Study of IL4 in Acute and Chronic ITP in Pediatric Patients

Thesis

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وعلَّمَكَ مَا لَمْ تَكُن
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List of Abbreviations

Abbr.	Full-term
ACTH	: Adrenocorticotropic hormone
AD	: Atopic dermatitis
ADO	: Adenosine
Ag	: Antigen
APC	: Antigen presenting cells
ASH	: American society of heamatology
CGRP	: Calcitonin gene related peptide
cITP	: Chronic ITP
CR	: Complete response
CRH	: Corticotropin releasing hormone
DAT	: Direct antiglobulin test
DC	: Dendritic cell
ELISA	: Enzyme–linked immunosorbent assays
EMBP	: Eosinophilic major basic protein
HPAA	: Hypothalamic pituitary adrenal axis
IFN	: Interferon
IL	: Interleukin
IQR	: Interquartile range
ITP	: Immune thrombocytopenic purpura
IVIg	: Intravenous immunoglobulin
IWG	: International Working Group

List of Abbreviations *(Cont.)*

Abbr.	Full-term
NE	: Norepinephrine
NK	: Natural killer cells
PaIgG	: Platelet associated IgG
PBQ	: Pediatric bleeding questionnaire
RBCs	: Red blood cells
ROC	: Receiver operating characteristic
SD	: Standard deviation
SNS	: Sympathetic nervous system
SP	: Substance P
Tc	: T-cytotoxic
TCR	: T cell's receptor
TGF	: Transforming growth factor
Th	: T-helper
TNF	: Tumor necrosis factor
TPO	: Thrombopoietin
WBCs	: White blood cells

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ABSTRACT

Background: Immune thrombocytopenia (ITP) is an autoimmune disease where platelets are destroyed prematurely. In the majority of children the disease resolves, but in some it becomes chronic. IL-4 is also termed B cell stimulatory factor 1 and is involved in B-cell activation and antibody production but also in T-cell activation. IL-4 is also known for its role in Th2 response **Aim of the Work:** This study was designed to compare IL4, bleeding score and lymphocytic count between acute and chronic ITP patient. **Subjects and methods:** The serum level of IL4 was assessed by ELISA in 20 newly diagnosed and 15 chronic ITP pediatric patients; we also compared bleeding score and lymphocytic count between both groups. **Results:** In this study IL4 differ significantly between newly diagnosed and chronic ITP patients with higher levels among newly diagnosed patients. However, there was no difference between both groups regarding bleeding score or lymphocytic count. **Conclusion:** Our data indicate that cytokine disturbances especially IL4 might be involved in the pathogenesis of newly diagnosed ITP.

Key words: Immune thrombocytopenia, Interleukin-4, bleeding score

Introduction

Immune thrombocytopenic purpura (ITP) is a heterogeneous clinical disorder characterized by immune-mediated platelet destruction. ITP is usually a benign, self-limiting disease in children ***(Provan et al., 2010).***

However, approximately 20% of childhood newly diagnosed ITP progress to a chronic form defined according to standardized criteria ***(Rodeghiero et al., 2009).***

Primary ITP was previously split into acute and chronic ITP depending on the outcome, however, the condition is today divided into 3 phases depending on the duration of thrombocytopenia after the initial diagnosis, that is newly diagnosed up to 3 months persistent ITP between 3 and 12 months, and chronic ITP beyond 12 months ***(Rodeghiero et al. 2009).***

The clinical differences between newly diagnosed and chronic ITP suggest the existence of different pathophysiological mechanisms in the two forms ***(Stasi et al., 2008).***

Many researchers have investigated the role of genetic factors, humoural and cellular immunity, and inadequate platelet production in the development of this condition, but failed to identify specific characteristics of children with ITP who will probably develop the chronic form of the disorder,

mainly because of the study design and differences in patients' immunomodulating therapy ***(Nugent et al., 2009).***

Clinical findings indicate that the development of chronic ITP in children is associated with older age, less mucosal bleedings, and an insidious onset. Furthermore, chronic ITP is less likely to have had a viral illness before onset and has higher platelet count at presentation than in children with a spontaneously resolving ITP ***(Glanz et al. 2008).***

At presentation there are no clinical useful biomarkers that can separate a spontaneously resolving disease from the chronic variant ***(Jernas et al., 2013).***

Nevertheless, ***Semple et al. (1996)*** found increased serum levels of interleukin 2 (IL-2), IL-10, and interferon-g in chronic ITP compared with acute ITP. ***Del Vecchio et al. (2012)*** also found increased serum levels of IL-10 in chronic versus acute ITP.

Recently ***Jernas et al. (2013)*** found increased levels of interleukin (IL) 16 and TNF – related weak inducer of apoptosis and lower levels of IL4 in newly diagnosed Compared with chronic ITP**.**

IL-4 is also termed B cell stimulatory factor 1 and is, as the name implies, involved in B-cell activation and antibody production but also in T-cell activation. IL-4 is also known for its role in Th2 response ***(Yakura et al., 1988).***

Aim of the Study

The aim of this study is to compare bleeding score and lymphocytic index between acute and chronic ITP patients, we will also measure level of IL4 in both groups to assess if there is a pathophysiologic difference between both disease processes. This may help to find tools to predict disease progression.