Silent Brain Abnormalities in Thalassemia Intermedia

Thesis

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عنوان الرسالة / / متلازمات المخ الصامتة فى الثلاسيميا انترميديا

الملخص:

هناك تحسن فى متوسط عمر مرضى أنيميا البحر الأبيض المتوسط فى العقود الأخيرة إلا ان المرضى لا يزالوا يعانون من مضاعفات هذا المرض الوراثى حيث تم تحديد حالة من فرط الخثورية. تسعى الدراسة إلى إكتشاف معدل حدوث جلطات بالمخ صامتة بين مرضى أنيميا البحر الأبيض المتوسط بالرنين المغناطيسى و أشعة الدوبلر على أوعية المخ و إكتشاف العوامل المساعدة . تعرض50 مريض لأنيميا البحر الأبيض المتوسط (بمتوسط عمر 11.2 سنة) و ممن تنطبق عليهم شروط الدراسة للفحص و التحاليل و الأشعات بعد موافقة شفهية.29 (58%) كانوا من الذكور بينما 21(42%) كانوا من الإناث. نسبة الهيموجلوبين بمتوسط 8.25 .معدل نقل الدم بمتوسط 4.78 شهر. 36(72%) مريض كانوا يتعاطون دواء الهيدرا بمتوسط 20.8 مجم/ك/اليوم . و قد تلقوا الجرعة بمتوسط مدة 31.6 شهر 7 مرضى (14.85%) كانوا قد استئصلوا الطحال من مدة أقصاها عامين.تم استبعاد 3مرضى بسبب عدم وضوح الأوعية بالمخ أثناء الفحص مما انتج 94 فحص كلى (أيمن و أيسر) . حيث أن 64(68%) من الفحوصات أظهرت ارتفاع فى PSV عن الطبيعى للسن المقابل له فى حين أن 70 (74.4%) فحص أظهر إرتفاع فى MV مما يدل على أن MV قد يكون معامل أكثر حساسية من PSV . أظهرت نتائج الدوبلر لأوردة المخ علاقة عكسية مع السن عند بداية ظهور أعراض المرض و السن عند الفحص ($P\leq0.05$) . 6من أصل 7 (85%) من المرضى اللذين استئصلوا الطحال أظهروا إرتفاع فى سرعة الدوبلر . أظهر كل من مدة تعاطى دواء الهيدرا و تعدد نقل الدم علاقة عكسية مع سرعة الدوبلر و لكن يحتاج إلى دراسة مطولة للتأكد من هذه العلاقة. الإستنتاجات :لم يتواجد ضيق فعلى بالأوعية الدموية بالمخ أثناء الفحص بالدوبلر و لا بالرنين المغناطيسى على المخ و لكن ارتفاع سرعة الدوبلر بأوعية المخ الدموية قد يوحى بوجود خطر الإصابة بجلطة (صامتة أو بأعراض). قد يساعد جهاز الدوبلر لأوعية المخ فى الإكتشاف المبكر للجلطات و من هم فى دائرة الخطر .

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Abstract

Background :Thrombo-embolic episodes (TEE) occurred 4.38 times more frequently in thalassemia intermedia (TI)than thalassemia major (TM), The prevalence of overt strokes in TI patients with a history of thrombosis ranges between 5% and 9%**.** Thrombosis in splenectomized TI patients is a chronic process . Aim of the work :This study aimed at detecting the prevalence of silent stroke in TI using MRI and TCD . Patients and Methods : Fifty TI patients (age range 5 to 34 years with mean age of 11.2 ± 5.72 years) fulfilling the inclusion criteria underwent history taking , clinical examination , laboratory investigations and imagings (MRI, TCD) after providing a verbal consent. Results : Steady Hb level ranged from 7 to 9.5 g/dl with mean of 8.25 ± 0.52 g/dl. Frequency of blood transfusions to maintain that Hb level ranged from 0 to 60 months with mean duration of 4.78 ± 11.77 months . Thirty six (72%) patients were on HU , on a compliance dose 20.8 ± 3.8 mg/kg/day. Only 7 (14.85%) were splenectomized within maximum period of 2 years. The examination of right and left MCAs of forty seven TI patients resulted into 94 total TCD examinations, 64(68%) showed PSV above normal for age while, 70 examinations (74.4%) showed MV above normal for age ; suggesting MV sensitivity over PSV.TCD velocities showed negative correlation with age at diagnosis ($P \leq 0.05$) as well as at time of examination ($P \leq 0.05$). Six (85%) out of the 7 splenectomized patients had high TCD velocity for age . Both blood transfusion frequency and HU duration of compliance showed negative correlation with TCD velocities for further longitudinal studies. Conclusion , TCD is a sensitive tool to be used for early detection of stroke (silent or overt) . The presence of high TCD velocities for age in TI may suggest the presence of a risk to develop stroke (silent or overt)

Key words: Thalassemia Intermedia , Transcranial Doppler , Silent Stroke , MRI brain , HU

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Abbreviations

- **ACA: Anterior cerebral artery**
- **ADCC :Antibody dependent cell cytotoxicity**
- **ADC: Apparent diffusion coefficient**
- **AHSP :Alpha hemoglobin stabilizing protein**
- **ALT: Alanine aminotransferase**
- **ANC : Absolute neutrophilic count**
- **ARC: Absolute reticulocytic count**
- **AST : Aspartate aminotransferase**
- **ATIII : Antithrombin III**
- **AVM : Arterio- venous malformations**
- **BA : Basilar artery**
- **BAEPs: Brain auditory evoked potential**
- **CBC : Complete blood counts**
- **CNS : Central nervous system**
- **CS: Carotid siphon**
- **CT : Computed tomography**
- **CVA: cerebrovascular accident**
- **DFO: Deferoxamine**
- **DFP: Defereprone**
- **DFX: Deferiserox**
- **DVT : Deep venous thrombosis**
- **DW: Diffusion weighted**
- **DWI: Diffusion weighted imaging**
- **DXA : Dual energy Xray absorptiometry**
- **ECs: Endothelial cells**
- **ECG : electrocardiogram**

- **EDTA: Ethylene diamine tetraacetic acid**
- **EEG : Electroencephalogram**
- **ELAM : E- selectin**
- **ELISA: Enzyme -linked immunosorbent assay**
- **EMH : Extramedullary hemopoeisis**
- **EPO : Erythropoitin**
- **Hb : Hemoglobin**
- **HC II : Heparin co factor II**
- **HPFH : Hereditary persistant fetal hemoglobin**
- **HPLC : High performance liquid chromatography**
- **HRC : Horse radish peroxidase**
- **HU : Hydroxyurea**
- **ICAM -1: Intercellular adhesion molecule -1**
- **ISCD: International Society for Clinical Densitometry**
- **IQ : Intelligent quotient**
- **L-carnitine : Levo carnitine**
- **LCR : Locus control region**
- **LIC : Liver iron concentration**
- **LT. :Left**
- **MCA: Middle cerebral artery.**
- **MRA: Magnetic resonance angiography**
- **MRI : Magnetic resonance angiography**
- **mRNA: Messenger RNA**
- **MTD : Maximum tolerated dose**
- **MTHFR: methyl tetra –hydro folate reductase**
- **MV : Mean velocity**
- **NO : Nitrous oxide**
- **NTBI : non -transferrin bound iron**

- **PCA: Posterior cerebral artery**
- **PC : Prothrombin concentration**
- **PT: Prothrombin time**
- **PTT: Partial thromboplastin time**
- **PET-CT: Positron emission tomography**
- **PF3: Platelet factor 3**
- **PHT : Pulmonary hypertension**
- **Plt: Platelet**
- **PS : Phosphotidylserine**
- **PSV : Peak systolic velocity**
- **QTLs : Quantitative trait loci**
- **RAM : Risk assessment model**
- **RBC: Red blood cell**
- **Rh- EPO: Recombinant human erythropoietin**
- **RT.: Right**
- **RVEF: Right ventricular ejection fraction**
- **RV: Right ventricle**
- **SCA: Sickle cell anemia**
- **SCD : Sickle cell disease**
- **SEPs : Somato-sensory evoked potential**
- **STOP: The stroke prevention trial in sickle cell anemia**
- **SQUID: Superconducting quantum interference device**
- **TAMMV: Time averaged maximum mean velocity**
- **TAT : Thrombin –antithrombin complex**
- **TCD : Transcranial Doppler**
- **TEE : Thromboembolic episodes**
- **TI : Thalassemia intermedia**
- **TM :Thalassemia major**

- **UDPG: Uridine 5’-diphospho-alpha-D-glucose**
- **VCAM -1 : Vascular cell adhesion molecule -1**
- **VEPs: visual evoked potential**
- **VWF : Von willibrand factor**
- **WBC: White blood cell**
- **WHO : World health organization**

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