IMPAIRED GLUCOSE TOLERANCE AND INSULIN SENSITIVITY IN TRANSFUSION-DEPENDENT β-THALASSEMIA

AMPAI SAENGWICHITR

A Thesis Submitted to the Graduate School of Naresuan University
in Partial Fulfillment of the Requirements
for the Master of Science Degree in Biomedical Science Program
February 2012

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This thesis entitled "Impaired Glucose Tolerance and Insulin Sensitivity in Transfusion-Dependent β-thalassemia" submitted by **Ampai Saengwichitr** in partial fulfillment of the requirements for the Master of Science Degree in Biomedical Sciences is hereby approved

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Ampai Pimanprom

Title	IMPAIRED GLUCOSE TOLERANCE AND INSULIN SENSITIVITY IN TRANSFUSION-DEPENDENT BETA THALASSEMIA
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ABSTRACT

Transfusion-dependent β-thalassemia patients invariably develop iron overload acquired from blood hemolysis and increase intestinal iron absorption. Ferritin is the major markers for iron storage compound of the body. The iron induces oxidative stress mainly thought the Fenton and Harber Weiss reaction. A total of 60 transfusion-dependent β-thalassemia patients were participated in the present study by Oral Glucose Tolerance test (OGTT) in the first and second period study. We found all of the fasting blood sugar (FBS) levels were significantly higher in β-thalassemia patients than normal control in each period (p<0.001). In OGTT, in the first period only at 2 Hr testing was significantly higher in β-thalassemia patients than normal controls, while in the second period of OGTT testing were significantly higher than normal control. When we compared OGTT of the first and second period only the 0.5 Hr and 1.0 Hr testing were significantly higher (p<0.05) in second period study of the β-thalassemia. And the association of FBS levels and serum ferritin levels were positive correlated (r = 0.314, p = 0.015) and positive correlated with insulin and Insulin Resistance Index (IRI) (r = 0.719, p < 0.001 and r = 0.840, p <0.001) respectively. Serum ferritin level and AST, ALT were positive correlated (r = 0.500, p < 0.001 and r = 0.473, p <0.001). In study, result showed that these patients have iron overload (higher serum ferritin levels). As the iron overload may be stimulated higher oxidative stress in β-thalassemia patients. Higher oxidative stress may cause

damage the liver and pancreas tissues. The insulin levels were significantly higher (p <0.001) in β-thalassemia patients than normal controls. These patients were not showed impaired glucose tolerance tests or pre-diabetes but all have hyperinsulinemia. These transfusion-dependent β-thalassemia patients were trend to high risk for impaired glucose tolerance or pre-diabetes by causing hyper-insulinemia.

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ABBREVIATIONS

β-thalassemia	=	Beta thalassemia
α-thalassemia	=	Alpha thalassemia
Hb	=	Hemoglobin
Hct	=	Hematocrit
ALA	=	aminolaevulinic acid
DMT1	=	divalent metal transporter-1
Fe (III)	=	ferric
Fe (II)	=	ferrous
RE	=	reticuloendothelial
ATPase	=	Adenisine triphophatase
IRPs	=	iron-regulatory proteins
IREs	=	iron-responsive elements
mRNA	=	messenger ribonucleic acid
GDF15	=	growth differentiation factor-15
ADP	=	adenosine di-phosphate
ATP	=	adenosine tri-phosphate
NTBI	=	Nontransferin-bound iron
FBS	=	fasting blood sugar
IGT	=	impaired glucose tolerance
IDF	=	International Diabetic Fedeartion
OGTT	=	Oral Glucose Tolerance Test
HOMA	=	Homeostasis model assessment
μU	=	microunit
μmol	=	micromole
mL	=	milliliter
L	=	litre
EDTA	=	ethelene diamine tetraacetate
HBsAg	=	Hepatitis B surface antigen
Anti-HCV	=	Hepatitis C antibody

ABBREVIATIONS (CONT.)

Anti-HCV	=	Hepatitis C antibody
LDL-C	=	low density lipoprotein cholesterol
HDL-C	=	high density lipoprotein cholesterol
AST	=	aspartate aminotransferase
ALT	=	alanine aminotransferase
ALP	=	alkaline phosphatase
MEIA	=	Microparticle Enzyme Immuno
Hr	=	Hours
IRI	=	insulin resistance index
BMI	=	body mass imdex
st	=	first
nd	=	second
DFO	=	Deferoxamine
H_2O_2	=	hydrogen peroxide
$O_2^{\cdot}$	=	superoxide
$OH^{\cdot}$	=	hydroxyl radical
mg	=	milligram
g	=	gram