EFFECT OF HEPATITIS C INFECTION ON PLATELET FUNCTION IN HEMODIALYSIS PATIENTS

Thesis

Submitted for partial fulfillment
Of master degree of internal medicine

By
Aida Osama Mohamed Zeidan
M.b.b.ch

Supervised by
Professor Dr. Mohamed El Tayeb Nasser
Professor of internal medicine and nephrology
Faculty of medicine Ain Shams University

Dr. Walid Ahmed Bichari
Lecturer of internal medicine and nephrology
Faculty of medicine. Ain Shams University.

Ain shams University
Faculty of medicine

2011

تأثير الإصابة بفيرس ج على وظائف الصفائح الدموية لدى مرضى الفشل الكلوى المزمن المعاشون على الإستصفاء الدموى

رسالة

توطئة للحصول على درجة الماجستير فى
أمراض الباطنة

مقدمة من

الطبيبة/ عايدة أسامة محمد زيدان

بكالوريوس الطب والجراحة العامة- كلية الطب جامعة عين شمس

تحت إشراف

الأستاذ الدكتور/ محمد الطيب ناصر

أستاذ أمراض الباطنة والكلى

كلية الطب جامعة عين شمس

الدكتور/ وليد أحمد بشارى

مدرس أمراض الباطنة والكلى

كلية الطب جامعة عين شمس

كلية الطب
جامعة عين شمس
٢٠١١

Summary

HCV has been proven to affect platelet function (aggregation and adhesion) in chronic renal failure patients and increase bleeding tendency in uremic patients on rgular hemodialysis this hemostatic effect has been related to the decrease in aggregation and adhesion tests especially adhesion and ristocation aggregation test.

Furthermore, a decrease in platelet aggregation in some patients have reported in uremic patients with negative HCV Abs.

Our study was to analyze the possible effect HCV on platelet function in uremic patients under regular hemodialysis. 30 patients, 11 woman and 19 men, with clinically stable end stage renal failure, who received maintenance hemodialysis 3 times weeks, with an age range between 24-67 years old, were enrolled in the study.

Individual base line values for Hb, and platelet count., and platelet aggregation tests using ristocetin, ADP (in concentration of 0.5 – m & 2.5 – m), and Epinephrine, were performed, there were significant decrease in platelet aggregation by using reistocetin, ADP significant decrease by using Epinephrine and significant, ADP in concentration There

CONTENTS

CONTENTS

List of abbreviations

vWF	von willebrand factor
(No)	nitric oxide
(CGMP)	cyclic guanosine monophosphate
(CKD)	chronic kidney disease
ADP	adenosine diphosphate
(AGA)	the american gastroenterological association
(CBC).	Complete blood counts
rh EPO	recombinant human EPO
(ASA)	acetylsalicylic acid
Tx A_2	thromboxane A_2
PGI_2	prostaglandin I_2
(TNF α)	tumor necrosis factor alpha
(GSA)	guanidinosuccinic acid.
(ACH)	adsorbable collagen hemostat
(PCR)	polymerase chain reaction
(TMA)	transcription mediated amplification
(B-DNA)	branched DNA
(TXA)	tranexamic acid
HCV	hepatitis c virus
DDAVP	(1-deamino-8-d-arginine vasopressin)
PTH	parathyroid hormone
(TMA)	transcription mediated amplification
TXB_2	2,3 dinor-thromboxane B_2
HD	Hemodialysis

List of Tables

List of Tables

List of Figures

O

قَالُوا سُبْحَانَكَ لَا عِلْمَ لَنَا
إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنتَ الْعَلِيمُ
الْحَكِيمُ

صدق الله العظيم

سورة البقرة الآية

INTRODUCTION

Hemostasis is the process that maintains the integrity of the circulatory system after vascular damage.It is a dynamic and tightly regulated process that we arejust beginning to understand. Under normal circumstances,vessel wall injury rapidly initiates a series of coordinated events designed to seal the breach generatedby the injury.

These events lead to clot formation and require both platelet recruitment and activation as well as

the generation of thrombin and fibrin.***(Furie and Furie 2008)***

In addition, thisprocess is modulated by multiple mechanisms that containit, thus preventing theotherwise imminent vascularinflammation and tissue damage ***(Lane et al.,2005).***

Deficiencies of platelet function or of the coagulation cascade typically lead to bleeding disorders, whereas platelet hyperreactivity and abnormalities in the regulatory mechanisms may result in excessive thrombin formation and pathological thrombosis. ***(Boccardo et al., 2004)***

Patients at various clinical stages of chronic kidney disease (CKD) display a wide range of derangements inall three aspects of hemostasis, and they experience a widespectrum of clinical manifestations that lead to consider-able morbidity and mortality in this patient population, one that

spans prothrombotic tendency leading to excessivec-ardiovascular events, as well as platelet dysfunctionleading to increased bleeding tendency. ***(Boccardo et al., 2004)*** .

This review summarizes the current knowledge on normal hemostasis, abnormalities in hemostatic pathways that have been described in CKD patients, and thedifferent therapeutic options for these individuals as wellas their effectiveness. ***(Boccardo et al., 2004)***

Aim of the Work

This study aims to asses platelet function in chronic renal failure patients on regular haemodialysis to show the prevelance of platelet dysfunction in this group of patients in relation to hepatits c status.

Review Of The Literature

Physiolog of Platelets :

Hemostasis & platelet function:

The participation of platelets in hemostasis is a fundamental component of this physiologic process. The reactions involved include adhesion to the cut end of a blood vessel, spreading of adherent platelets on the exposed subendothelial surfaces, secretion of stored platelet constituents (Including molecules involved in hemostasis and wound healing), and formation of large platelet aggregates. ***(Johnson et al., 2008)***

Production and kinetics:

The platelets develop in the inter medullary components of bone marrow. The platelet precursor of megakaryocyte undergoes a number of nuclear divisions leading in general to a 16 lobed cell which then begins to produce platelets.

When platelets mature , they circulate for aproximately l0 days . During this time , they decrease in size and increase in density primarily because of the loss of plasma membrane . ***(George and Lewis,2008)***

Studies showed age related changes in platelet survival , and a rough correlation between shortened survival and vascular disease suggesting that increased platelet turnover may result from vascular lesions ***(Abrahamsen, 2007).***

Morphology Of Blood Platelets:-

Platelets are small non nucleated discoid cells about 3M long and 1M thick, In stained blood films , the clear, blue cytoplasm is seen to contain a few granules , but the electron microscope reveals a very complex system of membranes , microtubules and organelles. Under the electron microscope platelets appear to be formed of 4 distinct divisions ***(Thompson, 2006)***

1- The peripheral zone .

2 - The sol-gel zone.

3 - The organelle zone.

4 - The membrane systems.

Under the peripheral membrane, there are helical coiled bundles of microtubules which are involved in platelet contraction. A gel like matrix embes the organelles and microfilaments.

There is a system of channels by which it is possible that the products of secretory granules reach the organelles. The metabolic requirements of the platelets are maintained by the mitochondria ***(Thompson, 2006)***