

مقارنة بين العلاج الجامع الإنترفيرون المعتاد ألفا مع الريبافيرين و العلاج الجامع
الإنترفيرون طويل المفعول مع الريبافيرين في التأثير العلاجي لكل منهما على
مرضى الإلتهاب الكبدي الفيروسي (سي) بعد عامين من نهاية العلاج

رسالة

مقدمة توطئة للحصول على درجة الماجستير في طب المناطق الحارة

من الطبيب

أحمد عبد الله غلوش

تحت إشراف

أ.د/محمد فوزي منتصر

عميد كلية الطب-أستاذ طب المناطق الحارة
جامعة عين شمس

أ.د/محمد رضا الوكيل

أستاذ طب المناطق الحارة
جامعة عين شمس

عميد.د/مدحت حسن السحار

دكتورة في طب المناطق الحارة
رئيس قسم الجهاز الهضمي و الكبد
مستشفى الشرطة.العجوزة

كلية الطب
جامعة عين شمس
2006

Two years retrospective study for Egyptian hepatitis C patients with
sustained response to pegylated versus standard interferon combined
therapy

Thesis

Submitted For Partial Fulfillment of
Master Degree in Tropical Medicine

By

Ahmed Abdallah Ghalwash

M.B.B,Ch

Supervisors

Prof. Dr. Mohamed Fawzy Montaser

Dean of Faculty of Medicine

Professor of Tropical Medicine

Ain Shams University

Prof. Dr. Mohamed Reda El-Wakil

Professor of Tropical Medicine

Ain Shams University

Brig. Dr. Medhat Hassan El-Sahhar

M.D Tropical Medicine

Head of Hepatology and Gastroenterology Department

Police Hospital, Agouza

Faculty of Medicine

Ain-Shams University

2006

Acknowledgment

First and foremost thanks to **ALLAH**, the most gracious and mercifull.

I wish heartily to express my deep appreciation and profound gratitude to my **Prof. Dr. Mohamed Fawzy Montaser**, Dean of Faculty of Medicine and Professor of Tropical Medicine, Ain Shams University, for his kind close supervision and encouragement. He has his finger prints in every single piece in this thesis.

Words stand short to express my deep respect and thanks to **Prof. Dr. Mohamed Reda El-Wakil**, Professor of Tropical Medicine, Faculty of Medicine, Ain Shams University, for his continuous encouragement and sincere work which have been the main factors to complete this work.

I wish to introduce my deepest gratitude, respect, and cordial thanks to **Brig. Dr. Medhat Hassan El-Sahhar**, Head of Hepatology and Gastro-enterology Department. Police Hospital. Agouza, for his kind care and great assistance throughout this work.

I am also delighted to express my deep gratitude and thanks to all my dear professors, my colleagues and to my family, without their help, this work couldn't be completed.

List of Contents

Title	Page
List of contents	I
List of figures	II
List of tables	V
List of Abbreviations	VIII
Introduction	1
Aim of the work	3
Review of literature	4
Patients & methods	90
Results	102
Discussion	137
Summary	156
Conclusions and recommendations	161
References	163
Arabic Summary	205

List of Figures

Figure	Title	Page
1	Gender distribution among studied cases	127
2	Comparison between the five groups as regards mean age	127
3	Comparison between the five groups as regards mean body mass index (BMI)	128
4	Comparison between the five groups as regards mean platelet at 0 month	128
5	Comparison between the five groups as regards mean platelet at 18 months	129
6	Comparison between the five groups as regards mean bilirubin at start of treatment	129
7	Comparison between the five groups as regards mean bilirubin at 0 month	130
8	Comparison between the five groups as regards mean bilirubin at 18 months	130

9	Comparison between the five groups as regards mean ALT at start of treatment	131
10	Comparison between the five groups as regards mean ALT at 0 month	131
11	Comparison between the five groups as regards mean ALT at 6 months	132
12	Comparison between the five groups as regards mean ALT at 18 months	132
13	Comparison between the five groups as regards positivity of ALT at 18 months	133
14	Comparison between the five groups as regards mean AST at start of treatment	133
15	Comparison between the five groups as regards mean AST at 0 month	134
16	Comparison between the five groups as regards mean AST at 6 months	134

17	Comparison between the five groups as regards mean AST at 18 months	135
18	Comparison between group I and group III as regards PCR positivity at 6 months	135
19	Comparison between group I and group III as regards PCR positivity at 12 months	136
20	Comparison between group I and group III as regards PCR positivity at 18 months	136

List of Tables

Table	Title	Page
1	Demographic data of the studied cases	109
2	Comparison between the five groups as regards Risk factors	110
3	Comparison between the five groups as regards hepatomegaly at start of treatment and after 18 months of follow-up	112
4	Frequency of pretreatment histopathology activity index (HAI) score among studied patients by modified Knodell score	113
5	Frequency of pretreatment histopathology activity index (HAI) grouped according to severity	114
6	Frequency of pretreatment fibrosis stages among studied patients according to modified Knodell score	114
7	Comparison between the five groups as regards GIT symptoms at start of treatment and at the end of follow-up	115

8	Comparison between the five groups as regards Fatigue at start of treatment and end of study	116
9	Comparison between the five groups as regards arthralgia at start of treatment and end of study	117
10	Comparison between the five groups as regards right hypochondrial pain at start of treatment and end of study	118
11	Comparison between the five groups as regards hypersomnia at start of treatment and end of study	119
12	Comparison between the five groups as regards the mean platelets at follow up periods	120
13	Comparison between the five groups as regards the mean bilirubin at follow up periods	121
14	Comparison between the five groups as regards the mean ALT at follow up periods	122
15	Comparison between the five groups as regards the ALT positivity after 18 months of follow-up	123

16	Comparison between the five groups as regards the mean AST at follow up periods:	124
17	Comparison between the five groups as regards PCR results at 0 month	125
18	Comparison between group II and III as regards PCR results at 6, 12, and 18 months	126

List of Abbreviations

AASLD	American Association for Study of Liver Disease
ALT	Alanine amino transferase
AMA	Anti-mitochondrial antibodies
ANA	Antinuclear antibodies
BMI	Body mass index
CTL	Cytotoxic T cells
EASL	European Association for the Study of the Liver
EIA	Enzyme immunoassay
ELISA	Enzyme linked immunosorbent assay
ETR	End of treatment virological response
EVR	Early virological response
HAI	Histopathology activity index
HBV	Hepatitis B virus
HBsAg	Hepatitis B surface antigen
HCC	Hepatocellular carcinoma
HCV	Hepatitis C virus
HVR	Highly variable regions
HS	Highly significant
IFN	Interferon
Kd	Kilodaltons
μ	Micrograms
NIH	National Institute of Health
NS	Not significant
ORF	Open-reading frame
PEG	Poly Ethylene Glycols
PCR	Polymerase Chain Reaction
RIBA	Recombinant immunoblot assay
RT	Reverse transcriptase
S	Significant
SD	Standard deviation
SPSS	Statistical Package for the Social Sciences
SVR	Sustained virological response
TSH	Thyroid stimulating hormone
WHO	World Health Organization

AIM OF THE STUDY

Is to study the patients who had shown sustained response to pegylated interferon plus ribavirin, patients who hadn't shown sustained response to pegylated interferon plus ribavirin, patients who had shown sustained response to standard interferon plus ribavirin, patients who hadn't shown sustained virological response to standard interferon plus ribavirin, and CHC patients who didn't receive interferon retrospectively to evaluate their clinical, biochemical, and virological parameters through one and half years of follow-up starting from zero point (6 months after end of treatment) to see if there is a sustained and progressive improvement or not.

INTRODUCTION

Since the discovery of HCV and the development of diagnostic tests, almost all of non-A non-B post transfusion hepatitis cases have been shown to be due to HCV infection. HCV has been encountered worldwide with WHO estimates of 170 million infected patients worldwide (**Booth et al., 2001**).

In Egypt, high rates were reported among several population groups including rural residents reaching up to 20% (**Habib et al., 2001 and Tanaka et al., 2004**).

In Egypt, a high homology of HCV genotypes, 90 % of which is accounted for by genotype 4a, strongly suggests a local epidemic of HCV throughout the general population (**Ray et al., 2000**).

The success of HCV in causing persistent infection is probably related to its extremely high mutation rate and its existence as multiple quasi-species, each slightly different in sequence from the other. Many patients have a clinical course characterized by peaks and depressions of clinical and biochemical activity suggesting that HCV is capable of down regulation in order to reduce immune pressure (**Brechot, 1994; Honda et al., 1994**).

Chronic hepatitis C is indolent disease extending over many years. The acute attack is usually unrecognized and has no clinical features which will predict chronicity. Nevertheless, 80% of patients will develop chronic hepatitis and 20% of them will go into cirrhosis.

The course is a slow one, marked by fluctuating transaminases over many years. Each elevation probably represent an episode of HCV viraemia perhaps due to quasispecies (**Koretz et al., 1996**).

Transaminase levels do not predict liver pathology and significant changes can be found with repeatedly normal values Serum HCV RNA is essential for measuring disease activity and monitoring the effects of treatment (**Healey et al., 1995**).

As regard treatment, the common antiviral interferon alpha is used, selection of patient for this treatment is difficult and many factors have to be considered (**Conjeervaram et al., 1995**).

The results with interferon alone were not satisfactory and because of the high mutation rate of the virus, combinations were suggested. Combination with ribavirin was tried, it enhances the antiviral effect of the interferon (**Lau et al., 1994**).