Case report

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To feed or not to feed in palliative medicine

Abstract

The problem of malnutrition concerns most patients in the advanced stages of cancer. Nutrition and food are synonymous with the continuation of life for patients and their families and friends. In this paper, the methods of oral, enteral and parenteral nutrition are discussed, together with their advantages and the controversies connected with them and their effects on survival time and the quality of life.

Key words: cancer disease, nutrition, hydration

"Deux extremes: exclure la raison, admettre uniquement la raison"
"Two extremes: to exclude reason, to act according only to reason"
"Thoughts," Blaise Pascal

Introduction

Those patients who, yesterday, were still dying of cancer, today, owing to progress in medicine, survive until malnutrition becomes the main factor causing death [1].

Malnutrition is a problem for most patients with advanced cancer. Malnutrition causes impairment to the quality of life, immunity and body functions. It is responsible for the increased incidence of diseases, mostly of various infections, and, in consequence, brings the patient's death forward. It is believed that in 5–20% of cancer patients, cachexia is the direct cause of death [2, 3]. Every year, two million people worldwide die from cachexia [4, 5]: these are mainly patients with gastrointestinal and lung cancers.

Malnutrition associated with cancer disease is determined by many factors: in the first place by reduction of the amount of food consumed (its main causes include obstruction rendering gastrointestinal passage difficult, vomiting, pain and depression), reduction of intestinal absorption, and metabolic changes (glucose intolerance, insulin resistance, increased gluconeogenesis from amino acids and lactates, decreased lipogenesis, and disrupted protein metabolism) [6]. Protein loss is the main factor responsible for mortality in malnutrition. In healthy adults 33–37% loss of ideal body mass, which corresponds to 60–75 days of starvation, is regarded as critical [7].

On the other hand, in the advanced stage of cancer, 63% of patients feel no hunger and 34% feel only slight hunger; 62% of patients feel no thirst or only slight thirst [8]. Thirst, however, is not connected with the degree of dehydration [14]. Oral hygiene measures, such as mouth rinsing, ice cube sucking and consumption of liquid food through a straw, bring relief.

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The problem of nutrition concerns mainly cancer patients who can be classified in the following groups:

— potentially curable patients who require aggressive chemo- and radiotherapy and surgical treatment;
— patients regarded as cured, presenting with intestinal failure due to resection or radiation-induced enteritis;
— patients with advanced cancer, refractory to treatment, presenting with alimentary failure.

Although nutrition of the first two groups of patients is widely accepted, patients from the third group still constitute a current problem open to discussion. These patients will die of disease progression irrespective of whether they are fed or not. Sometimes their being fed is still necessary, should we assume based on medical knowledge that they would die from starvation earlier than from the direct cause of the disease.

Oral nutrition

The American Dietetic Association (ADA) suggests the following mode of therapeutic management when starting nutrition for a palliative care patient [9]:

1. Consumption *per os* of food, in accordance with the patient's desires.
2. The introduction of artificial and natural nutritional supplements.
3. Family participation in nutrition.
4. The elimination of dietary restrictions, e.g. so called "unhealthy" food.
5. Respecting the patient's freedom of choice: many patients consume meals to please their families.
6. The treatment of symptoms and signs that make food consumption difficult.

The following can also be added to the list:

— adaptation of the consistency, volume and frequency of meals to the alimentary capabilities of the patient;
— prevention of mouth dryness: application of water 2–3 ml with a pipette, mouth rinsing, ice sucking, pineapple chewing, artificial saliva;
— treatment of anorexia: megestrol acetate, dexamethasone;
— treatment of nausea and vomiting: methoclopramide;
— treatment of complaints of pain in the oral cavity, or swallowing disorders;
— prevention of constipation;
— treatment of diarrhoea;
— diagnosis and treatment of depression.

Nutrition and survival time

The expected survival time is possibly the most important criterion when making the decision about the introduction of feeding, particularly artificial nutrition. Its determination is extremely difficult and it is usually optimistically overestimated [10]. The Karnofsky scale (index), which determines in percentage values the physical fitness of patients treated for cancer disease, seems to be a rather good parameter: a 50% result indicates the risk of death in six months (most frequently two months).

Other described criteria include:

— body weight loss of over 10 kg and a Mini Mental test result of below 24 and coexistent dysphagia — the estimated survival time is under four weeks [11];
— a palliative prognostic index combining the result on the ECOG scale describing a patient's vital activity, oral administration of food, absence of oedema, resting dyspnoea, and hallucinations. The index determines the expected survival time over six weeks with 77% specificity and 80% sensitivity [12];
— a palliative prognostic score uses the following symptoms and signs for the assessment of a patient's condition (prediction of survival time over 30 days with 87% probability): the Karnofsky index, anorexia, dyspnoea, leucocyte count and lymphocyte percentage [13].

Knowing that someone can survive for approximately two months without food, it seems reasonable to introduce artificial nutrition for patients requiring it, if the estimated survival time is over two or three months.

According to the ADA, the remaining criteria for the introduction of artificial feeding include the following:

— evaluation of benefits and risk;
— the choice of the patient, having previously been informed about the food administration route;
— the availability of staff providing enteral and parenteral feeding.

Enteral nutrition

The main indication for starting enteral nutrition are malignancies of the upper segment of the alimentary tract that render swallowing impossible, with normal function maintained in the gastrointestinal tract. Gastric tubes are replaced by a percutaneous endoscopic gastrostomy (PEG). Numerous clinical studies confirm a higher early mortality rate in

patients following PEG application [15, 16], which is connected with decreased albumin levels in such patients or those with dementia [17, 18]. In other studies, no high percentage of serious complications following PEG application were found, although the following complications were reported in 5-13% of cases: wound infection, gastric content leakage, intestinal obstruction [19–22].

Statistical data (1992) demonstrate that 415 patients per 1 million population in the USA and 40 per 1 million in Great Britain have been fed by the enteral route. On the either side of the Atlantic, patients with cancer account for 40% of those fed by the enteral route: most of them live only a month but 30% manage to survive a year.

Another group of palliative care patients are those with amyotrophic lateral sclerosis, in whom swallowing disorders develop rather early in the course of the disease. In such patients, the introduction of enteral nutrition can prolong life, reducing the risk of aspiration and choking. Of course, those patients are fully aware and take the decision about beginning the nutrition independently [23].

Compared with parenteral nutrition, enteral feeding is cheaper, has fewer adverse effects, allows for the maintenance of the intestinal barrier [24], and, although it causes no increase in lean body mass in cancer patients [25], it partially prevents its decrease, reduces the concern of the caregivers and improves the psychological condition of the patients themselves [26, 27].

Parenteral nutrition

In a review of international literature on the nutrition of patients in the terminal stages of diseases, the most controversial factor is the application of total parenteral nutrition (TPN) in palliative care patients [28]. Until now, no beneficial effect of TPN has been proven on parameters other than the strictly nutritional, and the adverse effects, which do not occur rarely, are also stressed.

Parenteral nutrition was applied for the first time in animals in 1656 by Wren. He administered wine, opium, and oleic acid intravenously. In 1840 Bernard subcutaneously injected animals with a solution of egg albumin, milk, and cane sugar. Biedl and Krause in 1896 administered glucose solution to humans intravenously but only in 1967 did Dudrick, applying completely parenteral nutrition, manage to obtain normal growth and development, first in puppies and, a year later, in a child. This started the development of parenteral nutrition as a therapeutic method and a great boom in the pharmaceutical industry, with the creation of a branch worth many billions of dollars [23,29].

Considering the pros and cons in the context of TPN in palliative care patients, it seems reasonable to answer the following questions:

— does parenteral nutrition prolong the survival time?
— does parenteral nutrition improve the quality of life?
— does parenteral nutrition prolong the process of dying?

Federico Bozetti from the Italian Enteral and Parenteral Nutrition Society believes that in the 21st century parenteral nutrition should not be regarded as an extraordinary therapeutic method: we all used that atypical administration route for nutrients during intrauterine life. TPN can be applied at home, with the family's help. Parenteral nutrition should not be made unavailable to patients with cancer disease refractory to treatment simply because its effectiveness has not been confirmed by evidence-based medical criteria [30]. Bozetti compares this situation with the administration of expensive therapy with gemcytabine in patients with advanced pancreatic cancer, in whom the survival time is 3–5 months and the therapy is applied routinely.

In another publication [31] the same author suggests using TPN in patients who could die earlier from malnutrition than from progression of the disease. Should any doubts arise as to the validity of the practice of parenteral nutrition, Bozetti suggests adopting the "try it and see" strategy. The effects of TPN are easily and rapidly reversible: in the case of the absence of benefits, nutrition can be stopped and the "wrong" decision is a lesser error than the lack of the introduction of a possibly beneficial treatment [32].

Duerksen et al carried out studies on a group of patients with alimentary tract malignancies refractory to surgical treatment and with alimentary tract obstruction, in whom the estimated survival time after aggressive chemotherapy was several months. On the basis of the results obtained, they concluded that TPN was beneficial in the case of an estimated survival time of over 60 days, the minor complications of TPN that occurred having no influence on mortality, and biological parameters were not helpful in identifying those patients in whom TPN could have been more beneficial [33].

Even Loprinzi from the Mayo Clinic, although sceptical in his opinion in Current Controversies in Cancer, admits that in spite of the absence of well-

documented data on the validity of the application of parenteral nutrition in patients with advanced cancer, there are some situations when such intervention is justified. They include post-resection intestinal failure, radiation- or chemotherapy-induced enteritis and cancer dissemination in the abdominal cavity (carcinomatosis) without failure of the remaining organs.

About 40% of patients fed parenterally are those with cancer disease at every stage of progression. That percentage varies in different countries: 80% in Sweden, 60% in the Netherlands, 40% in the USA, 27% in France, and only 5% in Great Britain. Those patients are fed for four months on average and about 30% of them survive for over a year [34].

Parenteral nutrition and the quality of life

Few publications are available describing the quality of life of patients with advanced cancer in whom TPN was applied. In a study in 2002 [36], Bozetti, quoted above, evaluated the quality of life for patients with advanced cancer subjected to parenteral nutrition in several Italian centres. For the assessment of quality of life, the Rotterdam scale was used with a form completed by the patients beginning TPN and again at monthly intervals. The mean TPN duration was four months. The condition of the patients assessed by the Karnofsky scale was stable until the third month before death. A month following the beginning of TPN, no impairment of the quality of life was observed. The quality of life level was stable until approximately the second month before death. In their final conclusion the authors reported that TPN can prolong survival time by up to seven months in one third of the patients, improve the quality of life in 20-40% or at least maintain it at an unchanged level until the second month before death. The patients who qualify for TPN should have a Karnofsky scale score of 50% and should give consent to the application of such treatment, the duration of which is estimated to be at least one month.

In Stockholm, a descriptive study of the quality of life was conducted in palliative care patients included on a programme of home parenteral nutrition, as well as in their families or caregivers [35]. The most frequently stressed positive aspects of that activity included a feeling of safety connected with frequent visits of "the feeding team", a reduction in internal tension connected with the "obligation" to have meals, and even body weight gain and increase of appetite. Only isolated adverse effects were observed, such as nausea, vomiting, headaches (connected with the rate of formula application rather than with the feeding itself), and limitations in social contact. In most patients parenteral nutrition administered at night 3–4 times weekly with weekend-long intervals was complementary to oral feeding. No negative opinions of the patients were recorded, possibly because some of them discontinued the home nutrition programme and were excluded from the study. In addition to that, Sweden is a country with a highly-developed social welfare system (a model of the welfare state), where the artificial nutrition of terminally ill patients is applied almost routinely.

In the study by Howard et al the financial cost, survival time and quality of life of patients subjected to a home TPN programme were evaluated [37]. It was found that the therapy was safe, particularly in its short-term application, as in the case of cancer patients: 2–6 months (a short survival time), and 2–3 years in female patients with metastatic ovarian cancer (there is a better prognosis in the case of malignancies associated with sex). According to the authors, TPN complications were responsible for only 1% of deaths; the remaining causes mainly included underlying disease progression and diseases of other organs. It was confirmed that 40% of parenterally fed patients were those with cancer disease, and 20% of the patients survived one year. The cost of the home nutrition programme was only half of that during hospitalization and was lower in younger patients. Quality of life was assessed in emotional and social terms and in respect of physical parameters. The observed quality of life level was low in the first year of feeding and increased gradually with TPN continuation, reaching a result comparable with that in a healthy population after about four years. Unfortunately, no separate analysis was carried out in cancer patients with a short survival time.

In Great Britain — the country where only a low percentage of parenterally fed patients are those with cancer disease — a study was conducted to assess how nutritional habits could be influenced and how patients with advanced disease could be helped [38]. Most patients with cancer present with an appetite decrease, an early feeling of satiety, an aversion to eating and a refusal to take food, which led in 30–80% of patients to anorexia precipitating death. Most patients and their caregivers accept these changes, regarding them as a transitional stage between life and death. Others try to deal with the

problem, only to be met with incomprehension from the caregivers, who believe that a good caregiver can persuade the patient to eat.

Nutrition in paediatrics

Considering the problem of nutrition for patients in the terminal stage of disease, the differences in the management of very young patients should be stressed [39]. This concerns four groups of children:

— children with potentially curable diseases (neoplasms, circulatory failure);
— children with diseases in which intensive treatment can prolong survival time (intestinal failure, cystic fibrosis);
— children with diseases in which only palliative treatment is applied (neurodegenerative diseases);
— children with diseases leading to invalidism, often neurological (e.g. metabolic, mitochondrial diseases).

Nutrition for children is one element of the global care of very young patients, although it cannot be forgotten that its purpose is not the prolongation of survival time at any cost.

In the first group, therefore, the main aim is improvement of a child's functioning and comfort and a reduction of the symptoms and signs of weakness. Enteral nutrition with a tube failed to give the expected results, in some cases a gastrostomy was better tolerated but TPN was the most frequently chosen method of nutrition.

Nutrition in the second group of children not only contributed to survival prolongation but also to an improvement in life quality. After 10–25 years of TPN, most of those patients reached a certain social and professional status.

In groups 3 and 4, the introduction of artificial nutrition is very often necessary and usually the appropriacy of such treatment is unquestionable. For most members of teams treating children in the terminal stage of disease, their nutrition is an integral part of the care provided for them. Is there, therefore, a time limit determining when the artificial nutrition of patients should be discontinued? The nutrition becomes permanent and then, for ethical and moral reasons, it should not be stopped. In spite of adverse effects, gastric tubes (with the risk of infection in the upper airways, accidental or intentional removals, inflammatory conditions of the oesophagus and stomach), a gastrostomy (insertion under general anaesthesia, tube obstruction, abdominal pain and vomiting caused by too rapid an administration of formula), and TPN (with a risk of disturbing the blood-intestine barrier and bacterial translocation) are used.

Hydration in palliative medicine

The last issue to discuss is the problem of the hydration of terminally ill patients. Cessation of the consumption of fluids and food, increased sweating, vomiting, and sometimes diarrhoea are the main causes of dehydration in the process of dying. The families of patients very often take note of the fact that their kin will not die of hunger because they simply will not have time: cancer will kill them sooner. However, they can die of thirst and dehydration. Are there any clear indications for hydrating all terminally ill patients?

Here also, the opinions of scientists are divergent: some believe that dehydration can be responsible for apathy, depression, dysphagia, or orthostatic arterial pressure drops [40, 41]; others, however, point to benefits connected with dehydration: the reduction of bronchial secretion leading to improvement of respiratory comfort, a decrease in central and peripheral oedema, the reduction of vomiting and urination frequency, and a decrease in pain and discomfort due to acidosis [42].

Presently, most physicians believe that dehydration is better tolerated by patients than the risk connected with intense hydration, especially if the dehydration developed gradually and was not caused by sudden reversible episodes (diarrhoea or vomiting). Of course, in some cases, e.g. in hypercalcaemia, hydration is desirable and even necessary.

Although 63% of terminally ill patients feel no hunger [43], the feeling of thirst in the case of dehydration is reported significantly more frequently — by over 80% of patients [44,45], or according to other authors by 62% [8] — but it is not proportional to the degree of dehydration [14].

The demand for water in cancer patients is far lower than that in healthy people. Firstly, cachexia leads to an increase of the extracellular space; secondly, there is possibly an overproduction of antidiuretic hormone; thirdly, cancer is frequently disseminated in the peritoneal cavity and excessive fluid supply can exacerbate its symptoms and signs. In 1946, Gamble had already proved that the supply of glucose solution (frequently used during hydration) decreases renal sodium excretion, thus increasing the extracellular space, which is already greater in cancer disease.

To hydrate or not to hydrate?

In 2006 the results were published of a multicentre study assessing biological parameters and water balance in patients with disseminated malignant process in the abdominal cavity who had been subjected, or not, to artificial hydration [46]. A significantly lower albumin level and, therefore, lower oncotic pressure were observed in the hydrated patients, while no differences were found in the levels of non-protein nitrogen/creatinine, sodium or potassium. The mean water balance was 400 ml daily and only 20% of the patients had a positive balance. It should be stressed that the non-protein nitrogen/creatinine level increased in the last three weeks of life, irrespective of whether the patients were hydrated or not.

The hypothesis was put forward that in terminally ill patients intravascular dehydration is caused by fluid escape into the intercellular space and not by complete loss of water. Active hydration of such patients, therefore, fails to increase the volume of intravascular space: water "escapes" from the vessels as a result of greater permeability of the endothelium and reduced oncotic pressure. The assessment of water balance in those patients was not correlated with clinical signs of dehydration/fluid retention.

In the light of these results, the active hydration of terminally ill patients seems pointless.

Mouth dryness is a frequent manifestation accompanying dehydration. The management in this case includes the treatment of mycosis, oral hygiene measures and dietary recommendations (if the patient takes food *per os*). Close attention should be paid to oral hygiene maintenance: rinsing with antiseptic solutions, moistening of the lips and tongue, the administration of low volumes of fluids, the sucking of ice cubes and lumps of pineapple, chewing gum, etc.

In the case of a necessity for hydration (e.g. as a result of dramatic dehydration due to diarrhoea or vomiting) the least invasive method should be chosen. If no central access point (vascular port) is available, the subcutaneous administration of 0.9% NaCl solution, 500 ml daily e.g. during the night seems appropriate.

Conclusions

In 2001, French specialists in malignant diseases, on the basis of the available world literature, prepared "The standards, options and recommendations for nutrition of adult patients with advanced and terminal cancer disease". These are as follows:

1. Nutrition and hydration of patients in the terminal stages of cancer disease should be instituted or continued if its purpose includes improvement of the quality of the patient's life or the alleviation of some clinical symptoms and signs. The priority is to maintain the oral route of food/fluid administration as long as possible.
2. Enteral nutrition is recommended in patients with malignancies of the upper airways and alimentary tract, which completely or partially render food taking impossible, which could lead to cachexia and death in a short time period.
3. Parenteral nutrition can prolong survival time in patients with malignancies of the alimentary tract or cancer dissemination in the abdominal cavity leading to intestinal obstruction in whom the estimated survival time is greater than three months [47].

The position of the Polish Society of Enteral and Parenteral Nutrition is similar: the oral route is the priority, with maintained alimentary tract function the enteral route should be used; while the introduction of parenteral nutrition is valid when the estimated survival time is longer than two months.

On the other hand, Polish specialists in palliative medicine approach the issue of nutrition slightly more rigorously. This is possibly connected with the British model of palliative care accepted in Poland (only 8% of patients receiving enteral and parenteral nutrition in Great Britain are those with cancer disease), or with underinvestment in the health service, or, possibly, with the logistical management of patients with an estimated survival time shorter than three months.

The question of whether to feed or not to feed remains, therefore, a topical issue.

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