Review paper

Nutritional intervention during radiotherapy of head and neck cancers

Interwencja żywieniowa podczas radioterapii nowotworów głowy i szyi

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Słowa kluczowe: radioterapia, leczenie żywieniowe, rak głowy i szyi.

Abstract

Radiotherapy is one of the main forms of treatment for head and neck cancer. This procedure is associated with high toxicity in the irradiated area resulting in patients' numerous complaints about: inflammation of oral mucous membranes, difficulties with food chewing and swallowing, dry mouth, or impaired taste and smell. Some of these pathologies are temporary and go away at a specific time after treatment, but some of the damage is permanent and irreversible. Complications at the level of the upper gastrointestinal tract cause considerable difficulties in food intake; therefore, intensive dietary counselling is recommended along with nutritional intervention in this group of patients. Adopted and recommended methods of nutritional support during radiotherapy include: modification of the basic diet in terms of consistency, oral nutritional supplements, enteral nutrition with the use of probes, and nutrient gastrostomy.

Streszczenie

Radioterapia jest jedną z głównych metod leczenia nowotworów głowy i szyi. Ta forma leczenia wiąże się z wysoką toksycznością w obszarze napromienianym, czego skutkiem są liczne dolegliwości, takie jak zapalenie błon śluzowych jamy ustnej, trudności z przeżuwaniem i połykaniem pokarmu, suchość w jamie ustnej, zaburzenia odczuwania smaku i zapachu. Część z tych patologii ma charakter przejściowy i ustępuje w określonym czasie po zakończeniu leczenia, jednak część uszkodzeń ma charakter trwały i nieodwracalny. Powikłania na poziomie górnego odcinka przewodu pokarmowego powodują znaczne trudności w przyjmowaniu pokarmów, w związku z czym zaleca się prowadzenie intensywnego poradnictwa dietetycznego i interwencje żywieniowe w tej grupie chorych. Do uznanych i zalecanych metod wsparcia żywieniowego podczas radioterapii należą: modyfikacja diety podstawowej pod względem konsystencji, doustne suplementy odżywcze, żywienie dojelitowe z wykorzystaniem sond i gastrostomii odżywczych.

Introduction

Cancer diseases are classified as the second cause of mortality in Poland, and their course is very often associated with disturbances of nutritional status, especially of those located in the region of the head, neck, and digestive system [1, 2]. According to data collected by the National Cancer Registry, head and neck cancer diseases constitute 5.5% to 6.2% of all malignancies [3]. Radiotherapy is one of the basic methods of oncological treatment, which can be used alone or in combination with chemotherapy and/or surgery – providing better treatment results. Despite the effectiveness of treatment with ionising radiation within the head and neck, this method of treatment brings the risk of developing many troublesome side effects [4]. The most common complications relate to oral and gastrointestinal mucosa inflammation, disturbed salivary secretion, impaired taste and smell sensation, nausea, vomiting, chewing and swallowing disorders, and decreased appetite [5, 6]. The mutual overlap of the above-mentioned factors in the treatment process very often leads to the development of

malnutrition in the patient, which results in a reduction in treatment tolerance or its prolongation, and sometimes even the interruption. In the face of this problem, the right planned nutritional support, tailored to the individual needs of the patient, at every stage of treatment plays a key role. There are several methods of nutritional support in this period, starting from a traditional diet with a modified consistency and enriched with oral nutritional supplements (ONS), through enteral nutrition (EN) using probes and nutrition tubes, ending in specific cases with parenteral nutrition (PN). Nevertheless, all the mentioned methods of support should be used to reduce the risk of developing malnutrition in the process of radiotherapeutic treatment, and the physician and dietitian are to play the key role here.

Energy and protein demand

Following the assessment of the nutritional status, the calculation of protein and energy demand including vitamins and trace elements is the compulsory element initiating nutritional support for a patient undergoing oncological treatment. The energy of the diet is closely related to the patient's condition. In the case of patients who are confined to bed an energy demand should be planned at 20–25 kcal/kg/day, and for the remaining patients it should be assumed at 30–35 kcal/kg/day [7]. The optimal amount of protein in the diet is not precisely specified; however, experts' recommendations advise that the minimum supply should be 1 g/kg/day, preferably 1.2–2.0 g/kg/day, and target supply should amount to 1.2–1.5 g/kg/day [1, 8]. The energy supply from individual macronutrients should be, respectively: 15–20% of protein, 30–50% of fat, and 35–50% of carbohydrates [9]. In everyday clinical practice, the values are transformed depending on the patient's support method and current metabolic needs. In the case of irradiation of advanced head and neck cancers, an increase in energy demand by up to 25% in relation to the basic should be considered.

Nutrition disorders

Malnutrition is a significant problem in the group of patients undergoing radiotherapy due to a tumour located in the head and neck area. Many factors contribute to the pathogenesis of the development of this pathology, e.g. increased need for nutrients or their loss, disturbances in metabolic processes, excessive activity of proinflammatory cytokines, increased catabolic processes, and increased energy expenditure [1, 9, 10]. Long-lasting deficit of energy and building substances leads to the development of cancer cachexia syndrome, defined as "a complex metabolic syndrome associated with the underlying disease and characterised by muscle loss with or without fat mass loss" [11]. Weight loss in the case of oncological patients is an important prognostic factor affecting patients' survival as well as an important predictive factor, which is why it is so important to take preventive measures. The factors affecting the reduction of food intake by patients with head and neck cancer include the following: loss of appetite, difficulties with chewing food, dry mouth, and pain during swallowing [12]. It is particularly important to recognise malnutrition in the patient, which can sometimes be very difficult. There are a number of possibilities to pre-diagnose this pathology. One of the simplest methods is to calculate the body mass index (BMI), which is the ratio of mass [kg] to the square of height [m^2]. Criteria determining the limits for proper nutrition are eloquent and slightly different. Body mass index < 18.5 kg/m^2 malnutrition, BMI 18.5–20 kg/m^2 risk of malnutrition, BMI 20–25 kg/m^2 standard, BMI 25–30 kg/m^2 overweight, and BMI > 30 kg/m^2 obesity [9]. A preliminary assessment of the nutritional status can also be made by measuring the triceps skin fold thickness (TSF) of the non-dominant arm or by measuring the mid-arm circumference (MAC). Another obligatory method in Polish hospitals is the evaluation of nutritional status using nutritional scales, e.g. Subjective Global Assessment of nutritional status (SGA) or Nutritional Risk Screening 2002 (NRS 2002). At the moment, however, biochemical testing is considered to be the most accurate method of diagnosing malnutrition. The biochemical indicators of malnutrition include: albumin (< 3.5 g/dl), prealbumin (< 18 mg/dl), transferrin (< 176 mg/dl), and the total number of lymphocytes (CLL < 1500 in 1 mm^3 blood) [13, 14]. It is recommended that patients undergoing chemoradiotherapy should be evaluated for the nutritional status from the beginning of treatment with subsequent regular assessments throughout the therapy period [15] (Table 1).

Side effects of radiation therapy

Side effects of radiation therapy around the head and neck significantly affect the quality of life of patients treated with this method. Radiotherapy damages not only the tumour, but also healthy, surrounding tissues, resulting in the formation of adverse clinical symptoms, being a consequence of the radiation reaction. Early and late complications of this treatment are distinguished. Early complications, which are acute radiation reactions, occur directly during treatment and/or up to 3–6 months after its completion and concern mainly the tissues of organs whose cells divide very quickly. In the case of head and neck cancers, the inflammation of mucous membrane of the mouth and throat and skin reactions are often reported. Late complications occur most often after 6 months or even years after the end of treatment and mainly include dry mouth, fibrosis, temporal bone and man-

Table 1. Interpretation of albumin, transferrin, prealbumin, and CLL levels in peripheral blood in relation to the nutritional status [14]

Nutritional status	Albumin [g/dl]	Transferrin [mg/dl]	Prealbumin [mg/dl]	CLL [in 1 mm^3 of blood]
Correct	3.5–5.0	176–315	18–45	> 1500
Light malnutrition	3.0–3.4	134–175	10–17	1200–1499
Medium malnutrition	2.1–2.9	117–133	5–9	800–1199
Severe malnutrition	< 2.1	< 117	< 5	< 800

dibular bone necrosis, or necrosis of the laryngeal cartilage. The type and intensity of radiation response development depend on, for example, type, dose and amount of radiation fraction, duration of treatment, and the use of other simultaneous treatment methods e.g. chemotherapy [16, 17]. Acute radiation reaction is a set of many different functional disorders as well as morphological ones, which occur not only in the cells themselves but also in the intercellular space of a given tissue. The radiation response usually develops in rapidly dividing tissues, i.e. bone marrow, epidermis, and epithelium lining the alimentary and respiratory tract. The mucous membrane of the mouth, throat, and larynx is built from multistratified squamous or ciliary epithelium; these epithelia consist of three types of cells: stem, transient, and mature. It is the damage to these cells that plays a key role in the pathogenesis of the radiation response. Ionising rays act mainly on cells with a short mitotic time, i.e. stem and transient ones, leading to epitheliolysis, thus causing an imbalance in their renewal, which results in a rapid and progressive loss of all epithelial strata [18]. Symptoms of acute radiation mucosal reaction in patients irradiated due to a tumour located in the area of the head or neck may appear several days after the start of treatment. Acute radiation mucosal reaction consists in four phases: inflammatory (erythema), epithelial (epitheliolysis), ulcerative-bacterial, and healing [18, 19]. The inflammatory phase is characterised by congestion of the mucous membrane and damage to vascular endothelial cells, which in the further course transforms into the epithelial phase by intensifying the destruction of epithelial cells filled by inflammatory exudation. Over time, the local epitheliolysis changes into a generalised and diffuse form covering the entire thickness of the mucosal epithelium – this condition persists during the subsequent days of therapy and after its completion. In special situations, infection, mycosis, and damage to the basal membrane may develop, initiating the ulcer-bacterial phase, most often manifested as seriously breathing obstructing oedema and bleeding of the mucous membranes [20]. It is the epithelial phase and ulcerative-bacterial phase when the patient requires special nutritional care and nutritional control. The physiological healing of acute radiation mucosal reaction involves the migration of cells from the healthy epithelium adjacent to the area subjected to irradiation. A disadvantageous functional consequence of this radiation-induced reaction is excessive dryness of the mucous membranes, difficulties and pain in the process of swallowing and chewing of food, and even in speech and breathing; this is when the patient refuses to eat food or significantly reduces the consumption. During treatment with ionising radiation, secretory functions of the parotid glands are impaired, which often results in dry mouth and changes in the consistency and viscosity of saliva, as well as impaired taste and smell sensation [6]. The first week of irradiation brings 80% decrease in salivary secretion [21]. Too little saliva in the mouth becomes the cause of the development of tooth decay, which, if neglected, may lead to infection of bones and expose the patient to even greater suffering [17]. The inflammation of mucous membranes usually disappears in the period from five to six weeks after the end of treatment; however, the final cessation of discomfort is an individual feature. The majority of secretory activities of damaged organs return to normal functioning up to 6 months after the end of radiotherapy; however, one must bear in mind that that in some patients the changes that occur during irradiation may be rebuilt for years or become irreversible and take the form of a late radiation reaction. Treatment of acute reaction is based on the use of local (mouth-rinses, artificial saliva substitutes, suspensions) and/or systemic pharmacological agents (antibiotics) combined with a properly planned nutritional intervention.

Forms of nutritional support

There are several nutritional techniques aimed at limiting the development of malnutrition among patients undergoing radiation therapy, who are struggling with pain complaints from the irradiated place.

– The simplest and the cheapest solution is to modify the basic diet in terms of its composition and consistency under the supervision of a nutritionist.
– Another solution is enriching the diet with oral nutritional supplements.
– In the case of the most severe radiation reactions that should be expected during the treatment peri-

od, it is advisable to use a percutaneous endoscopic gastrostomy (PEG) or a nasogastric tube.
– Parenteral nutrition should only be introduced in specific clinical situations, bearing in mind that enteral nutrition should always be the method of choice [8].

Gastrointestinal intervention is cheaper and has a much lower risk of complications related to, for example, access to nutrition, infections (bacterial translocation), and metabolic disorders (water-electrolyte disorders, glycaemic disorders or refeeding syndrome) in relation to parenteral nutrition [22].

Diet with changed consistency

A diet with altered consistency is a modification of an easily digestible diet. The modification consists of the change of consistency of the dishes, which are usually served to the patient in a pasty, semi-liquid, or liquid form. The purpose of the diet is to provide the patient with adequate nutrition, i.e. compatible with real energy and nutrient requirements, and to protect the diseased oral mucosa and oesophagus against mechanical, chemical, and thermal irritation of foods [23]. Meals should not contain sharp and sour spices, and the products they are made from should be fresh and cooked in water or steam, then subjected to crumbling to a form tolerated by the patient. The protein of animal origin, vitamin C, B vitamins, and minerals are important in this diet. The temperature of meals and drinks should be lukewarm or cold. The products mixed or sieved should be diluted with liquids, e.g. boiled water, broth, or milk, and minced food should be served with sauces. It is recommended that the diet is complete in terms of all nutrients and contains products from various food groups. In order not to irritate the oral mucosa, fluid should be drunk through a straw, it is also beneficial to replace large cutlery with smaller. To prepare diets with changed consistency, the following products can be used: groats in the form of gruel, biscuits, rusks, potatoes, wheat bread, rice, butter, milk, natural yoghurts and homogenised cheese, boiled eggs, lean meat and fish, sweet cream, vegetable oils, honey, liquid jelly, pudding, jelly, boiled vegetables, and fruits [23, 24]. It is important that this type of diet is carefully balanced by a clinical dietitian because only then can there be certainty that there will be no nutrient deficiency and the energy value of the diet will be correct.

Oral nutritional supplements

Oral nutritional supplements (ONS) in accordance with European Union Directive 1999/21/EC 25.03.1999 constitute a special category of medical food dedicated to nutritional support of malnourished patients or those threatened by the development of this pathology, under the supervision of qualified medical personnel (doctors, dieticians, pharmacists, qualified nursing staff). Oral nutritional supplements are available in various forms (liquid, powder, tablets, biscuits) and have a diverse composition, thanks to which it is possible to adapt the product to the specific nutritional needs of the patient [9, 25]. In the case of tumours localised within the head and neck, the most reasonable seems to be supplementation of ONS in liquid or powdered form, in the case when the patient is unable to eat at least 60% of the daily requirement by the oral route and there are no difficulties with swallowing and choking. Due to the fact that ONS differ in their composition, purpose, and form, the diet must be carefully selected, and its supply must be strictly controlled so that the patient would be benefit from it [26]. In terms of calorie content, ONS can be divided into: hypocaloric (0.5–0.9 kcal/ml diet), normocaloric (1–1.2 kcal/ml diet), and hypercaloric (1.3–2.4 kcal/ml diet) [9]. In terms of composition, incomplete and complete preparations are distinguished. Incomplete diets cannot be used as the only source of food because they contain only one ingredient, e.g. protein, but not all basic nutrients. Complete diets can be the only source of food because they contain all the necessary macro- and micronutrients of a diet [27]. Oral nutritional supplements for a patient with cancer should be hypercaloric and high in protein. From the research conducted in 2004 in the group of patients with head and neck and gastrointestinal region cancers, it is clear that patients during radiotherapy benefited from the use of ONS in combination with dietary counselling by reducing weight loss, thus improving the quality of life during treatment and after its completion [28]. A systematic review and meta-analysis of Elia *et al*. showed that the use of ONS during radiotherapy increases the amount of energy received by patients [29]. However, to draw reliable conclusions as for the effectiveness of ONS in patients with head and neck cancer, many randomised trials in this direction are required. However, it should be emphasised that the latest expert guidelines recommend that all patients undergoing radiotherapy of the gastrointestinal tract or of the head and neck area should be regularly evaluated for nutritional status, receive individual dietary counselling, and, if necessary, start nutritional support with the use of ONS [30, 31]. The European Society for Clinical Nutrition and Metabolism (ESPEN) strongly recommends the use of ONS during radiotherapy of the head, neck, chest, and gastrointestinal tract to prevent deterioration of nutritional status and to avoid breaks in radiotherapy [8].

Enteral nutrition: percutaneous endoscopic gastrostomy and nasogastric tube

Indications for the use of percutaneous endoscopic gastrostomy (PEG) among patients with facial and neck tumours have been changing over the past

years. It was previously believed that PEG should only be prescribed to palliative patients at the time of upper GI patency disorder, and a probe should be the method of choice. Currently, many doctors agree on the use of this form of support. However, the question remains regarding the period from the diagnosis of the disease in which an artificial nutritional access should be inserted. From a study conducted by Daly *et al.* on a group of 40 patients with head and neck cancers undergoing radiotherapy or chemoradiation, the early onset of nasogastric tube nutrition reduced weight loss compared to normal nutrition and feeding through PEG [32]. In several other studies, a similar improvement in body weight was observed and lower frequency of hospitalisations and interruptions in treatment in previously fed patients in comparison with its later start or complete lack [33–35]. The decision to start feeding by PEG should consider choosing the right industrial diet [36]. So far, only a few randomised clinical trials has shown higher efficacy of diets enriched with omega-3 acids compared to standard diets in the context of improving the parameters of screening the nutritional status of patients undergoing radiation therapy due to head and neck cancer [37–39]. The should not exclude gastrostomy in palliative patients due to the high stage of head and neck cancer because such a procedure may improve the quality of life of these patients and limit the rate of development of progressive malignancy [40]. However, it is necessary to aim at prophylactically setting up artificial access in order to spare patients additional pain and stress associated with the process of selecting gastrostomy in periods of exacerbation. ESPEN recommends enteral nutrition with a nasal or PEG probe as a strong recommendation in patients with severe radiation-induced disease [8]. The nasogastric tube is inserted in the case of expected short feeding time, i.e. < 30 days, and for feeding liquid and complete industrial diets should be used. It is not advisable to administer a liquid food diet by gavage, so as not to block the tube with improperly chopped food. The indication for the establishment of a gastrostomy is the expected feeding time over a period > 30 days.

It is recommended to administer industrial diet to PEG; in this case it is also possible to provide food diet adequately diluted; however, it should be realised that its use is more difficult, it requires more time and is subject to the risk of error in estimating the nutritional value of prepared meals [9, 41].

Parenteral nutrition

Although nearly 80% of patients undergoing head and neck radiotherapy lose weight, ESPEN does not recommend routine use of parenteral nutrition because this can bring more complications than benefits [8, 42–44]. Parenteral nutriotion during radiotherapy should be considered only in strictly defined situations, i.e. in case of poor tolerance of oral and gastrointestinal nutrition, which does not allow provision of the required amount of energy and nutrients, e.g. in severe radiation-induced enteritis or chronic inflammation of the intestines and related malabsorption (diarrhoea, vomiting) [8]. In order for PN to be effective, it should be remembered to provide the patient with all the necessary ingredients and, if necessary, additional substances resulting from individual physiological needs [45].

Summary

Despite the progress of medicine, the role of nutrition is still underestimated, but there are many forms of nutritional support for patients undergoing irradiation due to cancer located in the area of the head and neck. Benefits in the form of maintaining a proper nutrition status can be obtained using any of the methods discussed in this study. Nutritional intervention should always begin with a careful assessment of the nutritional status and determination of real demand for energy and nutrients. Some forms can be combined with each other, giving even better effect – for example, enriching the diet with ONS. When deciding on more advanced forms of nutritional intervention (EN, PN), one should always take into account the well-being of the patient and the benefits that he or she can get from its introduction. The doctor and dietitian should play a key role in the nutritional therapy.

Conflict of interest

The authors declare no conflict of interest.

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