شبكة المعلومات الجامعية

بسم الله الرحمن الرحيم

شبكة المعلومات الجامعية

جامعة عين شمس

التوثيق الالكتروني والميكروفيلم

قسم

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التوثيق الالكتروني والميكروفيلم

بعض الوثائق الاصلية تالفة

بالرسالة صفحات

لم ترد بالاصل

Study of MTHFR Gene Mutation in Normal Mothers and in Mothers with Down syndrome Children

Thesis submitted for fulfillment of the
Master degree in
Pediatrics

By

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October 2002

بسم الله الرحمن الرحيم

بناء على موافقة الأستاذ الدكتور / نائب رئيس الجامعة بتاريخ ٢٠٠٢/٨/٨م اجتمعت اللجنة المشكلة من الأساتذة :

١ – أ.د./ سعاد إسحاق وهبة (عن المشرفين)

٢ – أ.د./ سوسن حسن عبد الهادى (ممتحن داخلى)

٣ – أ.د./ مصطفى كامل العوضى (ممتحن خارجى)

بقاعة الدور الثانى لمناقشة علنية لرسالة الماجستير فى طب الأطفال المقدمة من الطبيبة / **علا حسنى السيد محمد على.**

وذلك فى تمام الساعة (١٢) صباحا يوم (الأحد) الموافق ٢٠٠٢/١٠/٢٠م.

عنوان الرسالة :

دراسة الطفرة فى جين ميثلين تتراهيدروفوليت ردكتيز فى الأمهات العاديين والأمهات لأطفال بمتلازمة داون

الملخص :

تم تحديد وجود الطفرة فى الأمهات العاديين والأمهات لأطفال بمتلازمة داون، ولم يثبت وجود الطفرة مما يدل على أن هذه الطفرة ليست عامل خطورة لزيادة نسبة الاصابة بطفل منغولى.

بتحليل النظام الغذائى لأمهات الأطفال المصابين بمتلازمة داون تبين أنهن يتناولن حمض الفوليك بكميات أقل من الحد الأمثل مما يثبت أن نقص حمض الفوليك يزيد نسبة الاصابة بطفل منغولى.

كذلك تم تحديد نسبة الحمض الأمينى الهوموسيستايين فى دم الأمهات كدلالة على نسبة حمض الفوليك فى الدم، وكان فى الحدود الطبيعية مما يثبت أنه يتأثر بعوامل أخرى غير حمض الفوليك.

وترى اللجنة قبول البحث

٢٠/١٠/٢٠٠٢

Acknowledgement

My great thanks and all my respects to Prof. Dr. Soad IshaK, Prof. of pediatrics, Faculty of Medicine, Cairo University for her kind care, encouragement and guidance. She enriched me with her experience and continuous help.

My profound thanks and gratitude to Prof. Dr. Nagwa Abdel-Meguid head of the Dept. of Research on children with special needs, National Research Centre for her great support, continuous encouragement and valuable observations. She was interested in this work and enriched me with constructive observations. Dr, Nagwa did her best to get this work in the final form. Her help and kindness are always kept in mind.

My deep thanks to Dr. Hanna Abou El Ghar for her kindness, cooperation and sound advice.

I also express my gratitude to Dr. Ahmed Dardir Researcher of pediatrics, National Research Centre for his sound observations, valuable help and encouragement.

Special thanks to all members of the Biomedical Technology Department, National Research Centre for their great help and continuous cooperation.

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List of Abbreviations

AAI	Atlantoaxial instability
AML	Acute myeloid Leukemia
AML	Acute myeloid leukemia
APP	Amyloid beta (A4) precursor protein
bp	Base pair
C	Cytosine
CAF1A	Chromatin assembly factor 1, p60 subunit
CBS	Cystathionine beta synthase
COL6A1	Collagen V1, alpha-1 polypeptide
CRYA1	Crystallin, alpha polypeptide
D.S.	Down Syndrome
DHA	Docasahexaenoic acid
ETS2	Oncogene ETS-2
FPIA	Fluorescence Polarization Immunoassay
GLUR5	Glutamate receptor, ionotropic, kainate
HCY	Homocysteine
IFNAR	Interferon (alpha, beta), receptor for
IQ	Intelligence Quotient
Kb	Kilo base
MB	Mega Base
MMI	Maternal Meiosis I
MMII	Maternal Meiosis II
MTHFR	Methylenetetrahydrofolate reductase
NTDs	Neural Tube Defects
ORF	Open reading fragment
PFKL	Phosphofructokinase, liver type
SAH	S-adenosylhomocysteine
SAM	S-adenosylmethionine
SOD	Superoxide dismutase
T	Thymine

Abstract

The main aim of the present study was detection of the frequency of MTHFR gene mutation in Egyptians as a risk factor for nondisjunction. Mothers were subjected to complete nutritional history, estimation of homocysteine level in blood and study of MTHFR mutation at site 677 .

The results showed absence of MTHFR gene mutation in D.S. mothers and control mothers. Folate intake was significantly low in mothers with D.S. children. This indicates that sufficient folate (400 μg/d) is important preventive strategy, for nondisjunction. Blood homocysteine was normal in both D.S. mothers, which indicate that homocysteine is affected by other factors than folate intake.

Key words:

Down syndrome, MTHFR gene, mutation, Homocysteine, Folate

Introduction And Aim of work

1. Introduction

The story of Down syndrome began in 1866, when a physician, John Langdon Down published an essay in England. He described a set of children with common features who were distinct from other children with mental retardation. He made the first distinction between children who were cretins and what he referred to as "Mongoloids. In the 1970s, an American revision of scientific terms called it simply "Down syndrome,"

The incidence differs at different maternal ages. It is 1/1500 at 20 years, 1/1350 at 25 years, 1/900 at 30 years, 1/380 at 35 years, 1/240 at 37years, 1//150 at 39 years, 1/85 at 41years, 1/28 at 45 years, (Cheffins et al., 2000).

The overall birth prevalence of Down syndrome is 1 in 700 live births,, (Cheffins et al., 2000). The incidence at conception is much greater, but more than 60% are spontaneously aborted and at least 20 % are stillborn. It is a leading genetic cause of mental retardation. About 80% of trisomy 21 conceptions result in pregnancy loss, (Freeman et al., 1996). Despite its prevalence and consequence, the biochemical and molecular mechanisms that predispose to maternal nondisjunction are not understood. Recent evidence indicates that abnormal recombination during the meiosis I prophase is associated