Biochemical and molecular study of Maple Syrup Urine Disease among Egyptian Children

Thesis

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List of Abbreviations

Abb.	Meaning
allo-Ile	allo-Isoleucine
αKGDH	α-ketoglutarate dehydrogenase complex
BCCAs	Branched chain amino acids
BCKAs	Branched chain α-keto acid
BCKDC	branched-chain alpha-ketoacid dehydrogenase complex
BCKDH	Branched chain ketoacid dehydrogenase
BCKDHA	The BCKDHA gene encodes the alpha subunit of E1
BCKDHB	The BCKDHB gene encodes the beta subunit of E1
BIA	bacterial inhibition assay
CNS	central nervous system
DBT	Dihydrolipoamide branched chain transacylase
DLD	Dihydrolipoamide dehydrogenase
DLDD	dihydrolipoamide dehydrogenase deficiency
El	branched chain α-ketoacid decarboxylase
E2	dihydrolipoyl transacylase
E3	dihydrolipoamide dehydrogenase
HPLC	high-performance liquid chromatography
IEM	inborn errors of metabolism

List of Abbreviations

Abb.	Meaning
MSUD	Maple Syrup Urine Disease
NBS	newborn screening
OADs	Organic acid disorders
PDH	pyruvate dehydrogenase complex
PKU	phenylketonuria

INTRODUCTION

Maple syrup urine disease (MSUD), originally described by Menkes in 1954, is an inherited genetic disease with an autosomal recessive pattern affecting approximately 1 out of 120,000 infants worldwide ***(Parmar et al.,2004)***.

Maple syrup urine disease (MSUD), or branched chain ketonuria caused by impaired Branched chain α-ketoacid dehydrogenase (BCKDH) complex activity ***(Danner and Elsas, 1989)***. The biochemical basis of this disease is the inability to metabolize branched chain α-keto acid (BCKAs) derived from the essential branched chained amino acids (BCAAs): leucine, isoleucine, and valine. The elevated BCAAs and BCKAs may have severe clinical consequences including ketoacidosis, mental retardation, and neurological impairment ***(Sakai et al., 2005)***.

The determination of branched chain amino acids, α - keto acid derived from BCAA, methionine, phenylalanine and tyrosine is currently the most reliable approach for the diagnosis of MSUD ***(Kandar et al., 2009)***. Diagnosis is also made clinically based on the peculiar maple syrup odor or sugar burnt of the urine, encephalopathy, and α-ketoacids in urine. The presence of plasma L-alloisoleucine and urinary α-hydroxyisovalerate are pathognomonic for MSUD ***(Sakai et al., 2005)*.**