بسم الله الرحمن الرحيم

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تم رفع هذه الرسالة بواسطة / مني مغربي أحمد

بقسم التوثيق الإلكتروني بمركز الشبكات وتكنولوجيا المعلومات دون أدنى مسئولية عن محتوى هذه الرسالة.

ملاحظات: لا يوجد

Effect of Dialysis Prescription Dose on Hepatitis B Vaccination Immunological Response in Hemodialysis Patients

Thesis

Submitted for Partial Fulfillment of Master Degree in Internal Medicine

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2022

سورة البقرة الآية: ٣٢

Acknowledgment

First and foremost, I feel always indebted to **ALLAH**, *the Most Kind and Most Merciful.*

I'd like to express my respectful thanks and profound gratitude to ***Prof. Dr. Saeed AbdelWahab Saeed,*** *Professor of Internal Medicine and Nephrology, Faculty of Medicine, Ain Shams University for his keen guidance, kind supervision, valuable advice and continuous encouragement, which made possible the completion of this work.*

I am also delighted to express my deepest gratitude and thanks to ***Prof. Dr. Hayam Ahmed Hebah,*** *Professor of Internal Medicine and Nephrology, Faculty of Medicine, Ain Shams University, for her kind care, continuous supervision, valuable instructions, constant help and great assistance throughout this work.*

I am deeply thankful to ***Dr. Ahmed Mohamed Tawfik,*** *Lecturer of Internal Medicine and Nephrology, Faculty of Medicine, Ain Shams University, for his great help, active participation and guidance.*

Nahla Elsayed

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INTRODUCTION

Hepatitis B virus (HBV) infection is an important public health problem affecting approximately 500 million people worldwide ***(Ozaras et al., 2015),*** According to 2010 data, 360 million people have chronic HBV infection that leads to more than 1 million deaths/year due to acute hepatitis, cirrhosis or hepatocellular carcinoma ***(Güthle and Dollinger, 2014)***. Clinical course of chronic HBV infection may vary from asymptomatic carrier state to cirrhosis or even hepatocellular carcinoma ***(Luca et al., 2014).***

Hepatitis B prevalence remains a challenge in dialysis. USRDS data indicates that 1% of dialysis patients tested positive for hepatitis B surface antigen (HBsAg) while in a registry study of Asian-Pacific countries the prevalence of HBsAg in hemodialysis populations ranged from 1.3% to 14.6% ***(Johnson et al., 2009)***. In general the incidence of HBsAg positivity among dialysis patients ranges from 0%-7% in low-prevalence countries to 10%-20% in endemic areas.

However, it is significantly higher in some areas like southeastern Asia and Middle East. The majority of southeast Asia and Middle East countries have an intermediate or high endemicity of HBV infection. Based on the data in 2009, the rate of HBsAg positivity was 4.4% in the Turkish population (ranging from 2.5% to 9.1%) ***(Sayan et al., 2012).***

The chronicity rate of HBV infection is 5%-10% in the general population, whereas it may be as high as 60%-80% in patients receiving renal replacement therapy (RRT) ***(Maheux, 2013),*** Nucleoside analogues and interferon(IFN) are choices of treatment; however, a sustained viral response is achieved in only 30%-40% of patients on dialysis ***(Grzegorzewska, 2014).*** Owing to the fact that the chronicity rate of HBV infection is high and success rate of antiviral therapy is low in dialysis population, preventive measures against HBV infection is of vital importance. Since the first recommendation of HBV vaccination by the Center for Disease Control and Prevention, the United States in 1982, administration of recombinant HBV vaccine which is composed of HBsAg is routinely used ***(Centers for Disease Control (CDC), 1982).***

HBV vaccination should be started before the initiation of RRT. Currently, intramuscular administration HBV vaccine at 0, 1, 2 and 6 mo at a dose of 40 μg is recommended. Instead of gluteal region which contains muscle and fat, deltoid muscle is a preferable area to increase response rates ***(Janus et al., 2008).*** There are variable response rates to HBV vaccination among HD patients. Inadequate seroconversion rates in the general population and patients on RRT are 5%-10%and 40%-50%, respectively ***(Grzegorzewska et al., 2013).*** According to another report, 20% of vaccinated patients on HD still do not achieve antibody formation against HBsAg ***(Lin et al., 2012).***

Patients with chronic kidney disease (CKD) exhibit an impaired immune response against host agents including HBV due to bone marrow suppression caused by uremia and loss of CD4 T cells by use of bio-incompatible dialysate and membranes ***(Noori et al., 2013)***. Patients on HD or peritoneal dialysis (PD) have an increased risk of HBV related complications. On the other hand, the rates of seroconversion induced by HBV vaccination in patients with CKD is significantly lower than those in the general population ***(Liu et al., 2009)***.

AIM OF THE WORK

The aim of our study is to determine the immunological response after HBV vaccination, and its relation to dialysis prescription dose in hemodialysis patients.

Chapter 1

HEPATITIS B VIRUS INFECTION

Introduction

An estimated 350 million persons worldwide are chronically infected with hepatitis B virus (HBV) ***(Lavanchy, 2004)***. In the United States, there are estimated 1.25 million hepatitis B carriers, defined as persons positive for hepatitis B surface antigen (HBsAg) for more than 6 months ***(Mast et al., 2005).***

Although most carriers will not develop hepatic complications from chronic hepatitis B, 15% to 40% will develop serious sequelae during their lifetime ***(Bosch et al., 2005).*** Carriers of HBV are at increased risk of developing cirrhosis, hepatic decompensation and hepatocellular carcinoma (HCC) ***(Beasley, 1988).***

HBV is one of the most frequent viral infections in humans. Infection can occur either through perinatal transmission, which is the cause of 35 to 40 percent of new infections worldwide or horizontally through exposure to infected blood or other body fluids. The perinatal (vertical) mode of transmission is of increasing concern in specific geographic regions ***(Fabrizi and Martin, 2000).***

Although safe and effective vaccines against HBV have been available for more than three decades, HBV infection remains a burden to global public health, resulting in 600000 to 1 million deaths per year worldwide ***(Kao and Chen, 2002)***.

Two billion people are estimated to be exposed to HBV infection once in their life and it causes a wide spectrum of liver disease, including acute or fulminant hepatitis, inactive carrier state, reactivation, chronic hepatitis, cirrhosis and HCC ***(Mizokami, 2009).***

The global prevalence of HBsAg varies greatly and countries can be defined as having a high, intermediate and low prevalence of HBV infection based on a prevalence of HBsAg carriers of ≥ 8%, 2%-7%, and <2% respectively ***(McMahon, 2005).*** In developed countries, the prevalence is higher among those who immigrated from high or intermediate prevalence countries and in those with high risk behaviors ***(Bosch et al., 2005).***

Historical view of HBV

The earliest record of an epidemic caused by HBV was made in Germany by Lurman in 1885 ***(Lurman, 1885).***

An outbreak of smallpox occurred in Bremen in 1883 and 1,289 shipyard employees were vaccinated with lymph from other people. After several weeks and up to eight months later, 191 of the vaccinated workers became ill with jaundice and were diagnosed as suffering from serum hepatitis. Other