

Assessment of Serum L-Carnitine Levels and its Role in Egyptian Asthmatic Children

Thesis

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Abstract

Bronchial asthma is a chronic airway disease with an underlying inflammatory component. Despite advances in modern medical care and the introduction of effective therapies, such as inhaled corticosteroids, poor asthma control exists in clinical practice. That can be attributed to two primary factors: (i) poor compliance and adherence to treatment; and (ii) poor efficiency of inhalation drug delivery, resulting from the inability of young children to correctly use inhalers . Free serum L- carnitine was not affected in 31 patients with mild acute asthma attacks (group I) , while decreased in 30 patients with moderate acute asthma attacks (group II) as compared to 20 healthy children (group III). Giving L-carnitine as an adjuvant therapy to the conventional asthma treatment for 3 months resulted in:

- (i) Statistically significant increase in serum l-carnitine after 3 weeks and after 3 months
- (ii) Statistically significant reduction in the frequency of moderate and severe acute attacks during 3 months follow up
- (iii) Statistically significant improvement in pulmonary functions(FEV1, FVC and FEV1/FVC).

Key words:

Asthma – L-carnitine – pulmonary functions

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List of Abbreviations

Ac-CoA: Acetyl – Co Enzyme A

ACQ: Asthma control questionnaire

ACT: Asthma control test

AIDS: Acquired immunodeficiency syndrome

ATAQ: Asthma therapy Assessment Questionnaire

BBD: C-butyrobetaine dioxygenase

C- ACT: Childhood asthma control test

CACT: Carnitine-acylcarnitine translocase

COPD: Chronic obstructive pulmonary disease

CPT I: Carnitine palmitoyl transferase I

CPT II : Carnitine palmitoyltransferase II

CPT: Carnitine palmitoyl transferase enzyme

DPI: Dry powder inhaler

DPPC: Dipalmitoyl phosphatidyl choline

DRI: Dietary Reference Intakes

EIB: Exercise induced bronchial asthma

ESRD: End-stage renal disease

FeNO : Fractional exhaled NO

FEV1%: FEV1/FVC ratio

FEV1: Forced expiratory volume in the first second

FNB: The Food and Nutrition Board

FVC: Forced vital capacity

GERD Gastro esophageal reflux disease

GINA: Global initiative for asthma

GM-CSF: Granulocyte-macrophage colony-stimulating factor

HIV: Human immunodeficiency virus

HPA: Hypothalamic- pituitary axis

HPETE: 5-hydroperoxy-eicosatetraenoic acid

HTML: 3-hydroxy- TML

HTMLA: HTML aldolase

ICSs: Inhaled corticosteroids

IFN- γ : Interferone – γ

IgE: Immunoglobulin E

IL-13: Interleukin 13

IL-4: Interleukins-4

IL-5: Interleukin-5

KOH: Potassium hydroxide

LABA: Long acting β 2 agonists

5-LO: 5-lipoxygenase enzyme

LTs: Leukotrienes

MDCs: Macrophage-derived chemokines

NK cells: Natural killer cells

NO: Nitric oxide (NO)

OCTN2: Carnitine organic cation transporter

PC: Phosphatidyl choline

PEEF: Peak end expiratory flow

PEF: Peak expiratory flow

PLA₂: Phospholipase A2 Enzyme

pMDI: Pressurized metered dose inhaler

RDA: Recommended dietary allowance

RDS: Respiratory distress syndrome

RSV: Respiratory syncytial virus

TARCs: Thymus and activation-regulated chemokines

Th1 cytokine : T helper 1 cytokine

Th2 cytokine: T helper 2 cytokine

Th2-cytokine: T helper cytokines

TMABA: 4-trimethylaminobutyraldehyde

TML: N-tri methyl lysine

TMLD: TML dioxygenase

TNF- α : tumor necrosis factor- α

INTRODUCTION

Bronchial asthma is defined as Chronic inflammatory disorder of the airways in which many cells and cellular elements play a role, in particular, mast cells, eosinophils, T- lymphocytes, macrophages, neutrophils, and epithelial cells. In susceptible individuals, this inflammation causes recurrent episodes of wheezing, breathlessness, chest tightness and coughing, particularly at night or in the early morning. These episodes are usually associated with wide spread but variable airflow obstruction that is often reversible either spontaneously or with treatment. Such inflammation also causes an associated increase in the existing bronchial responsiveness to a variety of stimuli. Reversibility of airflow limitation may be incomplete in some patients with asthma (**Pocket guide for asthma management and prevention, 2009**).

Asthma is a worldwide problem with 300 million affected individuals. It appears that the global prevalence of asthma ranges from 1% to 18% of population of different countries. Over the recent years, the percentage of the prevalence of childhood asthma increased significantly and this may be due to either increased parental recognition or improved diagnostic processes. The world health organization estimated among asthmatic patients that 15 millions having disability adjusted life due to asthma and 25.0000 deaths which do not correlate with the prevalence (**Expert Panel Report 3, 2007**).

The main goals for developing effective treatments for pediatric asthma are to improve the quality of life by both reducing symptoms and the frequency of exacerbations, to allow undisturbed sleep and performance of daily activities, and to ensure a more healthy adult future. Despite advances in modern medical care and the introduction of effective therapies, such as inhaled corticosteroids, poor asthma control exists in clinical practice. This lack of control can be attributed to two primary factors: (i) poor compliance and adherence to treatment; and (ii) poor efficiency of inhalation drug delivery, resulting from the inability of young children to correctly use inhalers that were designed for adults. Significant effort needs to be invested in the area of pediatric asthma to increase the availability of high-quality, patient-centric medication and delivery systems (**Eskandar and Fleming, 2010**).

Carnitine is an amino acid derivative biosynthesized from lysine and methionine, found in high energy demanding tissues (skeletal muscles, myocardium, liver and suprarenal gland). Carnitine is indispensable for both β oxidation of long chain fatty acids in the mitochondria and regulation of the concentration and removal of the produced acyl groups (**Evangelidou and Vlassopoulous, 2003**).

It was found that type II pneumocyte carnitine palmitoyl transferase (CPT) isolated from the rat lung plays an important role in remodeling phosphatidylcholine(PC) fatty acid composition and hence dipalmitoylphosphatidylcholine(DPPC) and surfactant synthesis (**Arduini et al, 2001**).

During asthma exacerbations, there is increased release of phospholipase A₂ (PLA₂) from inflammatory cells into the airways. PLA₂ has the capacity to hydrolyze phosphatidyl choline (PC), which is the principal component of pulmonary surfactant (**Ackerman et al, 2003**). Thus low level of total and free serum carnitine in asthmatic patients during or shortly after moderate acute asthma attacks might be attributed to decreased lung surfactant and the usage of body stores of L-carnitine to replenish it (**Asilsoy et al, 2009**). The normal serum levels of L- carnitine during mild acute attacks might be attributed to lesser destruction of pulmonary surfactant, thus no need for usage of L- carnitine to resynthesize it.

The present study hypothesized presence of changes in free serum L-carnitine levels during acute asthma attacks due to its utilization for synthesis of pulmonary surfactant that is consumed during acute attack. The utilization of L-carnitine as an adjuvant supplementation may reduce the frequency and intensity of acute asthma attacks.

AIM OF THE WORK

The objective of this study was to estimate free serum L- carnitine levels during mild and moderate acute asthma attacks in a group of Egyptian asthmatic children and to evaluate the effect of giving L-carnitine as an adjuvant therapy to the standard asthma treatment on free serum L-carnitine levels, frequency and severity of acute attacks and lung functions.