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MANAGEMENT AND TREATMENT OF SARCOPENIA IN FIFTY PATIENTS RECEIVING CHEMOTHERAPY WITH AHCC (ACTIVE HEXOSE CORRELATED COMPOUND)

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Abstract – *Objective:* *Malnutrition is a recurrent problem in cancer patients, which can condition the prognosis and compliance to therapeutic protocols. Therefore, an evaluation of the nutritional status is pivotal before therapeutic interventions, as well as* in itinere*, to confirm the possible presence of cachexia, evident and subclinical deficiencies.*

Alpha and β-glucans from the fungi (Lentinan) have been used as therapeutic support for thousands of years in oriental culture. Active Hexose Correlated Compound (AHCC) is a molecule rich in alpha-glucan derived from the mycelium of the shiitake mushroom (Lentinula edodes) *with antioxidant, anti-inflammatory and immunomodulatory properties, as well as antiproliferative. AHCC boasts multiple studies published in specialized international journals suggesting their integration to the diet to support the immune system and promote the reduction of side effects due to chemotherapy.*

Patients and Methods: *We evaluated fifty patients diagnosed with adenocarcinoma and malnutrition, during radio-chemotherapy. All patients were given a food therapy and a dose of AHCC of 1.5 g/day. Bioelectrical impedance assessed body composition at time 0 and after 3 - 6 months of nutritional therapy.*

Results: *There was no progression of cancer malnutrition/cachexia in 80% of the subjects, instead of a concomitant increase in body cell mass (BCM)..*

Conclusions: *The use of AHCC during chemotherapy helps to prevent cases of cachexia and sarcopenia, as evidenced in our study by the BCM analysis.*

These preliminary results could be related to longevity/environmental issue in order to plan a specific project of nutritional diet upper for people who lived in high environmental risk area.

KEYWORDS: *Alpha glucans, Cancer therapy, Nutrition.*

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INTRODUCTION

The majority of patients with advanced neoplasia often suffer an involuntary weight loss[1]. The main cause of this condition is neoplastic cachexia. As a complex metabolic disorder, cachexia involves the depletion of skeletal muscle and adipose tissue, anorexia, fatigue, anemia and alterations of the immunological and endocrine structure[2,3]. Furthermore, since cachexia is often accompanied by anorexia, it can lead to a reduction in physical activity and an increase in psychological distress[4]. Up to 80% of people with cancer have involuntary weight and appetite loss[5]; these conditions have been associated with a reduced quality of life and an increase in morbidity[6,7]. However, although cachexia has long been recognized as an adverse effect of cancer [8], weight loss in cancer patients is rarely understood and assessed by hospital staff [9,10]. Patients with severe muscle loss, due to severe catabolic status or metastatic disease refractory to therapy, unlikely benefit from clinically relevant multimodal treatments designed to result in gain of functionality and lean tissue mass [11]. Furthermore, the collection of signs and symptoms of cachectic syndrome makes this condition difficult to define, as well as extremely difficult to treat effectively[12]. Because of the prevalence of cachexia in patients with advanced cancer, physicians have focused efforts to assess and classify patients, in order to allow early identification of those who have an unusually high risk of developing this condition to enable more timely treatments[13]. Based on recent studies[14], the current international consensus includes skeletal muscle loss (sarcopenia) in the definition of cancer cachexia, regardless of the loss of fat mass. Cachexia is, therefore, defined as weight loss > 5% in subjects without previous muscle depletion or weight loss of > 2% in those who have already shown a body mass index depletion of < 20 kg/m^2 or a loss of skeletal muscle[2]. Therefore, sarcopenia must be considered as a critical diagnostic criterion. The term sarcopenia derives from the Greek meaning "poverty of meat" and is characterized by the progressive loss of skeletal muscle mass, muscular strength, and physical performance[15]. The predictive value of sarcopenia for health purposes is linked to the functional and metabolic relationship between muscle mass and physical strength, mobility and vitality[16-18]. In particular, sarcopenia is related to the increased risk of decreased muscle strength and physical activity linked to age[19,20]. It has been described initially in the non-cancerous elderly population and is often defined as a geriatric syndrome associated with functional impairment, increased risk of falls, fractures and reduced survival[16,21,22]. Recently, sarcopenia has received particular attention in the oncology literature because it is associated with reduced physical activity and increased mortality in cancer patients[23-25].

AHCC

The scientific literature does not give us much information about the properties of alpha-glucans, but many works since the late '80s speak of a mildly sweet monosaccharide produced by the mycelium of a Shiitake hybrid grown in rice bran extract. The rice bran itself has antiviral and immune system support. The AHCC was developed in 1987 at the Faculty of Pharmaceutical Sciences of the University of Tokyo by Dr. Toshihiko Okamoto, in collaboration with the researchers of Amino Up Chemical Co. Ltd. The AHCC is extracted from the strands forming the mycelium of the mixture of mushrooms grown in a pre-cultivation tank. In the successive forty-five days, the mushroom colonies grew in the primary culture tank. The AHCC is obtained through a patented process of culture, enzymatic decomposition, sterilization, concentration and cryo-drying. Among the main components of AHCC is partially acetylated α-glucan, which is known for its beneficial effects on the immune system [26]. One of the advantages of the fermentation process is linked to the breakdown of nutrients in a form more easily absorbed by the body. The AHCC has a molecular weight of only 5,000 daltons. The molecular weight of most of the fungal extracts is hundreds of thousands of daltons. A reduced molecular weight increases the effectiveness of the nutrients that are absorbed and used without their elimination. All this ensures that the powerful nutrients contained in the AHCC are quickly assimilated by white blood cells to be used immediately to destroy tumors or to strengthen the immune system. This is another reason, in addition to its immune-strengthening function, for which the AHCC is considered a superfood. The acronym AHCC is for Active Hexose Correlated Compound (active hexose linked compound). Developed in the late 1980s as a natural agent for regulating blood pressure, researchers soon observed its beneficial effects on the immune system. The AHCC has been used to treat some of the most serious diseases, including cancer, heart disease, hepatitis and AIDS. The AHCC has been widely publicized in Japan in hundreds of newspapers, magazines and in peer-reviewed scientific publications. There are many books written about it, such as, for example, Testimony of 11 Cancer Doctors: Why Is AHCC Effective? Gendai Shorin, Tokyo 1999; The Cancer Immunity Screening, K.Uno, Metamor Shuppan, Tokyo 2000. In addition, there are several testimonies of healing or marked improvement of many other diseases, such as slow lesions to heal, stomach ulcers, gingivitis, chronic fatigue, parasites, multiple sclerosis and other autoimmune diseases.

The word "cancer" is perhaps the most feared of the whole vocabulary. Conventional methods of treatment include chemotherapy, radiation, and surgery.

All these approaches, however, radically influence the patient's immunity and well-being. Not only chemotherapy and radiation weaken the immune system, but the former, in particular, damage the well-being of the patient, causing inappetence, nausea, vomiting, depression, fatigue, and hair loss. Furthermore, chemotherapy can have adverse effects on the liver function, causing numerous complications. A frequent damage to the bone marrow, which deeply compromises the immune system and the body's ability to produce white blood cells and red blood cells, is also added. The latest trend in cancer therapies is a non-toxic treatment to stimulate the immune system. This immunotherapy is based on the use of "biological response modifiers" (BRM - biological response modifiers) and is rapidly gaining favors from the traditional medical environment, especially in Japan, where AHCC often supports conventional anti-cancer treatments. In Japan, AHCC is considered the most potent biological response modifier capable of strengthening the immune system; for this reason, it is indicated for the treatment of any cancer. According to data on the treatment of over 100,000 patients affected by various types of cancer, 60% of these have benefited to some extent, and many have found it useful enough to induce remission of the disease.

AHCC has been shown to be particularly effective against liver, lung, stomach, colon, breast, thyroid, ovary, testicular, tongue, kidney and pancreas cancers[27]. The results vary from an effective reduction of the tumor mass to the arrest of the tumor growth, from stopping the spread of the tumor in the whole body (metastasis), to the increase of the survival times, up, above all, to a notable improvement of the life quality.

Improve survival rate: in a prospective cohort study conducted in Osaka, Japan, AHCC was given following surgery to a group of patients with liver cancer. Compared to the control group, which had not been given AHCC, the five-year survival rate of the AHCC group was 14% higher. At the end of the study, 79% of the patients taking the AHCC were still alive, compared to 51% of the patients in the control group. Furthermore, the onset of postoperative hepatitis or cirrhosis was greatly reduced as demonstrated by laboratory tests performed up to five years later. However, the most critical finding was that fewer patients had cancer recurrence: 49% of the AHCC group compared to 67% of the control group[28]. The survival rate of patients taking AHCC was on average higher of 23 months. The authors of the liver tumor study noted the absence of undesirable effects due to AHCC. The AHCC seemed to alleviate a large part, and sometimes even all, the extremely unpleasant effects of chemotherapy[29].

Japanese researchers analyzed 229 cancer treatment cases during 3 years, in which 127 patients were treated with AHCC, while the remaining 102 were not given supra-activity. In almost all cases, AHCC was used in combination with a conventional chemotherapeutic agent. The mean time and survival rate were compared with the control group that did not take the AHCC. The results showed that oral intake of AHCC prolonged the survival times of patients with various types of cancer.

A study published in 1998 showed how AHCC enhanced the therapeutic effects of chemotherapy, reducing its side effects. The AHCC prevented the inhibition of NK cell activity due to chemotherapy, improving the operation of macrophages, also generally suppressed by therapy. The AHCC associated with traditional chemotherapy has improved its effectiveness, reducing the size of the tumor by 20% more than the chemotherapy alone, and preventing metastases, the spread of the cancer to other parts of the body, 30% more compared to chemotherapy alone. One of the significant advantages of AHCC over conventional chemotherapy, which does not distinguish between healthy cells and cancer cells, is linked to the fact that it stimulates the action of NK cells, which only destroy abnormal cells[30].

PATIENTS AND METHODS

Patients

Fifty patients from the Province of Naples and Caserta, diagnosed with adenocarcinoma, were selected in our study. All patients were followed during the radio-chemotherapy regimen. Drugs predominantly used were: placlitaxel and gemcitabine (pancreatic adenocarcinoma), placlitaxel/alimta (pulmonary adenocarcinoma) FOLFOX (colorectal adenocarcinoma), Placlitaxel/doxorubicin/5-fluorouracil (breast adenocarcinoma). All patients showed cachectic syndrome at the first visit (weight loss > 5% in the last few months).

Body Composition Analysis

The measurement of body composition was performed using a Bioelectric Vector Impedance analysis with Akern BIA 101 device, at time 0 and after a variable period of 3-6 months, depending on the individual chemotherapy period. The bioelectrical impedance is a measurable property due to the ionic conduction of the tissues, indicating the hydration of the muscles. The alternating current at constant intensity and frequency (50 kHz) injected onto the skin by electrode-patches passes through the electrolytic solutions of LEC and LIC of all tissues, excluding fat and bone, generating a Vector impedance Z, expressed in Ohms. The cell membranes and the tissue interfaces phase out the current conduction (phase angle between voltage and current of the vector Z)

generating the capacitive component of Z, or Xc[26-29]. The Vector Z can be represented in polar coordinates with module and phase angle, or in the usual rectangular coordinates Z = (R, Xc), or Z = R + j Xc, with the two components Resistance (R, depending on the LIC + LEC solutions crossed) and Reactance (Xc, dependent on membranes and interfaces crossed). The rectangular representation (R, Xc) with R in the abscissae and Xc in the ordinates provides, in addition to the module | Z | = Ö (R2 + Xc2), also the phase angle as arctangent of Xc/R. The BIA can therefore specifically recognize and measure only the conductive compartment of the tissues, a chamber expressed as the value of R from the intra and extracellular electrolyte solutions, and as the value of Xc from the whole of the cell membranes of the compartment itself.

Nutritional Therapy

The diet dispensed to the subjects, without total exclusion of any alimentary category, has been elaborated with prevalence of vegetable proteins; only in one patient, the diet was characterized by a limitation of intake of animal proteins. It has the following characteristics:

a. The caloric levels and the macronutrient balance were calculated by combining the basal metabolic rate analysis, obtained by evaluating the Bioelectrical Impedance (direct method) together with the use of the most accredited mathematical formulas in the literature (indirect method).
b. Primary sources of macronutrients (whole grains rich in fiber and vegetable proteins): brown rice, buckwheat, barley, spelled, quinoa. Fish meat. Eggs and white meat, a weekly portion.
c. Main sources of Micronutrients: seasonal fruit and vegetables, whole and in juice (obtained by centrifugation/extraction). These foods come from the regional markets, suggesting a rotation of the type of plant and the place of purchase.
d. Other foods: non-creamy white yogurt, rice miso, turmeric, ginger, bitter almonds, walnuts. Blend 50% extra virgin olive oil and linseed oil. Low residual natural water with slightly alkaline pH.

Nutraceutical Diet Integration

Together with the diet, a dose of 2 gr/die of AHCC was administered at 10:00 pm.

RESULTS

The change in body cell mass (BCM) was assessed at entry and after a variable period of 3 to 6 months, depending on the individual chemotherapy period. In 80% of the subjects, there was no progression of malnutrition/cancer cachexia, instead of a concomitant increase in body cell mass (BCM) (Figure 1). Also, 90% of patients, for the duration of treatment, did not use myelostimulant drugs (Filgrastim, Pegfilgrastim), showing minimal fluctuations of the total blood count.

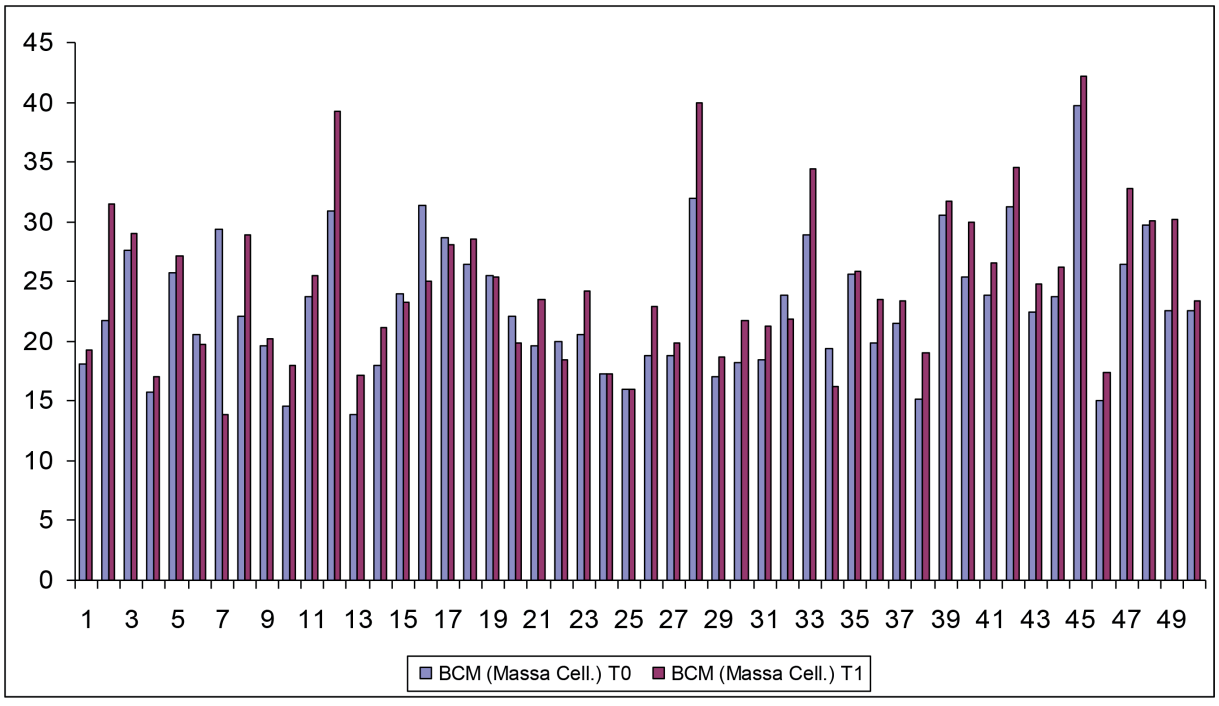

Fig. 1. The change in body cell mass (BCM) at T0 (entry) and T1(after a variable period of 3 to 6 months) in all patients.

DISCUSSION

More than half of patients with solid tumors experience excessive and progressive weight loss, defined as sarcopenia or, in advanced cases, cancer cachexia. This phenomenon is due to the exhaustion of adipose and muscular tissue. It increases the rate of morbidity and mortality, reduces the patient's quality of life and complicates management, reducing tolerance and response to drug treatments. Cachexia is the direct cause of death in 22-44% of cancer patients. This pathological weight loss cannot be countered only with a nutritional approach, but it would also be necessary to act at a pharmacological level. To do this, it is necessary to have a thorough knowledge of the pathological and molecular mechanisms underlying this complex phenomenon, which are still largely unknown, including the important concept of inflaming. In this context of immuno-inflammation, it is essential to evaluate the most active nutraceuticals, such as polysaccharides extracted from fungi, and in particular AHCC extracted from *Lentinula Edodes*. During the oncological treatments, the integration has helped to promote the anabolic process with a recovery of lean mass. Certainly more extensive cohort studies are needed to validate these preliminary results; however, the question is significant, as far as today the only remedy in use is constituted by the supply of high quality proteins (at dosage slightly higher than that physiological), associated with a light physical exercise.

CONCLUSIONS

The use of AHCC during chemotherapy helps to prevent cases of cachexia and sarcopenia, as evidenced in our study by the BCM analysis (Figure 1).

These preliminary results could be related to longevity/environmental issue in order to plan a specific project of nutritional diet [31] for people who lived in high environmental risk area.

Conflict of Interest:
The Authors declare that they have no conflict of interests.

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