Abstract

Reduced nutritional state is associated with unfavourable outcomes and a lower quality of life in patients with malignancies. Patients with active tumour disease frequently have insufficient food intake. The resting energy expenditure in cancer patients can be increased, decreased, or remain unchanged compared to predicted values. Tumours may result in varying degrees of systemic pro-inflammatory processes with secondary effects on all significant metabolic pathways. Therapeutic objectives are to stabilise nutritional state with oral/enteral nutrition and parenteral nutrition (PN) and thus to prevent or reduce progressive weight loss. The maintenance or improvement of quality of life, and the increase in the effectiveness and a reduction in the side-effects of antitumor therapy are further objectives. Indications for PN in tumour patients are essentially identical to those in patients with benign illnesses, with preference given to oral or enteral nutrition when feasible. A combined nutritional concept is preferred if oral or enteral nutrition are possible but not sufficient. There are generally no accepted standards for ideal energy and nutrient intakes in oncological patients, particularly when exclusive artificial nutrition is administered. The use of PN as a general accompaniment to radiotherapy or chemotherapy is not indicated, but PN is indicated in chronic severe radiogenic enteritis or after allogenic transplantation with pronounced mucositis or GvH-related gastrointestinal damage for prolonged periods, with particular attention to increased risk of bleeding and infection. No PN is necessary in the terminal phase.

Keywords: tumour, radiotherapy, chemotherapy, stem cell transplantation

Zusammenfassung

Ein reduzierter Ernährungszustand ist mit einer eingeschränkten Prognose und vermindriger Lebensqualität assoziiert. Patienten mit aktiver Tumorerkrankung haben häufig eine unzureichende Nährstoffaufnahme. Der Ruhe-Energieumsatz kann im Vergleich zum Erwartungswert unverändert, gesteigert oder vermindert sein. Bei manifesten Tumorerkrankungen kommt es in unterschiedlichem Ausmaß zu systemischen pro-inflammatorischen Prozessen mit sekundären Auswirkungen auf alle wesentlichen Stoffwechselwege. Durch eine parenterale Ernährung (PE) soll der Ernährungszustand stabilisiert und ein fortschreitender Gewichtsverlust verhindert oder reduziert werden. Weitere Ziele sind der Erhalt oder eine Verbesserung der Lebensqualität und eine Erhöhung der Effektivität sowie eine Reduktion von Nebenwirkungen der antitumoralen Therapie. Prinzipiell sind die Indikationen für eine PE bei Tumorpatienten identisch mit den Indikationen bei Patienten mit gutartigen Erkrankungen, wobei bei Tumorpatienten eine orale oder enteralere Nahrungszufuhr immer vor einer PE eingesetzt werden sollte. Bei möglicher oraler oder enteraler Zufuhr ergibt sich ein kombiniertes Ernährungskonzept. Für
The nutritional state influences the clinical outcome

- Reduced nutritional state is associated with unfavourable outcomes and a lower quality of life in patients with malignancies (IIa).

Commentary

Adult tumour patients who have lost weight or are malnourished show an unfavorable outcome in longitudinal studies. The response to antitumor treatment is decreased while treatment-associated side effects are more frequent; physical performance and quality of life are compromised; overall survival is significantly shorter than in patients without weight loss [1], [2], [3], [4], [5], [6], [7], [8], [9], [10], [11]. Cachexia is the most common cause of death in tumour patients other than sepsis [12]. In a recent study body nitrogen content was found to be the strongest predictor for protection against bone marrow toxicity during chemotherapy in patients with breast cancer [13].

The effect of malnutrition on the rate of cure in children with cancer is controversial. While a significantly lower rate of healing is reported in malnourished patients (Ib) [14], [15], [16], [17], [18], there appears to be no influence on patients’ survival (Iia) [19], [20], [21], [22]. These differences depend on the various definitions of malnutrition, the type and extent of the tumour, tumour therapy, supportive measures and the socio-economic status of the family. Malnutrition is known to decrease immune competence (Iia) [23], [24], decrease the tolerance to chemotherapy (Iia) [25] and increase the rate of infection (Iia) [26], [27]. Information on organ dysfunction as a result of malnutrition in children with cancer is scarce. In malnourished children there is an increased risk of cardiomyopathy after the administration of anthracyclines (IV) [28].

Influence of malignancies on energy expenditure

- Patients with active tumours frequently have insufficient food intake (II).

- The resting energy expenditure in cancer patients can be increased, decreased, or remain unchanged in comparison to the predicted value (II).

Commentary

Food intake is lower than the usual even in patients with early stage tumour disease, and there is often a large discrepancy between the actual energy and protein intake and the calculated requirements in advanced tumour stages [10], [29]. In approximately 25% of patients with active tumours, resting energy expenditure (REE), as measured by indirect calorimetry, is more than 10% above, and in another 25% more than 10% below the predicted value. A prediction as to the direction and extent of the deviation is not possible [30], [31]. The mean value of total energy expenditure in cancer patients is similar to that of a healthy reference group [31], [32]. Studies in patients with various tumour entities showed a normal REE in people with stomach or colorectal carcinomas, and an increased REE in patients with pancreatic or bronchial carcinomas [33], [34], [35], [36]. More detailed investigations in patients with advanced bronchial and pancreatic carcinomas revealed an increased REE coupled with diminished physical activity and a slightly lower overall energy expenditure when compared to healthy subjects [35], [36]. Therefore, in adult patients normal energy expenditure should be assumed if the actual resting energy expenditure cannot be measured in individual cases. Formulae (i.e. Harris Benedict, cf. chapter “Energy expenditure and energy intake” (http://www.egms.de/en/gms/2009-7/000084.shtml)) may be used to calculate the normal resting energy expenditure. In patients, the overall energy requirement is also determined by physical activity and may be estimated as 100–120% of REE (cf. chapters “Energy expenditure and energy intake” (http://www.egms.de/en/gms/2009-7/000084.shtml) and “Neonatology/Paediatrics” (http://www.egms.de/en/gms/2009-7/000074.shtml) for children’s energy expenditure). Studies have shown that children with leukaemia have a near normal resting energy expenditure at diagnosis and during anti-cancer treatment [24], [37], [38], [39], [40]. Resting energy expenditure, however, is increased in leukaemic children with large tumour mass [38], and
Malignancies may influence metabolic parameters

Clinically-relevant metabolic changes

Manifest tumours result in varying degrees of systemic pro-inflammatory processes with secondary effects on all significant metabolic pathways [42]. A large body of data suggests that the primary reaction of the tumour-bearing host is to release cytokines, catabolic hormones and other regulatory peptides locally and systemically [42], [43], [44]. The resulting systemic inflammatory reaction contributes significantly to the loss of appetite [45], [46] and weight [47], [48], [49], [50]. These cytokine-induced metabolic changes prevent a recovery of body cell mass [51], and are associated with reduced life expectancy [52] in cachectic patients [52], [53].

Effects on carbohydrate metabolism

• Insulin resistance and increased glucose production can often be detected in tumour patients (II).

Commentary

Impaired glucose tolerance due to insulin resistance is common in tumour patients [54]. The plasma ratio of insulin to catabolic hormones is abnormal with typical findings of increased cortisol secretion and a decreased insulin-cortisol ratio [44], [55]. This results in increased glucose turnover and gluconeogenesis [43]. Concomitant medication with high-dose glucocorticoids intensifies these changes.

Effects on lipid metabolism

• Weight loss in cancer patients is accompanied by a loss of lipid stores and increased serum triglycerides. The ability to oxidise lipids is normal to increased (II).

Commentary

The reasons for changes in lipid metabolism have not yet been clearly determined [44] although increased lipolysis is often observed [56], [57]. Increased [57], [58], [59] or at least normal [60], lipid oxidation is often detectable at the same time, while glucose oxidation is compromised. These observations may support the recommendation to increase the lipids to glucose ratio when composing nutrition for cancer patients.

Effects on protein metabolism

• Protein expenditure is usually increased, resulting in a loss of muscle mass and an increased production of acute phase proteins (II).

Commentary

While the underlying processes are complex, usually increases in overall body protein turnover and in proteolysis are measured [43], [61]. The ATP consuming and ubiquitin-dependent proteolysis system of proteasomes is activated at an early stage [62], [63], [64]. These changes are triggered by inflammatory mediators and, possibly, additional substances released by the tumour [65], [66].

Treatment aims for parenteral nutrition (PN) in cancer patients

• PN should stabilise the nutritional state and prevent or reduce progressive weight loss (C).
• PN should maintain or improve the quality of life (C).
• PN might increase the effectivity and reduce the side-effects of anti-cancer therapies (C).

Commentary

After curative antitumour treatment, PN can enhance survival chances in patients with severe gastrointestinal defects e.g. with radiation enteritis [67]. Due to the accompanying non-specific inflammatory processes in patients with active cancers anabolism usually cannot be achieved by only supplying energy and substrates [44], [50], [51]. According to data collected on body compartments, artificial nutrition results in a stabilisation of or an increase in body weight [68], [69], [70], [71] and body fat mass, while an improvement in lean body or muscle mass is observed only rarely [72]. Numerous studies reported a median overall survival of 50 to 150 days [69], [70], [71], [73], [74], [75], [76], [77], [78] when using PN in patients with advanced cancer and chronic small bowel defects. In the majority of these patients weight [69], [70], [71], and parameters to measure quality of life may be stabilized [69], [70], [71], [75]. The rate of PN-associated infectious complications is between 0.34 and 2.68 per 1000 catheter days [74], [76], [77], [78].

Orreval et al. reported that the provision of home PN was perceived as a positive alternative to progressive weight loss due to the inability to eat in a small group of patients with advanced tumours [79].

Meta-analyses indicate that PN may reduce postoperative complications in malnourished, but not in normally nourished, patients after extensive abdominal surgery [80]. In contrast, only few studies have evaluated the influence of PN on the therapeutic effects of non-surgical oncology. Parenteral nutrition in orally nourished patients undergoing chemotherapy may increase body weight [68].
(Ib), but does not improve anticancer treatment [68], [81] (Ib). The quality of these few studies, however, is restricted by the inhomogeneity of the patient groups and by the inclusion of patients without malnutrition or patients who were able to eat normal amounts of food [81].

**Indication for parenteral nutrition in cancer patients**

Indications for PN in tumour patients are essentially identical to those in patients with benign illnesses. Considering the limited data available in this area [82], [83], [84], [85], [86], [87], [88] the following recommendations are given:

- PN is indicated if oral and enteral food intake [83], [84] provide <500 kcal per day and this is expected to continue for >5 days, or for between 3 and 5 days in case of severe malnutrition, or if oral and enteral food intake reach <60% of calculated requirement and this is expected to last for 10–14 days in adult patients (C).
- PN should be commenced immediately when indicated, and increased to target dosages over 2–4 days if considered necessary (C).
- The amount of PN should supplement oral or enteral nutrition, providing full nutritional requirements in combination (C).
- PN in children is indicated (C):
  - in severe malnutrition
  - in borderline malnutrition and high risk for malnutrition through therapy, etc.
  - when oral food intake is <60% of the energy and protein requirements and there is a high risk for treatment-induced malnutrition, etc.
- PN is used in children if digestion or absorption of food is impaired and it is expected that the patient will require nutritional therapy for at least 7 days. PN should be commenced as soon as possible and continued until the gastrointestinal tract is fully functioning. Regular checks should be carried out if it is expected that the patient will require a nutrition therapy for less than 7 days (C).

**Commentary**

In tumour patients, who are not able to eat, digest or absorb foods, the nutritional state may be maintained or increased to target dosages over 2–4 days if considered necessary (C). The amount of PN should supplement oral or enteral nutrition, providing full nutritional requirements in combination (C).

Volume and substrate quantities in parenteral nutrition of cancer patients

- **Energy** expenditure is usually comparable to that of healthy subjects; only rarely is it necessary to supply daily energy exceeding 35 kcal per kg body weight (C) (for children’s intake, cf. chapter “Neonatology/Paediatrics” [http://www.egms.de/en/gms/2009-7/000074.shtml]).
- A daily **amino acid** supply of 1.2 to 1.5 g per kg body weight is usually appropriate in cancer patients (C) (for the appropriate dose for children, cf. chapter “Neonatology/Paediatrics” [http://www.egms.de/en/gms/2009-7/000074.shtml]).
- There is no agreement on an ideal ratio of **lipids** and carbohydrates; the proportion of lipids can be above 35% of the overall energy intake without disadvantages (C).
- **Glucose** should be the preferred parenteral carbohydrate (B).
• Micronutrients should be supplied in sufficient amounts; this should not be less than the iv doses recommended for healthy persons (C).

• Monitoring of PN should be carried out following the usual protocol for all PN patients (C).

Commentary

There are generally no accepted standards for the optimal energy and nutrient intake in oncological patients, particularly when artificial nutrition is administered exclusively. The energy intake should be adapted to the potentially increased energy requirements and the level of physical activity. Total energy expenditure of cancer patients was measured to be comparable to that of healthy subjects, even though REE was increased in cancer patients [30]. The cause of this is perhaps an adaptive decrease in physical activity in metabolically altered cancer patients [36]. The basis for dosing macro- and micronutrients currently remains the same as for healthy persons. There is no indication that an intake of protein above the normal dose (max. 1.5 g protein/kg body weight) has an antitumoral effect in oncological patients [109].

Tumour patients show increased lipid oxidation and utilisation of exogenously administered lipids [58]. Tumour cells preferentially utilise glucose for their energy requirements while healthy tissues display high lipid oxidation [110]. Therefore, it is recommended to increase the proportion of lipids to over 35% of the total energy supply in the nutrition of oncological patients [58]. More recent studies, however, showed that post-absorptive glucose turnover of malignant tissues is high and does not increase during an intravenous glucose infusion [111]; thus, the theoretical benefit of lipid over glucose solutions may be clinically irrelevant.

Metabolic and immunological effects of various lipid solutions (LCT, MCT) have been compared mainly in surgical environments. The postulated benefit of medium-chained triglycerides (MCT) over long-chained triglycerides (LCT) could not be established in various clinical studies [112], [113]. There are no data in cancer patients undergoing radiotherapy or chemotherapy substantiating benefits of more recently developed parenteral lipid emulsions, with increased contents of n-9 or n-3 fatty acids. Attention should be given to providing a sufficient supply of micronutrients. The recommendations for intake in other patient population should be followed (cf. chapter “Water, electrolytes, vitamins and trace elements” (http://www.egms.de/en/gms/2009-7/000080.shtml)). There are no data supporting a clinical advantage of very high doses of micronutrients.

Special substrates

• The provision of special substrates such as glutamine, arginine, taurine, branched-chain amino acids or n-3 fatty acids is not recommended due to lack of convincing data supporting their use (C).

Commentary

Glutamine has been studied as a possible oral supplement to reduce toxic side-effects of radiation or chemotherapy [114]. Parenteral glutamine has been used in haematopoietic stem cell transplantations (HSCT). Findings to date are inconsistent. In a randomized study of patients after allogeneic HSCT Ziegler et al. showed a significantly improved nitrogen balance, reduced infection rate and shorter length of stay (LOS) for patients supplemented with glutamine (0.57 g/kg/d) compared a control group on an isonitrogenic and isocaloric diet (Ib) [115]. In a randomized follow-up study these data, however, could only be repeated with respect to a reduction in LOS (Ib) [116]. In a later study, the same working group was not able to document any advantage of parenteral glutamine (0.57 g/kg/d) in a similar clinical situation [117] (Ib).

In a further randomised study patients after HSCT receiving 3–4 weeks of glutamine-enriched PN showed significant increases in total lymphocyte counts, T-lymphocytes, CD4 and CD8 cells, while the clinical outcome was unchanged [118] (Ib). In a randomised study in patients after autologous HSCT, high daily doses of intravenous alanyl-glutamine dipeptide (30 g glutamine) resulted in increased relapse and mortality rates as well as increased costs [119] (Ib).

One randomised study, which highlighted the possible protective role of glutamine infusions on hepatic functions during HSCT justifies further studies, especially with a focus on the prevention of veno-occlusive disease [120] (Ib).

In hematological patients undergoing intensive chemotherapy supplementation with glutamine dipeptide had no effect on hematological parameters or clinical toxicity; the glutamine group, however, showed significantly more weight gain during the study period [121].

In a randomised study of patients with acute myeloid leukaemia requiring PN supplementation with glutamine (20 g) resulted in a more rapid recovery of neutrophils after myelosuppressive chemotherapy, but no reduction in the incidence of neutropenic fever and no improvement in other immunological parameters [122] (Ib).

According to the current ASPEN guidelines [123], there is no indication for the administration of pharmacological doses of glutamine in patients after HSCT. Other recent recommendations agree with this [124].

There is only scarce evidence concerning other special substrates; particularly, there are no relevant data on the parenteral use of n-3 fatty acids.
Indications for parenteral nutrition during radiotherapy

- PN should not be used as a general accompaniment of radiotherapy (B), but PN is indicated if sufficient enteral intake cannot be achieved (B).
- PN is indicated in chronic severe radiation enteritis (C).

Commentary

During the last 10 years no prospective randomised studies have been published on the use of PN as an accompaniment to radiotherapy. So far it has not been demonstrated that routine PN during radiotherapy or radio-chemotherapy improves prognosis [81], [125], [126]. During radiation treatment, especially when treating head and neck areas, whenever possible, sufficient enteral nutrition should be supplied including the use of sip feeds or enteral tube feeding [109], [125], [127], [128].

PN is indicated if sufficient enteral nutrition is not possible, e.g., as a result of acute radiation enteritis; if nutritional deficits exist and radiation is intended to cover the upper gastrointestinal tract such that an intended PEG would need to be placed within the radiation field; and during neoadjuvant treatment, if insertion of a PEG system is not recommended, e.g., in oesophageal resections and planned gastric interposition. Chronic radiation enteritis develops in approx. 5% of cases subjected to abdominal radiation; this may be accompanied by intestinal failure, fistulae, perforation or chylosus ascites and these cases frequently require long-term PN [67], [129], [130], [131], [132].

No benefit of special parenteral substrates such as glutamine has been established for radiotherapy procedures.

Indications for parenteral nutrition during chemotherapy

- The indications for PN during chemotherapy are not different from general indications in malignant diseases. Routine PN therapy as an accompaniment to chemotherapy is not indicated (B).

Commentary

In 1990 McGeer et al. published a meta-analysis on the use of PN during chemotherapy (Ia) [133]. They reported that PN is associated with a trend towards shorter survival and reduced tumour response. They concluded that routine PN is not advisable in patients undergoing chemotherapy. Klein and Koretz analysed 18 randomised studies with clinically relevant end points on the effect of PN in patients treated with chemotherapy. They concluded that there were no evident advantages of PN with regards to overall survival, tumour responses and toxicity of chemotherapy, but there was an increased rate of infection in those receiving PN (lb) [81].

It is difficult to draw reliable conclusions from the existing data due to serious flaws in most study designs, such as insufficient number of patients treated, inclusion of extremely inhomogeneous patient groups, large variability of the nutrient solutions used, large variability of antitumor therapies, and inclusion of patients who were not suffering from malnutrition as well as patients who maintained normal oral food intake [81]. Randomised studies, i.e. by De Cicco et al, which differentiated between normal and malnourished patients undergoing chemotherapy, were able to detect an improvement in the nitrogen balance in severely malnourished patients while no effect was seen in patients without malnutrition [134] (Ib).

Recent recommendations by the American Gastroenterological Association (AGA) and the American Society for Parenteral and Enteral Nutrition (ASPEN) have come to similar conclusions. The AGA report reviewed 19 randomised studies and concluded that PN had no influence on the survival of patients who were treated with chemotherapy or radiation treatment, although a positive influence may be possible after bone marrow transplants. Accompanying PN has an unfavourable effect on other parameters in patients treated for chemotherapy, radiotherapy or bone marrow transplants, mainly an increase in infectious complications and a decrease of the response to chemotherapy (lb) [85].

The ASPEN recommendations specify that PN as routine accompaniment of chemotherapy is not justified and potentially dangerous due to the increased risk of infection. It is pointed out, however, that PN should be offered to patients who are malnourished and who are unable to absorb sufficient nutrients over a long time period [135].

Regarding all published recommendations it is important to note that all randomised studies on which they are based were performed more than 10 years ago and that many are flawed as mentioned above. More recent studies report fewer complications of long-term PN [67], [76], [77], [78], [136], [137], suggesting that the benefits and risks of PN administration during chemotherapy should be reviewed again in the near future.

Indications for parenteral nutrition during autologous/allogeneic stem cell transplantation

- PN is required only in selected patients after autologous transplantations, while after allogeneic transplantation PN is usually required in most patients and for prolonged time periods due to the development of pronounced mucositis and GvH-related gastrointestinal damage (C).
- Particular attention must be paid to the increased risk of bleeding and infection associated with PN (C).
Indications for parenteral nutrition independent of antitumor therapies in incurable cancer patients

- If food intake is insufficient survival of patients in advanced cancer stages may be compromised more by inadequate nutrition than by the underlying illness (C).
- Long-term PN should be initiated if intestinal absorption is severely impaired and if allof the following 4 criteria are fulfilled (C):
  1. enteral nutrition is insufficient to maintain nutritional state,
  2. the expected survival is more than 4 weeks,
  3. PN is expected to stabilise or improve quality of life,
  4. the patient explicitly wishes to receive PN.

Commentary

Oncological treatments today may allow patients with incurable cancer disease to survive up to a point at which further survival is significantly affected the nutritional state [153]. An inadequate oral or enteral intake results in progressive weight loss and impaired clinical outcome (see: The nutritional state influences the clinical outcome). Randomised studies on the value of PN appear unethical in these situations [87]. Despite a lack of effective antitumor treatment options, patients with advanced cancers may have a life expectancy of several weeks or months. If the expected survival exceeds 2 to 3 months (e.g. the period of survival in total starvation [154], [155], [156]), it can be reasonably assumed that PN will lengthen the survival of a patient who does not tolerate enteral nutrition [87]. In this situation

Commentary

In patients after autologous transplantations impaired food intake is usually of short duration (2–3 weeks). Nutritional problems in allogenic transplant patients usually are more severe and prolonged. Thus, there is no need for routine PN after autologous transplantations, but PN may be necessary if complications develop such as prolonged mucositis [138]. After allogenic transplantations, PN is routinely administered in most transplantation centres [138]. In 1987 Weisdorf et al. showed that prophylactic standardised PN significantly improved survival three years after HSCT [106]. The control group received only minerals and vitamins intravenously until a reduced nutritional state was detected. Because patients receiving early PN had a lower relapse rate, it was speculated that the better overall survival observed might have been caused by a possible positive effect of PN on transplant function, resulting e.g. in an increased graft versus leukaemia effect.

Enteral nutrition is not well tolerated in most cases after complete conditioning regimens [139]; if tolerated, however, enteral nutrition in patients with a functioning gastrointestinal tract has effects on nutritional status that are comparable to those of PN [124], [140] [141] (lb). The French Federation of Cancer Centres, as well as the authors of a review of relevant randomised studies recommend enteral nutrition as the primary approach in non-myeloablative conditioning, and PN only in cases of gastrointestinal complications [141]. It has been recommended to initiate PN when oral or enteral food intake provides less than 50–60% of calculated requirements [67], [141].

American and French panels on gastroenterology and nutrition emphasize that all HSCT patients carry a high nutritional risk and should, therefore, be monitored regularly for nutritional deficits before and after transplantation [123], [141].

A small randomised study has observed that a high dose of lipid (lipid:glucose ratio 80:20) after allogenic transplantation lowered the incidence of lethal acute graft–versus-host disease and hyperglycaemia [142]. This study has yet to be confirmed.

Certin et al. [143] reported that supplying total rather than partial PN after autologous transplantation resulted in a delayed rise in thrombocytes. At the same time, there were more cases of infection and hyperglycaemia associated with total PN as compared to partial PN, whilst a drop in the level of albumin was prevented. The study was not randomized and patients receiving total PN may have been more severely ill. The observation, however, may support the recommendation not to provide total PN as a standard treatment after autologous transplantations.

In children an autologous blood stem cell transplantation usually has only a low impact on nutritional status (III) [144], [145]. Thus, a targeted nutritional therapy should be based primarily on the above-mentioned criteria (see: Indication for PN in cancer patients) or be initiated if a conditioning therapy is chosen, which is associated with a high risk for severe mucositis.

In allogenic transplantations the criteria for using PN are usually given, and PN has been shown to have positive effects on maintaining the body weight [146], [147] (lb). Enteral nutrition is possible in many cases and then is as effective as PN. In a study by Hopman et al., enteral tube feeding was possible during 50% of the study period, although it could be used as the sole form of nutrition only in 3 of 12 children [148] (lb). In a retrospective analysis, Langdana et al. reported on their positive experiences and the high patient acceptance rate for a similar concept with the preferential use of enteral nutrition [149] (III).

In all cases the risks of enteral tube feeding (aspiration, bleeding, diarrhoea, sinusitis, intestinal perforation) should be weighed against the risks of PN (catheter sepsis and metabolic complications).

In most cases it appears to be sufficient to restrict the amount of energy provided to be slightly more than the resting energy expenditure (see: Influence of malignancies on energy expenditure) [150], [151], [152].

There are no generally accepted indications for the use of glutamine (see Special substrates).

4/14
PN, by providing essential nutrition, constitutes a basic care rather than a medical therapy [87], [157]. Specialised centres providing long-term PN to patients with advanced cancer disease report a median survival period of 2–5 months [69], [70], [71], [73], [74], [75], [76], [77], [78]. This means that a large proportion of patients cared for in this manner have a longer period of survival than that assumed for conditions of complete starvation. Weight stabilisation was successful in a majority of patients [69], [70], [71].

Quality of life scores are poorer in parenterally nourished cancer patients than in healthy subjects undergoing PN; cancer patients are further burdened by accompanying depressions and opioid requirements [158]. PN, however, may stabilise parameters determining quality of life [69], [70], [71]. Orrel et al. reported that the provision of PN was perceived as a positive alternative to progressive weight loss by a small group of patients with advanced tumours and their relatives [79]. Since the benefits of PN can only have an impact when life expectancy is impaired more by insufficient food intake than by the tumour itself, several expert groups recommend considering PN when the expected survival is at least 4 weeks [135] or 2–3 months depending on the tumour [85], [87], [159], [160]. No advantage of PN should be expected when survival is shorter.

It is extremely difficult to estimate the life expectancy of a cancer patient and, hence, the possible advantages of artificial nutrition. These patients should, therefore, be seen and evaluated cooperatively by their consultant oncologist, the nutrition specialist and the palliative care consultant in order to design a treatment plan that is in agreement with the patients expectations and wishes.

Parenteral nutrition in terminally ill patients

- No PN is necessary in dying patients (B).
- The occurrence of agitated confusion induced by dehydration can be controlled by parenteral infusion of saline solutions (or the appropriate paediatric solutions, respectively) (B).

Commentary

During the phase of dying the most important aims of treatment and care are the alleviation of agonising discomfort and the feelings of thirst and hunger. Fluids and nutrition are part of the basic care; however, the patient needs to consent to such offers [157]. Most patients do not feel hungry in the terminal phase of life and only require minimal quantities of fluid [161]. It is counterproductive since it may strain the patient severely and thus it should be avoided at all cost to continue standardised infusion regimens into the terminal phase without further consideration [162]. Regulation of fluid balance should be observed closely. Both dehydration, induced by diuretics or limited drinking, and hyperhydration caused by infusions can have adverse affects on a person’s well-being. The “dry mouth” is one of the main symptoms of the dying [163]. However, thirst and “dry mouth” do neither correlate with the degree of hydration [164] nor with the volume of intravenous infusion [165]. Terminal patients appear to receive too much fluid in general [162], increasing the risks for peripheral oedema, ascites, pleural effusions and the development of a pulmonary oedema.

Dehydration can result in drying of the mucous membranes with subsequent injuries and infections [163], it reduces alertness and promotes the occurrence of restlessness and confusion [166], thus contributing to the burden of the patients and their relatives [167]. Retrospective studies provided evidence that intravenous fluids may reduce neuropsychiatric symptoms like sedation, hallucinations, myoclonus and agitation [168], [169]. A randomised trial in dehydrated terminal cancer patients could show that subjective discomfort was significantly improved with the infusion of 1000 ml per day as compared to no infusions and only minimal oral fluid intake of 100 ml per day [170]. Recommendations for terminal care, therefore, emphasize that fluid intake should always be prescribed on an individual basis and should target the prevention of intolerable symptoms. Fluid quantities of 1000 ml per day are recommended in symptomatic dehydration [170], [171]; in children this corresponds to supplying approx. 50% of the daily fluid requirements.

Notes

This article is part of the publication of the Guidelines on Parenteral Nutrition from the German Society for Nutritional Medicine (overview and corresponding address under http://www EGMS DE EN GMS 2009 7 000086 shtml).

English version edited by Sabine Verwied Jorky, Rashmi Mittal and Berthold Koletzko, Univ. of Munich Medical Centre, Munich, Germany.

References

1. Tubiana M, Attié E, Flamant R, Gérard-Marchant R, Hayat M. Prognostic factors in 454 cases of Hodgkin’s Disease. Cancer Res. 1971;31(11):1801-10.
2. Swenerton KD, Legha SS, Smith T, Hortobagyi GN, Gehan EA, Yap HY, Gutterman JU, Blumenschein GR. Prognostic factors in metastatic breast cancer treated with combination chemotherapy. Cancer Res. 1979;39(5):1552-62.
3. DeWys WD, Begg C, Lavin PT, et al. Prognostic effect of weight loss prior to chemotherapy in cancer patients. Am J Med. 1980;69(4):491-7. DOI: 10.1016/S0149-2918(05)80001-3
4. Van Eys J. Effect of nutritional status on response to therapy. Cancer Res. 1982;42(2 Suppl):747s-53.
5. Pedersen H, Hansen HS, Cederqvist C, Lober J. The prognostic significance of weight loss and its integration in stage-grouping of oesophageal cancer. Acta Chir Scand. 1982;148(4):363-6.
6. Bruning PF, Egger RJ, Gooskens AC, et al. Dietary intake, nutritional status and well-being of cancer patients: a prospective study. Eur J Cancer. 1985;21(12):1449-59. DOI: 10.1016/0277-5379(85)90237-8.

7. Padilla GV. Psychological aspects of nutrition and cancer. Surg Clin North Am. 1986;66(6):1121-35.

8. Andreou HJN, Norman AR, Oates J, Cunningham D. Why do patients with weight loss have a worse outcome when undergoing chemotherapy for gastrointestinal malignancies? Eur J Cancer. 1998;34(4):503-9. DOI: 10.1016/S0959-8049(97)10909-9.

9. Argiris A, Lj Y, Forastiere A. Prognostic factors and long-term survival in patients with recurrent or metastatic carcinoma of the head and neck. Cancer. 2004;101(10):2222-9. DOI: 10.1002/cncr.20640.

10. Ravasco P, Monteiro-Grillo I, Vidal PM, Camilo ME. Cancer; disease and nutrition are key determinants of patients’ quality of life. Supp Care Cancer. 2004;12(4):246-52. DOI: 10.1007/s00520-003-0568-z.

11. Ross PJ, Ashley S, Norton A, et al. Do patients with weight loss have a worse outcome when undergoing chemotherapy for lung cancers? Br J Cancer. 2004;90:1905-11. DOI: 10.1038/sj.bjc.6601781.

12. Warren S. The immediate causes of death in cancer. Am J Med Sci. 1932;184:610-5. DOI: 10.1097/00000441-193211000-00002.

13. Aslani A, Smith RC, Allen BJ, Paviakis N, Levi JA. The predictive value of body protein for chemotherapy-induced toxicity. Cancer. 2000;88(4):796-803. DOI: 10.1002/(SICI)1097-0142(20000215)88:4<796::AID-CNCR10>3.0.CO;2-P.

14. Donaldson SS, DeWys WD, Suskind RM, Jaffe N, van Eys J. A study of the nutritional status of pediatric cancer patients. Am J Dis Child. 1981;135(12):1107-12.

15. Rickard KA, Detamore CM, Grosfeld JL, Kirksey A, Ballantine TV, Baehner RL. Effect of nutrition staging on treatment delays and outcome in Stage IV neuroblastoma. Cancer. 1983;52(4):587-98. DOI: 10.1002/1097-0142(19830815)52:4<587::AID-CNCR10>3.0.CO;2-T.

16. Lobato-Mendizabal E, Ruiz-Arguelles GJ, Marín-Lopez A. Leukaemia and nutrition: I. Malnutrition is an adverse prognostic factor in the outcome of treatment of patients with standard-risk acute lymphoblastic leukaemia. Leuk Res. 1989;13:899-906. DOI: 10.1016/0145-2126(89)9043-X.

17. Viana MB, Murao M, Ramos G, et al. Malnutrition as a prognostic factor in lymphoblastic leukaemia: a multivariate analysis. Arch Dis Child. 1994;71:304-10. DOI: 10.1136/adc.71.4.304.

18. Mejia-Aranguie JM, Fajardo-Gutierrez A, Reyes-Ruiz NI, et al. Malnutrition in childhood lymphoblastic leukaemia: a predictor of early mortality during the induction-to-remission phase of treatment. Arch Med Res. 1999;30:150-3. DOI: 10.1016/S0142-0100(99)0026-6.

19. Weir J, Reilly JJ, McColl JH, Gibson BE. No evidence for an effect of nutritional status at diagnosis on prognosis in children with acute lymphoblastic leukaemia. J Pediatr Hematol Oncol. 1998;20(6):534-8. DOI: 10.1097/00043426-199811000-00004.

20. Pedrosa F, Bonilla M, Liu A, et al. Effect of malnutrition at the time of diagnosis on the survival of children treated for cancer in El Salvador and Northern Brazil. J Pediatr Hematol Oncol. 2000;22(6):502-5. DOI: 10.1097/00043426-200011000-00005.

21. Wessels G. Nutrition, morbidity and survival in South African children with Wilms tumor. J Pediatr Hematol Oncol. 1999;16(4):321-7. DOI: 10.1080/088800199277146.

22. Yaris N, Akyüz C, Coskun T, Kutuk T, Büyükmumcuş M. Nutritional status of children with cancer and its effects on survival. Turk J Pediatr. 2002;44(1):35-9.

23. Rickard KA, Grosfeld JL, Kirksey A, Ballantine TV, Baehner RL. Reversal of protein-energy malnutrition in children during treatment of advanced neoplastic disease. Ann Surg. 1979;190(6):771-81. DOI: 10.1097/00000658-197912000-00018.

24. Picton SV. Aspects of altered metabolism in children with cancer. Int J Cancer Suppl. 1998;78(1):624-4. DOI: 10.1002/(SICI)1097-0215(1998)78:11<624::AID-IJC17>3.0.CO;2-V.

25. Halton JM, Scissons-Fisher CC. Impact of nutritional status on morbidity and dose intensity of chemotherapy during consolidation therapy in children with acute lymphoblastic leukaemia. J Pediatr Hematol Oncol. 1999;21(4):317. DOI: 10.1097/00043442-199907000-00052.

26. Hughes WT, Price RA, Sisko F, et al. Protein-calorie malnutrition; a host determinant for Pneumocystis carinii infection. Am J Dis Child. 1974;124:44-52.

27. Taj MM, Pearson AD, Mumford DB, Price L. Effect of nutritional status on the incidence of infection in childhood. Pediatr Hematol Oncol. 1993;10(3):283-7. DOI: 10.3109/08880019309029498.

28. Obama M, Gargir A, van Eys J. Nutritional status and anthracycline cardiotoxicity in children. South Med J. 1983;76(5):577-8.

29. Bosause J, Daneryd P, Svanberg E, Lundholm K. Dietary intake and resting energy expenditure in relation to weight loss in unselected cancer patients. Int J Cancer. 2001;93(3):380-3. DOI: 10.1002/jic.1332.

30. Knox LS, Crosby LO, Feurer ID, Buzby GP, Miller CL, Mullen JL. Energy expenditure in malnourished cancer patients. Ann Surg. 1983;197(1):152-61. DOI: 10.1097/00000658-198302000-00006.

31. Dempsey DT, Feurer ID, Knox LS, Crosby LO, Buzby GP, Mullen JL. Energy expenditure in malnourished gastrointestinal cancer patients. Cancer. 1984;53(6):1265-73. DOI: 10.1002/1097-0142(19840315)53:6<1265::AID-CNCR2820530609>3.0.CO;2-2.

32. Dempsey DT, Knox LS, Mullen JL, Miller CL, Feurer ID, Buzby GP. Energy expenditure in malnourished patients with colorectal cancer. Arch Surg. 1986;121:789-95.

33. Hansell DT, Davies JW, Burns HJ. Effects of hepatic metastases on resting energy expenditure in patients with colorectal cancer. Br J Surg. 1986;73(8):659-62. DOI: 10.1002/bjs.1800730828.

34. Fredrix EW, Soeters PB, Wouters EF, Deerenberg IM, von Meyenberg MF, Saris WH. Effect of different tumor types on resting energy expenditure. Cancer Res. 1991;51(22):6138-41.

35. Gibney E, Elia M, Jebb SA, Murgatroyd P, Jennings G. Total energy expenditure in patients with small-cell lung cancer: results of a validated study using the bicarbonate-urea method. Metabolism. 1997;46(12):1412-7. DOI: 10.1016/S0026-0495(97)90140-2.

36. Moses AW, Slater C, Preston T, Barber MD, Fearon KC. Reduced energy expenditure in patients with pancreatic cancer can be modulated by an energy and protein dense oral supplement enriched with n-3 fatty acids. J Pediatr Gastroenterol Nutr. 1997;24(6):585-9. DOI: 10.1097/00005123-199712000-00004.

37. Kim CL, Camitta BM. Close association of accelerated rates of whole body protein turnover (synthesis and breakdown) and energy expenditure in children with newly diagnosed acute lymphoblastic leukemia. J Pediatr Gastroenterol Nutr. 1987;11(2):129-34. DOI: 10.1177/0148607187011001219.
105. UICC Workshop. Nutritional morbidity in children with cancer: Mechanisms, measures and management. Int J Cancer. 1998;78(Suppl 1):I-92.

106. Weisdorf SA, Lyne J, Wind D, Haake RJ, Sharp HL, Goldman A, Schissel K, McGlave PB, Ramsay NK, Kersey JH. Positive effect of prophylactic total parenteral nutrition on long-term outcome of bone marrow transplantation. Transplantation. 1987;43(6):833-8.

107. Christensen ML, Hancock ML, Gattuso J, Hurwitz CA, Smith C, McCormick J, Miro J Jr. Parenteral nutrition associated with increased infection rate in children with cancer. Cancer. 1993;72(9):2732-8. DOI: 10.1002/1097-0142(19931101)72:9-2732:AID-CNCR282072934-3.0.CO;2-E

108. Bakish J, Hargrave D, Tariq N, Laperriere N, Rutka JT, Bouffet E. Evaluation of dietetic intervention in children with medulloblastoma or supratentorial primitive neuroectodermal tumors. Cancer. 2003;89(5):1014-20. DOI: 10.1002/cncr.11598

109. Nitenberg G, Raynard B. Nutritional support of the cancer patient: issues and dilemma. Crit Rev Oncol Hematol. 2000;34(3):137-68. DOI: 10.1016/S1040-8428(00)00048-2

110. Holm E, Hagnmüller E, Staedt U, Schloerb PR, Skikne BS. Oral and parenteral glutamine in bone marrow transplantation. J Parenter Enteral Nutr. 1999;23(3):117-22. DOI: 10.1177/0148607199023003177

111. Bozzetti F, Gavazzi C, Mariani L, Crippa F. Glucose-based total parenteral nutrition does not stimulate glucose uptake by human tumors. Clin Nutr. 2004;23(3):417-21. DOI: 10.1016/j.clnu.2003.09.012

112. Ulrich H, Pastores SM, Katz DP. Parenteral use of medium-chain triglycerides: a reappraisal. Nutrition. 1996;12(4):231-8. DOI: 10.1016/S0899-9007(96)00089-6

113. Ziegler TR, Young LS, Benfell K, Scheltinga M, Hortos K, Bye R, Savarese DM, Savy G, Vahdat L, Wischmeyer PE, Corey B. Metabolic efficacy of glutamine-supplemented parenteral nutrition after bone marrow transplantation. A randomized, double-blind, controlled study. Ann Intern Med. 1993;116(10):821-8.

114. Savarese DM, Savay G, Vahdat L, Wischmeyer PE, Corey B. Prevention of chemotherapy and radiation toxicity with glutamine. Cancer Treat Rev. 2003;29(6):501-13. DOI: 10.1016/S0305-7372(03)00133-6

115. Ziegler TR, Young LS, Benfell K, Scheltinga M, Hortos K, Bye R, Morrow FD, Jacobos DO, Smith RJ, Antin JH, et al. Clinical and metabolic efficacy of glutamine-supplemented parenteral nutrition after bone marrow transplantation. A randomized, double-blind, controlled study. Ann Intern Med. 1992;116(10):821-8.

116. Schroer PR, Amare M. Total parenteral nutrition with glutamine in bone marrow transplantation and other clinical applications (a randomized, double-blind study). JPEN J Parenter Enteral Nutr. 1993;17(5):407-13. DOI: 10.1177/0148607193017005407

117. Schroer PR, Skikne BS. Oral and parenteral glutamine in bone marrow transplantation: a randomized, double-blind study. JPEN J Parenter Enteral Nutr. 1999;23(3):147-22. DOI: 10.1177/0148607199023003117

118. Ziegler TR, Bye RL, Persinger RL, Young LS, Antin JH, Wilmore DW. Effects of glutamine supplementation on circulating lymphocytes after bone marrow transplantation: a pilot study. Am J Med Sci. 1998;315(1):4-10. DOI: 10.1097/00000441-199801000-0002

119. Pytlík R, Benes P, Patorková M, Chocenská E, Gregora E, Procházka B, Kozák T. Standardized parenteral alanine-glutamine dipeptide supplementation is not beneficial in autologous transplant patients: a randomized, double-blind, placebo controlled study. Bone Marrow Transplant. 2002;30(12):953-61. DOI: 10.1038/sj.bmt.1703759

120. Brown SA, Goringe A, Fegan C, Davies SV, Giddings J, Whittaker JA, Burnett AK, Poynton CH. Parenteral glutamine protects hepatic function during bone marrow transplantation. Bone Marrow Transplant. 1998;22(3):281-4. DOI: 10.1038/sj.bmt.1701321

121. Van Zaane HC, van der Leele H, Timmer JG, Fürst P, Sauerwein HP. Parenteral glutamine dipeptide supplementation does not ameliorate chemotherapy-induced toxicity. Cancer. 1994;74(10):2879-84. DOI: 10.1002/1097-0142(19941115)74:10<2879::AID-CNCR2820741122>3.0.CO;2-H

122. Scheid C, Hermann K, Kremmer G, Holsing A, Heck G, Fuchs M, Waldschmidt D, Herrmann HJ, Söhngen D, Diehl V, Schwenk A. Randomized, double-blind, controlled study of glycyl-glutamine-dipeptide in the parenteral nutrition of patients with acute leukemia undergoing intensive chemotherapy. Nutrition. 2004;20(3):249-54. DOI: 10.1016/j.nut.2003.11.018

123. ASPEN Board of Directors and the Clinical Guidelines Task Force. Specific guidelines for disease – adults: Cancer – hematopoietic cell transplantation. JPEN J Parenter Enteral Nutr. 2002;26:83SA-85SA.

124. Arfons LM, Lazarus HM. Total parenteral nutrition and hematopoietic stem cell transplantation: an expensive placebo? Bone Marrow Transplant. 2005;36(4):281-8. DOI: 10.1038/sj.bmt.1709039

125. Fietkau R. Principles of feeding cancer patients via enteral or parenteral nutrition during radiotherapy. Strahlenther Onkol. 1998;174 Suppl 3:47-51.

126. Body JJ. Metabolic sequelae of cancers (excluding bone marrow transplantation). Curr Opin Clin Nutr Metab Care. 1999;2(4):339-44. DOI: 10.1097/00075197-199907000-00016

127. Celaya Pérez S, Valero Zanuy MA. [Nutritional management of oncological patients]. Nutr Hosp. 1999;14 Suppl 2:43S-52S.

128. Schattner MA, Willis HJ, Raykher A, Brown P, Quesada O, Scott B, Shike M. Long-term enteral nutrition facilitates optimization of body weight. JPEN J Parenter Enteral Nutr. 2005;29(3):198-203. DOI: 10.1177/0148607105029003198

129. Miller DG, Ivey M, Young J. Home parenteral nutrition in treatment of severe radiation enteritis. Ann Intern Med. 1979;91(6):858-60.

130. Lavery IC, Steiger E, Fazio W. Home parenteral nutrition in management of patients with severe radiation enteritis. Dis Colon Rectum. 1980;23(2):91-3. DOI: 10.1007/BF02587600

131. Lentz SS, Schray MF, Wilson TO. Cylous ascites after whole-abdomen irradiation for gynecologic malignancy. Int J Radiat Oncol Biol Phys. 1990;19(2):435-8.

132. Silvain C, Besson I, Ingrand P, Beau P, Matuchansky C, Carretier M, Morichau-Beauchant M. Long-term outcome of small bowel resection for gynecologic malignancies. Int J Gynecol Cancer. 1998;8(4):373-9. DOI: 10.1089/0890084002600399

133. McGeer AJ, Detsky AS, O'Rourke K. Parenteral nutrition in cancer patients undergoing chemotherapy: effects on toxicity and nutritional status. JPEN J Parenter Enteral Nutr. 1993;17(6):513-8. DOI: 10.1177/0148607193017006513

134. ASPEN Board of Directors and the Clinical Guidelines Task Force. Specific guidelines for disease - adults: cancer. JPEN J Parenter Enteral Nutr. 2002;26:83SA-85SA.
136. Bozzetti F, Mariani L, Bertinet DB, Chiavenna G, Crose N, De Cicco M, Gigli G, Micklewright A, Moreno Villares JM, Orban A, Pertkiewicz M, Pironi L, Vilas MP, Prins F, Thul P. Central venous catheter complications in 447 patients on home parenteral nutrition: an analysis of over 100,000 catheter days. Clin Nutr. 2002;21(6):475-85. DOI: 10.1054/cinu.2002.0578

137. Ireton-Jones C, DeLegge M. Home parenteral nutrition registry: a five-year retrospective evaluation of outcomes of patients receiving home parenteral nutritional support. Nutrition. 2005;21(2):156-60. DOI: 10.1016/j.nut.2004.04.024

138. Muscaritoli M, Grieco G, Capria S, Iori AP, Rossi Fanelli F. Nutritional and metabolic support in patients undergoing bone marrow transplantation. Am J Clin Nutr. 2002;75(2):183-90.

139. Herrmann VM, Petruska PJ. Nutrition support in bone marrow transplantation. Bone Marrow Transplant. 2001;27(7):741-6. DOI: 10.1038/sj.bmt.1702855

140. Szeluga DJ, Stuart RK, Brookmeyer R, Utermohlen V, Santos GW. Effects of different parental nutrition regimens in patients undergoing autologous bone marrow transplantation. Transplantation. 1998;66(5):610-6. DOI: 10.1097/00007890-199809150-00011

141. Raynard B, Nitenberg G, Gory-Delabaere G, Bourhis JH, Bachmann P, Bensadoun RJ, Desport JC, Kere D, Schneider S, Senesse P, Bordigoni P, Dieu L; FNCLCC. Summary of the Standards, Options and Recommendations for nutritional support in patients undergoing bone marrow transplantation (2002). Br J Cancer. 2003;89 Suppl 1:5101-6. DOI: 10.1038/sj.bjc.6601091

142. Muscaritoli M, Conversano L, Torelli GF, Arcese W, Capria S, Cangiano C, Falcone C, Rossi Fanelli F. Clinical and metabolic effects of different parental nutritional support in patients undergoing autologous bone marrow transplantation. Bone Marrow Transplant. 1996;8(1):19-27. DOI: 10.1038/sj.bmt.1702855

143. Cetin T, Arpaci F, Dere Y, Turan M, Oztürk B, Kömürcü S, Ozet A, Beyzadeoğlu M, Kaptan K, Beyan C, Yalçin A. Total parenteral nutrition: an analysis of over 100,000 catheter days. Clin Nutr. 2005;24(6):475-85. DOI: 10.1054/clnu.2005.0578

144. Kajiume T, Yoshimi S, Kobayashi K, Kataoka N. Nutritional assessment of peripheral blood stem cell transplantation in children. Pediatr Hematol Oncol. 2000;17(5):389-92. DOI: 10.1080/08880010050034328

145. Pedrón C, Madero L, Madero R, García-Novó MD, Díaz MA, Hernández M. Short-term follow-up of the nutritional status of children undergoing autologous peripheral blood stem cell transplantation. Pediatr Hematol Oncol. 2000;17(7):559-66. DOI: 10.1080/088800100500122925

146. Yokoyama S, Fujimoto T, Mitomi T, Yabe M, Yabe H, Kato S. Use of total parenteral nutrition in pediatric bone marrow transplantation. Nutrition. 1989;5(1):27-30.

147. Udoto C, Rogelli A, Bonomi M, Femia L, Piromano L, Masera G. Total parental nutrition and nutritional assessment and leukaemic children undergoing bone marrow transplantation. Eur J Cancer. 1991;27(6):758-62. DOI: 10.1016/0277-5379(91)90183-E

148. Hopman GD, Peña EG, Le Cessie S, Van Weel MH, Vossen JM, Mearin ML. Tube feeding and bone marrow transplantation. Med Pediatr Oncol. 2003;40(6):375-9. DOI: 10.1002/mpo.10284

149. Langdana A, Tully N, Molloy E, Bourke B, O'Meara A. Intensive enteral nutrition support in paediatric bone marrow transplantation. Bone Marrow Transplant. 2001;27(7):741-6. DOI: 10.1038/sj.bmt.1702855

150. Ringwald-Smith KA, Heslop HE, Kranze RA, Mackert PW, Hancock ML, Stricklin LM, Bowman LC, Haie GA. Energy expenditure in children undergoing hematopoietic stem cell transplantation. Bone Marrow Transplant. 2002;30(2):125-30. DOI: 10.1038/sj.bmt.1703608

151. Duggan C, Bechard L, Donovan K, Vangel M, O'Leary A, Holmes C, Lehmann L, Guinan E. Changes in resting energy expenditure among children undergoing autologous stem cell transplantation. Am J Clin Nutr. 2003;78(1):104-9.

152. Forchielli ML, Azi N, Cadrel P, Paolucci G. Total parenteral nutrition in bone marrow transplant: what is the appropriate energy level? Oncology. 2003;64(1):7-13. DOI: 10.1159/000066513

153. MacFie J. Ethical implications of recognizing nutritional support as a medical therapy. Br J Surg. 1996;83(11):1567-8. DOI: 10.1002/bja.1800831125

154. Grozek J, Wells S, Keys A. Medical aspects of semistarvation in Leningrad (siege 1941-1942). Am Rev Sov Med. 1946;4:90-66.

155. Fliederbaum A. Clinical aspects of hunger disease in adults. In: Winnick M, editor. Hunger disease: Studies by the Jewish physicians in the Warsaw ghetto. New York: John Wiley & Sons; 1975. p. 11-43.

156. Winnick M, editor. Hunger disease: Studies by the Jewish physicians in the Warsaw ghetto. New York: John Wiley & Sons; 1975.

157. Bundesärztekammer. Grundsätze der Bundesärztekammer zur ärztlichen Sterbebegleitung. Dtsch Arztebl. 1998;95:B1851-8.B1855.

158. Winkler MF. Quality of life in adult home parenteral nutrition patients. JPN En Parenter Enteral Nutr. 2005;29(3):162-70. DOI: 10.1177/0148607105029003162

159. Bachmann P, Marti-Massoud C, Blanc-Vincent MP, Desport JC, Vercruysse V, Kere D, Melchior JC, Nitenberg G, Raynard B, Roux-Boumary P, Schneider S, Senesse P. Standards, options et recommandations: nutrition en situation palliative ou terminale de l'adulte porteur de cancer évolutif [Standards, options and recommendations: nutritional support in palliative or terminal cancer care of adult patients with progressive cancer]. Bull Cancer. 2001;88(10):985-1006.

160. McKinlay AW. Nutritional support in patients with advanced cancer: permission to fail out? Proc Nutr Soc. 2003;63(3):431-5. DOI: 10.1079/PNS2004377

161. McCann RM, Hall WJ, Groth-Juncker A. Terminal patients. The appropriate use of nutrition and hydration. JAMA. 2001;284(16):2063-6.

162. Bruera E, Belzile M, Watanabe S, Fainsinger RL. Volume of hydration in terminal cancer patients. Support Care Cancer. 1996;4(2):147-50. DOI: 10.1007/BF01845764

163. Burge FL. Dehydration symptoms of palliative care cancer patients. J Pain Symptom Manage. 1993;8(7):454-64. DOI: 10.1016/0885-3924(93)90188-2

164. Ellershaw JE, Sutcliffe JM, Saunders CM. Dehydration and the dying patient. J Pain Symptom Manage. 1994;7(1):16-21. DOI: 10.1016/0885-3924(94)90123-3

165. Musgrave CF, Ostajd J. Fluid retention and intravenous hydration in the dying. Palliat Med. 1996;10(1):53. DOI: 10.1177/02692163960100111

166. Fainsinger RL, Bruera E. When to treat dehydration in a terminally ill patient? Support Care Cancer. 1997;5(3):205-11. DOI: 10.1007/s005200500681

167. Michaud L, Bournand B, Stiefel F. Taking care of the terminally ill cancer patient: delirium as a symptom of terminal disease. Ann Oncol. 2004;15 Suppl 4:i199-203. DOI: 10.1093/annonc/mdh927
168. Bruera E, Franco JJ, Maltoni M, Watanabe S, Suarez-Almazor M. Changing pattern of agitated impaired mental status in patients with advanced cancer: association with cognitive monitoring, hydration, and opioid rotation. J Pain Symptom Manage. 1995;10(4):287-91. DOI: 10.1016/0885-3924(95)00005-J

169. De Stoutz ND, Bruera E, Suarez-Almazor M. Opioid rotation for toxicity reduction in terminal cancer patients. J Pain Symptom Manage. 1995;10(5):378-84. DOI: 10.1016/0885-3924(95)90924-C

170. Bruera E, Sala R, Rico MA, Moyano J, Centeno C, Willey J, Palmer JL. Effects of parenteral hydration in terminally ill cancer patients: a preliminary study. J Clin Oncol. 2005;23(10):2366-71. DOI: 10.1200/JCO.2005.04.069

171. Bachmann P, Marti-Massoud C, Blanc-Vincent MP, Desport JC, Colomb V, Dieu L, Kere D, Melchior JC, Nitenberg G, Raynard B, Roux-Bournay P, Schneider S, Senesse P; FNCLCC. Summary version of the Standards, Options and Recommendations for palliative or terminal nutrition in adults with progressive cancer (2001). Br J Cancer. 2003;89 Suppl 1:S107-10. DOI: 10.1038/sj.bjc.6601092

Please cite as
Arends J, Zuercher G, Dossett A, Fietkau R, Hug M, Schmid I, Shang E, Zander A, Working group for developing the guidelines for parenteral nutrition of The German Association for Nutritional Medicine. Non-surgical oncology – Guidelines on Parenteral Nutrition, Chapter 19. GMS Ger Med Sci. 2009;7:Doc09.

This article is freely available from http://www.egms.de/en/gms/2009-7/000068.shtml

Received: 2009-01-14
Published: 2009-11-18

Copyright ©2009 Arends et al. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by-nc-nd/3.0/deed.en). You are free: to Share — to copy, distribute and transmit the work, provided the original author and source are credited.