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Research Paper

Maximum Voluntary Contraction of Muscle, Body Composition & Ergoreflex in Adult Male Cancer Patients

Medical Science

KEYWORDS :

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ABSTRACT

Cancer is a disease in which a group of cells display unregulated growth. Almost half of all the cancer patients show a syndrome of cachexia. Ergoreflex is a peripheral reflex originating in skeletal muscles. Metabolic abnormalities in skeletal muscles with early acidosis and accumulation of catabolites on exercise, have been shown to be responsible for their enhanced activity. So the aim of the study is to see if there is any association between peripheral muscle wasting and Ergoreflex. In the present study it was observed that muscle mass was significantly reduced in cancer patients. Also there was statistically significant decrease in mid arm circumference in experimental group. changes in body composition are also an important indicator adjuvant index in the assessment of cachexia. Education about risk factors, early detection, treatment and palliative care can be helpful in decreasing the incidence as well as morbidity and mortality of the disease.

INTRODUCTION

Cancer is a disease in which a group of cells display unregulated growth. Almost half of all the cancer patients show a syndrome of cachexia. Cachexia is characterized by weight loss involving depletion of host adipose tissue and skeletal muscle mass [1]. Cachexia occurs in number of diseases like COPD, CHF, AIDS, and Anorexia Nervosa. Weight loss in Anorexia Nervosa, is predominantly from fat tissue. The muscle mass being mainly preserved. In cancer patients weight loss is equally from fat and lean tissue with significant loss of muscle tissue [2]. Although anorexia is common in cancer patients, the body composition changes suggest that anorexia alone is not responsible for cachexia. In cancer patients loss of both muscle and adipose tissue has been reported to precede the fall in food intake [3].

A number of cytokines including TNF-α, IL-1, IL-6, and Interferon-α have been proposed as mediator of cachetic process [1]. Loss of muscle tissue in cancer patients is reflected in functional changes of various reflexes arising from them e.g. Ergoreflex.

The muscle wasting maybe associated with reduced muscle strength and fatigue on physical exertion. These functional changes are accompanied by increased sympathetic activity, manifested as reflex increase in heart rate, respiratory minute volume, and constriction of peripheral blood vessels and increased blood pressure. This is well established as one of the factors contributing to fatigue and dyspnoea in heart failure patients

Ergoreflex is a peripheral reflex originating in skeletal muscles. Nerve endings that are sensitive to metabolites exist in skeletal muscles and have been named ergoreceptors [4]. Ergoreceptors are intramuscular afferents, and are functionally differentiated into Mechanoreceptors and Chemoreceptors. The Mechanoreceptors are finely myelinated group III afferents and they respond mainly to mechanical stimuli. Chemoreceptors are group IV afferents which are sensitive to acid metabolites in muscles, but also to prostaglandins and bradykinin. Once the ergoreceptors are stimulated they cause sympathetic drive, increase in blood pressure and ventilation. This combined effect is beneficial in diverting more oxygenated blood to the working skeletal muscles [5]. Ergoreceptors activation has been subject of several recent studies in heart failure syndrome, where metabolic abnormalities in skeletal muscles with early acidosis and accumulation of catabolites on exercise, have been shown to be responsible for their enhanced activity. [6]

So the aim of the study is to see if there is any association between peripheral muscle wasting and Ergoreflex.

MATERIALS AND METHODS

The study was conducted in Department of Physiology, Himalayan Institute of Medical Sciences (HIMS), Swami Ram Nagar, Dehradun, over a period of 12 months. Study group was selected from the patients presenting in Cancer OPD of HIMS Dehradun with primary diagnosis of cancer. Written informed consent was obtained from the subjects for inclusion in the study.It is observational, analytical cross-sectional study in cancer patients. Control subjects (n=30)were selected from the people working in HIMS belonging to the age group of 45 to 60 years .Control group included healthy adults.

Experimental group included (n=30) cancer male patients of the age group 45-60 years who were histologicaly diagnosed cancer Diagnosed cancer patients before beginning of treatment. Cancer patients after 3 months of completion of treatment.

The other cachetic conditions like CHF, COPD, Anorexia nervosa, Tuberculosis, Liver Diseases, Thyrotoxicosis were excluded.

Data acquisition was done using window based computerized polygraph i.e. physiopac (Medicaid systems). Physiopac is capable of simultaneously recording signals of different physiological parameters.

Harpenden type skin fold caliper [Model-SFCG80 Galaxy Scientific New Delhi

(India)] - used for measuring skin fold thickness

Handgrip Dynamometer device was used for measurement of isometric force and sustained static exercise stimulation.The subject held the dynamometer in the non-dominant hand, with the arm by the side of the body. The pointer on the dial of the dynamometer was adjusted at zero and the base rested on the palm. The subject squeezed the dynamometer with maximum isometric effort, and maintained for at least 5 seconds for obtaining Maximum Voluntary Contraction (MVC). No other body movement was allowed. The subject was strongly encouraged to give a maximum effort. 50% of MVC thus recorded, was used for Sustained Hand-Grip (SHG) as given in the protocol.

Relevant medical history was taken involving present illness, past illness, personal and family history. Also relevant clinical examination was done.

Anthropometric and basal cardio respiratory parameters were recorded in both the groups. Height was taken as standing height, without shoes with light clothes, using the wall mounted measuring tape in centimeters. Weight was taken with light

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clothes on, without shoes on "Krups" weighing machine.Body Mass Index was calculated as weight in kilograms (kg) divided by height in m^2 (Kg/ m^2).

Mid arm circumference (cm) was measured by measuring tape at a fixed point midway between acromian and olecranon process, without applying any pressure.Skin fold thickness was measured using Harpenden type skin fold caliper. It was ensured that caliper was clean and opened freely and smoothly. Reliability of zero value was checked. The caliper was placed perpendicular to the skin fold, on the site marked with dial facing up. The subject was asked to keep the muscle relaxed during the test. Triceps skin fold (TSF) was measured as a vertical fold on the posterior aspect of arm over the triceps muscle, mid way between the acromian process and olecranon process. Subject was asked to keep the elbows extended and arms relaxed during the test. A minimum of two measurements were taken and the average of two values was taken. Body composition parameters like Body Fat Fat Mass (kg) ,Fat Free Mass (FFM) (kg), Corrected Arm Muscle Area (CAMA) , Muscle Mass were done using various formulae . [7, 8]

Ergoreflexwas was done by asking Subjects to avoid strenuous physical activity for at least 24hrs before assessment test and to refrain from smoking and having caffeinated beverages for at least 3hrs prior to test. The subjects were briefed and familiarized with the process, so as to remove apprehension regarding the test. The demonstration of the test was done to make them familiar with the procedure.

The environment in the laboratory was quiet, with dimmed lighting, and the subject was asked to rest for 15min prior to any data collection. Tests were performed in morning from 8am-10am in thermo neutral zone to avoid the effect of diurnal variation and temperature. Data was recorded, with subject in seated position in chair. To evaluate Ergoreflex in forearm, post exercise regional circulatory occlusion method (PE-RCO) was used [5]. The test consisted of following steps-

The protocol included two exercise bouts which were performed in random order- Protocol I- SHG exercise without PE-RCO. Protocol II- SHG followed by 3min of venous occlusion by inflation of Riva Rocci cuff i.e. SHG exercise followed by PE-RCO . [9] There was a period of rest of at least 30min between 2bouts of exercise to minimize the effect of muscle fatigue.

Briefly the test consisted of following steps- (a)Determination of Maximum voluntary contraction (MVC) of hand muscles using hand grip dynamometer.

Subject was asked to perform sustained hand grip (SHG) at 50% MVC for 3 minutes. From 10 seconds before the end of exercise, 3minutes of circulatory (venous) occlusion was done at 40mmHg. Recovery phase started with release of pressure at the end of occlusion period. Data was recorded for 10 minutes during recovery phase.

The degree of activation of Ergoreflex was assessed during recovery phase as the difference in the parameters between recovery with occlusion and non occlusion.

Statistical Analysis was done using SPSS (version 16) using Unpaired t-test Repeated measures ANOVA .Pearson correlation was used to study the correlation between muscles mass with Ergoreflex.

Result :

Variable	Control group means±SEM (n=30)	Experimental group means±SEM(n=30)
BMI(kg/m^2)	25.5 ± 0.6	19.3 ±0.5***
MVC(kg)	34.8 ± 1.2	23.3 ± 1.3***

Body composition parameters and MVC in control group and experimental group

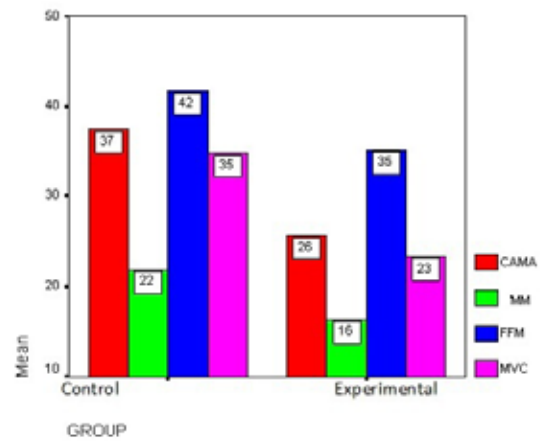

Figure 2 shows all the parameters decreased in experimental group (cancer patients) are lower when compared with control group

DISCUSSION

Exertional fatigue is directly and inversely related to skeletal muscle mass and strength. Cancer related fatigue is a highly prevalent and multifactorial symptom that is classically defined as a "persistent, subjective sense of tiredness related to cancer, or cancer treatment that interferes with usual functioning". A reduction in muscle mass coupled with muscle weakness could be the objective measure that partially explains the degree of tiredness and exhaustion experienced by many patients with advanced cancer. There is a definite link between muscle mass/ strength and fatigue .[10]

In cachexia patients body seems to consume more energy than normal. Even at rest their metabolic rate is higher than normal which leads to patient's weight loss in spite of sufficient daily calorie intake. This serious malnutrition state leads to reduction in patient's ability to be independent and simple daily tasks become difficult. There are cases where severe cachexia has even resulted in death. [11]

In the present study it was observed that muscle mass was significantly reduced in cancer patients. Studies show that possible mechanism for increased catabolism results from activation of various catabolic pathways, though we have not studied them in our study. One of them is lysosomal system which degrades plasma proteins or membrane receptors by acid activated cathepsin proteases B, H and D [12]. Second pathway is by calpin proteolytic system [13]. Third pathway is cytosolic, ATP-dependant ubiquitin proteosome pathway. This pathway has been known to play important role in cancer cachexia, sepsis, weightlessness, starvation and denervation atrophy [14]. It has been clear from the studies of Goldberg and coworkers that various conditions of skeletal muscle

wasting are associated with activation of ubiquitin proteosome system [15].

In our study there was statistically significant decrease in mid arm circumference in experimental group. Reduction in muscle mass coupled with muscle weakness could be one of the objective measures that partially explains the degree of tiredness and exhaustion experienced by many patients with advanced cancer. Stone et al [16] found that mid arm circumference was significantly related to subjective feeling of fatigue in patients with advanced forms of lung, breast and prostate cancer.

In our study there was no statistically significant reduction in food intake before and after diagnosis of cancer in experimental group. Experimental studies have documented that plasma leptin levels are found to be decreased, while Hypothalamic Neuropeptide Y (NPY) mRNA was found to be raised. It was seen that suppression of hunger is probably due to tumor products that inhibit NPY transport, release or it interferes with neuronal targets downstream of NPY. [17]

In our study there was statistically significant decrease in body weight, fat free mass, muscle mass and BMI in experimental group. Recent communications have emphasized that gross weight changes in patients with advanced cancer may be minimal even when large amounts of body fat are being lost. Under these conditions it has been shown that there may be great gain of total body water, without detectable edema. In addition these patients exihibit high rates of caloric expenditure. It is pertinent to compare the changes in body composition in cancer patients to those in normal subjects. The study by Craig AB et al [18] showed that patients with cancer showed that gross weight loss was less than calculated fat loss. There was direct evidence of a gain of total body water in every patient. It has been demonstrated that water content of malignant tissue, itself is increase. Greenstein [19] has postulated that changes in the host tissue represent "generalized systemic 'cancerousness' of the organs". This implies that host tissue assume some of the biochemical aberrations of the tumor. [20]

Maximum Voluntary Contraction was decreased in experimental group as compared to control group. The cancer patients were unable to perform SHG for 3 minutes (decrease in duration). This may be due to fatigue which is a common symptom seen in cancer patients. Fatigue is also reported in other cachetic conditions like COPD, Heart Failure and more than half of HIV patients. One study [21] has stressed the qualitative difference of cancer related fatigue in everyday life as 'Fatigue in cancer patients is a subjective feeling of unusual tiredness affecting the body (physical), the emotion (affective), and mental function (mental), persisting for several weeks and relieved only partially or not at all with rest or sleep. Reduced muscle strength and endurance has been linked to changes in histology in muscles and metabolism in patients with chronic heart failure. These changes seem to be related to imbalance of anabolic and catabolic factors. The cause of this shift may be due to continuous haemodynamic stress from decreased perfusion. Fatigue may be aggravated by ergoreflex. The accumulation of metabolites stimulates the ergoreceptors in muscle, causing increased ventilation and sympathetic activation after exercise .[17]

In our study there was increased activation of Ergoreflex in cancer patients. Increased ergoreceptors contribution to ventilation predicted central chemo sensitivity activation. Stimulation of central chemoreceptors produced both respiratory and cardiovascular effect. [6] Peripheral Hypoxic chemoreflex sensitivity was assessed by transient hypoxic ventilatory response by Chua et al [7] In our study there was exercise intolerance in cancer patients which may be due to enhanced chemo sensitivity. Favourable effects of transient hypoxic deactivation of peripheral chemoreceptors on exercise tolerance has also been demonstrated. [6]

Cachexia is characterized by low fat free mass, decreased muscle strength and early fatigue. As disease progresses there is increased mortality.

The treatment strategies can include increased nutritional intake by dietary counseling, oral nutritional supplements or by artificial means. Drugs like anabolic steroids, Non Steroidal Anti Inflammatory Drugs along with therapeutic strategies aimed at modulating the mediators of catabolic response e.g (cytokines, eicosanoids etc) are more promising alternatives for future. These can reduce the morbidity and mortality in cancer cachetic patients.

In addition to it, changes in body composition are also an important indicator adjuvant index in the assessment of cachexia. Education about risk factors, early detection, treatment and palliative care can be helpful in decreasing the incidence as well as morbidity and mortality of the disease. Cancer rates are increasing alarmingly all over the world and are expected to increase to15 million by 2020 (World Cancer Report).

Cachexia is a debilating wasting syndrome that affects majority of cancer patients. There is progressive muscle wasting caused due to various inflammatory processes. Other associated symptoms include systemic inflammation, loss of lean body tissue, skeletal muscle dysfunction, exercise limitation and cardiorespiratory alterations.

Ergoreflex is a reflex which is initiated by mechanical and metabolic changes in the working muscles. Afferent information is carried by ergoreceptors which are mechanoreceptors and metaboreceptors. Efferent sympathetic and vagal neurons innervate heart, blood vessels and respiratory muscles. Once they are activated they stimulate ventilatory drive, vasoconstriction and ventilation in non-exercising muscle which is initially beneficial but in long term can lead to disease progression.

Peripheral muscle wasting contributes to activation of Ergoreflex in cancer patients and may be responsible for exercise limitations, increased heart rate, and increased ventilatory response further contributes to disease pathology. Therefore therapeutic interventions, aimed at improving the quality of life in cancer patients may includes nutritional and rehabilitation program's, in addition to pharmacological treatment of cancer cachexia.

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