شبكة المعلومات الجامعية

التوثيق الإلكتروني والميكروفيلم

بسم الله الرحمن الرحيم

HANAA ALY

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جامعة عين شمس

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قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها
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HANAA ALY

Zinc as a Supplement in Reduction of Relapses in Children with Nephrotic Syndrome

Thesis

Submitted for Partial Fulfillment of Master Degree in Pediatrics

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Walid Soliman

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Abb	Fullterm
ACE	Angiotensin-converting enzyme
AIDS	Acquired immunodeficiency syndrome
AKI	Acute kidney injury
ANA	Anti-neucler antibody
ANP	Anti naturetic peptide
APO	Apolipoprotein
ARBs	Angiotensin II receptor blockers
C3GN	C3 glomerulonephritis
CBC	Complete blood count
CGN	Crescentic glomerulonephritis
CI	Confidence interval
CKD	Chronic kidney disease
CNIs	Calcineurin inhibitors
CSN	Canadian Society of Nephrology
DMP	Diffuse mesangial proliferation
EM	Electron microscope
ESKD	End-stage kidney disease
ESL	Endothelial cell surface layer
FENa	Fractional excetrion of sodium
FGS	Focal and global glomerulosclerosis
FRNS	Frequently relapsing nephrotic syndrome

FSGS…...……..Focal segmental glomerulosclerosis

GBM…..……Glomerular basement membrane

GFB…….Glomerular filtration barrier

GFR……Glomerular filtration rate

Gm……Gram

GN……..…..Glomerulonephritis

Hb……..……..Heamoglobin

HDL…..……...High density lipoprotein

HSP……..Henoch-Schönlein purpura

IDL…….…….Intermediate-density lipoprotein

IF……..……Immunoflurecence

IFN……Interferon

IFRNS…….....Infrequent relapses nephrotic syndrome

INS……..….Idiopathic nephrotic syndrome

ISKDC….....The international study of kidney disease in children

KDIGO……..Kidney Disease: Improving Global Outcomes

LDL……Low density lipoprotein

LM……..Light microscopy

LMWH……...Low molecular weight heparin

MCD……..…..Minimal change disease

MCGN…..……..Mesangiocapillary glomerulonephritis

MCNS…….Minimal change nephrotic syndrome

MesPGN…….Mesangial proliferative glomerulonephritis

MGN……..Membranous glomerulonephritis

MMF……...Mycophenolate mofetil

MN…….Membranous nephropathy

MPGN…….Membranoproliferative glomerulonephritis

NEUT…….Neutrophil

NF-KB……...Nuclear transcribtion factor kappa b

NS……..Nephrotic syndrome

NSAIDs…….Non-steroidal anti-inflammatory drugs

Podo……...Podocytes

PPSV23…….Polyvalent pneumococcal-23 polysaccharide vaccine

Pr/Cr……..Protein : Creatinine ratio

PV……...…..Plasma volume

QP…….Plasma flow rate

RDAs…….Recommended Dietary Allowances

RPGN……Rabidly progressive glomerulonephritis

SD…….Slit diaphragm

SDNS……Steroid dependent nephrotic syndrome

Sig…….Significance

SLE……Systemic lupus erythematosus

SRNS……Steroid-resistant nephrotic syndrome

SSNS……Steroid sensitive nephrotic syndrome

TE……Thromboembolism

TEE……..Thromboembolic event

TGF……..Tumor growth factor

UL……Upper tolerable limit

VLDL……..Very-low-density lipoprotein

ABSTRACT

Background: Most cases of nephrotic syndrome (NS) have disease relapse and 50% develop frequent relapsing NS or steroid dependent NS. Eighty percent of plasma zinc is bound to albumin which is lost in urine in NS during relapse period so, serum zinc level is decreased during NS attacks and more decreased in frequently relapsing NS. Zinc (Zn) supplementation reduces morbidity and mortality, especially among children due to infectious diseases, and also has immune-modulator effects.

Aim of the work: To assess whether zinc supplementation can reduce the relapse and infection rates in children with nephrotic syndrome or not?

Patients and Methods: This interventional study was conducted at Pediatric Nephrology Clinic, Children's Hospital, Ain Shams University. It comprised 40 patients with frequent relapsing NS divided into two groups (zinc and control groups). Both received routine medical care of nephrotic syndrome, but zinc group received also oral zinc supplementation 10 mg/day for 6 months with doubling the dose during infection period and relapse time. Serum zinc was measured at the start and at the end of the study. Relapse rate, hospitalization rate, number of days of hospitalization, time of relapse, and investigations were compared before and after zinc supplementation.

Results: There was low serum zinc level in most cases of frequently relapsing nephrotic syndrome. Oral zinc supplementation in FRNS improved serum zinc level by 22.72%, reduced relapse rate by 28% and reduced hospitalization days by 33.7%. Although there was no significant improvement as regards hospitalization rate and time of relapse, sustained remission occurred in 80% of patients of zinc group.

Conclusion: Oral zinc supplementation in frequently relapsing nephrotic syndrome children is useful for reduction of relapse rate and hospital stay, and achieving sustained remission.

Key words: Zinc, supplement, relapse, children, nephrotic syndrome

INTRODUCTION

After initial successful treatment of nephrotic syndrome (NS), around 80% of children with steroid sensitive nephrotic syndrome have disease relapses requiring further courses of high dose prednisolone. About 50% develop frequently relapsing nephrotic syndrome (two or more relapses within six months of presentation or four relapses within 12 months) or steroid dependent nephrotic syndrome (relapse while receiving prednisolone or within 14 days of stopping the drug ***(Larkins et al., 2016).***

Zinc (Zn) is an essential trace element that functions as a cofactor for certain enzymes involved in metabolism, and cell growth. It is found in nearly 300 specific enzymes ***(Osredkar and Sustar, 2011).***

Approximately 75–80% of plasma zinc is bound to albumin, accounting for as much as 98% of the exchangeable fraction of Zn in blood plasma. Serum albumin effectively acts as an extracellular "zinc buffer" that controls the concentrations of "free" Zn^{2+} ions that are available to other plasma proteins or for cellular uptake through membrane-bound zinc transporters (***Handing et al.,2016)***.

A positive correlation has been found between urinary zinc and protein excretion. In spite of high dietary intake and normal intestinal absorption, children with NS have zinc deficiency caused by increased urinary zinc loss ***(Haque et al., 2017).***

During NS attacks with a low protein level, there is a reduction in the serum zinc level. Mechanisms for the low zinc level in NS include concomitant nutritional deficiency with reduced oral zinc intake, decreased intestinal absorption, and increased intestinal zinc secretion ***(Hamik et al., 2019).***

The mean serum zinc level in frequently relapsing cases of

nephrotic syndrome is significantly lower than that of infrequently relapsing cases ***(Hashim and Jabur, 2020).***

There is strong evidence from developing countries that zinc supplementation can reduce morbidity and mortality, especially among children due to infectious diseases***(Yakoob et al., 2011).***

It is suggested that zinc deficiency can lead to down-regulation of T-helper 1 (Th1) cytokines, resulting in a relative T-helper 2 (Th2) cell over activity and an increased risk of clinical infections ***(Canani et al., 2005)***.

Zinc supplementation may result in restoration of Th1 immune response through suggested augmentation of gene expression for interleukin (IL)-2 and interferon-α ***(Prasad, 2008)***.

The Th1/Th2 cytokine imbalance is believed to be implicated in relapses of steroid sensitive nephrotic syndrome (SSNS) ***(Prasad, 2008)***.