ALPHA-1-ACID GLYCOPROTEN & HAPTOGLOBIN IN PROTEIN CALORIE MALNUTRITION

Thesis
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بسم الله الرحمن الرحيم

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بعد فحص الرسالة بواسطة كل عضو منفردا وكتابة تقارير منفردة لكل منهم إنعقدت اللجنة مجتمعة في يوم الثلاثاء بتاريخ ٦ / ٧ / ١٩٩٩ بقسم الباثولوجيا الاكلينيكية مدرج [illegible] بكلية الطب ـ جامعة القاهرة وذلك لمناقشة الطالب في جلسة علنية في موضوع الرسالة والنتائج التي توصل اليها وكذلك الأسس العلمية التي قام عليها البحث .

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List of Abbreviations

AAG	Alpha-1-acid glycoprotein
A/G	Albumin /Globulin
AGP	Alpha-1-acid glycoprotein
APPs	Acute phase proteins
CEA	Carcino Embryonic Antigen
CRP	C-Reactive protein
CSPM	Center for Social and Preventive Medicine
C_3	Complement 3
HAP	Haptoglobin
KWO	Kwashiorkor
IL-1	Interleukin-1
IL-II	Interleukin-II
IL-6	Interleukin-6
PCM	Protein Calorie Malnutrtion
PEM	Protein Energy Malnutrtion
PMN	Polymorphnuclear
SRI	Single Radial Immunodiffusion

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Abstract:

Acute phase proteins include α-1-protease inhibitor, α-1-acid glycoprotein, ceruloplasmin, C-reactive protein, fibrinogen and the haptoglobins.

The purpose of the present work is to assess the serum levels of α-1-acid glycoprotein and haptoglobin in infants and children suffering from protein calorie malnutrition to demonstrate any possible diagnostic or prognostic value of these parameters.

The study included thirty infant patients from the Nutritional Rehabilitation Unit in the center for Social and Preventive Medicine (C.S.P.M.) suffering from protein calorie malnutrition, their ages ranged from 3 to 36 months Group I kwo and Group II marasmus.

Ten healthy infants of the same age and sex served as a control group, Group III.

The results of our study showed that there was significant decrease in the total plasma proteins, in albumin and in A/G ratio in the groups of PCM and these results were expected as PCM is always associated with decrease in the total plasma proteins and fractionated proteins. Whereas the α-1-acid glycoprotein and haptoglobin were significantly higher among the PCM groups than the normal controls. These results could be explained by the presence of high incidence of infection (respiratory tract infection and gastrointestinal tract infection) among the PCM groups.

Those proteins increase significantly as a response to the inflammatory responses and infections that is common in the PCM patients

Key words:

Protein calorie malnutrition, alpha-1-acid glycoprotein and haptoglobin.

INTRODUCTION AND AIM OF WORK

Introduction

The acute-phase response is the term given to the coordinated series of events that occur nonspecifically in response to infection, inflammation, or trauma. Clinical signs of the acute-phase response include fever, anorexia, and increased slow wave sleep, and laboratory findings include neutrophilia, hypoalbuminemia, hypozincemia, hypoferremia, and elevations in a number of plasma proteins, termed "acute-phase proteins" ***(Dinarello, 1984).*** The acute-phase proteins include C-reactive protein, serum amyloid A protein, fibrinogen, gamma globulins, α-1-globulins, haptoglobin, ceruloplasmin and the third component of complement (C3) ***(Daniel, 1996).*** It is now known that these events are controlled through the activity of cytokines, especially interleukin-I (IL-I) ***(Dinarello, 1984; Kushner, 1991).***

A number of plasma proteins collectively termed acute phase proteins show a dramatic increase in concentration in response to infection or tissue injury ***(Roitt, 1994).***

The concentration of a number of plasma constituents is substantially altered within the first few days after an inflammatory stimulus as a part of the general systemic and metabolic response to tissue injury and infection ***(Kushner, 1982).***

Tissue damage of any kind triggers the sequence of biochemical and cellular events associated with inflammation. The biochemical

changes include stimulation of synthesis of the so-called acute phase reactants ***(Zilva et al., 1988).***

In the acute phase, these reactants appear in the serum in detectable amounts within hours or days of acute physical or chemical trauma, infection, inflammation, tissue damage, as well as in response to immunological reaction or pregnancy ***(Syrjanen et al., 1989).*** Following appropriate stimuli, the concentration of acute phase proteins rise to levels at least 25 percent greater than normal. Several hundred- folds to 1000–folds or more above these levels may be seen with sever inflammatory states, usually infections ***(Morley, 1982).***

The major site of the production of acute phase proteins is the liver, but mononuclear phagocytes in other tissues also synthesize and secrete these proteins ***(Pepys & Baitz, 1983).***
A number of different cytokines have been reported to regulate the synthesis of human acute phase proteins ***(Granabathi et al., 1988).***

Acute phase proteins include α_1–protease inhibitor, α_1- acid glycoprotein, ceruloplasmin, C–reactive protein, fibrinogen and the haptoglobins ***(Whitby et al., 1988).*** α_1- acid glycoprotein or orosomucoid is a normal constituent of serum which increases in acute inflammation ***(Chiu et al., 1977),*** indicating that this protein is typically an acute phase reactant ***(Shibata et al., 1977).*** A certain degree of homology exists among the amino acid sequence of α_1- acid glycoprotein, the immunoglobulins, and the haptoglobin chain, suggesting a common ancestry or role in the immune system ***(Carl et al., 1996).***

Alpha–1-acid glycoprotein is synthesized mainly in the liver hepatocytes ***(Schreiber et al., 1981).*** More recent studies have shown that some tumours are able to synthesize α_1- AGP ***(Carl et al., 1996).***

The haptoglobins are a group of proteins, all α_2-globulins, that bind haemoglobin to form haptoglobin/haemoglobin complexes; the complexes are then rapidly broken down in the lymphoreticular system. Plasma haptoglobin is increased in acute infections, in the nephrotic syndrome and following trauma. Haptoglobin is one of the acute phase reactants. ***(Whitby et al., 1988).***

In chronic inflammatory states including collagen disease and in patients suffering from chronic renal failure, nephrotic syndrome, and nephritis, a significant increase in serum haptoglobin levels was observed ***(Gray & Howarth, 1980).***

Protein calorie malnutrition is one of the leading causes of morbidity and mortality in childhood especially in the industrially under developed countries ***(Barness,1987).*** Intestinal mucosal injury was reported in protein calorie malnutrition. ***(Romer et al., 1983: Butzner and Gall, 1990: Omoike et al., 1990).*** Infection is usually the major cause of death in protein energy malnourished patients ***(Douglas et al., 1977).*** The commonest sites of infection are the gastrointestinal, respiratory and urinary tracts ***(Hansen et al., 1976).***

Aim of work

The purpose of the present work is to assess the serum levels of α-1- acid glycoprotein and haptoglobin in infants and children suffering from protein calorie malnutrition to demonstrate any possible diagnostic or prognostic value of these parameters.

REVIEW OF LITERATURE