To Our Readers

The current issue of the Update Series “Nutrition in Disease Management” is the 14th. The topic contained in this issue is a very important, yet a relatively neglected one, in the field of Surgical Nutrition – nutrition support in enterocutaneous fistula.

The article, which is an original publication, in addition to underscoring the importance of appropriate nutrition support in the management of this specific clinical situation, also provides an insight into the physiological mechanisms responsible for offsetting nutrient deficiencies and fluid losses in patients with fistulae involving the gastrointestinal tract.

We thank our readers, many of whom are of the opinion that the ‘Pick your Brains’ set of multiple-choice questions with answers and detailed explanations is a welcome addition. The current issue is the second one which contains the ‘Pick your Brains’ section. We do hope these questions stimulate your little grey cells!

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Nutritional Support In Enterocutaneous Fistula

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Enterocutaneous fistulas might develop spontaneously or, more commonly, as a catastrophic postoperative complication of virtually any intra-abdominal surgical procedure. The formation of such a fistula not only threatens life but can have profound impact on the patient’s psyche, emotional health, self-esteem and social relationships. The loss of gastrointestinal contents including digestive juices, water, electrolytes and nutrients through the fistula may precipitate or accentuate dehydration, dyselectrolytemia, acid-base imbalance and malnutrition which in turn might progress to hypovolemia, cardiac dysrhythmia, immune incompetence, sepsis, pulmonary complications, hepatic or renal insufficiency ultimately leading to shock and death1. The predominant causes of death in these patients have been and continue to be malnutrition, electrolyte imbalances and sepsis, especially in patients with high output duodenal or jejunal fistulas which is associated with a mortality rate of about 35 per cent1-3. Recent improvement in management of these patients has resulted from a combination of factors including a better understanding of the optimal timing for surgical intervention, availability of better nutritional support and antibiotics as well as advances in critical care and imaging techniques.
Edmunds et al4 analysed 157 patients with enterocutaneous fistulas and demonstrated the fact that 53 per cent of patients with gastro-duodenal fistulas, 74 percent with jejuno-ileal fistulas and 20 per cent with large bowel fistulas were malnourished and the corresponding mortality rates, with and without definitive therapy, were 62 per cent, 59 per cent and 64 per cent, respectively. The authors concluded that despite antibiotics and modern methods of replacement therapy there was no evidence that the mortality of enterocutaneous fistula had decreased significantly over the previous 20 years. Subsequently, Chapman et al 5 in a study of 56 patients established the role of nutritional support in the management of enterocutaneous fistulas. In this study, one third of patients received optimal nutritional support (>3000 calories/day) as evidenced by positive nitrogen balance and had a mortality rate of 12 per cent and fistula closure rate of 89 per cent. The remaining two thirds of patients received suboptimal nutritional support (<1000 calories/day) and had a mortality rate of 55 per cent and fistula closure rate of 37 per cent. The authors stressed the importance of ensuring optimal nutritional status prior to attempting definitive surgical repair. Malnutrition as defined by loss of >15 per cent of usual body weight and/or hypoalbuminemia of <3.5 gm/dl occurs in a majority of patients (66 per cent-74 per cent) with enterocutaneous fistulas which appears to be related to the site and volume output of fistula and correlates directly with increased morbidity and mortality in this group of patients2,6. Weight loss is due to inadequate food intake, excessive losses of gastrointestinal secretions and increased energy expenditure due to sepsis. Hypoalbuminemia results from decreased nutrient intake, excessive losses of protein in gastrointestinal secretions and muscle proteolysis consequent to sepsis.

In patients with enterocutaneous fistulas, the role of nutritional support in the form of enteral or parenteral nutrition is essentially supportive and prevents further deterioration of malnutrition in an already debilitated patient7. Besides, nutritional support decreases the amount or modifies the composition of gastrointestinal and pancreatic secretions which might have therapeutic implications8-10. An extensive review analysed 404 patients with enterocutaneous fistulas spanning 30 years which included the first period (1945-1960) during the introduction of antibiotics, the second period (1960-1970) which saw rapid improvements in patient monitoring, parasurgical care and respiratory support, improvements of antibiotics and introduction of nutritional support and the third period (1970-1975) which saw the introduction of parenteral hyperalimentation in the management of patients with enterocutaneous fistulas. The principal causes of death in this group of patients were malnutrition, sepsis and electrolyte imbalance. Mortality among patients with enterocutaneous fistulas decreased between the first and second periods from approximately 48 per cent to 15 per cent. However, mortality did not decrease further in the third (hyperalimentation) period although spontaneous closure rate of enterocutaneous fistulas increased, which suggested that the improvement in mortality in these patients was mostly due the introduction or improvement of parasurgical care. The addition of parenteral hyperalimentation might thus improve the spontaneous fistula closure rates without altering the mortality rates6.

Similar observations have been reported in recent studies which have concluded that although the mortality rate for enterocutaneous fistulas has remained stable,
Table I: Assessment of nutritional status

Clinical evaluation
- Nutritional history
- Physical examination
- Anthropometry (body weight, height, skinfold thickness, mid-arm circumference)
- Subjective global assessment (SGA)

Laboratory evaluation
- Complete blood counts
- Serum proteins (albumin, prealbumin)
- Serum transferrin and total iron binding capacity
- Urinary creatinine (24 hour creatinine excretion, creatinine-height index)
- Serum cholesterol and triglycerides
- Serum electrolytes (Sodium, Potassium, Chloride, Bicarbonate, Calcium, Phosphate, Magnesium)

Functional evaluation
- Immune function (Total lymphocyte count, delayed cutaneous hypersensitivity)
- Muscle function (ability to perform work on ergometer, changes of heart rate during maximal exercise, dynamometry/hand grip, respiratory muscle strength, muscle fatigability to electrical stimulation)

Measurement of body composition
- Isotope dilution
- Bioimpedence analysis
- Dual energy X-ray absorptiometry
- Whole body counting and neutron activation
- Computed tomography and magnetic resonance imaging

Discriminant analysis
- Prognostic nutritional index (PNI)

Spontaneous fistula closure rates continue to improve which may be attributed to improved parasurgical care, appropriate nutritional support as well as early and aggressive control of sepsis3,11.
ASSESSMENT OF NUTRITIONAL ST STATUS

Nutritional status of an individual can be assessed by clinical evaluation, biochemical evaluation, functional evaluation, measurement of body composition and discriminant analysis (Table 1). However, each of these methods has methodological and practical limitations. An ideal method of nutritional assessment should be able to predict whether the subject would have increased morbidity and mortality, that is, nutrition associated complications (NAC) in the absence of nutritional support.

Clinical assessment of nutritional status is a dynamic evaluation process which not only provides a picture of current nutritional status but also the future status by identifying the initial nutritional state and the interplay of factors influencing the progression or regression of nutritional abnormalities12. The data used for evaluating nutritional assessment is documented on a nutritional evaluation form at the time of initial interview and thereafter every week. The data serves as baseline nutritional assessment data, allows adequate delivery of nutrients and ensures that the patients are responding to nutritional therapy7. A focussed nutritional history and physical examination suggesting nutritional depletion such as weight loss of 10 per cent, pre-existing illness, weakness, muscle wasting and edema might be helpful in obtaining a subjective assessment of nutritional status13. Anthropometric assessment in the form of skin-fold thickness attempts to estimate body fat reserve while mid-arm muscle circumference estimates muscle mass. A patient with triceps skin-fold thickness <60 per cent of the standard (12.5 mm in men and 16.5 mm in women) would be considered as having abnormalities of fat reserves, while those demonstrating mid-arm muscle circumference <60 per cent of standard (25.5 cm in men and 23 cm in women) are considered as having abnormal somatic or skeletal muscle protein stores14. Clinical assessment of nutritional status should ideally encompass a variety of factors rather than a simple assessment of weight loss and wasting and should be able to identify patients likely to develop nutrition-associated complications. A structured type of clinical assessment which has been validated to predict nutrition associated complications thereby identifying patients likely to benefit from nutritional therapy is called subjective global assessment (SGA) and includes historical and physical parameters of clinical assessment13,15. The historical aspect of SGA focuses on five chief components namely weight change, dietary intake, gastrointestinal symptoms and metabolic demands. The percentage of weight loss in the past two weeks and six months is further categorised as mild <5 per cent, moderate 5-10 per cent and severe >10 per cent. Dietary intake, as determined by a change in intake and the fact that the current diet is nutritionally adequate, is classified as normal or abnormal. The presence of gastrointestinal symptoms like anorexia, nausea, vomiting, diarrhoea and abdominal pain persisting for at least two weeks is taken into consideration. The patient’s functional capacity is categorised as no dysfunction, suboptimally active and bedridden. Finally, metabolic demands/stress of the patient’s underlying disease state is taken into consideration and is classified as no stress, moderate stress (mild infection or limited malignant tumour) or high stress (major trauma, burns, sepsis or severe inflammation).

The physical parameters taken into consideration include loss of subcutaneous fat, muscle wasting, edema, ascitis, mucosal lesions as well as skin/hair changes which in turn are categorised as normal, mild deficit or established deficit. Based on subjective weighting, the findings of history and physical examination are used to categorise patients as being well-nourished (category A), having moderate or suspected malnutrition (category B) or having severe malnutrition (category C). In clinical studies, subjective global assessment (SGA) was found to give reproducible results with more than 80 per cent inter-observer variability13,15 and preoperative SGA was a better predictor of post-operative infectious complications than serum albumin, serum transferrin, delayed cutaneous hypersensitivity, anthropometry, creatinine-height index and prognostic nutritional index16.
Determination of serum albumin and prealbumin levels gives an indirect estimate of visceral protein stores. The most commonly used marker of visceral protein stores is albumin. Since the plasma half life of albumin is 20 days, acute changes in nutritional status are unlikely to be reflected in changes in serum albumin and it is therefore of greater value in assessment of chronic nutritional status of an individual. Prealbumin is a transport protein for thyroid hormones, which exists in the circulation as a retinol binding-prealbumin complex. Prealbumin has a half-life of two or three days and therefore changes in its levels are more suggestive of acute changes in nutritional status. Although prealbumin is responsive to nutritional changes, it is influenced by several disease-related factors thereby making it unreliable as an index of nutritional status.

Functional assessment aims at evaluating immune competence and muscle function. Immune function might be assessed by determination of total lymphocyte count and delayed cutaneous hypersensitivity (DCH) to a battery of intradermal antigens including candida, mumps, trichophyton, streptokinase, streptodornase and tuberculin (PPD). However in critically-ill patients, a number of factors can non-specifically alter DCH thereby rendering it meaningless in the evaluation of nutritional status. Immune function is therefore neither a specific indicator of malnutrition nor is it easily assessed. Skeletal muscle function serves as an index of nutritional status as well as risk of nutrition-related complications and may be assessed by the ability to perform work on ergometer, changes of heart rate during maximal exercise, dynamometry (hand-grip strength), respiratory muscle strength and study of muscle fatigue. It has been shown that the study of muscle fatigability on electrical stimulation is the most sensitive and specific predictor of nutrition associated complications as compared to hand grip strength, mid-arm muscle circumference as well as serum albumin and transferrin levels.

A number of techniques may be used to determine body composition like isotope dilution and bioimpedence analysis for estimating total body water. Dual energy X-ray absorptiometry (DEXA) helps in estimation of bone mineral mass and appendicular muscle mass while whole body counting and neutron activation assesses body cell mass, fat, fat-free body mass, skeletal muscle mass and various fluid volumes. Computed tomography and magnetic resonance imaging measure components at the tissue level of body including skeletal muscle, fat, viscera and brain. However, most of these techniques are experimental, not widely available, lack validation and have not been correlated with clinical outcome.

The prognostic nutritional index (PNI) is an equation which takes into consideration four variables used for nutritional assessment, namely serum albumin (gm/dl), serum transferrin (mg/dl), triceps skin-fold thickness (mm) and delayed cutaneous hypersensitivity to a three antigen panel (rated as 0: nonreactive, 1:<5mm in duration, 2:= 5mm in duration): PNI ( per cent)= 158 – 16.6 x (Sr Albumin) – 0.78 x (Triceps Skin-fold Thickness) – 0.20 x (Sr Transferrin) – 5.8 x (Delayed Cutaneous Hypersensitivity).

Based on PNI the patients may be categorised as low risk when PNI is less than 40 per cent, intermediate risk when PNI = 40-49 per cent (complication rate = 30 per cent, mortality rate = 4.3 per cent) and high risk when PNI is equal to or more than 50 per cent (complication rate = 46 per cent, mortality rate = 33 per cent).
ASSESSMENT OF NUTRITIONAL REQUIREMENTS

Optimal nutritional support aims at providing adequate provision of energy, water, electrolytes and micronutrients. While calculating the energy requirements of an individual, three factors have to be taken into account, namely, resting energy requirements (5-10 per cent more than basal requirements), increased energy expenditure secondary to disease process (stress factor), and energy for physical activity (activity factor). In clinical practice, energy requirements to meet basal metabolic expenditure (BME) are calculated using the Harris-Benedict equation:

For men: BME (kcal/day) = 66.5 + (13.7 x weight) + (5.0 x height) + (6.8 x age)
For women: BME (kcal/day) = 655.0 + (9.6 x weight) + (1.8 x height) + (4.7 x age)

However, these methods tend to both overestimate and underestimate caloric requirements7,14. Indirect calorimetry has been developed as a technological advance for evaluating energy requirements20. A balance of nutrients is required for optimal nutritional support and a mixed substrate of glucose and fat is optimal to meet energy requirements. If glucose is administered as the sole source of nonprotein calories, oxygen consumption and carbon di-oxide production might be markedly increased. With increasing stress, energy requirement increases but the fractional demand for glucose decreases and severely stressed septic patients might develop fat intolerance as a late finding14,21. Protein calories are usually not included in calculations of daily energy requirements. Protein requirements are 1.0-1.2 gm/kg/day for maintenance, 1.5-2.0 gm/kg/day for repletion and 2.0-2.5 gm/kg/day for patients with excess losses7.

Maintenance fluid requirements can be calculated using a standard formula: 100 ml/kg of body weight for the first 10 kg of body weight, 50 ml/kg for the next 10 kg and 20 ml/kg for each additional kg of body weight14. Alternately, based on the fact that 1 ml of water is for every calorie of energy spent, maintenance water requirement is 1 ml/kcal/day. These requirements might require alteration in patients with pre-existing chronic illness who are unable to tolerate large fluid load, and patients with additional losses of fluids, fever and sepsis7. Maintenance requirements for sodium are 1-1.5 mEq/kg/day, chloride 1.5-2 mEq/kg/day, potassium 0.7-1 mEq/kg/day, calcium 0.2-0.3 mEq/kg/day and magnesium 0.35-0.45 mEq/kg/day. The dose of electrolytes needs to be treated according to individual needs on a daily basis14.

ASSESSMENT OF THE ROUTE OF ADMINISTRATION

The choice of parenteral versus enteral nutrition will primarily be dictated by the fact whether the latter is feasible, as enteral nutrition is always to be preferred. The use of the alimentary tract is advocated because of simplicity of technique, greater availability, lower cost, lower complication rates and increasing recognition of the fact that abnormal trophism of intestinal mucosa plays a central role in surgical stress, hypermetabolic states, bacterial translocation with consequent endotoxemia and multisystem organ failure22-24. Moreover, evidence suggests that nutrients delivered enterally are used more efficiently by reaching the liver directly via the portal vein than when given by peripheral vein25. Besides, the current enteral nutrition formulae are superior to currently available parenteral nutrition solutions as they are enriched with arginine, glutamine, omega fish oils, nucleosides and nucleotides1,7. The addition of these nutrients supports growth of intestinal mucosa and immune competence26.
These apparent advantages of the enteral route must be weighed against the fact that enteral nutrition may increase fistula output especially in high output fistulas, may increase the caustic effects of fistula drainage on the skin, is more difficult to control initially and is accompanied by significant incidence and severity of complications. Total parenteral nutrition is preferred in patients with enterocutaneous fistula in the presence of the inability to obtain enteral access, intolerance to enteral nutrition, high output fistulas and presence of multiple unfavourable factors. Based on the aforementioned factors, the ideal route to administer nutritional support must be tailored to the individual patient.

Reasonable fistula closure rates have been reported using enteral nutrition, although the rates are lower than those achieved with parenteral nutrition, which may partly be attributed to the fact that at least four or five days are required to achieve optimal caloric and nutritional balance with enteral nutrition alone. Hence, during this initial period, the patient should be supported with parenteral nutrition to achieve optimal nutritional replenishment. When at least 4 feet of functional small intestine exists between Ligament of Treitz and enterocutaneous fistula, oral, nasogastric or nasoduodenal tube feeding of highly absorbable, low residue nutrients can be administered with reasonable results. If feasible, a small, soft feeding tube may be passed into the bowel below a fistula high in the alimentary tract for continuous infusion by a pump. Often a combination of these two techniques may be required for optimal nutritional support. Hyperosmolar solutions are not well tolerated by small bowel and whereas parenteral nutrition virtually never increases the fistula output, enteral nutrition frequently does so followed by a decrease in fistula output if the fistula is destined to close. During nasogastric feeding, osmolality of feed is increased, first until hyperosmolality is tolerated which is followed by an increase in volume till optimal nutritional requirements are met. Conversely when enteral feed is directly administered into the small bowel, the volume should be increased first followed by increase in osmolality to full nutritional dose.

Elemental diet consists of basic definable constituents in ultra-compact form, which does not stimulate digestive enzyme secretions and is ready for intestinal absorption. In a study of 13 patients with enterocutaneous fistulas, the use of elemental diet was associated with a 14-80 per cent decrease in fistula output and fistula closure rate of 54 per cent.

In order to ensure a consistent level of nutritional supportive care, standardised total parenteral nutrition (TPN) order forms with appropriate guidelines have been used to aid the inexperienced house staff in writing appropriate orders without compromising the quality of patient care. This form is based on the single delivery system of the three-in-one mixture concept and consists of an enteral purpose standard formula concentration or a space for individualised solutions, the average daily recommendations for electrolytes, vitamins and trace elements in paediatric as well as adult doses, the provision for weekly doses of vitamin K, the addition of heparin to prevent catheter thrombosis, the option to add insulin and H2-blocking agent, nursing and dietary orders to start and stop TPN and laboratory tests to monitor TPN. The introduction of ethyl vinyl acetate bags has made the admixture of a fat emulsion to glucose and amino acid solutions possible (three-in-one mixture) with the following advantages: cost saving, more uniform administration, less risk of contamination consequent to less manipulation, ease of delivery and storage for patients on home TPN programmes, the option of delivering nutritional support peripherally, decreased lipid toxicity due to dilution of lipid emulsion and longer duration of its administration. The complications of parenteral and enteral nutrition have been enumerated in Tables 2 and 3.
Table II: Complications of parenteral nutrition

- Mechanical complications: Malposition, arterial injury, pneumohydrohemothorax, vessel thrombosis, thrombophlebitis, catheter embolism
- Catheter sepsis
- Metabolic complications: Hyperglycemia, hypoglycemia, hyperosmolar syndromes, hypertriglyceridemia, abnormal lipid profile, hyperinsulinemia, elevated epinephrine, derangement of liver function, hypercarbia, deficiency of essential acids

Table III: Complications of enteral nutrition

- Mechanical complications: Dislodgement of feeding tubes, free peritoneal leak, bowel perforation and fistulisation, bowel obstruction, pneumatosis intestinalis, injury along the tube insertion site, aspiration pneumonitis
- Metabolic complications: Fluid overload, electrolyte imbalance, hyperglycemia, uremia, dehydration
- Infectious complications

END POINT FOR NUTRITIONAL SUPPORT

The persistence of enterocutaneous fistula, despite control of sepsis and four or six weeks of aggressive nutritional therapy, is the chief indication for definitive surgery. Three clinical scenarios dictate cessation of nutritional support in patients with enterocutaneous fistula, namely, development of a life-threatening complication like sepsis or severe metabolic complication, achievement of rehabilitative end point for nutritional support so that surgery is contemplated for definitive closure of fistula, progression of the patient’s underlying disease to terminal stage.

HOME NUTRITIONAL SUPPORT

Home nutritional support (both enteral and parenteral) is associated with psychological, clinical and economical benefits. The factors influencing the decision to initiate home nutritional support include underlying disease, clinical condition and the available support system for maintaining care at home. Home nutritional support is recommended if surgical closure of fistula fails or the patient remains a poor surgical risk despite all conservative measures.
REFERENCES


**PICK YOUR BRAINS!**

1. To avoid metabolic complications in the low birth weight infant receiving a parenteral lipid infusion, the best guideline to follow is to?
   
   (a) Use only 10 per cent fat emulsion preparation
   (b) Use only an intermittent infusion regimen
   (c) Monitor triglycerides to maintain below 300 mg/dl
2. When is the normal growth curve most likely to diverge from the standard curve?

(a) First six months of life
(b) Second six months of life
(c) Three to eight years
(d) Late adolescence

3. At what age should full-term, formula-fed infants receive supplemental iron?

(a) Birth
(b) Four months
(c) Eight months
(d) One year

4. How is creatinine height index used in the nutritional assessment of children?

(a) To assess total body nitrogen
(b) To reflect skeletal muscle mass
(c) To provide an index of protein turnover
(d) To assess adequacy of the visceral protein pool

5. Which of the following vitamins are available in water miscible formulations to use in paediatric patients with fat malabsorption?

(a) A, E, and K
(b) C, D, and K
(c) D, E, and K
(d) D, E, and folate

6. Which of the following is not a home parenteral nutrition management principle for a paediatric patient with short bowel syndrome?

(a) Gradual introduction of enteral nutrition
(b) Nutritional replenishment with parenteral nutrition
(c) Avoidance of enteral nutrition which worsens diarrhoea associated with short bowel syndrome
(d) Gradual weaning of enteral infusions over to a more normal diet once patient is free of parenteral nutrition

7. Which of the following best describes the use of amino acids in premature neonates?

(a) Taurine toxicity may be manifested by retinopathy More...
(b) Histidine plays an essential role in the conjugation of bile salts
(c) Taurine is an essential amino acid due to a deficiency of arginase
(d) Cysteine is an essential amino acid due to a deficiency of cystathionase

8. Which of the following is not associated with the administration of parenteral nutrition supplemented with lipid emulsion to premature neonates?

(a) Weight gain for carnitine-supplemented premature neonates
(b) Significant reduction in plasma carnitine concentrations
(c) Faster implementation of enteral feedings when carnitine supplementation is allowed
(d) Significant elevation of plasma carnitine concentrations when carnitine is supplemented

9. Determination of normal linear growth requires

(a) A stadiometer
(b) Tanner staging
(c) Interval measurements
(d) Determination of midparental height

10. Which of the following characterises the Frisancho Standards used to determine normal skin-fold thickness?

(a) They are most applicable in the first year of life
(b) They allow early detection of caloric deprivation
(c) They are also used for measuring mid-arm muscle circumference
(d) They require the use of the Harpenden and Holtain caliper

11. Which of the following would be the most likely access site for central parenteral nutrition?

(a) Femoral vein
(b) Basilic vein
(c) Subclavian vein
(d) Right atrial appendage

12. The Healthcare Financing Administration developed separate categories for premixed parenteral solutions based on the amount of

(a) Solution used daily
(b) Total calories per day
(c) Nonfat calories per day
(d) Amino acids prescribed per day

ANSWERS