

SEROPREVALANCE OF HEPATITIS A, B AND C AMONG MULTITRANSFUSED CHILDREN IN RED CRESCENT HOSPITAL IN KENA

Thesis

Submitted for partial fulfillment of the Master
Degree (MSc) in Pediatrics

By

Galal Helmy Hussein

M.B.B.ch.

Assuit University

Under the supervision of

Dr. Omnia Fathy El – Rashidy

Assist. Prof of Pediatrics, Ain Shams University

Dr. Perihan Hamdy Tawfik

Prof. of Clinical Pathology, Ain Shams University

Dr. Amel El – Faramawy

Lecturer of Pediatrics, Ain Shams University

Department of Pediatrics

Faculty of medicine

Ain shams university

2010

معدل انتشار العدوى بالفيروسات الكبدية أ و بى و سى

بين الأطفال الذين يتلقون نقل دم بصورة دورية

فى مستشفى الهلال الأحمر بقنا

بروتوكول مقدم من

الطبيب / جلال حلمي حسين

بكالوريوس الطب والجراحة – جامعة اسيوط

توطئة للحصول على درجة الماجستير في طب الأطفال

تحت إشراف

د/ أمنية فتحي الرشيدى

أستاذ م. طب الأطفال – جامعة عين شمس

د/ بريهان حمدي توفيق

أستاذ الباثولوجيا الإكلينيكية – جامعة عين شمس

د/ أمل الفرماوى

مدرس طب الأطفال - جامعة عين شمس

Introduction:

Though regular blood transfusion improves the overall survival of multitransfused children and In spite of the progress made in the prevention of transfusion - transmitted infections over the last years, these still occur. Transmitted infections (TTI) continue to be a problem in many parts of the world, and multi-transfused patients (MTP) are at a particularly increased risk of TTI. (1)

Monitoring infectivity markers in multi-transfused patients is an important indicator of the efficiency and quality of testing in blood centers.(2)

Blood transfusion is the main risk factor in transmission of viral hepatitis especially in patients with hematological diseases. They are exposed to frequent transfusion of blood and blood products which are risk factors for HCV infection in children with hemophilia (80-95%) and thalassemia (60-75%).(3)

Although the risk of post-transfusion HCV infection dropped significantly after the national screening of blood in 1993, more than 20% of children who were multiply transfused after that date were HCV-RNA positive.(4)

Blood transfusion remains a major risk of HCV transmission among Egyptian children. HCV infection is not always benign in the childhood period. ALT levels remain elevated in half of the children and histological abnormalities are detected in three quarters of HCV RNA-positive cases.(5)

Also, as regarding HAV, patients with chronic liver disease who acquire hepatitis A, are at increased risk for fulminant hepatitis. (6)

Aim of the study:

The purpose of the study is to estimate the prevalence and epidemiological data on hepatitis A (HAV), hepatitis B virus (HBV) and hepatitis C (HCV) among multitransfused children in blood bank of the Red Crescent hospital in Kena which is serving children of Upper Egypt (Kena , Luxor and the Red Sea governorates) and the impact of serological screening; to evaluate the role of number of transfusions and other potential risk factors

for the acquisition of HBV , HCV and HAV infections and contribute to a better understanding of the state of blood safety in this region.

Patients and methods:

This study will be carried out at the blood bank of the Egyptian Red Crescent Hospital in Kena . One hundred (100) multitransfused children aged between 2 and 18 years will be included in our study.

Eligibility criteria:

Selected children will be:

Thalassemics, hemophilics and of other blood diseases receiving multiple blood transfusions i.e. Aplastic anemia, sickle cell anemia...etc.

- They should be previously treated with 10 or more units of allogenic blood or blood components.

Clinical methods:

- A standardized questionnaire will be completed for all study subjects obtaining an informed consent from children's parents or their legal guardians.

- Data recorded will provide epidemiological history and risk factors pertaining to hepatitis virus infections, including maternal and family history of HAV, HBV and HCV infections or chronic liver disease, history of surgery, blood transfusions

(Type and numbers), hospitalization, schistosomiasis , sharing sharp household material and multiple injections will be emphasized .

- Through clinical examination:

- Presence of pallor or jaundice

- Abdominal examination for liver or spleen enlargement

Laboratory tests :

- Complete blood picture (C.B.C).
- Liver enzymes: - Aspartate transaminase (AST)
- Alanine transaminase (ALT)
- Using second-generation enzyme-linked immunosorbent assay (ELISA), sera of them will be tested for:
 - HAV (IgG).
 - Hepatitis B markers:
 - HBsAg
 - HBcAb
 - HBsAb
- HCV Ab (anti – HCV).

References:

- (1) Lopez L, Lopez P, Arago A, Rodriguez I, Lopez J, Lima E, Insagaray J, Bentancor N. (2005) Risk factors for hepatitis B and C in multi-transfused patients in Uruguay. (J Clin Virol. 2005 Dec; 34 Suppl 2:S69-74.).
- (2) Vinelli E, Lorenzana I. (2005) Transfusion-transmitted infections in multi-transfused patients in Honduras. (J Clin Virol. 2005 Dec; 34 Suppl 2:S53-60).
- (3) El-Raziky MS, El-Hawary M, El-Kofy N, Okasha S, Kotb M, Salama K, Esmat G, El-Rizky M, Abouzied AM, El-Karakasy H.(2004) Hepatitis C infection in Egyptian children:single center experience .(J Viral Hepat.2004; 11:471- 6.)
- (4) Khalifa AS, El-Sayed MH, Moustafa AO, Mohammed MM, Rady MS, Salama II, Karim AM. (2002) Hepatitis C virus infection in children with hematological diseases: risk factors and reliability of diagnosis assays. (Egypt J Pediatr 2002; 19:293– 308).
- (5) El-Raziky MS, El-Hawary M, El-Koofy N, Okasha S, Kotb M, Salama K, Esmat G, El-Raziky M, Abouzied AM, El-Karakasy H.(2004) Hepatitis C virus infection in Egyptian children: single centre experience. (J Viral Hepat.2004 Sep; 11(5):471-6).
- (6) Vento. S., T. Garofano,C.Renizi, et al (1998) fulminant hepatitis associated with hepatitis A virus superinfection in patients with chronic hepatitis. (C.N Engl J Med 1998; 338: 286 – 90).

مقدمة :

على الرغم من ان نقل الدم المنتظم يحسن الحالة العامة للأطفال المرضى المحتاجين لنقل الدم و على الرغم من التقدم الذى حدث فى منع العدوى الناتجة عن نقل الدم خلال السنوات الماضية فأنها مازالت تحدث .وتستمر العدوى الناتجة عن نقل الدم لتمثل مشكلة فى أجزاء عديدة من العالم و خصوصا للمرضى المحتاجين لنقل الدم باستمرار حيث أنهم تزداد خطورة نقل العدوى لهم .

وملاحظة دلالات العدوى فى المرضى المحتاجين لنقل الدم لهو مقياس مهم لكفاءة و جودة الاختبارات فى مراكز نقل الدم .

ويشكل نقل الدم الخطورة الرئيسية لنقل الفيروسات الكبدية بخاصة فى مرضى مختلف أمراض الدم فهم معرضون باستمرار لنقل الدم ومشتقاته وبالتالي تزداد فرصة العدوى بفيروس الكبد (سى) فتبلغ فى الأطفال مرضى الهيموفيليا (80 – 95%) وفى الأطفال مرضى انيميا البحر المتوسط (60 – 75%).

فبالرغم من ان معدل الإصابة بالالتهاب الكبدى الفيروسي (سى) بعد نقل الدم قد انخفضت وذلك بعد الفحص الشامل للدم سنة 1993 الا أن أكثر من 20% من الأطفال الذين يتعرضوا لنقل الدم المتكرر مصابون بالالتهاب الكبدى الفيروسي (سى).

ولذا يظل نقل الدم الخطورة الرئيسية لنقل الفيروس الكبدى (سى) بين الاطفال المصريين.وهو ليس بالضرورة حميدا فى مرحلة الطفولة فمستويات انزيمات الكبد مثل (ALT) يظل مرتفعا فى نصف الأطفال المصابين وكذلك فالتغيرات الهستولوجية ملحوظة فى ثلاثة أرباع الأطفال المصابين .

أما بالنسبة للفيروس الكبدى (أ) فالمصابون بأمراض الكبد المزمنة ويتعرضون للأصابة بالفيروس الكبدى (أ) يكونون أكثر عرضة للالتهاب الكبدى بصورة شديدة .

هدف البحث :

هو معرفة معدل الإصابة بالفيروسات الكبدية (أ و ب و ج) بين الاطفال المعرضون لنقل الدم المتكرر فى بنك الدم بمستشفى الهلال الأحمر بقنا والذى يخدم الأطفال المرضى فى صعيد مصر من محافظات (قنا والأقصر و البحر الأحمر) و جدوى الفحوصات المتبعة ومعدلات الخطورة المحتملة للإصابة بالفيروسات الكبدية (أ و ب و ج) ومدى توفر الدم الآمن فى هذا الأقليم .

المرضى و الطريقة المتبعة :

سيجرى هذا البحث فى وحدة بنك الدم بمستشفى الهلال الأحمر بقنا و سيجرى على مائة طفلا (100) من الأطفال الذين يتم نقل الدم المتكرر لهم بالوحدة على ان يكون متوسط العمر من سنتين وحتى 18 سنة .

الطريقة الاكلينيكية :

سيتم اختيار الأطفال المرضى بامراض الدم المزمنة المختلفة مثل أنيميا البحر المتوسط و الهيموفيليا و أنيميا الخلايا المنجلية ...

- أن يكون الطفل قد تم نقل دم أكثر من عشر وحدات من الدم أو مشتقاته .
- سيكون هناك مجموعة من الأسئلة سيجيب عنها سواء من الأطفال أو ذويهم بعد أخذ موافقة منهم بذلك لمعرفة معدل انتشار و عوامل خطورة العدوى للألتهاب الكبدي و تشمل تاريخ المرض العائلي للألتهاب الكبدي و تاريخ حدوث عمليات جراحية و نقل دم (عدده و نوعه) و دخول المستشفى و حدوث إصابة بالبلهارسيا و حدوث حقن متكررو استخدام ادوات حادة مشتركة كأدوات الحلاقة.

- الفحص الأكلينيكي : 1- ملاحظة وجود الشحوب أو الصفراء .
- 2- فحص البطن لملاحظة وجود تضخم بالكبد أو الطحال .

- الفحوصات المعملية :

1- صورة دم كاملة .

2- وظائف الكبد و تشمل : AST – ALT

نسبة البليروبين بالدم .

3- الفحوصات الفيروسية و تشمل :

- HAV (IGg).

- Hepatitis B markers:

- HBsAg

- HBcAb

- HBsAb

- HCV Ab (anti – HCV).

SEROPREVALANCE OF HEPATITIS A, B AND C AMONG MULTITRANSFUSED CHILDREN IN RED CRESCENT HOSPITAL IN KENA

Omnia Fathy El-Rashidy^{*}, Perihan Hamdy Tawfik^{**}, Amel El-Faramawy^{*},
Galal Helmy Hussein^{*}

^{*} Department of Pediatrics – ^{**} Department of Clinical Pathology
Ain Shams University

ABSTRACT

Background: Though regular blood transfusion improves the overall survival of multitransfused children and In spite of the progress made in the prevention of transfusion - transmitted infections over the last years, these still occur. Transmitted infections (TTI) continue to be a problem in many parts of the world, and multi-transfused patients (MTP) are at a particularly increased risk of TTI.

Aim of the Work: The purpose of the study is to estimate the prevalence and epidemiological data on hepatitis A (HAV), hepatitis B virus (HBV) and hepatitis C (HCV) among multitransfused children in blood bank of the Red Crescent hospital in Kena which is serving children of Upper Egypt (Kena , Luxor and the Red Sea governorates) and the impact of serological screening ; to evaluate the role of number of transfusions and other potential risk factors for the acquisition of HBV, HCV and HAV infections and contribute to a better understanding of the state of blood safety in this region.

Patients and Methods: This study was conducted in the Blood Bank established for serving children in the Red Crescent Hospital, Kena, between January 2008 and June 2008. One hundred children attending the children's Blood Bank, were included in the study suffering from diseases which require repeated blood transfusion. Among the 100 patients included in this study, thalassaemia was the most common diagnosis as it was found in fifty patients (50%) and fifty patients (50%) were diagnosed to have other blood diseases (33 patients (66%) were hemophilics. 11 patients (22%) had aplastic anaemia; 6 patients (12%) had sickle cell anaemia).

Results: Anti HAV Antibodies IgG was detected in 68% of thalassemic group of patients, compared to 72% of the other causes group with no

significance between 2 groups of the study, indicating that those patients are immune to Hepatitis A by past infection as history of hepatitis A vaccination was negative for all the included children. Immunity to Hepatitis B due to successful vaccination was found in 42% of group 1 and 50% of group 2 as they had positive HBsAb (while, HBsAg and HBcAb were negative). Chronic infection accounts for 4% of group 1 and 10% of group 2 as they had positive HBsAb and HBsAg (while, HBcAb was negative). Acute infection accounts for 4% of group 1 and 6% of group 2 as they had positive HBsAg and HBcAb (while, HBsAb was negative). Immunity due to natural infection accounts for 4% of group 1 and 2% of group 2 as they had positive HBsAb and HBcAb (while, HBsAg was negative). Susceptibility to infection accounts for 46% of group 1 and 32% of group 2 as they were negative to all hepatitis B markers, such patients need hepatitis B vaccination. As regards, hepatitis B markers, no significant difference was found between the two groups of the study. On the other hand, HCV antibodies were detected in 48% of group 1 and 42% of group 2, indicating that those patients had past or recent infection with HCV. While, the frequency of patients who were negative to all studied hepatic markers was 8% of group 1 and 2% of group 2, indicating that those patients are susceptible to infection and need vaccination against Hepatitis A and B.

Conclusion: Transfusion transmitted hepatitis is still a major problem for children who require repeated blood transfusion and this needs more effort to reduce the infection rate by blood transfusion through proper screening of blood and blood products, regular follow up for those children by hepatitis B antibodies titre and giving booster doses for those in need. HAV vaccination is recommended to multi-transfused children to reduce the exposure of their livers to infection with hepatitis A. Our study confirmed the increased risk of HBV and HCV among surveyed polytransfused children. The risk of infection with HCV is more than what has been previously reported due to the higher prevalence of HCV in the population and the nature and frequency of exposures. Also we can conclude that the frequency of HBV and HCV infection is still high among multi-transfused children in Egypt inspite of improving blood screening for these viruses and donor selection.

Key Words: Polytransfused children, Hepatitis markers, Immunity, thalassaemia,

List of Contents

Introduction	1
Aim of the work	3
Review of Literature	4
- Chapter (1) Hepatitis B Virus	4
- Chapter (2) Hepatitis C Virus	53
- Chapter (3) Blood Components Therapy	101
Patients and Methods	120
Results	133
Discussion	179
Summary and Conclusion	210
Recommendations	213
References	218
Arabic Summary	—

List of figures

Figure No.	Title	Page No.
1	Global distribution of hepatitis B	6
2	Genetic organization of hepatitis B virus genome	8
3	Infection cycle of hepadnaviruses	9
4	Outcome of hepatitis B virus infection by age at infection	19
5	Acute HBV infection	21
6	Clinical and virological course of acute infection with HBV or HCV	22
7	Chronic HBV infection (HBeAg positive)	23
8	Chronic HBV infection (HBeAg negative)	23
9	One possible evaluation algorithm for children with chronic HBV infection	24
10	Investigation of hepatitis B virus (HBV) immunity	25
11	Genomic organization of hepatitis C virus.	56
12	HCV genotypes in Egypt.	60
13	Progression of HCV mono-infection over 10-25 years.	73
14	Genomic organization of HCV. First generation, second generation refer to serologic assays for detection of HCV antibodies	76
15	laboratory diagnosis of hepatitis C infection (except infants)	79
16	Natural history of acute HCV infection	88
17	Production of blood components and plasma derivatives	104
18	Sex distribution of the patients of the study	134
19	Percentage of different studied hepatitis markers among all patients of the study (n=100).	140
20	Sex distribution among group 1	142
21	Hepatitis markers in group 1 (n=50).	148
22	Sex distribution among group group 2	157
23	Disease distribution among group 2	157
24	Hepatitis markers in group 2 of patients (n=50)	162
25	Comparison between both groups of the study as regards the mean value for age, disease duration and blood units.	169
26	Comparison between the 2 groups as regards source of transfused blood, and history of hepatitis B vaccination.	171
27	Comparison between the 2 groups as regards history of jaundice, history of hepatitis and chelation therapy.	171
28	Comparison between group 1 and group 2 as regards clinical jaundice	172
29	Comparison between the 2 groups as regards the mean value for the liver span, splenic size and splenectomy	173
30	Comparison between both groups as regards the mean value for Hb level and WBCs count.	174
31	Comparison between both groups as regards the platelets	175

	mean value.	
32	comparison between both groups as regards the mean value of AST and ALT	176
33	comparison between both groups as regards the mean of total, direct and indirect bilirubin	176
34	comparison between group 1 and 2 as regards hepatitis markers (each group = 50 patients)	178

