Liver Biopsy Based Study of Inactive Chronic HB Carrier Patients

Thesis
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Internal Medicine

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List of Abbreviations

AASLD	:	American Association for the study of liver Disease
AFP	:	Alpha fetoprotein
ALT	:	Alanine aminotransferase
AST	:	Aspartate aminotransferase
cccDNA	:	Covalently closed circular DNA
CDC	:	The Center of Disease Control & Prevention
CHB	:	Chronic hepatitis B
CTL	:	Cytotoxic T-lymphocyte
DR	:	Direct repeats
E	:	Core
GRE	:	Glucocorticoid-responsive element
HAI	:	Histologic activity index
HBCAb	:	Hepatitis B Core Antibody
HBeAg	:	HepatitisB e antigen
HBIG	:	Hepatitis B immunoglobulin
HBsAg	:	Hepatitis B surface antigen
HBV	:	Hepatitis B virus
HBx	:	Hepatitis B virus X protein
HCC	:	Hepatocellular carcinoma
HDV	:	Hepatitis D virus
HIV	:	Human Immunodeficiency Virus
IFNs	:	Interferons
Ig	:	Immunoglobulin
MS	:	Multiple sclerosis
NAs	:	Nucleotide analogs
NAT	:	Nuclric acid testing
ORF	:	Open reading frame
P	:	Promoters
PCR	:	Polymerase chain reaction
Peg	:	Pegylated
Pg	:	Pregenomic
rc	:	Relaxed circular

List of Abbreviations (Cont.)

RIA	:	Radioimmunossay
RNaseH	:	The ribonuclease
RT	:	Real-time
RT	:	The reverse transcriptase
SOI	:	Secondary occult infection
TCR	:	T-cell repertoire
Th	:	T- helper cell
TP	:	Terminal protein

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دراسة عملية قائمة على أخذ عينات من الكبد فى المرضى
الحاملين غير الناشطين للفيروس الكبدى الوبائى ب

رسالة

توطئة للحصول على درجة الماجستير فى **الأمراض الباطنة العامة**

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الملخص العربى

الفيروس الكبدى الوبائى ب مازال مشكله صحية كبيرة فى أجزاء متعددة من العالم ، المرضى المصابون بفيروس ب يمرون بمراحل مختلفة من المرض تقابل الدرجات المختلفة من التلف فى أنسجة الكبد .

إن الفيروس الكبدى الوبائى ب يمر بمراحل متعددة خلال تاريخه المرضي و يمكن تقسيم هذه المراحل إلى خمس مراحل.

وتضمن هذه الدراسة المرضى الحاملين غير الناشطين للفيروس ويتميز مرضى هذه المرحلة بكمية قليلة من الفيروس بالدم و تكون إنزيمات الكبد ضمن معدلاتها الطبيعية و في هذه المرحلة نسبة حدوث التليف بالكبد أو سرطان الكبد تمثل نسبة قليلة جدا.

وتهدف هذه الرسالة إلى تقييم العلاقة بين كمية فيروس الكبد الوبائى ب ومدى الضرر اللاحق بأنسجة الكبد فى الحاملين غير الناشيطين للفيروس.

ولكن لم نتمكن من اثبات علاقة بين كمية فيروس الكبد الوبائى ب ومدى الضرر اللاحق بأنسجة الكبد فى الحاملين غير الناشيطين للفيروس برغم من وجود نسبة تليف فى20% من هؤلاء الحاملين غير الناشطين للفيروس.

Bun	ALK.ph	T.P	Alb	HBsAg	HBeAg	HBVDNA	U/S	liver biopsy,grading	liver biopsy,stage	gender	age	HC Ab
11	155	7,3	4,1	positive	negative	555	NAD	3 from 18	0 from 6	female	33	negative
9	200	7,7	4,4	positive	negative	1900	NAD	3 from 18	1 from 6	male	27	negative
11	59	6,9	4	positive	negative	2000	NAD	5 from 18	1 from 6	female	30	negative
12	100	7	4,3	positive	negative	1900	NAD	3 from 18	1 from 6	male	32	negative
18	88	6,9	4,4	positive	negative	1800	NAD	4 from 18	2 from 6	male	33	negative
12	61	7	4,4	positive	negative	600	NAD	5 from 18	2 from 6	male	39	negative
20	70	7,1	4,4	positive	negative	200	NAD	4 from 18	1 from 6	female	41	negative
18	90	6,8	3,7	positive	negative	45	NAD	3 from 18	1 from 6	male	25	negative
10	100	7	4,5	positive	negative	460	NAD	5 from 18	1 from 6	female	30	negative
12	80	6,9	3,9	positive	negative	330	NAD	4 from 18	2 from 6	male	37	negative
13	113	7	4	positive	negative	1600	NAD	2 from 18	1 from 6	male	29	negative
8	98	6,8	4,4	positive	negative	2000	NAD	3 from 18	1 from 6	male	33	negative
11	109	7,2	4,7	positive	negative	12	NAD	3 from 18	0 from 6	male	22	negative
10	103	6,9	3,8	positive	negative	142	NAD	3 from 18	2 from 6	male	28	negative
7	116	7,1	4,3	positive	negative	1350	NAD	4 from 18	1 from 6	male	20	negative
12	124	8	4,4	positive	negative	10	NAD	3 from 18	1 from 6	male	23	negative
17	182	7,4	4,3	positive	negative	950	NAD	5 from 18	1 from 6	male	35	negative
12	130	6,9	4,2	positive	negative	below det	NAD	3 from 18	2 from 6	male	24	negative
13	113	7	4,4	positive	negative	1800	NAD	3 from 18	1 from 6	male	20	negative
15	150	6,8	4,2	positive	negative	1330	NAD	2 from 18	2 from 6	male	30	negative
14	160	7,3	3,9	positive	negative	below det	NAD	4 from 18	1 from 6	female	26	negative
11	90	7,6	4,8	positive	negative	15	NAD	5 from 18	1 from 6	female	38	negative
8	72	6,8	4	positive	negative	222	NAD	3 from 18	1 from 6	female	42	negative
6	111	6,7	3,8	positive	negative	2000	NAD	4 from 18	1 from 6	female	40	negative
10	141	7	4,2	positive	negative	686	NAD	3 from 18	1 from 6	male	21	negative
11	131	7	4,1	positive	negative	950	NAD	5 from 18	1 from 6	male	44	negative
19	133	6,5	3,8	positive	negative	600	NAD	3 from 18	1 from 6	male	27	negative
12	135	6,4	3,5	positive	negative	1200	NAD	3 from 18	1 from 6	female	25	negative
16	120	6,8	3,9	positive	negative	500	NAD	2 from 18	1 from 6	male	33	negative
10	111	6,9	4	positive	negative	1800	NAD	3 from 18	1 from 6	male	32	negative

patient.n	WBC	Hb	PLT	INR	AST	ALT	T.B	D.B	S.k	Na	s,cr
1	6,6	11,8	300	1,08	20	19	1,2	,3	3,8	135	,8
2	7	14,4	329	,9	20	12	,7	,2	4	140	1
3	5,5	11,9	274	,9	27	22	,6	,1	3,7	145	,7
4	6,5	13	270	,8	21	18	,9	,3	4	137	,6
5	6,9	14	250	1	19	23	,4	0	4	140	,9
6	7,3	13,7	204	1,2	24	27	,3	0	3,5	135	1
7	8,7	12	243	1,1	12	14	,4	,1	3,9	137	1,1
8	4,1	13	230	1	25	26	,9	,2	4,1	133	1,2
9	6	12	326	,8	15	13	,6	,1	4	137	,6
10	10	14	230	,9	27	23	,7	0	3,6	140	,7
11	5	15	400	1,2	24	29	,8	,1	4,2	141	1
12	7	14,4	329	1	23	13	1,2	,2	4,5	144	,6
13	6	11,8	280	,9	19	19	,9	,1	3,8	137	,7
14	5,9	15,9	257	1	27	17	1,1	,3	4,7	145	1
15	8	14	300	1,2	24	29	,2	0	3,9	147	,5
16	10,3	14,3	210	1	30	24	,3	0	3,6	136	1
17	6	14,4	151	,9	19	19	1,2	,4	4,2	141	,8
18	4,3	11,2	257	,9	14	21	,8	,1	4,4	144	,8
19	4,4	15,2	226	1,1	12	22	1	,3	4,6	139	,8
20	4,4	13,9	203	,7	12	13	,6	,1	3,7	137	,9
21	5,8	12,8	225	1	20	22	1	,4	3,9	138	1
22	4,7	11,3	188	,9	19	13	1,2	,6	3,5	136	,6
23	4	12	250	1	12	11	,2	0	4,6	142	1
24	4,6	11,8	320	,9	15	19	,7	,2	3,6	135	,5
25	5,6	13	270	1	13	12	,9	,3	3,9	140	,9
26	5,9	14	320	,8	19	19	,6	0	4	139	,8
27	6	12	200	1	22	23	,9	,1	4,3	135	,7
28	5,6	13	230	,9	17	18	1,1	,2	,4	138	,8
29	7	12,5	280	,8	20	19	,6	,1	3,9	139	,9
30	6,5	11	311	,7	23	20	1,2	,3	3,8	140	1

Introduction

Viral hepatitis B is still a major health problem in many parts of the world. Patients infected with HBV have different disease stages, which accompanies with varying degrees of liver damage, assessment of disease activity over time is of great importance in the management of chronic HBV infection **(Meraat *et al*., 2000)**.

Chronic hepatitis B is a dynamic process. The natural history of CHB can be schematically divided into five phases, which are not necessarily sequential.

(1) Immune tolerance
(2) Immune reactive phase
(3) Inactive HBV carrier state
(4) HBeAg-negative CHB
(5) HBsAg-negative phase

The "inactive HBV carrier state" may follow seroconversion from HBeAg to anti-HBe antibodies. It is characterized by very low or undetectable serum HBVDNA level and normal aminotransferases. As a result of immunological control of the infection, this state confers a favorable long-term outcome with a very low risk of cirrhosis or HCC in the majority of patients **(EASL *et al.*, 2009).**

The evaluation of patients with HBV infection has evolved from serological to molecular diagnostic assays within the molecular assays, the new highly sensitive techniques of quantification of serum HBV DNA titer have improved our understanding of the pathogenesis and natural history of HBV infection and facilitated the monitoring of response to treatment **(Noborg *et al*., 2003; Yalcin *et al*., 2003).**

Several studies have assessed the correlation between serum HBV viral load and severity of liver damage, as judged

by means of clinical and laboratory parameters **(Yuen *et al.*, 2003)**.

For the case of HBeAg-negative, most studies have shown that patients with less liver damage have lower viral load **(Hasan *et al.*, 2002)**; however some others have failed to observe such an association **(Xie *et al.*, 2003) .**

Aim of the Work

The aim of the study to determine if there is liver damage in inactive chronic HB carrier patients and if there is any correlation with HBV viral load.

Review of Literature

Introduction:

Hepatitis B virus (HBV) infection is a major health problem worldwide. Some individuals can develop acute HBV infection and achieve complete immune clearance of virus, yielding a life-long immunity, while others can develop chronic HBV infection depending on the host immune response. Chronic HBV infection is associated with a wide range of clinical manifestations, from an asymptomatic carrier state with a normal liver histology to severe and chronic liver diseases, including cirrhosis and hepatocellular carcinoma (HCC) **(McMahon, 2005).**

Chronic HBV infection is a dynamic process with a replicative or a non-replicative (or low replicative) phase based on virus-host interaction which is pivotal to the pathogenesis of liver disease. Understanding the dynamic nature of chronic HBV infection is crucial in the management of HBV carriers **(He *et al*., 2006)**. Long-term monitoring and optimal timing of antiviral therapy for chronic HBV infected patients can help to prevent progression of HBV related liver disease to its later stage **(Lupberger *et al*., 2007).**

Regions of High Prevalence :

Hepatitis B infections are major health problems in Egypt and the entire continent of Africa. Egypt is considered to be a region of intermediate prevalence for HBV infection with a reported figure of 4.5% **(Shaaban *et al*., 2007)**.

In Egypt some studies showed that the prevalence of hepatitis B virus infection was 51.8% and 55.7% among hemodialysis patients **(Gohar *et al*., 1995) (Cao *et al*., 2007)** respectively.