

Nutritional problems among patients affected by cancer during chemotherapy

Problemy żywieniowe u pacjentów dotkniętych chorobą nowotworową w trakcie chemioterapii

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Abstract

Chemotherapy is one of the primary methods of treating cancer. Symptoms occurring during this form of therapy affect patients' general health status, cause malnutrition, and deteriorate the quality of life of oncology patients, which results in cachexia. Malnutrition during treatment and the resulting bad general health status of patients may lead to disqualification from chemotherapy treatment. Cachexia is a complex and multi-factorial process, characterised by the nearly unknown mechanism of its development. What is extremely crucial is the evaluation of the state of malnutrition among patients qualified for cytostatic therapy and regular control of this state during therapy and immediately after its termination. Clinical practice indicates the importance of applying pharmacotherapy, nutritional treatment, and targeted education for the patient and their closest family regarding diet and correct behaviour, which significantly reduces anxiety and stress.

Streszczenie

Chemioterapia to jedna z podstawowych metod leczenia choroby nowotworowej. Objawy towarzyszące tej formie terapii wpływają na stan ogólny chorych, powodują niedożywienie i pogarszają jakość ich życia. Niedożywienie w trakcie leczenia i zły stan ogólny chorego będący konsekwencją wyniszczenia nowotworowego może spowodować wykluczenie go z chemioterapii. Skutkiem niedożywienia jest systematyczne pogarszanie się stanu klinicznego chorych poprzez osłabienie, zanik tkanki mięśniowej, zmniejszenie odporności, niedokrwistość, redukcję stężenia albumin w osoczu, podatność na zakażenia oraz zaburzenia gospodarki wodno-elektrolitowej i węglowodanowo-białkowo-tłuszczowej. Niezmiernie ważna jest ocena stanu odżywienia u pacjentów kwalifikowanych do leczenia cytostatykami. W praktyce klinicznej duże znaczenie ma zastosowanie farmakoterapii, leczenia żywieniowego oraz ukierunkowana edukacja pacjenta dotycząca stosowanej diety.

Patients subjected to chemotherapy due to tumour disease face problems with proper nutrition and often show malnutrition symptoms [1]. Malnutrition is a frequently occurring, multi-factorial, and still too rarely recognised state [2]. Chemotherapy is one of the methods characterised by complex oncological treatment, which involves administering cytostatic drugs (chemotherapeutic agents) that destroy tumour cells or hinder their replication. The way cytostatic drugs work is non-specific. It means that they affect all living cells of human internal organs in the same way, proportionally to their growth and divide rate.

One of the results of anticancer treatment may be immediate toxicity symptoms (nausea and vomiting), early complications (haematological toxicity, inflammatory changes of gastrointestinal mucositis, lack of

appetite, and alopecia), delayed complications (cardiomyopathy and peripheral neuropathy) as well as late complications (gonadal damage and secondary tumours) [1]. Undesirable effects of chemotherapy also include anaemia, taste disturbance, disorders when it comes to sensing food temperature, constipation, diarrhoea, dysphagia (i.e. swallowing difficulties), fatigue, dry mouth, and early saturation, which may decrease the amount of consumed food and consequently lead to extreme weight loss [3]. Occurring symptoms are often the reason for nutritional status deterioration, weight loss, and deterioration in the quality of patients' lives. On the other hand, malnutrition results in systematic deterioration of patients' clinical state due to fatigue, muscle tissue atrophy, decrease in organism immunity, anaemia, decrease in

albumin in plasma, vulnerability to infections, and water-electrolyte balance and carbohydrate-protein-fat balance disorders, which, ultimately, may lead to disqualification from chemotherapy [4].

Cancer cachexia is a multi-factorial health condition characterised by systemic inflammation, and a decrease in the significant level of intensification of skeletal muscle mass along with or without fat loss [4–7]. This condition cannot be completely withdrawn by adapting conventional nutrition, and it leads to progressing functional impairment [8]. Cachexia is not only determined by the stage of progress of cancer but also by its type [4]. What is emphasised is the influence of malnutrition on the decrease in tolerance and response to anticancer treatment, increase in risk of complications, deterioration in the quality of life, and increased mortality [9–11]. Over 50% of patients suffering from malignant tumours face cachexia at the time of their death, and over 30% of them die from emaciation [12].

Another consequence of cancer emaciation may be an activity decrease that causes decubitus as well as being dependent on others and feeling that one is a burden to them. Some patients show unfavourable changes in appearance, which contributes to low self-esteem and a feeling of guilt, which may sometimes be accompanied by severe dejection, discouragement, and embarrassment since the image of one's own body reflects one's self-esteem and self-acceptance [13]; therefore, psychological support should be provided not only for the patient but also for their family [14].

Cancer cachexia is a condition that could be potentially withdrawn; however, only in its early stage, where weight loss amounts to less than 10%. Advanced emaciation is resistant to treatment, and nutritional interventions are very often unsuccessful [15], defined as 20–30% weight loss [8]. Therefore, it is of a great importance to promptly intervene in malnutrition, which is advised by experts to be carried out if there is a 5% weight loss [15] within five months [16].

Mechanism of development

The reason for development of cachexia is multifactorial and not fully recognised [5]. Research reveals the importance and participation of intestinal flora, intestinal barrier, endotoxins, chronic inflammation, pro-inflammatory cytokines, pro-cachectic factors released by tumour cells, neuroendocrine hormones, insulin-like growth factor 1 (IGF-1), and acute-phase protein response (APPR) in the process of cachexia development [4].

Inflammation is commonly diagnosed among patients suffering from cachexia. Moreover, it is believed that it plays a crucial role in the aetiology of this condition. Metabolic changes occurring in ca-

chexia are similar to changes typical for infections rather than the feeling of hunger. Products of acute phase proteins, such as C-reactive protein (CRP) and fibrinogen are considered to be precise markers for inflammatory, and the activity of pro-inflammatory, cytokines. The increase in production of CRP and fibrinogen among patients suffering from cachexia is also connected with deterioration in the quality of patients' lives and shorter survival time [4, 6]. The level of CRP increases simultaneously with progressing weight loss among cachectic patients, which suggests that the activity of pro-inflammatory cytokines increases as the disease progresses. Pro-inflammatory cytokines whose increased concentration is recognised during the process of cachexia include: tumour necrosis factor receptor (TNF), interleukin 1 (IL-1), and interleukin 6 (IL-6). Research indicates that the activation of pro-inflammatory cytokines is connected with decreased appetite and the amount of consumed food, intensified loss of muscle, and increased metabolism. Other hypothetical mechanisms with genetic background that take part in a metabolic effect connected with cancer cachexia include overexpression of inflammatory gene through nuclear factor κ -light-chain-enhancer of activated B cells (NF- κ B), overexpression of myostatin protein leading to decrease in muscle gain and underexpression of IGF-1. The exact casual link between APPR and a lot of cancers as well as cachexia is not entirely known. Scientists suggest that the high level of pro-inflammatory cytokines in cachexia results from direct production of tumour cells or is caused by host inflammatory response to tumour cells. It is also possible that interference of intestinal barrier function is connected with disturbance of intestinal microflora, which may result in chronic activation of immune response. There is more and more evidence that disturbance of epithelial continuity of the intestinal barrier caused by intestinal pathogens or other harmful substances may lead to local inflammation and penetration of pro-inflammatory antigens and other substances present in intestines, for instance undisturbed bacteria, lipopolysaccharides, or other bacterial elements, or digestive enzymes. Intestinal inflammation may lead to release of pro-inflammatory cytokines, which may additionally intensify impairment of intestinal mucosa and permeability of intestine walls. Intestinal barrier dysfunction may intensify systemic inflammation caused by another source. Moreover, it may lead to anorexia, fatigue of muscle strength, and other hypermetabolic changes recognised in cachexia [4]. While trying to find a cause of cancer cachexia, scientists also suggested that cancer decreases the effectiveness of energy transformation and increases resting energy expenditure (REE) by inducing lipids, carbohydrates, and protein metabolism disorders, which may be the main reason for cachexia develop-

ment. Friesen *et al.* suggest that in the advanced stage of cancer both tumour mass and anaerobic metabolism stage play a pivotal role in energy expenditure of the malignant tumour, which causes the increase of REE and use of glucose, and leads to cachexia. This process takes place through constant glucose demand of tumour during anaerobic energy production, especially during fasting [17].

Evaluation

Patient's nutritional status should be evaluated in every cancer stage. What is extremely crucial is evaluation of malnutrition status among patients qualified for chemotherapy. The most frequently used markers for nutritional status are weight loss in a specific time frame, the level of albumin in serum, total amount of lymphocytes in peripheral blood, and the level of transferring. On the date of admission to hospital every patient should have their body mass and height checked. Body mass is evaluated through the Quetelet index – body mass index (BMI) – by interpreting results according to the recommendations of the World Health Organisation (WHO). Body mass index is calculated using the formula $\text{weight [kg]}/\text{height}^2$, where the ratio of weight (Wt) to height (Ht) is expressed in such a form so as to allow to the comparison of women and men in the majority of age groups with respect to the narrow range of normal values [18]. According to the interpretation of BMI, the risk of malnutrition is considered under 20.0 kg/m^2 . People whose BMI ranges from 17.0 to 23.5 kg/m^2 belong to the group risking malnutrition. It is also supposed that BMI under 19 kg/m^2 indicates malnutrition and increased risk of complications, for instance after surgery or injury. It is advised to recognise malnutrition requiring nutritional intervention among patients over 65 years old when their BMI is less than 24 kg/m^2 and weight loss is under 5% within 1 to 6 months, due to significantly worse tolerance of malnutrition among elderly people [19–21]. In addition to weight and height measurements (usually the current body mass (kg) is compared with the patient's normal body mass), by every evaluation of nutritional status it is advised to carry out nutrition interview evaluating the patient's current nutrition and energy requirement, to conduct anthropometrical measurements, to assess results of laboratory examinations and urine testing, as well as to determine intensification of side effects during chemical treatment [22–24]. Anthropometrical measurement is a common, affordable, non-invasive, objective, and widely available evaluation [2], where, in addition to weight and height measurement as well as BMI calculation, the thickness of skin fold above the three-headed arm muscle is measured, which gives information on weight loss connected to disease within 3 months prior to the date of admission to hospital is gathered [19].

Symptoms

One of the clinical symptoms defining cancer cachexia is malnutrition that reaches over 10% of the initial body weight [3]. Depending on the type and stage of cancer, around 30–80% of patients show weight loss. The significant weight loss, i.e. over 10% of the initial body mass, is recognised in 15% of patients [25].

The consequences of malnutrition can be divided into primary and secondary. Primary consequences include: weight loss caused by muscle and fat loss, fatigue of muscle strength, deterioration of the immune system, hypochromic anaemia, decrease in concentration of plasma proteins, digestive and absorption disorders, and functional impairment of all organs and systems. Secondary consequences include an increase in the frequency of inflammations, impaired healing, anastomosis leaks, and an increase in vulnerability to diseases and the costs of medical treatment [9, 25].

During physical examination of oncology patients being undernourished or subject to malnutritional status the following symptoms may be shown: emaciation, epidermal keratinisation, seborrhoea, hair loss, brittleness of nails, decrease in or atrophy of subcutaneous tissue, inflammation of gums, inflammation of the corners of the mouth, inflammation of tongue, enlargement of heart muscle, resting tachycardia, exudates in pleural cavities, and dyspnoea. Moreover, there are also symptoms observed such as ascites, pains, muscle atrophy, and joint swelling [22–24].

Oncology patients showing cachexia development usually report that they have lost their appetite or have stopped eating, as first symptoms. There are certain cases in which loss of appetite was connected with the feeling of satisfaction after having eaten a small amount of food (early satisfaction) or the feeling of "aversion" as a reaction to certain food products (unwillingness to eat). Moreover, there are other physical factors contributing to loss of appetite and cessation of eating, such as: oral ulceration, nausea, or gastrointestinal disorders. A number of these symptoms are related to the side effects of oncological treatment [16].

Treatment

Early treatment of cancer cachexia plays a crucial role. The purpose of nutritional treatment is to prevent development or later progression of malnutrition as well as to increase the patient's physical activity and functioning [26]. Nutritional intervention carried out among these patients aims at improvement of their nutritional status by alleviating the side effects of treatment, offering an individual approach to each patient and increasing the amount of consumed food while respecting individual eating habits and gradually increasing calorie supply. Not only does the im-

provement of nutritional status favour better response to treatment but it also improves the quality of life. It is recommended that patients eat small meals, but frequently (5–6 times a day), so as to increase the total amount of consumed calories among patients experiencing loss of appetite that results from metabolic disturbances and chemotherapy [3]. Emaciation is treated through pharmacotherapy along with nutritional treatment [27, 28], which mainly aims at increasing the intake of calories by the patient [16].

There are three groups of drugs that have proven their effectiveness in treating emaciation and are applicable in clinical practice [26]:

- progestogens (megestrol acetate and medroxyprogesterone acetate) – improve appetite and wellbeing and cause weight gain,
- glycocorticosteroids (dexamethasone, less frequently prednisolone or methylprednisolone) – increase appetite during the first week of their use; they have non-specific antiemetic effect and boost wellbeing and happiness,
- prokinetics (metoclopramide, cisapride, domperidone) – improve alimentary track function, accelerate gastric emptying, and have an antiemetic effect.

Nutritional treatment is, along with pharmacology, yet another important element of treating cancer cachexia. It is of a great importance to maintain the natural way of intaking food, when it is possible. The oral route is the most convenient and physiological nutrition route for the patient. The energy and nutritional value of applied diets as well as proper food choice and techniques for preparing meals may significantly improve the quality of life among patients battling the advanced stages of cancer, especially through alleviating pain and other somatic symptoms [15]. It has been proven that the amount of consumed energy improves when the patient intakes 500–600 calories a day, especially among patients receiving chemotherapy and radiotherapy, provided that there is radical treatment involved and a good response to therapy [17]. If the amount of consumed food does not cover 60% of daily recommendation, enteral or intravenous feeding should be applied [3]. It is necessary to create stoma (gastric tube, gastro- or jejunostoma) among patients who require enteral feeding for a longer time [26].

There are a number of substances and drugs that could provide an advantage in treatment of cachexia during clinical examinations. One of them is eicosapentaenoic acid (EPA) that belongs to the omega-3 fatty acids group [4, 29]. Potentially, EPA has an impact on metabolic disturbances, which are the main reason for body mass loss in cachexia and for changing inflammatory response. Supplementation with EPA is characterised by many advantages, among which are a decrease in the production of different cytokines, an increase in total body weight and appetite, and an improvement in the quality of life among patients with cancer cachexia.

Probiotics and prebiotics may also have a positive impact on human health. It has been shown that probiotics have a beneficial impact on the development and stability of bacterial flora, strengthen the mucosal barrier by exerting a trophic effect on intestinal mucosa, and stimulate the immune system [4].

Conclusions

Cachexia affects a big number of oncology patients, especially in the advanced stage of disease. It is a really serious and crucial problem. Currently, it is too rarely recognised, diagnosed, and cured. Cachexia influences, to a large extent, the efficiency and tolerance of therapy as well as the quality of patients' lives. Proper nourishment is extremely important due to increased demand for nutrients during anticancer treatment. It is also worth remembering that the daily energy requirement for an organism that is emaciated by cancer is significantly greater than it is for a healthy person. The diet should be easily digestible, high-energy, and high-protein. The diet should be adjusted to the patient's individual taste preferences. What is also very important is nutrition education for the patient and his/her family. The patient should not be "forcefully" fed; meals should be provided often and in small portions, and common family meals should be introduced. Cachexia treatment should become a permanent part of complex oncological treatment.

Conflict of interest

The authors declare no conflict of interest.

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