individual calculation of the requirement depending on the patient's condition, route of feeding, and feeding tolerance (21). Before that, Chapmanet al. (1964) found that patients who were given 1500–2000 kcal/day had a mortality rate of 16%, and those who were given less than 1000 kcal/day had a mortality rate of 58%. Moreover, they reported that 89% of fistula closure achieved among ECF patients with optimal nutrition support (1500–2000), and only 37% of those who were underfed (1000 kcal/day) (37). Dundrick et al. (1969) highlighted that the spontaneous closure of fistula was associated with restored nutritional status manifested by normal body weight, normal serum albumin, and total protein levels (38). Sheldon et al. (1997) found a decrease in the mortality rate, from 45% to 14%, in ECF patients provided with 3000 kcal/day (39). It was important to note that over feeding a patient with an ECF might result in worsening hyperglycemia and hepatic stenosis and increase risk of sepsis (40). Later Dundrick et al. (1999) recommended a starting point with 20–30 kcal/kg/day of non-protein calories, and 1.5–2.5 g/kg/day of protein. In high output fistula, 1.5–2 times of the usual calories were needed and vitamins and the trace elements recommended must be five to ten times the daily allowance (41).

Routes of feeding in ECF patients

The number of experimental studies that have investigated the optimal routes of feeding in ECF patients was scarce (2). Several factors influenced the selection of rout of feeding, including origin of fistula, length of healthy bowel available for absorption, and fistula output. If there was sufficient functioning bowel for adequate nutrients absorption and no intra abdominal sepsis and manageable fistula output, the enteral feeding would have been the optimum choice. If the nutritional requirement could not have been achieved enterally or the fistula output was high, the parenteral feeding should have been used (42).

Total parenteral nutrition (TPN)

The nutrition management usually began with TPN in the resuscitation phase. A short period of TPN feeding was preferable to avoid the disadvantages and complications related to it, especially when administered by central line (21). 30–40 ml/kg water, 30–40 kcal/kg calories and 1.5–2 g/kg protein required each day were achieved only by central line. Tight control of blood glucose level was necessary to avoid hyperglycemia (6). Carbohydrate, fat, and protein calories ratio in TPN could be modified according to patient's medical history, i.e. presence of co-morbidities such as diabetes mellitus. Pulmonary disease required increase fat and decreased dextrose percentages in order to reduce the carbon dioxide production by dextrose oxidation. The electrolytes requirements (sodium, potassium, chloride, calcium, phosphorus, manganese) were provided in crystalloid nutrient form, and all trace elements vitamins (fat, water soluble) were included in the TPN bag. Adjustment of the acetate, bicarbonate, phosphate, and chloride was essential to maintain the acid-base balance (21). Duplication of the dosage of vitamins and trace elements was recommended in high output fistula (41).

TPN was used for the first time in ECF patients (41), in a large trial that included 300 adult patients with variety of diseases that prevent feeding via the gut. They provided patients intravenously different amounts of calories for different periods of feeding. They reported an increase in body weight, positive nitrogen balance, persistent and spontaneous fistula closures, and noticeable decreases in the mortality rate (38). These findings were supported by MacFadyen et al. (1973), who presented exciting results; decreasing the mortality rate to 6.45%, and spontaneous fistula closure to 70% among the study subjects (43). These preferable results were due to the ability of TPN to decrease gastrointestinal secretions by 30–50%, which made surgeons believe that TPN was the key in managing proximal and high output fistulae (21).In (2003) Li et al. published their 30 years of experience in treating 1168 ECF patients in China. They reported the preferable outcome was by using a combination of TPN and enteral feeding in patients with ECF (44). These findings were supported by other findings of different researches in different parts of the world (21).

Enteral feeding

In clinical practices, enteral nutrition was highly recommended unless it is contraindicated, due to its relatively lower cost, greater availability and fewer complications. Early enteral nutrition in ECF fistula has been associated with earlier fistula closure (6), lower pneumonia rate and lower rate of fistula recurrence (45). The contraindications of enteral feeding include intestinal discontinuity, ileus (6), short bowel length (shorter than required (75 cm of small bowel for successful enteral feeding), not achievable enteral access, or not tolerated enteral feeding (46). The increase in fistula output was an ECF additional contraindication for enteral feedings (21,47). The use of enteral nutrition in high output fistula was found useless, and didn't provide any benefit to the patients, and had compounded metabolic and management complications (21).

In enteral feeding, the calorie requirement could be achieved on the first day. In some cases it needed 5–10 days to achieve the total requirement. In such situations TPN could be kept until the patient was able to achieve the requirement. A combination of the two feeding techniques was necessary for optimal nutritional support (48). This combination could also be applied when enteral feeding was accessible but not well tolerated, keeping 20% of the required calories achieved by enteral and 80% by TPN. It would be enough to protect the mucosal integrity and maintain immune and hormone function,(18). Highly absorbable formulae with low residue nutrients could be administered with reasonable results. The volume and the concentration of tube feeding usually was low at the beginning of feeding, and then it was increased gradually to achieve the full strength as tolerated (6).

Oral feeding

Oral feeding starts when the patient would be able to tolerate fluids and solid food. The recommendation was that patients be educated as to how to select high calories, high salt, low fiber, and low residual diet. In some cases, despite the patients having normal gut absorption, oral feeding might increase the fistula output, especially if the food was solid (47). This, in turn, would make the oral feeding of no value as a means of nutritional management (1).

Fistuloclysis

Fistuloclysis has been defined as "a technique of using fistula as the primary enteral portal for access and infusion of food stuff, formula, or gastrointestinal secretion" (21). It has been considered an efficient and successful method of feeding in fistula patients (42) with proven cost effectiveness (49). Fistuloclysis has not been a popular practice in fistula management due to technical and anesthetic issues. It has been indicated when the fistula location was in the small bowel and not distal enough to allow adequate enteral absorption (42), or when TPN was not available or contraindicated (21). Fistuloclysis could be a suitable choice if there was enough unobstructed bowel distal to the fistula to enable adequate nutrient absorption. Teubner et al. (2004) demonstrated that fistuloclysis could successfully replace TPN for 11 out of 12 patients using polymeric formula without re-feeding the secretions (50). This is supported by a recent study, conducted by Coetzee et al. (2014), they compared prospectively the effectives of this method compared with TPN, they investigated the effect of chyme refeeding on the complications and mortality among distal ECF patients, the safety of re-feeding the secretion was proved (51). It remained a viable option to be considered in order to increase the tolerance of tube feeding and maintain fluid and electrolyte homeostasis (21). The review reported that fistulae will be epithelialised when using fistuloclysis, which would decrease the chance of spontaneous closure of the fistula (21,42). The technique of fistuloclysis needs specialised and experienced enterostomal care to stabilise the feeding tube in the fistula; otherwise the effluents would be leaked and lead to skin corrosion, and the tube could be pulled into the bowel by the peristalsis movement of the bowel (52).

Nutritional management of ECF, summary of the published studies

Table 1 showed a brief summary of studies that have been done on the nutritional management in ECF patients. All the studies were reviewed in terms of study design, subjects' characteristics and nutritional management.

Table 1 revealed that ECF management was first reported at the beginning of the previous century, and has continued until today, with much concern about describing the clinical and nutritional management scenarios. In their study, Lilienthal (1901) and Cackovic (1903) reported a management plan for an ECF patient at the beginning of the 19th century, and 100%

Table 1: Nutritional management in Enterocutaneous Fistula – Summary of the original studies

Author/ year	Country	Study design	Number of subjects	Nutritional management
Coetzee et al. (2014)	South Africa	Prospective study	20	Fistuloclysis vs TPN
Badrasawi et al. (2014)	Malaysia	Retrospective study	22 patients	TPN, enteral, oral
Kumar et al. (2011)	India	Prospective study	41 patients	Not reported
Harriman et al. (2011)	Canada	Retrospective observation study (1994– 2009)	89 adult patients	Not reported
Yuan et al. (2011)	China	Retrospective observation study (2001–2009)	87 patients with ECF	EN or success entericus reinfusion (SER)
Taggarshe et al. (2010)	US	Retrospective observation study (1997–2007)	83 ECF	TPN and EN
Singh et al. (2008)	India	Observation study (2005–2008)	92 subjects with ECF 14 years and above	Not mentioned
Ahmad & Fawzy (2007)	Iraq	Prospective observation	70	TPN and EN
Cawish et al. (2007)	Jamaica	Case study	High output ECF case	Fistuloclysis
Chaudhry (2004)	US	Observation study (1995–2001)	17 subjects with small intestine – ECF	Plan of nutritional support with priority to utilise the gut when possible
Hollington (2004)	Austria	Retrospective analysis study (1992–2002)	227 ECF	TP in high output ECF Oral when output decreased
Teubner et al. (2004)	UK	Observation study	12 ECF	TPN, EN through the fistula
Li et al (2003)	China	Retrospective observation study (1971–2000)	1168 ECF	TPN and EN with TPN
Amodeo et al. (2002)	Italy	Prospective observation study	14	TPN and EN
Kuvshinoff et al. (1993)	USA	Retrospective observation study (1982–1991)	79 ECF anatomical favorable features	Not reported
Dardai et al. (1991)	Hungary	Retrospective observation study	64 ECF	TPN and/or EN
Daradi (1991)	Hungary	Prospective observation (1971–1988)	45 (postoperative small bowel ECF)	TPN, EN
Doglietto et al. (1989)	Italy	Retrospective observation study	38	TPN and EN
Levy et al (1989)	France	Retrospective observation study	135 with high output ECF	EN or fistuloclysis
Zera (1983)	USA	Observation retrospective study	50 ECF patients	TPN
Haffejee et al. (1980)	South Africa	Intervention study	63 high output ECF	TPN and EN using elemental low residue formula
Soeters et al. (1979)	USA	Retrospective observation study (1945–1975)	404 patients with ECF	EN and TPN
Howard et al. (1978)	USA	Retrospective observation study (1968– 1977)	186 ECF	TPN and EN

mortality rate was reported in both studies. In 1931, Bohrer and Milici introduced a conservative management for acute cases and surgical management for chronic cases with "maintenance of chemical balance," which had the key to effective management of ECF up until today. In 1964, Chapman et al. determined four main principles in ECF management, i.e. correction of intravascular volume deficit, drainage of abscesses, control of fistula effluent, and protection of the skin (13). In 1969, for the first time Dudrick et al. tried the total parenteral nutrition in various categories of patients, including ECF patients. Weight restoration, malnutrition prevention, nitrogen balance, and spontaneous closure of the fistula were achieved by feeding the patients intravenously (38). A few years later, Reber et al. (1978) assessed the clinical value of using TPN in the management of ECF. Their study reported the nutritional treatment of 186 ECF patients during 8 years, and they divided the study period into two phases. The difference between these two phases was the percentage of implication of TPN for ECF patients. In the first phase, only 30% of the subjects were fed by TPN, while in the second phase, 71% of the subjects were fed by TPN. They reported that the two groups were similar in the mortality rate and the clinical outcome (53). The research methodology showed that both groups were similar in the fistulae anatomical and physiological classifications, but the study only determined the caloric intake by EN or TPN more than once during the treatment period. Nutritional status differences between the two groups was not determined, presence of covariances such as the etiology of the fistula, and other confounding general clinical conditions were not reported or adjusted in the methodology part. Additionally, in the same period, Soeters et al. (1979) published their retrospective observation study to determine the impact of TPN on ECF management using the same methodology in Reber et al. (1978). However, the results were different. They found a decrease in the mortality rate between the time periods due to implication of TPN to the fistula management (40).

Later, in the late eighties, Levy et al. (1989) conducted an observation study, where they compared the outcome of high output small bowel ECF management in conservative, surgical treatment and non-intervention. The results showed better outcomes of the conservative treatment compared to surgical treatment in the mortality rate. Nonetheless, the study had a limitation: they classified the subjects according to the treatment which was chosen according to patients condition, i.e. in the non-intervention group all the patients were admitted in a moribund state and nothing was given to them. Therefore, the mortality rate (100%) among this group was not due to different ways of management. There was a similar limitation for the surgically treated group; all the group subjects were operated on as an emergency. The rest of the patients who were supposed to be in one group were managed in a non-standardised method. The feeding process involved reinfusion of the fistula effluents in some cases and in the others it was only limited to nutritional formula. Having discussed the limitations, the findings of this study were not enough to make a solid conclusion (54).

Haffejee et al. (1980) studied more specific management of high output fistulae in a prospective observation study on 63 patients with high output fistulae. Three nutritional management regimens were used in the study: TPN, TPN mixed with enteral nutrition (EN), and EN. EN was done using an elemental low residue formula. They found that the low residue elemental diet was beneficial in ECF without risks of sepsis and other complications related to TPN (55). Focusing on TPN, Zera (1983) concluded that the management of ECF should include TPN up to four weeks in the conservative period, then followed by the surgical treatment provided that there was no improvement with conservative therapy (56). Doglietto et al. (1989) compared the outcomes in the nutritional management and surgery in ECF treatment utilising retrospective data. The study included 38 patients with different type of fistula. The findings suggested that the treatment of ECF should include early control of infections and appropriate nutritional support. They recommended an earlier surgical approach for patients with large bowel fistulae (57).

A few years later, Dardai et al. (1991) conducted a study to determine the efficacy of parenteral and enteral nutrition in ECF patients, and determine the factors affecting the clinical outcome. The nutrition protocol was administration of enteral and/or parenteral nutrition as adjuvant therapy. They determined the factors that affected the outcomes in ECF patients such as age, nutritional status, etiology, and classification of the fistulae. This study had similar limitations to the previous ones. It was only retrospective observation. The patients were divided into two groups based on the way they were fed and the choice of enteral or TPN was done according to the treatment plan based on the patient's condition. So, the findings of the study were not enough to compare between the enteral and parenteral as a route of feeding to the fistulae patients (58). In the same year, the same authors published the results of a three year prospective observation study, that included 45 ECF patients, by comparing the nutritional complication using TPN and EN. The findings supported the efficacy of TPN and EN on ECF management (58).

Other studies aimed to determine the indicator factors of spontaneous closure of fistulae. For instance, Kuvshinoff et al. (1993) investigated the biochemical data that predicted the spontaneous closure of the fistulae, using retrospective data from 79 patients with favorable anatomical and physiological location of fistulae. The findings indicated that serum transferrin was a predictor for fistula closure; however, the nutritional management data were not recorded (29). Early in 2000s, Li et al. (2003) conducted a study with the largest sample size (1168 subjects, using 30 year-retrospective data) to explore the successful models of management of ECF. The findings showed a significant difference in the clinical outcomes between the time periods (44). With more focus on TPN, Amodeo et al. (2002) investigated the effect of nutritional support on the fistulae outcome in a prospective observation study conducted on 14 patients mainly treated with TPN. They concluded that nutritional support was very useful in the management of patients undergoing surgery in order to reduce the postoperative complications (59).

The effectiveness of fisuloclysis in nutritional management of ECF was studied by Teubner et al 2004, in an observation study. It aimed to determine whether feeding via an intestinal fistula would obviate the need for TPN. They found that fistuloclysis replaced TPN entirely in 11 patients out of the total of 12 patients (50). In dealing with ECF management for 11 years, Hollington et al. (2004) aimed to demonstrate the complex nature of fistulae and the extensive therapy necessary to treat them. The study included 227 subjects observed retrospectively, and the nutritional management was fully described. TPN was given in high output ECF, followed by enteral or oral when the output decreased. However, no details were mentioned regarding the provided calories and protein. The conclusions focused on the treatment outcome as spontaneous closure, mortality rate, and causes of the mortality, while no conclusions or comments on the nutritional management were found (60). Singh et al. (2008) from India determined the factors that can predict the spontaneous closure of ECF by observing 92 adult subjects prospectively. Here, the nutritional status assessment, using some biochemical parameter, was done regarding the relation with spontaneous closure of the fistula. Serum transferrin above 140 mg and serum albumin 3 g/dl were significantly associated with spontaneous fistula closure (24). In 2007, Ahmad & Fawzy conducted a prospective observation study on 70 ECF patients to determine the factors related to successful ECF treatment, including TPN and EN. They found that duodenal fistulae, and to lesser extent ileal fistulae, responded more to conservative treatment (61). In their case study, Cawish et al. (2007) examined the cost effectiveness of fistuloclysis in ECF patients compared to TPN. The findings of this study cannot be extrapolated and generalised because it was done only on one case (49). A recent study conducted by Taggarshe et al. (2010) aimed to compare the outcome of conservative treatment vs. surgical treatment ECF regarding the fistula recurrence rate during a 10 year retrospective review. They found no significant differences in the fistula recurrence rate between conservative and operative treatment. Yuan et al. (2011) studied the benefit of early enteral nutrition on the fistulae outcomes utilising 10 year retrospective study. They divided the nutritional regimen according to the day they initiated the EN feeding. They defined early EN as when the EN started before 14 days from the first day of fistula management. They found that the spontaneous closure was accomplished more rapidly in patients with early EN feeding (62). The latest was conducted by Badrasawi et al. (2014) utilising retrospective design also, but with more focus on the feeding regimen, specialized formula mainly using glutamine as immunomodulator nutrients, however they didn't find any significant effect of using the specialized formula on the clinical outcome, due to same limitation, which is lack of experimental design (63).

Conclusion

To conclude, although all of the references highlighted the importance of nutritional support in ECF patients, detailed nutritional status assessment was not identified. Nutritional status assessment was done mainly using the biochemical assessment, and most of the biochemical data focused on albumin, prealbumin, and CRP. For anthropometric measurement, only weight and body mass index were mentioned in the articles. Muscle and functional assessment were not included in any of the studies. In addition, the majority of the studies did not signal the occurrence or absence of re-feeding syndrome among the ECF. Tracing for this syndrome was very important to detect re-feeding syndrome and differentiate it with the electrolytes disturbances that commonly occur as ECF complications. The literature lacks clinical trials as a study design, which would be used to compare the clinical benefit between different nutritional regimens in terms of calories and protein requirement, onset, duration of feeding, and rout of feeding. It also lacked specialised studies to determine the energy requirement in ECF patients in the light of nutritional status, fistula classification, and patient clinical condition. Moreover, it lacked intervention studies that determined the efficacy of specialised formula such as immune enhanced formula, elemental formula, low residue formula, or additional dietary supplement on the clinical outcome of the management plan.

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