SPECIAL ARTICLE

Nutrition in Critically Ill Cancer Patients

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There is a general impression amongst clinicians that good nutrition in cancer before, during and after surgery and also prior to and during radiation and chemotherapy results in a favorable outcome. A lot of manpower and money is being expended to achieve this end. In the USA, a 21-day stay in a surgical ICU costs $84,000 (approximately Rs 2,100,000 at current rates). Is this colossal expense justified?

Many factors modify nutrition in a cancer patient. It is important to know about these as well as the types of nutritional support available for such patients before embarking on any expensive regime.

a) Tumor Necrosis Factor (TNF; Cachectin) It is so called because injection of this factor produces necrosis of tumor cells. It is produced in cancer patients in response to endotoxins by mononuclear cells, macrophages and lymphocytes. If injected in animals it produces anorexia, weight loss, increased protein turnover, negative nitrogen balance and increased lipolysis. These result in hormonal imbalance, metabolic dysfunction and increased energy expenditure. TNF produces anemia, hypoproteinemia, increased nitrogen catabolism, glucose intolerance, lactic acidosis and increased serum lipids. The half life of TNF in rabbits is 6 months. TNF has been successfully extracted and its effect can be abolished by anti-TNF antibodies.

b) Adaptation during starvation For survival, vital organs such as the brain, heart and lungs require nourishment. The body requires at least 100 mg of glucose per minute (2 mg/Kg/minute) for survival. Starvation has a deleterious effect on body metabolism. Protein breakdown supplies amino acids, especially alanine and glutamine, which are then used for gluconeogenesis. A daily supply of 100-150 g carbohydrates has a protein-sparing effect by reducing protein catabolism. Fat breakdown provides glycerol and fatty acids; glycerol also provides glucose. With prolonged starvation, the brain and the heart adapt to utilization of ketones and fatty acids for energy. The gastrointestinal mucosa responds to starvation by decreased cell migration leading to subtotal villous atrophy; in addition, there is decreased pancreatic secretion. These result in poor digestion and absorption due to decreased secretion of lipase, trypsin, amylase and intestinal lactase.

e) Stress: Stress occurs during burns, trauma, sepsis and post-operative periods. During stress, there is increased metabolism, glucose production, and protein and fat breakdown (Table 1).

<table>
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<th>Table 1: Energy and Protein Requirements during Stress</th>
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<td>Normal</td>
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<td>Protein (amino acids) (g/Kg)</td>
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<td>Energy expenditure above basal level (%)</td>
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Loss of one gram of nitrogen equals loss of 30 g of lean tissue. The protein metabolism in the critically ill is highly complex. At least 30 acute phase proteins are generated as a response to body trauma, and these have varying and sometimes opposite biological effects.

Albumin Degradation of albumin continues despite its deficiency in critical conditions. There is a wrong impression that intravenous infusion of albumin raises serum levels. Infused albumin diffuses into the extracellular space which expands. This increases the albumin pool in the body but not its serum concentration. Infusion of amino acids does not reverse the hypoalbuminemia seen in cancer patients. Successful nutritional support produces loss of weight and body water which denotes reduction in extracellular fluid in the lungs and the brain. Normal serum albumin level is not always synonymous with good nutrition. In anorexia nervosa, despite poor food intake, serum albumin level is usually normal. Increase in body protein synthesis can be detected early by a rise in serum transferrin, retinol binding protein and fibrinogen.

Nutrition and Drugs The effect of drugs given to critically ill patients on their nutrition is poorly understood. Whatever little we know is related only to protein malnutrition. The liver is the main organ metabolizing most drugs, which are usually excreted through the kidneys. With poor nutrition there is fatty infiltration of the liver; this decreases mitochon-
dria, endoplasmic reticulum and cytochrome P-450, causing
deranged metabolism of antipyrine, chloramphenicol
and sulphadiazine.

Renal excretion also regulates availability of drugs.
Some drugs are bound to serum proteins. The greater
the extent of protein binding, lesser free drug is available
for kidney excretion. With low plasma protein there is
decreased protein binding of ampicillin, streptomycin and
gentamicin and these are more easily eliminated through
the kidneys by filtration or active tubular excretion.

Modes of Feeding
In critically ill patients nutrients are supplied enterally or
intravenously (Table 2).

Table 2: Advantages of Enteral over Intravenous Feeding
- Easily tolerated
- Sterilization of tubes and nutrients not required
- Inexpensive
- Convenient
- No hospitalization
- In short bowel syndrome, intestinal mucosal mass
  regenerates more rapidly
- Insulin injections not usually necessary
- Expert supervision not necessary
- Avoids catheter sepsis and infections
- Blood electrolytes and trace element disturbances
  uncommon hence their laboratory estimation not necessary

External Nutrition. This may be given orally or through a
nasogastric tube or percutaneous gastrostomy. Enteral
tube feeding is recommended in patients who cannot eat
due to paralysis of swallowing muscles, refusal to eat,
persistent anorexia, semicongious state, severe malab-
sorption requiring unpalatable formula diet, short bowel
syndrome, or cancer of the pharynx, larynx or esophagus.
The reserve capacity of intestinal absorption being enor-
mous, even with a short residual gut, enteral feeding is
the best. After surgery, motor activity of the stomach and
large bowel is sluggish while that of the small intestine
remains intact. Hence, in the postoperative phase, slow
nasoduodenal or nasogastric feeding avoids distension,
bloating, pain and nausea.

The cancer patient is usually depressed due to surgery, anorexia and apathy. Forced
oral feeding produces conflict with nurses. Enteral feeding
may be required in such instances. The best time for
enteral feeding through a nasogastric tube is at night.
Osmolarity is not an important factor in the causation of
diarrhea, which sometimes accompanies tube feedings
this is usually due to the administration of antibiotics.

Percutaneous endoscopic or other form of gastro-
tomy is required when the food passage is obstructed
due to cancer of the mouth, pharynx, larynx or esophagus.
In patients with a short bowel, the length of the remaining
bowel and the region that has been resected are important
factors. If the duodenum and terminal 20 cm of the small
bowel are intact adequate absorption can occur; this is
made possible by hypertrophy and elongation of the
residual bowel. Elemental diet (predigested foods con-
taining proteins, fats and carbohydrates) itodes over the
immediate needs till functional regeneration occurs in the
residual bowel. Enzyme replacement then helps digestion
of orally ingested natural foods. Intestinal mucosal mass
regeneration and resumption of absorption are more
rapid with oral or nasogastric (enteral) than with intra-
venous feeding.

Complications of tube feeding include aspiration
pneumonia, gastrointestinal reflux and impaired gag
reflex. A post-operative regime without nasogastric tube
allows early oral feeding and early recovery of bowel
function.

Intravenous Parenteral Nutrition. This requires a team
consisting of clinicians, dieticians, highly trained nurses,
pharmacist, microbiologist and biochemist. It requires
expertise to pass the catheter in the deep veins. Nutrients
given intravenously include carbohydrates, lipids, amino
acids, vitamins and minerals.

The preferred carbohydrate source is 50% glucose,
which supplies half of the required calories. If more than
50% of calories are supplied as glucose, hormonal secre-
tions are disturbed and increased amount of carbon
dioxide is produced. The latter, during elimination
through the lungs, may embarrass respiration. Lipids are
meant not merely to supply essential fatty acids, as was
originally conceived, but also to supply 30% of required
calories. The lipid source must contain nearly equal pro-
portions of long and short chain triglycerides. Carnitine
is required for the metabolism of the former and is
deficient in critically ill patients; however, its replacement
has not proved to be of value. Coagulase-negative staph-
lococcal bacteremia is more frequent in infants admin-
istered intravenous lipid emulsions. The protein source
is 1.2 g/kg body weight of a mixture consisting of essential
as well as non-essential amino acids. The role of glut-
amic acid as non-essential amino nitrogen source is now better
appreciated. Branched chain amino acids (BCAA) (leucine,
iso-leucine and valine) are initially metabolized in the
peripheral muscle rather than in the liver. The usual
amount of BCAA in intravenous amino acid mixtures is
about 21%. Solutions enriched with BCAA (upto 45%) are
claimed to increase the rate of synthesis of liver
proteins and acute phase proteins. There is no general
agreement whether the amount of BCAA should be
increased above 25%. Intravenous feeding also requires
inclusion of multivitamin and trace element preparations
Perioperative intravenous feeding

In 1987, the American College of Physicians, based on a
meta-analysis of controlled trials concluded that "the
routine use of perioperative parenteral nutrition for major
surgery is not justified". This conclusion was criticized as
the study criteria did not include malnourished patients.
In a subsequent multicentric trial, 395 malnourished pa-
tients given intravenous feeding 7-15 days before surgery
and 3 days after surgery showed no advantage over those
given enteral feeding, and the risk of post-operative sur-
gical complications was not reduced.12 On the contrary,
infection rate was higher in those given intravenous feed-
ing.

Chemotherapy and nutrition

Chemotherapists advocate that improving the nutrition of
cancer patients results in improved response to cancer
chemotherapy. However, critical evaluation of cancer
chemotherapy reveals that it is useful only in malignancies
of the hematopoietic and lymphoreticular tissues, testic-
ular tumors and some ovarian tumors. On the other hand
chemotherapy is of no benefit in carcinoma of the stom-
ach, pancreas and colon.13-15 Twelve randomized con-
trolled trials15 have shown that parenteral nutrition in
patients receiving anti-neoplastic chemotherapy leads to
the following: 1) four-fold likelihood of acquiring infec-
tion; 2) chances of survival only 80% compared with those
not given parenteral nutrition; 3) increased risk of com-
plications like pneumothorax, subclavian and axillary ve-
nous thrombosis and catheter related sepsis.16

Occasional reports of better results with improved nutri-
tion may be fallacious as higher survival rate with
chemotherapy may be in those whose disease was initially
less malignant.16 Neither total parenteral nutrition nor
enteral feeding prolongs life in patients with advanced
cancer. In fact aggressive nutritional support causes de-
terioration in the quality of life.

"Routine use of total parenteral nutrition (intrave-
nous feeding) in patients receiving chemotherapy should
be strongly discouraged". TPN in a patient on chemother-
apy increases the risk of infection, catheter sepsis and
sepsis.15,17

Conclusions

Ten billion dollars are spent in USA annually on dubious
methods of treating patients with advanced cancer dis-
ease. There was no difference in the length of survival
and quality of life in patients treated with unproven
methods or at an academic center with accepted modes
of chemotherapy or radiotherapy.15

All attempts should be made to give cancer patients
enteral feeding (orally or through nasogastric tube) rather
than intravenous feeding which is not only expensive but
also liable to produce dangerous complications. Intrave-
nous therapy also necessitates hospitalization. It can only
comfort a naive therapist that the patient is being treated
with the latest technology. Intravenous nutrition merely
guarantees administration of food components but not
their utilization. It is like applying all the ingredients of
hair on bald skin with the fond hope that it will promote
hair growth.

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