

Possibility of pain reduction by dietary intervention in patients with advanced cancer

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Abstract

Pain in advanced cancer can have many causes, and they are not necessarily associated with the presence of cancer. Invalid daily food rations in terms of energy, nutritional value, and cooking techniques used can significantly impair quality of life, increase patients' pain and other somatic symptoms and aggravate malnutrition and cachexia. Basic dietary factors affecting the quality of life and severity of somatic symptoms are the nutritional value of the diet, the frequency of meals and their consistency, the presence of fiber, fat, sugars, lactose, gluten and nutraceuticals. Extremely important is the role of a team of specialists, that offers professional nutritional advice to the patients and their carers.

Key words

diet, pain, palliative care

INTRODUCTION

Palliative care is an interdisciplinary approach to the problems faced by terminally ill patients and their families, and an attempt to prevent or release from suffering is understood as an early diagnosis, assessment and treatment of pain and other symptoms, regardless of their origin, e.g. physical, mental or spiritual. The primary goal of palliative care is to improve the quality of life.

Pain management in palliative care is based on pharmacological procedures, but specialists have begun to notice the importance of psychotherapy and physical therapy for pain relief. However, proper dietary intervention may also directly and indirectly affect the perception of pain and the quality of life.

PAIN, EMACIATION AND THE ABILITY TO CONSUME FOOD

Pain and cachexia are the predominant symptoms in the terminal stages of life of the patient with cancer. As much as 80% of patients with advanced cancer suffer from pain of medium and high intensity [1], and 31–87% of patients suffer from malnutrition which is a part of cancer cachexia [2]. It is now known that up to 90% of pain can be effectively treated with appropriate medical therapy. The problem with cancer cachexia is potentially reversible, but only in the early stages, when weight loss is less than 10%. Advanced cachexia is a refractory phenomenon and dietary intervention is often ineffective. Current experts' position promotes taking an early intervention (nutrition, physical therapy, or pharmacological) at the stage of weight loss of 5% [3]. The problem of chronic pain and malnutrition are two mutually intertwined phenomena, the driving mechanism of each is within a vicious circle. The more exhausted the patient, the lower the threshold of perception of pain stimuli [4]; the

more the patient suffers from pain – the lower the possibility of food intake, thus causing reduction in the energy value of the diet.

In oncology, the cause of pain is not always associated with the presence of a tumour and its metastases (60–70%) [5, 6]. It may also be the result of the methods of cancer treatment, diagnostic procedures, cachexia, or may be related to the cause of non-tumour pain, such as osteoarthritis.

The presence of expansively-invasive type of tumour growth can be responsible for the pain by:

- mechanical compression of the neighboring organs and structures; – subileus or obstruction of the digestive tract, respiratory tract, or urinary tract; – infiltration of the nerves and nerve trunks, neuropathies;
- infiltration of bone and pathological fractures; – metastases to the brain and increased intracranial pressure; – inflammation and ulceration of the mucous membranes and skin, pressure ulcers; – ischemia of organs and tissue through infiltration of the blood vessels or their abnormal development.

Oncological therapy causes pain by various mechanisms, depending on the type of therapy. Pain associated with the treatment is the cause of 10–20% of pain in cancer [6]. Surgical procedures cause pain by mechanical and thermal damage to the tissue, but can also cause pain in a different time distance in the course of post-amputation and post-resection syndrome (after resection of limbs, parts of the gastrointestinal tract, etc.). Radiotherapy can cause pain by radiation reaction (acute and late), expressed as inflammation of the mucous membranes and skin, myelotoxicity and neurotoxicity. Chemotherapy can become a cause of pain because of the patient's persistent vomiting, mucositis, neuropathy, or myelotoxicity [7].

Dietary intervention can affect the reduction in the somatic pain syndromes after resection of the various parts of the gastrointestinal tract, as well as in the case of mucositis in different parts of the gastrointestinal tract, which develops as a result of chemotherapy and radiation, and the presence of tumour invasion [8].

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The role of dietary intervention in palliative care. The main goal of nutritional intervention in palliative care is to maintain and improve the quality of life, the difficult part of which is to achieve and maintain normal nutritional status and prevent of malnutrition. It is extremely important that in the nutritional care of the patient a team of professionals: a doctor, dietician, pharmacist, nurse, psychologist, physiotherapist and social worker should be actively involved. The role of the dietitian is to assess the patient's needs for nutrients and to identify the main problems that hinder nutrition [9]. The main obstacles in the proper food intake are anorexia in the course of cachexia, as well as 'voluntary anorexia', in which the patient does not eat because of fear of ailments that food can cause, changes in taste and smell, difficulty in swallowing, pain while chewing or swallowing or after eating, nausea and vomiting, diarrhea and constipation, eating disorders associated with current cancer therapies, cultural or religious issues that affect the eating habits. In a study by the authors (results not yet published) one third of patients had significant appetite disorders, and the greatest decrease in appetite was observed in patients diagnosed with abdominal cancer, especially pancreatic cancer and of the head and neck, as well as tongue, pancreas, prostate cancer, mainly due to nausea associated with anticancer therapy. The biggest change was observed in the preferences of sweet taste, sweet aversion concerned especially dairy products.

In addition, social reasons are often the cause of not eating: lack of strength and/or resources for the preparation of meals, lack of access to a diet with the right consistency and texture, lack of assistance in the preparation of meals, and family or staff patience during feeding. The nutritionist, after assessing the needs and problems of the patient, should propose a solution in the form of specific meal guidance: the frequency of meals, consistency and texture of the diet, food fortification of natural products, the addition of oral nutritional supplements if they are medically justified, and supplementation of vitamins, minerals and other bioactive compounds [10, 11]. It is worth noting that these guidelines should be discussed not only with patients but also with their families and caregivers. The dietitian working as a member of the team is required to give nutritional advice and training to other professionals in the team. It turns out that many professionals, including clinical oncologists, do not recognize malnutrition and are unable to offer appropriate advice. [12].

If patients are not able to consume a standard or enriched diet that cover 60% of the daily requirement for calories and nutrients, and such a situation can take 7–10 days and this condition is not reversible, artificial nutrition should be considered: enteral or parenteral nutrition [13]. Qualification for artificial feeding in palliative care is an extremely difficult decision, because apart from medical indications there are also ethical issues, and the key to the decision is the will of the patient. The administering of artificial feeding to a patient whose survival time is estimated to be less than two months is questionable. The current position of the European Society for Clinical Nutrition and Metabolism (ESPEN) states that in the last days the patient should be feed with small amounts of fluids to prevent dehydration, and provided with the best possible palliative care [14].

In the case of a patients with a longer survival prognosis the primary selected route is always the digestive tract – either by nasogastric or nasojejunal tube, gastrostomy or jejunostomy.

The usage of tube or stoma is determined by the time factor – if feeding extends beyond 3- 4 weeks, it is advisable to apply the stoma. Indications for parenteral nutrition are few and may be offered only when the gastrointestinal tract cannot be used as a way to provide the food [15]. These include intestinal obstruction, bowel failure (severe mucositis, ischemia), extensive resection of the small intestine (left less than 150 cm of the small intestine). The multi-level, often high gastrointestinal obstruction, occurs most often in the course of cancers of the oesophagus and stomach, pancreas, bile tract, as well as the genitalia: ovaries, cervix, endometrial cancer and gynaecological sarcomas.

Influence of dietary factors on pain perception. The definition of pain is very broad: 'the unpleasant physical and / or emotional experience associated with actual or potential tissue damage.' In this sense, any discomfort, including bloating, gas, belching, hiccups, nausea, diarrhea and constipation can cause pain.

Proper selection of nutrients can affect the somatic perception and the quality of life of the patient by the following:

- frequency, consistency and texture of the diet;
- nutritional value of the diet;
- presence of fibre;
- presence of fat and simple sugars in the diet;
- presence of lactose and gluten in the diet;
- presence of nutraceuticals in the nutrition.

Frequency, consistency and texture of the diet. As many as 60% of patients with advanced cancer complain of anorexia and early satiety. Dysphagia is a problem referred in 23 – 46% of patients [16]. This is common among patients with malignancies of the head and neck, but may occur in the course of any other cancer (cancers of the lung, breast, Hodgkin's disease and non-Hodgkin lymphoma, and brain tumours). The traditional meal schedule understood as three main meals and extra snacks is very difficult to achieve at the end of life. Products that require long-biting and chewing, such as some meats or vegetables or tough products, crisp (waffles, crisps, cereals, hard sweets), or sharp, sour (some spices, vinegar, natural silage, some fruit and vegetable juices) can significantly aggravate pain in the mouth and oesophagus. This is especially accurate in patients with mucosal reaction after radiation and chemotherapy, with a syndrome of dryness of mucous membranes of the oral fungal, inflammatory diseases of the teeth and periodontal with severe tooth decay, or with poorly fitting dental prosthesis. The solution to this problem is the increased frequency of meals – 8–10 per day, with small volume portions (not exceeding the volume of a cup – 150–250 ml). The consistency of the meals should be smooth or semi-smooth, without hard or sharp particles. This might include a the diet with soups, cream, milk shakes, mashed fruit and vegetable purees, mousse, jelly, soft cottage cheese. Meat should be ground and served as puddings, mousses, meatballs, homemade bread paste. Carbohydrate products such as breakfast cereals or bread should be soft and soggy, for instance in milk products or watered down broths. Patients with severe inflammatory and necrotic reaction in the mouth should be cautious when eating meals containing natural fruit acids such as citrus juices or berries, silage and natural hot spices, as they may trigger or exacerbate pain in the mouth. Natural soothing, anti-inflammatory and

astringent infusions are flaxseed, marigold and sage, used as a mouth rinse.

Nutritional value of the diet. In order to maintain and improve the quality of life of patients it is additionally crucial to maintain the nutritional status of patients and prevent their further deterioration. Inadequate nutritional value of a diet and caloric intake is one of the pillars that sustain cancer cachexia, and lowers the pain threshold in the emaciated patient. Among other things, inflammatory mediators are responsible for this state (TNF-alpha, IFN-gamma, IL-1, IL-6), and can be produced by the body as well as by tumour cells (PIF, LMF) [17].

The development of bone marrow failure and impaired function of all cell lines occurs quickly: red cell, and platelet and white blood cells. This leads to the development of anaemia, as well as a decrease in resistance, both humoral and cellular, which translates into an increased risk of infection [18]. With the decrease of the patient's anthropometric parameters (weight and height) the decrease in body surface area can be observed. This makes the doses of chemotherapeutic agents suboptimal, henceforth increasing the proportion of side-reactions [19]. This can also exacerbate pain and negatively affect the quality of life. The basis of nutritional intervention is to determine the demand for energy, protein and other nutrients. In patients with advanced disease, indirect calorimetry should be used as the 'Gold Standard'.

Patients whose body weight decreases during cancer therapy by less than 5%, perceive their physical fitness as good or very good, while those with the greatest weight loss experienced a significant reduction in physical fitness. People with prostate cancer and breast cancer significantly more often report average or good physical fitness, compared to those with lung cancer and gastrointestinal cancer.

However, in a patient with anorexia and early satiety, providing the right amount of energy and nutrients can be very difficult. Achieving this goal may become possible not only by varying the frequency and consistency of the food, but also through fortification of the diet and by applying oral nutritional supplements [20]. Fortification of a diet can be carried out using natural products: cream, butter, vegetable oil, honey, nuts, flour, potato flour or rice, as well as adding ground meat, fish or eggs. For fortification, formulas can also be used, usually in the form of powders or solutions containing various macronutrients: carbohydrates, proteins, fats. It appears that the fortification of natural products is better tolerated by patients in palliative care.

In order to achieve the daily demand for energy and protein in a diet, oral nutritional supplements can be provided, usually in a form of complex products (all macro- and micro-diet), with high-calorie and osmolality. These products contain an average of 250–400 calories per 200 ml of the product, and may be a valuable addition to the diet. They are sterile packed, ready to use, do not contain any potentially problematic additives, such as lactose, gluten, cholesterol or purine. However, they are not always well tolerated. Their high osmolality can be responsible for diarrhea and nausea, and despite the wide range of flavors, patients complain of an unpleasant taste of these products. It should also be noted that the improvement in the number of calories can be achieved through psychotherapy (reduction of anxiety, depression), physical therapy (to improve peristalsis, the

potential impact on the growth of muscle mass) and the relevant social welfare [21, 22].

Presence of fibre in the diet. Adequate dietary fibre content in the diet of patients in the palliative stage of life is an extremely important and often entirely overlooked issue. Recommendations for fibre consumption for a healthy human diet is about 25–40 g per day. In the case of a patient with advanced cancer, this demand falls and is set at the level of 15–20 g. A diet with high fibre supply is not only poorly tolerated, but may aggravate constipation, abdominal pain, and even become the cause of gastrointestinal obstruction. This applies particularly to patients who eat very little, are dehydrated, confined to bed and receiving opioids [23]. In this case, insoluble fibre increases constipation and pain, enhances the formation of faecal stones which, in extreme cases, can even lead to bowel perforation and / or obstruction.

Products containing a lot of fibre require a long chewing process, which is often not possible. The patient swallowing large pieces of food, suffers from nausea, bloating and vomiting. Dietary fibre is a component that absorbs at their surface a variety of nutrients, which reduces their availability to the already often malnourished patient. Often occurring in advanced disease and exocrine pancreatic insufficiency, fibre also interferes with digestion and absorption of nutrients. The diet of a patient with advanced cancer should be easy to digest, therefore low in fibre. Passage of stool should be adjusted using proper hydration, natural sorbitols occurring in products such as prunes, pears or using fermented dairy products or products containing a large amount of pectin (apples, oats) [24].

Presence of fat and simple sugars in the diet. An excess of fat and simple sugars in the menu of a patient with advanced cancer may translate into abdominal pain, nausea, bloating, gas and diarrhea. Sugars have the ability to ferment in the intestine, which clinically translates into flatulence and abdominal pain. Fats in the diet of a patient with coexisting exocrine pancreatic insufficiency can cause abdominal pain and fatty diarrhea. At the same time, their presence in the diet enhances satiety which, in cancer patients with anorexia, also reduces caloric intake [25]. In clinical practice, this relationship can be seen particularly in patients with pancreatic cancer. The most common error in this case is the supply of diets containing more than 40–50g of fat a day, high in fibre, as well as with a high fat intake and the administration of oral supplements high in fiber. Such a diet significantly increases pain and fatty diarrhea in this group of patients. From our own experience, a diet low in fat, that is easy to digest, lactose-free, with the administration of pancreatic enzymes formulas and probiotics supplementation, significantly improves the quality of life and largely relieves pain, bloating and diarrhea.

Lactose and gluten content in the diet. Secondary lactose intolerance is a common phenomenon associated with chemotherapy or radiotherapy. In the Polish population, lactose intolerance is present in up to 20% of healthy people and its incidence increases with age [26]. In the course of cancer treatment that causes damage to the intestinal epithelium which produces lactase, which hydrolyses lactose. This relative and usually temporary lactase deficiency is responsible for causing problems after the consumption

of dairy products such as: nausea, abdominal pain, bloating, diarrhea [27]. It is worth noting that the lactose content in dairy products is different: most of it comes from the milk, but also from cheeses, whereas butter contain trace amounts of lactose, and typically can be consumed safely. Definitely better tolerated are fermented dairy products (yogurt, kefir) because the lactose is already pre-digested by bacteria. There are not many cancer treatment regimens that require mandatory exclusion of dairy products from diet like e.g. radio – and chemotherapy in gastric carcinoma. Chemotherapeutic agents associated with a high risk of developing lactose intolerance are: 5-fluoropyrimidine irynotecan, tyrosine kinase inhibitors for the EGFR, temozolomide, and capecitabine, lapatinib, and many others [28]. The risk of lactose intolerance is also associated with radiation in the area of the abdomen and pelvis, as well as with the presence of diabetes and old age. At the beginning of the clinical treatment, only fresh milk should be excluded, and the fermented products with probiotic supplementation should be left in order to further improve lactose digestion, which may reduce the frequency of diarrhea [29]. If this is not enough and symptoms still persist, the patient should be completely taken off dairy products; they may be partially replaced by products of vegetable origin which are rich in calcium and protein.

Gluten intolerance in oncology patients is rare. However, if present, it requires specialized food due to the exclusion of the four basic grains and their derivatives, which may result in a significant depletion of many nutrients: carbohydrates, protein, B vitamins, and many minerals. On the other hand, maintaining the supply of gluten will worsen malabsorption which means the deepening of malnutrition and severity of somatic symptoms: abdominal pain, bloating and diarrhea. Secondary gluten intolerance can occur in women treated with regimens of chemo- and radiotherapy for cancer of the cervix and endometrium, less frequently in patients of both sexes treated for rectal cancer, or men with prostate cancer [30]. Although some patients benefit from the use of such a diet (lower abdominal pain and diarrhea), in the literature there is no evidence for a positive effect of gluten-free diet in oncology and the use of such a procedure. In the presented study, the frequent occurrence of diarrhea was observed in subjects with bowel cancer and prostate cancer, whereas in the patients with kidney, pancreas and lung cancer, constipation was often present.

Presence of nutraceuticals in the diet. In cancer cachexia the supply of appropriate fatty acids, such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) is important. Their source in the diet are sea fish. A certain amount of EPA and DHA precursors α -linolenic acid can be found in soybean oil, rapeseed, flax products, walnuts. EPA and DHA are precursors of eicosanoids: prostaglandins, thromboxanes and leukotrienes. Omega-3 are known for their beneficial effects on the cardiovascular system, as well as anti-inflammatory and analgesic effects in diseases of the musculoskeletal system [31].

In cancer cachexia, the influence of EPA and DHA on the inhibition of proteolytic factor produced by the tumour (PIF), the production of the key pro-inflammatory cytokines (IL-1, 6, TNF- α) and the stimulation of PPAR- α receptor, which is a factor of the transcription of genes for the degradation of leukotrienes (reduction of the inflammatory response), have been described. The stimulation of the PPAR- γ receptor

inhibits the production of NF- κ B, resulting in the induction of apoptosis in tumour cells. In addition, omega-3 fatty acids have a synergistic effect with chemotherapeutic agents, and increase the sensitivity to chemotherapy while decreasing its toxicity [32, 33]. The doses used in the treatment of patients affected by emaciation should be in the range of 1.5 – 2.0 g per day. Omega-3 polyunsaturated fatty acids could indirectly help the treatment of cachexia by reducing the inflammatory response, and may have an impact on the perception of pain by releasing endorphin [34].

A common problem in clinical practice is pain in the course of chemotherapy-induced peripheral neuropathy (CIPN). There is now a systematic review of studies where, in pain control as well as paresthesia in the course of CIPN, various nutraceuticals were used [35]. Efficacy of compounds such as vitamin E, B₆, the omega-3 group polyunsaturated fatty acids, carnitine, glutamine, glutathione, magnesium, calcium, α -lipoic acid, and N-acetyl-cysteine were evaluated. To date, no convincing evidence has been found regarding the use of any nutraceuticals in the prevention or treatment of CIPN in clinical practice.

CONCLUSIONS

Properly planned dietary intervention can reduce or prevent the increase of malnutrition and cachexia in patients with cancer. The energy and nutritional value of applied diets and a suitable selection of foods and cooking techniques can significantly improve the quality of life of patients with advanced cancer, in particular reducing the severity of pain and other somatic symptoms.

REFERENCES

1. Nekolaichuk CL, Fainsinger RL, Aass N, Hjermstad MJ, Knudsen AK, Klepstad P, Currow DC, Kaasa S. For the European Palliative Care Research Collaborative (EPCRC). The Edmonton Classification System for Cancer Pain: Comparison of Pain Classification Features and Pain Intensity Across Diverse Palliative Care Settings in Eight Countries. *J Palliat Med.* 2013; 16(5): 516–523.
2. DeWys WD, Begg C, Lavin PT, Band PR, Bennett JM, Bertino JR, et al. Prognostic effect of weight loss prior to chemotherapy in cancer patients. *Am J Med.* 1980; 69 (4): 491–497.
3. Muscaritoli M, Anker SD, Argilés J, Aversa Z, Bauer JM, Biolo G, et al. Consensus definition of sarcopenia, cachexia and pre-cachexia: Joint document elaborated by Special Interest Groups (SIG) „cachexia-anorexia in chronic wasting diseases” and „nutrition in geriatrics”. *Clin Nutr.* 2010; 29 (2): 154–159.
4. Bonica JJ. Anatomic and physiologic basis of nociception and pain. In: Bonica JJ. The management of pain. Ed. 2. Lea & Febiger, Philadelphia, London 1990, p. 28–95.
5. Daut RL, Cleeland CS. The prevalence and severity of pain in cancer. *Cancer.* 1982; 50: 1913–1918.
6. Stuver ShO, Isaac Th, Weeks JC, Block S, Berry DL, Davis RB, Weingart SN. Factors associated with pain among ambulatory patients with cancer with advanced disease at a Comprehensive Cancer Center. *J Oncol Pract.* 2012; 8(4): 17–23.
7. Zhu J, Davis RB, Stuver ShO, Berry DL, Block S, Weeks JC, Weingart SN. A Longitudinal study of pain variability and its correlates in ambulatory patients with advanced stage cancer. *Cancer.* 2012; 118: 6278–6286.
8. Foley KM: Pain syndromes in patients with cancer. In: Bonica JJ, Ventafridda V (eds.), *Advances in Pain Research and Therapy.* Raven Press, New York 1979, 2: 59–78.
9. Omlin A, Blum D, Wierecky J, Haile SR, Ottery FD, Strasser F. Nutrition impact symptoms in advanced cancer patients: frequency and specific interventions, a case-control study. *J Cachexia Sarcopenia Muscle.* 2013; 4: 55–61.

10. Jarosz J, Kapała A, Kłęk S, Misiak M, Bakinowska B., Czaplinska M., et al. Konferencja Uzgodnieniowa: Problemy żywieniowe w polskiej onkologii. *Postępy Żywienia Klinicznego*. 2012; 1: 29–38 (in Polish).
11. Stratton RJ, Elia MA. A review of reviews: A new look at the evidence for oral nutritional supplements in clinical practice. *Clin Nutr Suppl*. 2007; 2(1): 5–23.
12. Bourdel-Marchasson I, Barateau M, Rondeau V, Dequae-Merchadou L, Salles-Montaudon N, Emeriau J-P, et al. A multi-center trial of the effects of oral nutritional supplementation in critically ill older inpatients. *Nutrition* 2000; 16(1): 1–5.
13. Spiro A, Baldwin C, Patterson A, Thomas J, Andreyev HJN, et al. The views and practise of oncologists towards nutritional support in patient receiving chemotherapy. *Br J Cancer*. 2006; 95(4): 431–434.
14. Sobotka L (ed.). *Basics In Clinical Nutrition. Techniques of nutritional support*. 5th ed. ESPEN, Prague 2011.
15. Arends J, Bodoky G, Bozzetti K, Fearon M, Muscaritoli G, Selga MAE, et al. ESPEN guidelines of enteral nutrition: non surgical oncology. *Clin Nutr*. 2006; 25(3): 245–259.
16. Bozzetti F, Arends J, Lundholm K, Micklewright A, Zurchere G, Muscaritoli M, et al. ESPEN Guidelines on Parenteral Nutrition: Non-surgical oncology. *Clin Nutr*. 2009; 28(4): 445–454.
17. Roe JW, Leslie P, Drinnam MJ. Oropharyngeal dysphagia: the experience of patients with non-head and neck cancers receiving specialist palliative care. *Palliat Med*. 2007; 21(7): 567–574.
18. Argilés JM, Busquets S, Toledo M, López-Soriano FJ. The role of cytokines in cancer cachexia. *Curr Opin Support Palliat Care*. 2009; 3(4): 263–268.
19. Van Bokhorst-de van der Scheuren MAE, von Blomberg-Van der Flier BME, Riezebos RK, Scholten PET, Quak JJ, Snow GB, van Leeuwen PAM. Differences in immune status between well-nourished and malnourished head and neck cancer patients. *Clin Nutr*. 1998; 19(6): 437–444.
20. Sánchez-Muñoz A, Pérez-Ruiz E, Sáez MI, Trigo JM, Galindo MM, Manzanque L, Jiménez B, Muros B, Alba E. Limited impact of palliative chemotherapy on survival in advanced solid tumours in patients with poor performance status. *Clin Transl Oncol*. 2011; 13(6): 426–429.
21. Ravasco P, Monteiro Grillo I, Maria C. Cancer wasting and quality of life react to individualised nutritional counseling. *Clin Nutr*. 2007; 26(1): 7–15.
22. Robison J, DuPen S, Stillman M, Fredrickson M, Rivkin S, Feldman E, Gralow J, Rieke JW, Raish RJ, Lee DJ, Cleeland ChS, DuPen A, Syrjala KL, Abrams JR, Polissar NL, Hansberry J. Patient training in cancer pain management using integrated print and video materials: A multisite randomized controlled trial. *Pain*. 2008; 135: 175–186.
23. Capozzi LC, Lau H, Reimer RA, McNeely M, Giese-Davis J, Culos-Reed SN: Exercise and nutrition for head and neck cancer patients: a patient oriented, clinic-supported randomized controlled trial. *Cancer* 2012; 12: 446–454.
24. Power J. Fact Sheet 14: If your bowel is blocked. London 2009. <http://www.ovacom.org.uk> (access: 26.11.2013).
25. Xue H, Sawyer MB, Wischmeyer PE, Baracos VE. Nutrition modulation of gastrointestinal toxicity related to cancer chemotherapy: from preclinical findings to clinical strategy. *J Parenter Enteral Nutr*. 2011; 35: 74–90.
26. Hutton JL, Martin L, Field CJ, Wismer WV, Bruera ED, Watanabe ShM, Baracos VE. Dietary patterns in patients with advanced cancer: implications for anorexia-cachexia therapy. *Am J Clin Nutr*. 2006; 84: 1163–1170.
27. Hutyla T, Iwańczak B. Nietolerancja laktozy: patofizjologia, objawy kliniczne, rozpoznanie i leczenie. *Pol Merk Lek*. 2009; 36(152): 148–152 (in Polish).
28. Wedlake L, Thomas K, McGougha C, Andreyev HJN. Small bowel bacterial overgrowth and lactose intolerance during radical pelvic radiotherapy: An observational study. *Eur J Cancer*. 2008; 44(15): 2212–2217.
29. Benson AB, Jaffer A, Ajani A, Catalano RB, Engelking C, Kornblau SM. Recommended guidelines for the treatment of cancer treatment-induced diarrhea. *J Clin Oncol*. 2004; 22(14): 2918–2925.
30. Delia P, Sansotta G, Donato P, Frosina P, Messina G, De Renzis C, Famularo G, et al. Use of probiotics for prevention of radiation-induced diarrhoea. *World Journal of Gastroenterology* 2007; 13(6): 912–915.
31. Jervoise H, Andreyev N, Davidson SE, Gillespie C, Allum WH, Swarbrick E: Practice guidance on the management of acute and chronic gastrointestinal problems arising as a result of treatment for cancer. *Gut*. 2012; 61: 179–192.
32. Hardman WE. (n-3) Fatty Acids and Cancer Therapy. *J Nutr*. 2004; 134: 3427S–3430S.
33. Laviano A, Rianda S, Molfino A, Fanelli FR. Omega-3 fatty acids in cancer. *Curr Opin Clin Nutr Metab Care*. 2013; 16(2): 156–161.
34. Lee YH, Bae SC, Song GG. Omega-3 polyunsaturated fatty acids and the treatment of rheumatoid arthritis: a meta-analysis. *Arch Med Res*. 2012; 43(5): 356–362.
35. Nakamoto K, Nishinaka T, Matsumoto K, Kasuya F, Mankura M, Koyama Y, Tokuyama S. Involvement of the long-chain fatty acid receptor GPR40 as a novel pain regulatory system. *Brain Res*. 2012; 13(1432): 74–83.
36. Schloss JM, Colosimo M, Airey C, Masci PP, Linnane AW, Vitetta L. Nutraceuticals and chemotherapy induced peripheral neuropathy (CIPN): A systematic review. *Clin Nutr*. 2013 <http://dx.doi.org/10.1016/j.clnu> (access: 2013.04.07).