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Research Article

Therapeutic approach with anabolic steroids in chronic obstructive pulmonary disease: Their role in improving patients' quality of life

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Abstract

Introduction: Aging can be defined like a progressive and irreversible natural process. Chronic smoking shows the health care absence, 47% male smoking and 12% female smoking. Cigarette contains more than 4000 substances, in which 50 can develop neoplasm and many varied comorbidities like pituitary, thyroid, adrenal and gonadotrophic mismatch. It also affects calcium metabolism, atherosclerosis, type 2 diabetes, skeletal striated musculature dysfunction, muscle mass loss - mainly thighs and arms - and exercise capacity reduction with fatigue complaint and dyspnea at minimal effort.

Objective: Search endorsement to hormonal therapy in Chronic Obstructive Pulmonary Disease (COPD) patients older than 55 years and treatment parameters, such as drugs and dosage, using ergogenic resources.

Methodology: Bibliographic review in the data basis, such as SciElo and PubMed, with scientific articles in English, Portuguese and Spanish from the last 10 years.

Discussion: COPD is characterized by a pulmonary disease with many systemic dysfunctions and can be associated with hypogonadism. The skeletal striated musculature dysfunction, muscle mass loss, mainly thighs and arms and exercise capacity reduction with fatigue complaint and dyspnea at minimal effort can be minimized by hormonal replacement therapy use. Pharmacological treatment of COPD with new ergogenic therapies are being studied with the objective of increasing exercise tolerance, decreasing fatigue and increasing protein synthesis. However, Anabolic Steroids (AS) therapy has adverse effects like a gynecomastia, polycythemia, suppression of sperm production and others. The main objectives of testosterone treatment are increasing energy, physical capacity, sexual life, memory and concentration and improve life quality.

Conclusion: The use of AS in patient with moderate and severe COPD may bring benefits with respect to muscle and strength gain, and improvement in quality of life.

Introduction

The aging can be defined like a progressive and irreversible natural process, but it can be accelerated by some habits, such as smoking. It is common in all being of a specie, can suffers social factors, politics, economic and psychological influence [1]. The health care must increase in a proportional form, but it doesn't occurs. The built stereotype around the male picture brings to the health care absence, even though the women currently doesn't take care with theirselves [2]. Chronic smoking shows the health care absence: 47% male smoking and 12% female smoking [3].

Cigarettes contain more than 4000 substances, in which 50 can develop neoplasm [4]. Tobacco consumption and smoking can result in many varied comorbidities like pituitary, thyroid, adrenal and gonadotrophic mismatch, calcium metabolism disorders, atherosclerosis, type 2 diabetes, skeletal striated

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musculature dysfunctions, muscle mass loss, mainly thighs and arms and exercise capacity reduction with fatigue complaint and dyspnea at minimal effort [5-13]. These symptoms are present with the smoking habit maintenance and are associated with the manifestation of the Chronic Obstructive Pulmonary Disease (COPD) starting from the sixth decade of life.

COPD can be definite like a preventable and treatable air way disease with some important extrapulmonary effects that can contribute to an aggravation in many patients. The pulmonary component is characterized by chronic limitation of air flow and many pulmonary pathologic irreversible changes. This limitation is progressive and is associated at pulmonary abnormal inflammatory answer to particles or harmful gases.

The disease gravity can be defined with a simple spirometer classification in four stages: light, moderate, serious and very serious [6,14].

In this sense, Hormonal Replacement Therapy use (HRT) is prevalent in hypogonadism treatment, but is studied to be used with severe COPD patients too. The hypogonadism symptoms are softened with the start of therapy [10,15-18]. Besides that, it reduces the mortality by cardiovascular disease and improving metabolic parameters [19]. The association of aging with COPD can reduce muscular mass, induce a diabetes type 2, androgenic hormones reduction, cardiovascular disease risk, metabolic alterations. HRT intervention can reach both of diseases and ensure symptoms reduction, improving the life quality.

This paper search endorsement to hormonal therapy in COPD patients older than 55 years, treatment parameters, using drugs, dosage and other ergogenic resources use.

Methodology

This review article was developed from the data survey found in the literature. The related bibliographic researches were made from January to April 2020 in indexers and scientific databases such as SciELO (Scientific Electronic Library Online), PUBMED (National Library of Medicine of the National Institute of Health), BVS-Bireme (Virtual Library in Health Sciences) and Science Direct.

The keywords used in the research were: “COPD”, “anabolic steroids”, “inflammatory answer”, “pulmonary disease”, “smoking”. Their respective correspondents in Portuguese and Spanish were also consulted. Only the works considered more significant, that is, in line with the approach cutout of this review, were analyzed in order to guarantee the adequate theoretical basis for the evolution and discussion of the theme.

In this way, review articles, original articles, theses, books, guidelines and recommendations from official scientific bodies published from 2009 to 2019 were included. From this chronological filtering a total of 150 texts were analyzed and read. Of these, 30 sources were duly cited as references, which present original scientific properties that are more relevant to the approach of this work, in order to carry out the development and structuring of this article. Articles that were not published in the period of 10 years described above, and scientific manuscripts which did not matched the selected types of literature for research were excluded from this review.

Results and Discussion

The COPD is characterized by the progressive presence of obstruction or chronic airflow limitation associated with the normal inflammatory response of the lungs to harmful particles or gases, which is not reversible. Although COPD affects the lungs, the inflammatory process provides several systemic manifestations that include peripheral muscle dysfunction, nutritional changes, endocrine deregulation and recurrent exacerbations [10,12,20,21]. Intolerance to physical exercise can arise as a consequence of loss of muscle mass, changes in the constitution of muscle fibers and decrease blood flow, associated with increased lactic acidosis [6].

Still in this context, exercise intolerance is a constant manifestation in patients with COPD, a fact that was previously attributed exclusively to respiratory disorder. Currently, the importance of skeletal muscle dysfunction has been verified, with loss of muscle mass mainly in the thighs and arms, resulting in the reduction of the exercise capacity, appearance of fatigue and dyspnea to the minimum effort [5,7]. These symptoms lead to a significant decrease in the patient’s physical activity with increased muscle hypotrophy. Another important factor is dyspnea, which makes patients avoid roam, with restriction in the activity of daily that involves lower limb movement [8].

Muscle dysfunction in COPD affects respiratory and locomotors muscles, which can be caused by hypoxemia, loss of capillary capacity, production of oxygen free radicals, changes in metabolism, conversion of muscle fiber types and inflammation [22].

Therefore, the COPD patient has significant dyspnea to perform trivial activities. Two possible mechanisms are related: neuromechanical dysfunction with thoracoabdominal asynchrony of the respiratory muscles - diaphragm and auxiliary breathing muscles - and alteration of lung volumes during activities performed with upper limbs [11].

Muscle atrophy is related to decrease myotubes, inhibition of protein synthesis route by positive modulation of the proteasome pathway, suggesting that protein synthesis decreases and protein degradation increases [10]. Atrophy of type II muscle fibers is related to hypoxemia, due to the reduced number of capillaries. Other associated factors are aging, malnutrition and treatment with corticosteroids, which worsen the atrophy of the fast-twitch fiber [12,20]. COPD patients have a higher proportion of glycolytic type II fibers than oxidative type I fibers. This increase in glycolytic fibers is associated with an increase in the mortality rate [9,23].

Smoking, in turn, is the main cause of COPD and leads to a significant decrease in exercise tolerance, which may suggest that the muscle effect of carbon monoxide alters the oxygenation and functioning of myoglobin and hemoglobin, causing the effect of muscular resistance and fatigue [3,20].

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Several forms of treatment have been studied, including pulmonary rehabilitation.

Strength training of upper limbs in patients with moderate and severe COPD proved to be important because it was well tolerated [6]. Inspiratory and expiratory muscle treatment is beneficial in improving the strength of these muscles, and there is even evidence that muscle strength training is favorable to improving quality of life related to general health [5,24].

Smoking systematically influences pituitary, thyroid, adrenal, testicular, ovarian function calcium metabolism and also insulin activity. Along with nicotine, other substances in cigarettes alter hormonal secretion, including endogenous steroid hormones, accentuating the expected hypogonadism with the advancing of age [19,4]. One of the hormones altered by smoking is undoubtedly testosterone. The mechanism of influence of smoking on testosterone levels is not clear [4].

Hypogonadism has a negative effect on the individual's physical, social and mental function, which may show decreased energy, emotional social, mental, physical and sexual dysfunction [15].

With the advancing of age, men decrease the production of several hormones, especially sexual steroids. Symptoms related to this condition include: increased body fat, changes in lipidogram, decrease in muscle mass, hypertension, metabolic syndromes, tendency to osteoporosis, sweating, decreased libido, difficulty in erection, difficulty in concentrating, memory problems, fatigue, apathy, discouragement, anxiety, depression, shedding, irritability, insomnia and decreased feeling of well-being [18,19,25,26].

In the context of treatment, the pharmacological approach to COPD must be individualized according to the availability of medication severity of the disease, patient preference, drug interactions and comorbidities. The treatment includes smoking cessation, encouraging physical activity, pulmonary rehabilitation and vaccination to prevent infections. In advanced diseases, measures such as oxygen therapy, surgical, endoscopic treatment and lung transplantation are used. The objectives of pharmacological treatment of COPD are to reduce the symptoms of dyspnea and cough, including improving health and exercise tolerance [27].

Despite the current protocol for pharmacological treatment of COPD, new ergogenic therapies are being studied, with the objective of increasing exercise tolerance, decreasing fatigue and increasing protein synthesis, which can improve physical conditioning, decreasing catabolism [28]. Were tested: creatine, which resulted in an increase of lean mass, strength and endurance in peripheral muscles; L-carnitine, which has not shown satisfactory results; BCAA (Branched-Chain Amino Acids), under study and still without conclusions; somatotrophic Hormone (GH), which increases muscle mass without impact on respiratory muscle performance or exercise capacity; anabolic steroids, which showed increased respiratory muscle strength and increased lean mass - mainly associated with a high-calorie diet [28].

However, the therapy with Anabolic Steroids (AS) has side effects, such as erythrocytosis, edema, gynecomastia, polycythemia, suppression of sperm production, worsening of sleep apnea, increased lipoproteins and plasma cholesterol concentration. Nevertheless, anabolic steroids can be administered in the absence of contraindications, such as liver problems, cardiac disorders and prostate cancer [28,26].

The AS have effect on protein synthesis, energy reserves increase and reduced recovery time after training. It is widely used by athletes who want to gain muscle mass and strength. The use, however, for aerobic exercise has a controversial effect. Studies have shown that AS associated with strength training increased the performance of athletes by 1 to 5%, with an increase in strength and lean mass from 2 to 5 kg. There are studies that have not found an increase in muscle mass and strength in individuals treated with AS, but it may be due to the protocol and dose used. Aerobic athletes usually use AS to decrease catabolism promoted by sport [29,30].

AS are synthetic hormones similar to testosterone, which is the most important hormone secreted by the interstitial cells of the testicles. Testosterone promotes male sexual differentiation, such as hair growth, voice changes, and acts on muscle hypertrophy and reduction of body fat [28].

AS can be used for sexual dysfunction in men who have reduced sexual desire and reduced spontaneous erection. However, erectile dysfunction can still be found in patients using AS. Testosterone treatment has shown increased libido, sexual activity, night-time erection and sexual satisfaction. Studies show that testosterone treatment has neurological implications with improved symptoms of concentration and memory. It is also helpful in the treatment of osteoporosis, which is an independent risk factor for osteoporotic fractures in men. Moreover, testosterone treatment has cardiovascular and metabolic implications. A lower level of testosterone is associated with several cardiovascular risk factors, including increased body fat, increased insulin resistance, decreased HDL, increased LDL and even higher mortality rates [18].

Metabolic Syndrome (MS) is characterized by abdominal fat, insulin deregulation, abnormal level of lipids and hypertension, which leads to risks of cardiovascular diseases and type II diabetes. The use of testosterone treatment has shown a positive effect in patients with MS, decreasing the risk of cardiovascular and endocrine complications [18,19].

In a recent study, authors administered 250mg of testosterone every 4 weeks for 26 weeks to men with moderate to severe COPD (FEV1 < 60%) and found a decrease in fat mass, an increase in lean mass and an improvement in sexual function. The improvement in lean mass in COPD patients, decreasing mortality, may justify the use of AS in these patients [28]. Furthermore, studies have shown that increased levels of testosterone and its neuroactive metabolites influence in smoking cessation [4]. Testosterone treatment in elderly and frail men with low testosterone levels prevents deterioration and increases body composition, improving symptoms related to the quality of life [17].

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The main objectives of testosterone treatment are increasing energy, physical capacity, sexual life, memory and concentration, beyond improving the patient's self-confidence [15]. The quality of life of patients with hypogonadism is impaired by sexual dysfunction, decreased energy, mood and cognitive function [18]. COPD patients have reduced muscle mass, which has a major impact on morbidity and mortality. The use of AS seems to be promising in increasing muscle mass, strength, sexual function, which improves the quality of life of these patients. It is observed that the use of these AS must be administered in adequate doses and for a limited time [28].

Conclusion

The use of AS in patients with moderate and severe COPD may bring benefits with respect to muscle and strength gain, and improvement in quality of life. The administration of 250mg of testosterone once a month, with medical monitoring, to men with moderate to severe COPD (FEV1 < 60%) has showed many benefits in the gain of lean mass, loss of fat mass and even in smoking cessation. However, there are few articles relating this treatment to COPD, which suggests new researches should be evaluated, aiming to clarify dosage, type of drug and treatment time, in order to establish guidelines for the administration of these drugs.

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