

## The alteration in serum amino acid profile in patients with chronic obstructive pulmonary disease.

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### الخلاصة

هدف الدراسة هو لمعرفة ماهية التغيرات المحتملة حدوثها لمستويات البروتين، الدهون، الألبومين وكذلك (BCAA) في مصل المرضى بالانسداد الرئوي المزمن. اشترك في هذا البحث 14 مريض بحالة الانسداد الرئوي المزمن و 14 متطوع اصحاء جميعهم من الذكور المتقاربين بالعمر والمرضى منهم متشابهين بالحالة المرضية وبوضعية مستقره من الناحية الطبية لمقارنة المستويات للمواد المذكوره سابقا في مصل المرضى وفرقتها عن الاصحاء أظهرت النتائج وجود تغيرات و بدلاله احصائية معنويه (0.05) في المرضى وهذا يؤكد على وجود حاله من التغيرات البنائيه السلبيه لدى المرضى والتي يجب متابعتها و محاولة وضع الحلول المناسبه لها.

### Abstract

The aim of this study was to identify whether there is a difference in serum (BCAA) concentration in COPD, and is this alteration associated with changes in total protein concentration, total cholesterol, Albumin and triglyceride (TGL). Fourteen patients with COPD their age is (62.3±2.4), and fourteen healthy volunteers their age (60.32±1.56) were examined. All subjects were men, furthermore the patients have irreversible obstructive air way diseases (emphysema due to heavy smoking) but they were clinically in stable condition and not suffering from respiratory tract infection or exacerbation of their diseases. Serum sample were obtained from all patients and control group for the measurement of BCAA, total protein, albumin and total cholesterol.

The results show that the concentration of BCAA were reduced in patients with COPD (P<0.05) in addition to that there were a significant differ in serum concentration of total protein, total cholesterol, TGL and albumin between the patients with COPD and control group.

### Introduction

There is increasing evidence of abnormal protein metabolism in patient with chronic obstructive pulmonary disease (COPD) as reflected by lower serum branched chain amino acid (BCAA) concentration.

Chronic obstructive pulmonary disease also known as chronic obstructive lung disease(COLD) is characterized by a limitation of the airflow in the lung which increase overtime and is not totally reversible<sup>(1)</sup>.

So over time the COPD will cause low oxygen levels *hypoxia* and high carbon dioxide *hypercapnia*. In order to increase oxygen delivery, the body has number of ways:-

1-Increase the rate of breathing.

2-Increase the heart rate to pump more blood.

3-Vessels in the lung constrict to force blood and oxygen through the circulation.

The above will have serious effect on metabolic process due to the changes that happen in internal respiration which occur at the tissue level<sup>(2)</sup>.

Amino acids play a pivotal role in intermediary metabolism both as building blocks of proteins and as precursors for other functionally important compounds such as nucleotides and neurotransmitters<sup>(3)</sup>.

Skeletal muscles is the body major protein store and under certain condition like fasting muscles supplies amino acids to other tissues<sup>(4)</sup>. However muscles also has a characteristic pattern of amino acid metabolism. The branched chain amino acid leucine, isoleucine and valine are rapidly degraded as are other non essential amino acids, including alanine, glutamate, and aspartate<sup>(5)</sup>.

However unlike other tissue, muscle does not degrade the carbon skeleton of several other amino acids such as phenylalanine and tyrosine<sup>(6)</sup>.Leucine is an important energy source for muscle tissue particularly during fasting, and under these conditions leucine inhibits oxidation of glucose<sup>(7)</sup>. So measuring the amino acid concentration in muscle and plasma may give important information about changes in amino acid metabolism in COPD<sup>(8)</sup>.

In an average 70 kg male there is 7 kg of skeletal muscle protein of which the majority is formed by contractile proteins including actin and myosin<sup>(9)</sup>. In addition 60% of free amino acid in the body is thought to derive from muscle<sup>(10)</sup>.All muscles proteins are continually being synthesized and degraded and the combined effect of changes in synthesis and degradation alter the total protein turnover<sup>(11)</sup>.

Several factor influence muscles protein turnover including contractile activity, changes in nutritional intake and the circulating levels of variety of hormones<sup>(12)</sup>. Clearly measurement of muscles or lean body mass may fail to reveal important imbalances in the rates of muscles protein synthesis or degradation<sup>(13)</sup>.

Metabolic studies using isotopically labeled amino acid have been used extensively for investigation in human subjects, though only a

limited number of studies have used this technique in the context of COPD<sup>(14)</sup>.

## **Subjects and Methods**

### **1-study population**

Twenty-eight persons were involved in this study, (14) with COPD the other (14) a healthy volunteers. The patients were in clinically stable condition all of them attended the pulmonary health center in Hilla Governorate in the period between January and September 2007. All patients had chronic air flow limitation defined as a measured forced expiratory volume in 1s (FEV1) of <70% of the predict value, FEV1 is the maximum of air expired in one second. Airflow is considered to be limited if the forced exhalation is persistently low over the course of one second as measured by pulmonary function test by spirometry furthermore the patients had irreversible obstructive airway diseases moreover non of the patients had a fever or a bacterial infection on the basis of sputum culture. Exclusion criteria were malignancy, cardiac failure, distal arteriopathy, recent surgery, infection, use of anticoagulant medication, or sever endocrine, gastrointestinal, and renal disorders.

### **2-Venous blood sample collection and analysis**

10ml of blood samples were collected into tubes. Serum was immediately separated from blood by centrifugation after collection. Serum sample were stored at (-8) °C until analyzed. The amino acid were measured in serum samples by using fully automated HPLC method which is a very sensitive method with high resolution and relatively short analysis time the system consisted of refrigerated(4°C)auto sampler( model 9300;Varian, Palo Alto, CA)a pump(model 9012;Varian), a column oven(29°C; Croco-Cil, Riemerling, Germany), a guard column(model 69080; Varian), a 250x4.6 mm octadecylsilance(C98)analytic column packed with 5-µm particles(Varian Res Elut, 90°A), and an ultraviolet visual light detector(model 9050; Varian).The mobile phase was acetonitrile(product number C 2502; Lab scan sciences): ethanol(65:35, by volume) added to 0.05%triethylamine(product number 23,962-3; Aldrich chemical Co Mil Waukee); the flow rate was 1.5 ml/min.

Serum total cholesterol concentration was measured by enzyme colorimetric testing (Biomerieux kit), and serum triglyceride (TGL) was measured by enzyme colorimetric testing kit (Biomerieux kit). Serum total protein was also measured by colorimetric biuret method (Spinreact Girona Spain Kit). Albumen measurement in serum was done by the biuret method (Spinreact Kit).

## Results

Table (1) shows the clinical characteristic of the study groups, the mean age of the control group were  $60.32 \pm 1.56$  while the mean age of chronic obstructive pulmonary disease (COPD) were  $62.3 \pm 2.4$ . The COPD patients have a significant lower body weights than control group ( $p < 0.05$ ). The mean concentration of serum leucine amino acid were significantly higher in control group than in COPD patients ( $p < 0.05$ ). Isoleucine and valine amino acid were also reduced in patients with COPD as shown in table (2). Table (2) also show the mean concentration of total protein which were significantly higher in control group than in COPD patients group ( $p < 0.05$ ), while there were no significant differ in serum albumin concentration in patient with COPD and control group. Furthermore, the mean concentration of TGL and total cholesterol were significantly higher in the serum of control group more than patients with COPD ( $p < 0.05$ ), table (3).

**Table1: the clinical characteristics of the study groups.**

	control	COPD
Age	$60.32 \pm 1.56$	$62.3 \pm 2.4$
weight	$88.53 \pm 2.32$	$71.64 \pm 2.14$

**Table2: mean concentration of serum branched chain amino acid, total protein triglyceride, total cholesterol and albumen in control and COPD.**

	Control M $\pm$ SD	COPD M $\pm$ SD	P<0.05
Leucine	$97.96 \pm 1.45$	$56.4 \pm 2.09$	S
Isoleucine	$77.42 \pm 2.15$	$49.2 \pm 3$	S
Valine	$207.85 \pm 4.69$	$188.9 \pm 3.6$	S
Total protein	$72.71 \pm 3.35$	$52.5 \pm 3.63$	S
Triglyceride	$92.64 \pm 6.38$	$44.21 \pm 3.46$	S
Total cholesterol	$180.28 \pm 13.64$	$108.9 \pm 5.96$	S
Albumen	$37.60 \pm 2.45$	$31.07 \pm 0.86$	NS

## **Discussion**

In COPD the hypoxia will lead to the reduction in protein turnover, this reduction was principally due to significant lower whole body protein synthesis rate <sup>(15)</sup>. Some studies suggest that in order to investigate the effect of COPD on protein metabolism before clinical signs of muscle wasting are apparent we can depends on measurement of amino acid profile in muscle, plasma and serum <sup>(16)</sup>.

Many studies have confirmed that plasma levels of branched chain amino acid are reduced in patients with COPD <sup>(17)</sup>. A significant association was found between low levels of branch chain amino acid and reduction of TGL and cholesterol <sup>(18)</sup>. In one study muscle to plasma leucine gradient was greater in COPD patients compared with control group, and this was associated with corresponding higher plasma insulin concentrations (which would favor retention of amino acids within insulin sensitive tissues like muscle) <sup>(19)</sup>. However the exact reasons for the raised insulin levels observed in this group of patients with COPD are unclear <sup>(20)</sup>.

In this study there were significant differences in serum amino acid concentration between the COPD patients and the control subjects. Changes in serum amino acid concentrations are difficult to interpret unless there is some consistency in finding among studies <sup>(21)</sup>. In the past, several studies examined serum amino acid concentrations in COPD patients and all of them observed lower BCAA concentration than in control subjects <sup>(22)</sup>.

Some research confirmed a relation between reduced serum level of total protein and COPD <sup>(23)</sup>. In this study the mean concentration of total protein was significantly higher in control subject than patient with COPD, while for albumin concentration there were no significant differ between the two group. Some studies shows that serum albumin concentration was reduced in COPD patients <sup>(24)</sup>, while other studies confirm no relation between them <sup>(19)</sup>.

So Patients with chronic obstructive pulmonary disease not only suffer from alteration in amino acid serum concentration but also from abnormal metabolism of amino acid, protein, TGL and cholesterol that lead to loss of weight and many other serious problem. The hope for further studies to concentrate on muscle wasting and changes in amino acid profile in skeletal muscle and the effect of that on glucose and insulin concentration.

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