YKL-40 (A chitinase-like protein) In the Circulation of Children with Severe Asthma

PROTOCOL

Submitted For Partial Fullfillment Of

Master Degree in Pediatrics

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INTRODUCTION

YKL-40 is a chitinase homolog, also called human cartilage glycoprotein 39 [HCgp-39] and chitinase 3–like 1, but it lacks chitinase activity***(Lee et al ,2007) .***

YKL-40 is a plasma protein secreted by macrophages , neutrophills , chondrocytes, vascular smooth muscle & cancer cells ***(Rathcke et al , 2006) .***

It is synthesized at neutrophill precursors at the myelocyte–metamyelocyte stage; it is stored in the specific granules of neutrophils and released from fully activated cells ***(Volck et al, 1998) .***

YKL-40 has a role in inflammation and tissue remodeling in human disease***(Hakala et al,1993 – kelleher et al, 2005 and Johansen et al, 2006) .***

A number of studies revealed that serum YKL-40 levels are elevated in patients with asthma and that circulating YKL-40 levels are correlated with asthma severity, thickness of the subepithelial basement membrane, and pulmonary function suggesting that circulating YKL-40 levels are a future biomarker for asthma**.** It is strongly upregulated in the airway epithelium and alveolar macrophages of patients with asthma ***(Chupp et al , 2007) .***

HYPOTHESIS :-

We hypothesized that the level of expression of YKL-40 would be increased in patients with asthma and would correlate with the severity of asthma .

AIM OF THE WORK :-

The purpose of this study is to measure the level of YKL-40 in asthmatic children and correlate its level to the severity of clinical presentation and the other clinical data .

PATIENTS :-

We will select the patients from pediatric Ain Shams Hospital with their ages range from one month to eighteen years old .

These patients will be classified into four groups:

Group 1 :

Known asthmatic patients who are used to follow up in pulmonary clinic .

Group 2 :

Patients with acute severe asthma admitted to PICU .

Group 3 :

Patients with wheezy chest due to any cause other than asthma , for example : bronchiolitis .

Group 4 :

Healthy children matched with age and sex as a control group.

We will exclude children with other medical conditions which increase YKL-40,for example : rheumatoid arthritis , inflammatory bowel disease and diabetes mellitus .

METHODS:

All the patients included in the study will be subjected to :

a. Full medical history ,Laying stress on chest symptoms.
b. Thorough clinical examination .
c. Chest X-ray.
d. Asthma scoring.
e. Arterial blood gases.
f. Pulmonary function tests if possible.
g. Measurig serum YKL-40 concentrations by ELIZA method .

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قياس نسبة البروتين واى كى أل-40 فى حالات الربو

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2008

مقدمة:-

ان البروتين واى كى ال 40 مشابه للإنزيمات المحللة للمواد الكيتينية وله اسماء أخرى عديدة.

وهذه الانزيمات لها القدرة على تكسير السكريات المتعددة الغنية بالكتينات .

ويفرز هذا البروتين بواسطة خلايا متعددة فى الجسم منها خلايا المناعة و الخلايا الغضروفية و الخلايا العضلية المبطنة للأوعية الدموية .

وهذا البروتين له دور فى الالتهابات التى تحدث داخل جسم الانسان سواء حادة او مزمنة.

و هذا النوع من البروتينات يزيد فى الغشاء المخاطى المبطن لجدار الجهاز الهوائى و الخلايا الهاجمة فى الحويصلات الهوائية فى حالات الربو الشعبى وله دور فى التغيرات التى تحدث فى الشعب الهوائية والأنسجة المبطنة لها .

ولقد أوضحت بعض الدراسات أن هذا البروتين يزيد فى مرضى الربو الشعبى لذا يستعمل كأحد الدلائل التى تشخص هذا المرض .

و هذا النوع من البروتينات يزيد فى الغشاء المخاطى المبطن لجدار الجهاز الهوائى و الخلايا الهاجمة فى الحويصلات الهوائية فى حالات الربو الشعبى وله دور فى التغيرات التى تحدث فى الشعب الهوائية والأنسجة المبطنة لها .

الهدف من الدراسة :-

الغرض من هذه الدراسة هو قياس مستوى واى كى ال 40 فى دم الاطفال الذين يعانون من الربو وعمل علاقة بين زيادته وشدة الحالة المرضية .

المرضى و طرق البحث:-

سيتم اختيار الحالات من مستشفى طب الاطفال في كلية الطب ، جامعة عين شمس أعمارهم تتراوح من شهر إلى ثمانية عشر عاما , وسوف يقسم الاطفال الى اربع مجموعات و هى :

المجموعة الأولى : يعانون من الربو من عيادة الصدر .

المجموعة الثانية : تعانى من أزمة ربوية شديدة بقسم العناية المركزة للأطفال .

المجموعة الثالثة : تعانى من أزيز صدرى لأسباب أخرى كحالات النزلات الشعيبية.

المجموعة الرابعة : أطفال كمجموعة مقارنة فى نفس عمر وجنس المرضى .

كل طفل سوف يخضع الى ما يلى :-

- اخذ التاريخ المرضى الكامل , ومعرفة الأعراض الصدرية التى يشتكى منها .
- الفحص الاكلينيكى العام و الخاص بالامراض الصدرية .
- عمل أشعة على الصدر .
- عمل غازات بالدم .
- عمل وظائف التنفس إن أمكن .
- بالإضافة لقياس واى كى ال – 40 فى الدم بطريقة إليزا .

YKL-40 (A chitinase-like protein) In The Circulation of Children with Severe Asthma.

By **BOTHAINA MAHROUS ELBIALY** M.B.,B.Ch.(Cairo university,2001) Resident at Damietta General Hospital

Aim of the work:

The purpose of this study is to measure the level of YKL-40 in asthmatic children and correlate its level to the severity of clinical presentation and the other clinical data.

Methods:

Serum samples were taken from sixty children whom were subdivided into four groups: group I (mild to moderate asthmatic cases), group II (severe asthmatic cases), group III (non-asthmatic wheezy cases) and group IV (controls) and the protocol for this study will be approved by the local ethics committee, and informed consent was obtained from the parents.

Serum YKL-40 levels was detected by ELISA kits supplied by *(Metra™ YKL-40 EIA Kit-QUIDEL CORPORATION)*

Results:

The results of our work showed that YKL-40 is a good screening test for asthma , with best cut off value (45 ng/ml) and sensitivity (89%) and is considered better negative test in prognosis as well with sensitivity (86.7%) , when its value below 90 ng/ml, it means better prognosis.

Conclusions:

The observed increase in serum concentrations of total YKL-40 suggest that measurements of it may be useful in monitoring asthmatic children and can be used as bimarker of asthma and may in assessment in degree of control of asthma

Introduction

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YKL-40 is a plasma protein secreted by macrophages, neutrophills, chondrocytes, vascular smooth muscle & cancer cells ***(Rathcke et al., 2006) .***

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Aim of Work

The purpose of this study is to measure the level of YKL-40 in asthmatic children and correlate its level with the severity of clinical presentation and the other clinical data.

Pediatric Bronchial Asthma

DEFINITION:

Asthma is a disorder defined by its clinical, physiological, and pathological characteristics.

The predominant feature of the clinical history is episodic shortness of breath, particularly at night, often accompanied by cough, wheezing appreciated on auscultation of the chest is the most common physical finding ***(GINA, 2008).***

The main physiological feature of asthma is episodic airway obstruction characterized by expiratory airflow limitation. The dominant pathological feature is airway inflammation, sometimes associated with airway structural changes ***(GINA, 2008).***

EPIDIMIOLOGY:

Asthma is a problem worldwide, with an estimated 300 million affected individuals ***(Masoli et al.,2004).***

It appears that the global prevalence of asthma ranges from 1 % to 18% of the population in different countries ***(Masoli et al., 2004).***

The World Health Organization (WHO) has estimated that 15 million disability-adjusted life years (DALYs) are lost annually due to asthma, representing 1% of the total global disease burden ***(Beasley,2004).***

Annual worldwide deaths from asthma have been estimated at 250,000 and mortality does not appear to correlate well with prevalence ***(Masoli et al.,2004).***

Factors influencing the development and expression of Asthma:

Factors that influence the risk of asthma can be divided into those that cause the development of asthma and those that trigger asthma symptoms; some do both. The former include host factors (which are primarily genetic) and the latter are usually environmental factors ***(Busse and Lemanske, 2001).***

However, the mechanisms whereby they influence the development and expression of asthma are complex and interactive. For example, genes likely interact both with other genes and with environmental factors to determine asthma susceptibility ***(Ober, 2005).***

In addition, developmental aspects such as the maturation of the immune response and the timing of infectious exposures during the first years of life are emerging as important factors modifying the risk of asthma in the genetically susceptible person ***(Holgate, 1999).***

A.Host Factors:

Genetic:

Asthma has a heritable component, but it is not simple. Current data show that multiple genes may be involved in the pathogenesis of asthma ***(Holloway et al.,1999; Wiesch et al.,1999)*** and different genes may be involved in different ethnic groups.

Ober and Hoffjan (2006) conducted a comprehensive review of the literature covering 500