سامية محمد مصطفى

شبكة المعلومات الجامعية

بسم الله الرحمن الرحيم

سامية محمد مصطفى

شبكة المعلومات الجامعية

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التوثيق الالكتروني والميكروفيلم

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جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

قسم

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بالرسالة صفحات لم ترد بالأصل

EVALUATION OF THE EFFICACY OF INTERFERON IN TREATMENT OF CHRONIC VIRAL HEPATITIS WITH FOLLOW UP OF THE PATIENTS AFTER CESSATION OF THERAPY

Thesis

Submitted in Partial Fulfillment of Requirements of the M.D. Degree in

"Internal Medicine "

By

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"وما أوتيتم من العلم إلا قليلا"

صدق الله العظيم

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CONTENTS

LIST OF ABBREVIATIONS

- ALT = alanine aminortansferase.
- AST = aspartate aminotransferase.
- Bil. = bilirubin.
- CAH = chronic active hepatitis.
- CDNA = complementary deoxy nucleic acid.
- CHB = chronic hepatitis B.
- CHC = chronic hepatitis C.
- CPH = chronic persistent hepatitis.
- CVH = chronic viral hepatitis.
- EIA = enzyme immunoassay.
- ELISA= enzyme linked immunosorbentassay.
- ETR = end-of-treatment -response.
- HAV = hepatitis A virus.
- Hb = hemoglobin.
- HBV = hepatitis B virus.
- HBcAb = hepatitis B core antibody.
- HBcAg = hepatitis B core antigen.
- HBeAb = hepatitis B envelop antibody.
- HBeAg = hepatitis B envelop antigen.
- HBsAb = hepatitis B surface antibody.
- HBsAg = hepatitis B surface antigen.
- HBV DNA = hepatitis B virus deoxy nucleic acid.
- HCC = hepatocellular carcinoma.
- HCV = hepatitis C virus.
- HCV RNA = hepatitis C virus ribodeoxy nucleic acid.
- HDV = hepatitis D virus.
- HDV Ag = hepatitis D virus antigen.
- HIV = human immunodeficiency virus.
- IFN-α = interferon- alpha.
- NANB = non-A,nonB.
- NRs = non-responders.
- PCR = polymerase chain reaction.
- RIA = radioimmunoassay.
- RIBA = recombinant immunoblot assay.
- RIFN = recombinant interferon.
- Rs = relapsers.

INTRODUCTION

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There are at least five forms of viral hepatitis caused by five different viral agents which are hepatitis A virus (HAV), hepatitis B virus (HBV), hepatitis C virus (HCV), hepatitis Delta or D virus (HDV)1, hepatitis E virus (HEV) and hepatitis G virus (HGV) .They have been named according to the disease they cause and are designated by the first five letters of the alphabet [1]. All five viruses can induce acute hepatitis, but only three can lead to chronic infection which are HBV, HDV and HGV. The other two viruses cause acute, self limited disease only [2].

Recent findings suggest that there is an additional form of viral hepatitis to which two recently discovered human viruses, the hepatitis G virus (HGV) and the hepatitis GB virus C (HGBV-C) have been linked [2].The five viruses of hepatitis are distinct and show no homology of structure, virus family or replication. Yet the five diseases are all very similar and cannot be distinguished reliably by clinical features, routine laboratory tests, or liver biopsy results [1].

Chronic viral hepatitis (CVH) is the principal cause of chronic liver disease, cirrhosis, and hepatocellular carcinoma (HCC) in the world and now ranks as thē chief reason for liver transplantation in adults [2]. Chronic HBV is an important and common form of chronic

liver disease. Approximately 200 million persons worldwide, including at least 1 million Americans, are chronic carriers of hepatitis B surface antigen (HBsAg)[3]. Chronic HBV infection may be complicated by chronic hepatitis, cirrhosis or HCC[4]. Glomerulonephritis is an uncommon but well described complication of chronic hepatitis B (CHB)[5].

Hepatitis C virus (HCV) is the major aetiological agent of human posttransfusion hepatitis and community-acquired non-A non-B(NANB) hepatitis[6,7].Nearly 4 million Americans are infected with hepatitis C with an estimated incidence of 150.000-170.000 new cases per year. It is estimated that approximately 80% of these new cases will develop chronic hepatitis and that 20% to 50% of these patients will develop progressive liver disease leading to cirrhosis and up to 25% of cirrhotic patients may eventually develop liver failure and /or HCC[8,9]. Nowadays, HCV infection is among the major health problems facing the Egyptian population[10].

Delta hepatitis is a serious medical problem worldwide[11]. It is the least common form of chronic viral hepatitis but is the form most likely to lead to cirrhosis[2].HDV is a defective virus and require a helper function of HBV[12,13]. Thus , HDV can replicate only in people who are also infected with HBV[14]. It increases the inflammatory activity in the liver of HBsAg carriers, inducing severe liver injury[15]. Superinfection of HBsAg carriers may cause a self-limiting, often severe acute hepatitis or persisting replication of delta

antigen, which enhances the severity of liver damage and leads to chronic active hepatitis (CAH) and cirrhosis [16].

Currently, there is no standard therapy for CVH and the therapeutic aim is early eradication of the virus in order to prevent long-term clinical complications [14]. IFN-α is the only agent currently licensed for therapy of chronic hepatitis [17], because of its wide spectrum of antiviral actions, and it is being investigated as a possible treatment for the disease [14]. INF-α is a proinflammatory cytokine with a wide spectrum of antiviral activities and has been used to treat several human viral infections including hepatitis viruses [19]. They are proteins with antiviral, antiproliferative, and immunoregulatory effects [20].

Recombinant interferon (r-IFN) has been shown to be effective in decreasing serum aminotransferase levels and the level of viremia and in reducing histologic evidence of hepatic inflammation in patients with CVH [21].

Unfortunately, the response to IFN occurs in fewer than half of patients and is usually not maintained after the drug is stopped [22]. Thus the ability to achieve and sustain a long-term response to IFN is only 13-25% [22].However, the response rate may increase on high dose regimens or with long-term treatment, but there is concomitant increase in side effects and cost of treatment and decrease in patient compliance. New treatment regimens are