Nutritional status in relation to treatment modalities

An J.V. Vandebroek *

ZNA Middelheim, Department of Oncology, Antwerp, Belgium

1. Influence of nutritional status on chemotherapy and radiotherapy

The prevalence of disease-related malnutrition in patients with cancer ranges from 40% to 80%, which is the highest of all hospital groups. This variation in prevalence is the result of the different definitions of malnutrition used, and it also depends on tumour type, stage and anticancer treatment. Malnutrition is associated with negative outcome, including increased morbidity, poor prognoses and tolerance to treatment, decreased quality of life and increased health-care costs [1]. Head and neck cancer patients who experience a weight loss >20% of their total body weight during or following radiotherapy are at an increased risk of toxicity and mortality. Stage 3 or 4 disease and smoking more than 20 cigarettes a day should be reason enough for early enteral feeding. A prophylactic percutaneously placed endoscopic gastrostomy (PEG) feeding tube is also beneficial when there is pretreatment weight loss [2].

Nutrition screening is the process of identifying patients with characteristics commonly associated with nutritional problems that may require full nutritional assessment. Screening can be applied to all patients. The malnutrition screening tool (MST) is a validated, quick and simple nutrition screening tool. The patient-generated subjective global assessment (PG-SGA) can be applied for a full nutritional assessment [1].

The identification of baseline risk factors to assess a patient's fragility or ability to tolerate treatment is desirable to predict outcome of chemotherapy toxicity, not only for medically unfit patients but also amongst patients with an apparently good medical condition, since the high inter-individual variability in drug exposure remains an unresolved issue. Chemotherapy-induced DNA damage might become more cytotoxic to normal tissue in the presence of perturbations of the cellular immune response because of high protein catabolism and stimulation of acute-phase protein responses (APPRs). The nutritional and inflammatory status (NIS) appears to correlate with increased risk of severe haematological toxicity following anticancer chemotherapy. This status takes in account (1) C-reactive protein, (2) alpha-1-acid glycoprotein, (3) albumin and (4) prealbumin: NIS = $(1 \times 2)/(3 \times 4)$ [3].

Malnutrition has been associated with changes in drug disposition, including changes in absorption, protein binding, hepatic metabolism and renal elimination. In malnourished patients reduced concentrations of plasma proteins may significantly increase the likelihood of toxicity from the administrations of agents that are highly protein-bound, such as prednisolone, etoposide, teniposide, cisplatin, paclitaxel and SN-38 [4].

Anticancer treatment can induce a poor nutritional status by inducing nausea, vomiting and anorexia and gastrointestinal disorders as mucositis and diarrhoea [4]. Reversible lactose intolerance – associated with diarrhoea, flatulence and poor nutritional status – is not infrequent in patients treated with chemotherapy based on 5-fluorouracil (5-FU). Hypolactasia can easily be diagnosed with a lactose tolerance test. Dietary lactose restriction might improve tolerability of treatment [5]. Malabsorption may be caused not only by fluorouracil but also by other drugs affecting cell proliferation such as thioguanine, methotrexate, vinca's alkaloid, actinomycin D, hydroxyurea and daunomycin [6].

2. Influence of nutritional deficiencies on chemotherapy and vice versa

Trace elements consist mostly of metal ions which act mainly as basic components of essential enzymatic systems or proteins that play major roles in the physiology of the gastrointestinal tract (Jackson, 1989). Studies suggest that trace elements serve as cofactors in several metabolic pathways, and a decrease in their concentration may facilitate the malnutrition process that takes place in cancer patients. Negative acute-phase reactants such as selenium and zinc are decreased in cancer patients, whereas serum levels of copper are increased. Selenium deficiency may interfere with

* Tel.: +32 32803340; fax: +32 32810719.
E-mail address: an.vandebroek@zna.be.
1359-6349/$ - see front matter
http://dx.doi.org/10.1016/j.ejcsup.2013.07.057

free-radical-mediated damage. Zinc regulates the function of cytochromes, stabilizes plasma membranes, reduces lipid peroxidation and has a role in the detoxification of ammonia. A deficiency in zinc potentiates the toxicity of other metals and decreases the plasma values of vitamin A. Supplementation of these trace elements can delay cachexia with its consequent depression of the immune system, influencing the neoplastic process and the success of chemotherapy [7].

Cetuximab, a monoclonal antibody against the epithelial growth factor receptor (EGFR), can induce an inappropriate urinary excretion of magnesium through the inhibition of reabsorption of magnesium in the ascending loop of Henle, since EGFR is strongly expressed in the kidney [8]. This leads to symptomatic hypomagnesaemia, a side effect also commonly known to be associated with the use of cisplatin.

Cachectic patients with decreased dietary carnitine uptake may develop carnitine deficiency when treated repeatedly with chemotherapies that include cisplatin. They have a ten-fold increase in renal carnitine excretion [9].

Pemetrexed, a multitargeted antifolate, is associated with life-threatening toxicity, especially myelosuppression, if not administrated after supplementation with folic acid and vitamin B12. One week prior to commencing pemetrexed, folic acid (0.5 mg by mouth each day) and vitamin B12 (1 mg by intramuscular injection every 9 weeks) should be given [10].

3. Influence of nutritional supplements on chemotherapy

More than 80% of the patients with cancer surveyed in 2000 in the United States reported using complementary and alternative medicine (CAM) [11]. While the body of literature related to the use of CAM is growing, the extrapolation and application to patient care remain complex. Clinicians must establish whether the supplement is an antioxidant, is an anticoagulant or procoagulant, has immunosuppressive or immunomodulatory properties, has hormonal properties, has known safety issues and has known or theoretical drug interactions [12].

Antioxidants represent one of the largest categories of dietary supplements. Reactive oxygen species (ROSs) are a natural consequence of living in an aerobic environment. Oxidative stress occurs when natural defence systems are inadequate to combat the production of ROSs. Antioxidants could be protective against the adverse effects of chemotherapy, but some of these agents rely for their antineoplastic activity on the production or interaction with ROSs. Agents with a high reliance on ROSs for their antineoplastic activity are alkylating agents and mitomycin C. Mitoxanthrone is less likely to be dependent on ROSs.

The use of dietary supplements with anticoagulant properties, alone or concomitantly with conventional anticoagulants or antiplatelet medication, may pose a risk for bleeding due to additive or synergistic effects on the coagulation pathway. Agents with coumarin constituents – such as angelica root, agents that inhibit platelets such as panax ginseng, agents with salicylate constituents such as black cohosh, garlic, ginkgo, saw palmetto – may increase the risk of bleeding. Supplements with procoagulant properties should be avoided with hormonal treatments such as tamoxifen, and with erythropoietic growth factors, estramustin or thalidomide.

4. Conclusion

Nutrition and nutritional status are influenced by the presence of cancer but also have an important influence on anticancer treatment and treatment outcome. It is important that the oncologist has an insight into the possible interactions and complications that nutritional agents may have with chemotherapeutic agents.

The ability to identify and locate reliable information regarding dietary supplements is vital.

The use of more than one reference is necessary to complete the analysis of dietary supplements for a patient. Counselling patients with cancer about dietary supplements requires a systematic thought process that considers the available theories and data, as well as the patient's views about these agents [13]. More attention should be paid to patient nutritional status, and cooperation with a dietician is essential in the care of the cancer patient.

Conflict of interest statement

None declared.

REFERENCES

[1] Isenring E, Cross G, Daniels L, Kellett E, Koczwara B. Validity of the malnutrition screening tool as an effective predictor of nutritional risk in oncology outpatients receiving chemotherapy. Support Care Cancer 2006;14:1152–6.
[2] Kiyomoto D. Head and neck cancer patients treated with chemo-radiotherapy require individualized oncology nutrition. J Am Diet Assoc 2007;107:412–5.
[3] Alexandre J, Gross-Goupil M, Falssard B, et al. Evaluation of the nutritional and inflammatory status in cancer patients for the risk assessment of severe hematological toxicity following chemotherapy. Ann Oncol 2003;14:36–41.
[4] Murry D, Riva L, Poplack D. Impact of nutrition on pharmacokinetics of anti-neoplastic agents. Int J Cancer 1998;11:48–51 [Supplement].
[5] Österlund P, Ruotsalainen T, Peuhkuri K, et al. Lactose intolerance associated with adjuvant 5-fluorouracil-based chemotherapy for colorectal cancer. Clin Gastroenterol Hepatol 2004;2:696–703.
[6] Trier JS. Morphologic alterations induced by methotrexate in the mucosa of the human proximal in.
[7] Federico A, Iodice P, Federico P, et al. Effects of selenium and zinc supplementation on nutritional status in patients with cancer of digestive tract. Eur J Clin Nutr 2001;55:293–7.
[8] Schrag D, Chung KY, Flombaum C, Saltz L. Cetuximab therapy and symptomatic hypomagnesemia. J Natl Cancer Inst 2005;97:1221–4.
[9] Heuberger W, Berardi S, Jacky E, Pey P, Krähenbühl S. Increased urinary excretion of carnitine in patients treated with cisplatin. Eur J Clin Pharmacol 1998;54:503–8.
[10] Li KM, Rivory LP, Clarke SJ. Pemetrexed pharmacokinetics and pharmacodynamics in a phase 2 study of doublet chemotherapy with vinorelbine: implications for further

optimisation of pemetrexed schedules. Br J Cancer 2007;97:1071–6.
[11] Richardson MA, Sanders T, Palmer JL, et al. Complementary/alternative medicine use in a comprehensive cancer center and the implications for oncology. J Clin Oncol 2000;18:2505–14.
[12] Michaud LB, Karpinski JP, Jones KL, Esperito J. Dietary supplements bin patients with cancer: risks and key concepts, Part 1. Am J Health Syst Pharm 2007;64:369–81.
[13] Michaud LB, Karpinski JP, Jones KL, Esperito J. Dietary supplements bin patients with cancer: risks and key concepts, Part 2. Am J Health Syst Pharm 2007;64:467–80.