LIVER DISEASE OUTCOME IN HEPATITIS B AND HEPATITIS C VIRUS COINFECTED CHILDREN UNDER IMMUNOSUPPRESSIVE THERAPY

Thesis

Submitted for partial fulfillment of Master Degree of Pediatrics

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2010

تاثير العدوى المزدوجة بفيروسى الالتهاب الكبدى بى وسى على كبد الاطفال الخاضعين للعلاج بمثبطات المناعه

رسالة
توطئة للحصول علي درجه الماجستير في طب الاطفال

مقدمه من
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كليه الطب
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2010

Acknowledgement

First of all, thanks to GOD for his grace and mercy and for giving me the health & effort to complete this work.

I would like to thank ***Professor Doctor Manal Hamdy El Sayed,*** professor of pediatrics, Ain Shams University; for her kind support, her constant guidance, experienced advice and great encouragement which have been of utmost importance and to whom I will always be indebted.

I owe special thanks to ***Professor Doctor Iman Ibrahim Salama,*** for guiding me in the statistical work in this study.

My gratitude is dedicated to ***professor doctor Alaa El Haddad,*** professor of paediatric oncology, National Cancer Institute, for his valuable guidance and willing cooperation throughout this work.

I would like to express my thanks to ***Dr Nevine Gamal,*** lecturer of paediatrics, Ain Shams University for her continuous attention and follow up.

Finally I would like to express my warm feelings to my dear husband & my two daughters who suffered a lot with me until I finished this work & also for all my family for their support & helps.

Contents

List of abbreviations

- AASLD: American Association for the Study of Liver Diseases.
- ACIP: Advisory Committee on Immunization Practices.
- ALL: Acute Lymphoblastic Leukemia.
- ALT: Alanine Aminotransaminase
- Anti-HBc: Anti hepatitis B core antigen.
- Anti-HBe: Anti hepatitis B envelop antigen.
- Anti-HBs: Anti hepatitis B surface antigen.
- Anti-HCV: Antibodies against HCV.
- APASL: Asian Pacific Association for the Study of the Liver.
- AST: Aspartate Aminotransferase.
- BCP: Basal core prometor.
- BMT: Bone marrow transplantation.
- CD8: Cluster of differentiation or cluster of determination number 8.
- CDC: Centers for Disease Control and Prevention.
- CLD: chronic liver disease.
- DNA: Deoxyribo nucleic acid.
- EASL: European Association for the Study of the Liver.
- EIA: Enzyme immunoassay.
- ELISA: Enzyme linked immunosorbent assay.
- EOTR: end of treatment response.
- EVR: early virological response.

- FDA: Food & drug administration.
- FS: Fibrosis stage.
- HAI: Histologic activity index.
- HBcAg: Hepatitis B core antigen.
- HBeAg: Hepatitis B envelop antigen.
- HBIG: Hepatitis B Immunoglobulin.
- HBsAg: Hepatitis B surface antigen.
- HBV: Hepatitis B virus.
- HCC: Hepatocellular carcinoma.
- HCV: Hepatitis C virus.
- HCV-4: Hepatitis C virus genotype 4.
- HCW: Health care workers.
- HD: Hemodialysis
- HIV: Human immune deficiency virus
- IDU: Intravenous drug users.
- IgG: Immunoglobulin G.
- IgM: Immunoglobulin M.
- IFN- α: Interferon –Alfa.
- INR: international normalized ratio.
- LAM: Lamivudine.
- MHC: Major histocompatability complex.
- MU: Mega units.
- NIH: National Institutes of Health.
- PCR: Polymerase chain reaction.
- PEG-IFN: Peginterferon.

- PNET: Primitive neuroectodermal tumour.
- P-P septa: Periportal septa.
- RBV: Ribavirin.
- RIBA: Recombinant immunoblot assays.
- RNA: Ribo nucleic acid.
- RT / Pol: Reverse transcriptase / polymerase.
- RVR: Rapid virologic response.
- SVR: Sustained virologic response.
- VHPB: Viral Hepatitis Prevention Board.
- WHO: World health organization.

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Introduction

Hepatitis B virus (HBV) and Hepatitis C virus (HCV) infections are the most common causes of chronic liver diseases worldwide. Both viruses could induce chronic hepatitis, which may progress to cirrhosis and eventually hepatocellular carcinoma ***(Fan et al., 2003).***

HBV is a double stranded DNA virus and its genome has 4 genes ***(Wormann and Lin, 2002)***. The prevalence rate of hepatitis B surface antigen in the Egyptian population is intermediate (4.5%) ***(Mohammed et al., 2006).*** About 90% of infected neonates and 50% of infected young children (1-5 years) will develop chronic hepatitis whereas the percent is only 2-6% of acutely infected older children and adults. In immunocompromised children there is increased risk for chronicity (30-100%) ***(Pol, 2006).***

HCV is a single stranded RNA enveloped virus and a member of flaviviridae family with 6 genotypes, the commonest in Egypt is genotype 4 **(Penin F et al; 2004, Abdel Aziz F et al; 2000).** Egypt has the highest prevalence of HCV worldwide (15%) ***(Egyptian Ministry of Health Annual Report: 2007).*** Asymptomatic HCV is detectable in 2.02% of Egyptian children ***(El-Raziky et al., 2007).*** In Egypt, 8.8% of blood donors' sera in 13 governorates were positive for anti-HCV ***(Tanaka et al, 2004).***

As a result of shared routes of infection, HBV and HCV coinfection is not uncommon, especially in areas with a high prevalence of HBV infection. Patients who are coinfected represent

a unique group with diverse serologic profiles. Combined chronic hepatitis B and C leads to more severe liver disease and increased risk for hepatocellular carcinoma. Furthermore coinfected patients represent a treatment challenge ***(Crockett and Keeffe, 2005).***

In general, the prevalence of coinfection is around 10-20% in patients with chronic HBV infection, and 2-10% of anti-HCV positive patients to have markers of HBV infection ***(Liu and Hou, 2006).***

Immunocompromised children are considered high risk population for infection with hepatitis B and C concurrently. They include those with malignant neoplasms, receiving radiotherapy or chemotherapy, on chronic haemodialysis, organ transplant patients, human immunodeficiency virus infected patients and haematological patients with frequent blood transfusion as haemophilics and thalassemics ***(Liu and Hou, 2006).***

Infection by HBV rather than HCV causes more severe liver disease in children with haematological malignancies ***(El-Sayed et al., 2003).***

Aim

The objective of this study is to assess the impact of coinfection with HBV and HCV on the outcome of liver disease in children receiving immunosuppressive therapy.

Viral hepatitis

The term hepatitis describes inflammation of the liver. Hepatitis may be caused by alcohol, drugs, autoimmune diseases, metabolic diseases, and viruses. Viral infection accounts for more than half the cases of acute hepatitis in the world ***(Mahoney et al, 1997).***

In the strictest sense, the term "viral hepatitis" includes a series of clinical conditions of infectious origin caused by five phylogenetically unrelated human viruses that have developed specific tropism to hepatocytes. In a broader sense, it also includes acute liver diseases due to infection by other viruses that do not display specific liver tropism, but may produce liver disease as a complication of the infection. Hepatitis B and C viruses have, in addition, developed strategies that allow them to establish long-lasting, chronic infections in some patients ***(Echevarria–Mayo JM; 2006).***

*Acute hepatitis: *(Wasley et al, 2007)*

Clinical Case Definition: Acute hepatitis was defined as acute illness with 1) discrete onset of symptoms (e.g., nausea, anorexia, fever, malaise, or abdominal pain) and 2) jaundice or elevated serum aminotransferase levels.

*Chronic hepatitis:

Hepatitis B virus (HBV) and Hepatitis C virus (HCV) infections are the most common causes of chronic liver diseases worldwide. Both viruses could induce chronic hepatitis, which may progress to cirrhosis and eventually hepatocellular carcinoma ***(Fan et al., 2003).***