Effect of Steroids Therapy on Serum Levels of Interleukin1beta (IL-1β) in Children and Adolescents with Intractable Epilepsy

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بسم الله الرحمن الرحيم

قالوا سبحانك لا علم لنا الا ما علمتنا
انك أنت العليم الحكيم

صدق الله العظيم

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List of Abbreviations

ACTH	Adrenocarticotrophic hormone
AEDS	Antiepileptic Drugs
ALT	Alanine transaminase
AST	Aspartate transaminase
ATP	Adenosine triphosphate
BBB	Blood brain barrier
BOE	Benign occipital epilepsy
Ca^{++}	Calcium
CAE	Childhood Absence Epilepsy
CBC	Complete blood count
Cl^{-}	Chloride
CNS	Central Nervous system
CPS	Complex partial seizures
CRH	Corticotropin-releasing hormone
CS	Corticosteroids
CSF	Cerebro Spinal Fluid
CT scan	Computerized tomography scan
ECSWS	Epilepsy with continuous spike waves during slow-wave sleep
EEG	Electro Encephalography
ELISA	Enzyme-linked immunosorbent assay
ENT	Ear, nose and throat
FDA	Food and drugs administration
FMRI	Functional MRI
GABA	Gamma Amino Butyric Acid
GABRA1	alpha 1 subunit of GABA-A receptor
GAD	Glutamic acid decarboxylase
GCA	Giant cell arteritis
GLUR3	Glutamate receptor 3
GR	Glucocorticoid receptors

List of Abbreviations (Cont.)

GSW	Generalized spike wave
GTC	Generalized Tonic colonic
HPA	Hypothalamo-pituitary-adrenal
ICE	interleukin-1 converting enzyme
IE	Intractable epilepsy
IED	Interictal epileptiform discharge
IFN-G	interferon gamma
IgA	Immunoglobulin A
IL-1	Interleukin-1
IL-IR	Interleukin-1 Receptor
IL-1RA	Interleukin-1 Receptor antagonist
IL1-B	Interleukin1-beta
ILAE	International League Against Epilepsy
IS	Infantile spasm
IvIgs	Intravenous immunoglobulins
JAE	Juvenile Absence Epilepsy
JME	Juvenile myoclonic epilepsy
K^+	Potassium
LGS	Lennox Gastaut syndrome
LKS	Landeu-kleffner syndrome
LT	Leukotrienes
MDR-1	Multiple drug resistance gene
Mg^{++}	Magnesium
MHC	Major histocompatibility complex
MMP	Matrix –metalloproteinase
Mphi	Monocyte-macrophages
MRI	Magnetic resonant Imaging
mRNA	Messenger ribonucleic acid
MRS	Magnetic resonance spectroscopy
MS	Multiple sclerosis
MTLE	Mesial temporal lobe epilepsy
Na^+	Sodium
NK	Natural killer
NOS	nitric oxide synthetase

PET	Proton emission tomography
PGE2	prostaglandin E2
PMR	Polymyalgia rheumatic
RE	Rasmussen's encephalitis
SD	Standard deviation
SIADH	Syndrome of inappropriate secretion of antidiuretic hormone
SLE	systemic lupus erythematosus
SPET	Single photon emission computerized tomography
SPS	Simple partial Seizures
SUDEP	Sudden unexpected death in epilepsy
Th	T helper
TLE	Temporal lobe epilepsy
TNF	Tumor necrosis factor
VNS	Vagus nerve stimulation
VPA	Sodium valproate
WS	West syndrome
χ^2	Chi-square test

Introduction

Epilepsy may be defined as "the occurrence of transient, paroxysms of excessive or uncontrolled discharges of neurons, which may be caused by a number of different etiologies, leading to epileptic seizures **(Thomas & Gregory, 2004).** In recent years, increasing evidence has indicated that immune and inflammatory reactions occur in brain in various central nervous system (CNS) diseases. Furthermore, inflammatory processes, such as the production of pro-inflammatory cytokines and related molecules, have been described in brain after seizures induced in experimental models and in clinical cases of epilepsy. Although little is known about the role of inflammation in epilepsy, it has been hypothesized that activation of the innate immune system and associated inflammatory reactions in the brain may mediate some of the molecular and structural changes occurring during and after seizure activity **(Vezzani A; 2005).**

Cytokines are soluble proteins involved in regulation of growth, development, and activation of immune system cells and mediation of the inflammatory response **(Haynes and Fauci, 2005).** Elevated serum cytokines have been documented in neurological disorders: cerebral ischemia, epilepsy, CNS trauma, multiple sclerosis, amyotrophic lateral sclerosis (ALS), Alzheimer's disease, and Parkinson's disease **(Perry, 2004).** The first clinical insight into a possible role of inflammation in epilepsy is the evidence that selected anti-inflammatory drugs, including steroids, display anticonvulsant activity and may control seizures which are otherwise refractory to classical antiepileptic drugs **(Vezzani and Granata, 2005).**

Corticosteroids (predominantly prednisolone, hydro-cortisone and adreno-corticotrophin hormone ACTH) have been used in the treatment of the epilepsy for over 50 years. Over the past 30 years most reports have focused on epilepsy syndromes and epileptic encephalopathies resistant to treatment with the more conventional anticonvulsive and antiepileptic drugs specifically West syndrome and Rasmussen encephalitis ***(Gupta and Appleton, 2005).***Steroids are used as effective adjunctive treatment for children with intractable epilepsy who have failed conventional antiepileptic therapy ***(Sinclair 2003, Azam etal., 2005).*** Successful use of corticosteroids as one of the anti-inflammatory and immuno-modulatroy treatment in some cases of intractable childhood epilepsies suggests that immune mechanisms are involved in the pathogenesis ***(Tamas et al., 2009).***

Aim of the work

The aim of this study is:

1- To evaluate serum levels of interleukin1-beta and to correlate them to different studied parameters in intractable epilepsy patients with diverse etiologies.
2- To evaluate the effect of steroids therapy on clinical, neurophysiological and serum levels of interleukin1-beta of these patients.

Epilepsy

Definition :

The word epilepsy comes from the Greek word which means "to be seized by forces from without", it refers to the old magic concept that diseases were "attacks or seizures" by gods and demons ***(Aicardi, 1986)***.

Epilepsy is a chronic disorder or group of chronic disorders, in which the indispensable feature is recurrence of seizures that are typically unprovoked and usually unpredictable ***(Carl et al., 2005).***

Recently, it has been defied as recurrent convulsive and non-convulsive seizures caused by partial or generalized epileptogenic discharge in the cerebrum ***(John et al., 2000)***.

A seizure can be defined as a sudden, transient disturbance of brain function manifested by involuntary motor, sensory, autonomic or psychic phenomena, alone or in combination, often accompanied by alteration or loss of consciousness ***(Moe and Benke, 2005).***

Epidemiology :

Epilepsy is one of the most common of the serious neurological disorders ***(Hirtz et al., 2007)***.

Epilepsy is a highly prevalent disease, affecting 0.5-1.5% of the world's population ***(Hauser, 1995)***, the overall prevalence of the epilepsies in childhood and adolescence is 4-6 per 100 ***(Cowan et al., 1989)***.

Epilepsy's approximate annual incidence rate is 40–70 per 100,000 in industrialized countries and 100–190 per 100,000 in resource-poor countries ***(Hirtz et al., 2007)*** . This high rate in developing countries is mainly due to acute infections, parasitic infestations and poor postnatal care ***(Jallon, 2002)***.