Correlation of Serum Levels of Interleukin-6 with the Severity of Ulcerative Colitis

Thesis

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in Internal Medicine

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Abstract

This study was done to assess the serum level of IL-6 in patients with Ulcerative colitis to correlate these levels with the severity of the disease which determined by TrueLove & Witt classification.

This study included 60 patients subdivided into three main groups.

20 Patients with active ulcerative colitis were included in this study (group A), 20 patients with inactive Ulcerative colitis (group B), 20 healthy individuals as controllers (group C).

Patients were subjected to full medical history and clinical examination, abdominal ultrasonography, Colonoscopy, laboratory evaluation including CBC, liver and kidney function tests, INR, ESR, serum electrolytes, in addition to assessment of plasma level of IL-6.

It was found that the serum IL-6 was highly significant bêtween group I and III and it was found that it’s values between group II and group III were significant, this also found between group I and II. Values in group I were higher than other groups.

There was Negative correlation between the values of IL-6 and Pulse, Temperature, Diarrhea, Hb, ESR. On the other hand, there was highly significant positive correlation between the values of Il-6 and severity of ulcerative colitis.

Key words: IL6, ULCERATIVE COLITIS

Contents

Abbreviations

ANCA --------- Anti neutrophil cytoplasmic antibodies

ASCA ---------- Anti saccharomyces cerevisiae antibodies

CD ---------- Crohn's disease

CT ---------- Computerized tomography

ESR---------- Erythrocyte sedimentation rate

G-CSF --------- Granulocyte colony stimulating factor

GH ---------- Growth hormone

Gp---------- Glycoprotein

Hb---------- Hemoglobin

HLA ---------- Human leukocyte antigen

HMPAO ------- Hexa methyl propylene amine oxime

IBD ---------- Inflammatory bowel disease

IL ---------- Interleukin

INR ---------- International normalized ratio

LPMNC ------- Lamina propria mononuclear cells

MadCAM-1 -- Mucosal addressin cellular adhesion molecule-1

MRI ---------- Magnetic resonance imaging

NF-κB --------- Nuclear factor-κB

NOD ---------- Nucleotide-binding oligomerization domain receptors

NSAIDs ------- Non steroidal anti-inflammatory drugs

STAT3 --------- Signal transducer and activator of transcription 3

TLR ---------- Toll like receptors

TNF ---------- Tumor necrosis factor

UC ---------- Ulcerative colitis

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Introduction

Interleukin-6 (IL-6) is a proinflammatory cytokine implicated in the pathogenesis of inflammatory bowel disease. It is locally up regulated in inflammatory bowel disease patients **(Targan and Karp, 2005)**.

Cytokines of the interleukin-6 (IL-6) family act via receptor complexes containing at least one subunit of the signal-transducing protein gp130 **(VanSnick, 2008)**.

Cytokines are the main mediators of the mucosal healing in IBD; ulcerative colitis is characterized by a Th2 atypical immune response since, beside the classical proinflammatory cytokines, such as IL-1, IL-6, and TNF-α, in the pathogenesis of UC, There is complex network in which the Th2 cytokines, IL-10 and IL-13, play a key role, but little IL-4 was found **(Vasiliauskass, 2000)**.

The determination of proinflammatory cytokine secretion may be a sensitive method for monitoring the severity of mucosal inflammation in IBD patients **(tuttolomondo et al., 2010)**.

A growing body of evidence suggests that interleukin-6 (IL-6) plays a crucial role in the uncontrolled intestinal

inflammatory process responsible for inflammatory bowel disease (IBD) **(Tolia et al., 2001)**.

Patients with active UC had significantly more IL6 and p-STAT3-positive epithelial cells than both patients with inactive UC and controls **(Peeters, 2001)**.

In quiescent ulcerative colitis the enhanced spontaneous secretion of IL-6 may be a consequence of mucosal T-cell or macrophage activation: the smaller increase after T-cell stimulation suggests that one or both of these two cell types are already pre-activated **(Travis, 2006)**.

Serum IL-6 concentrations decreased gradually in the active UC during the treatment and were unchanged in the inactive UC **(Carolina Guzman et al., 2010)**.

The serum IL-6 concentrations correlate with endoscopic and histopathologic UC activity but serum IL-6 concentration is unchanged in the inactive UC **(Dielh et al., 2002)**.

Aim of Work

Assessment of serum level of IL-6 as a marker of severity for Ulcerative Colitis patients.

Chapter One

ULCERATIVE COLITIS

Inflammatory bowel disease:

Inflammatory bowel disease (IBD) is an idiopathic disease caused by a dysregulated immune response to host intestinal microflora. The 2 major types of inflammatory bowel disease are ulcerative colitis (UC), which is limited to the colon, and Crohn's disease (CD), which can involve any segment of the gastrointestinal tract from the mouth to the anus, involves "skip lesions, " and is transmural. There is a genetic predisposition for IBD, and patients with this condition are more prone to the development of malignancy **(Carucci et al., 2012)**.

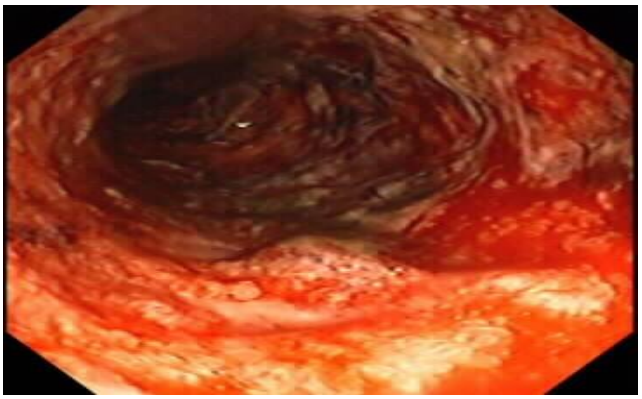

Figure (A): Severe colitis noted during colonoscopy in a patient with inflammatory bowel disease. The mucosa is inflamed and ulcerated with