Predictive Value of Quantitative Estimation of Hepatitis B Surface Antigen and DNA load in serum of Chronic Hepatitis B Patients

Tarek A. El-Shazly Assistant professor of Internal Medicine Department, Faculty of Medicine, Mansoura University, Egypt

Background

The proposed diagnostic criteria for differentiation between different phases of CHB disease relied mainly on the positivity of serum for HBeAg as the main diagnostic criterion for differentiating cases as two main categories; among each category differentiating parameters provided gray zone of diagnosis. Liver biopsy has long been essential to evaluate the degree of liver damage and to decide therapeutic plan in these subjects. Besides establishing the diagnosis, the biopsy is often used to assess the severity of the disease in terms of both grade and stage. (Lee et al., 2001, Goodman, 2007, Ganji et al., 2011).

Aim of the Work

the current study was designed to evaluate the diagnostic yield of quantitative estimation of serum HBsAg level and DNA viral load in differentiation between the main categories of CHB disease and their subtypes and to define their applicability for differentiating between phases of CHB disease and to predict the outcome of liver biopsy.

Patients & Methods

This current prospective study was conducted on all patients with CHB disease irrespective of being on treatment or not. Patients with undetectable HBV DNA levels, patients with co-infection with HCV, Human Immunodeficiency Virus (HIV) or Hepatitis D virus (HDV), chronic renal failure patients with serum creatinine >4 mg/dl and patients with autoimmune liver disease were not enrolled in the study. All patients underwent clinical examination for determination of the current clinical status, disease duration, preliminary lab data. Blind liver biopsies were done. The histopathological grading and staging were performed using Ishak Modified HAI system (Ishak et al., 1995). Sampling: blood sample was divided in to three parts: The first part was used for serum AST, ALT, total and direct bilirubin and ELISA estimation of hepatitis B serological markers (HBsAg, HBeAg, anti-HBe, anti-HBc).The second part was collected in dry plain tube and centrifuged and serum was stored at -80°C to be used for quantitative estimation of HBsAg. The third part was collected in EDTA tube and centrifuged in the PCR unit and plasma was stored at -80°C to be used for and HBV quantitation by PCR.

Result

Patients' laboratory data

Data			Number (%)	Level
HBeAg	Positive		53 (46.9%)	
	Negative		60 (53.1%)	
Serum ALT (U/L)	<ULN	Males	0	0
		Females	3 (2.7%)	18±1 (17-19)
	≤2ULN	Males	14 (12.4%)	52.9±3.2 (46-58)
		Females	33 (29.2%)	29.5±6.1 (21-38)
	>2ULN	Males	53 (46.9%)	85.9±15.4 (67-136)
		Females	10 (8.8%)	43.4±2.5 (39-46)
HB VDL (IU/ml)	Low		32 (28.3%)	
	High		81 (71.7%)	
	Low VDL (<2000)	Level	1530±255.7 (1100-1980)	
		Median of Log10	3.19	
	High VDL (≥2000)	Level	3451.1±700 (2300-5200)	
		Median of Log10	3.52	
HBsAg (103 IU/ml)	Low VDL (<2000)	Level	23±5.1 (12-37)	
		Median of Log10	1.36	
	High VDL (≥2000)	Level	25.3±6.1 (13-39)	
		Median of Log10	1.38	
HB VDL/HBsAg ratio (Log10/Log1	Low VDL (<2000)		0.42	
	High VDL (≥2000)		0.40	

ROC curve analysis of parameters for diagnosis of liver fibrosis, irrespective of histopathological examination of liver biopsy

	AUC	Std. Error	Sig.	CI	
				Lower	Upper
Positive HBeAg	0.369	0.054	=0.022	0.262	0.476
Serum ALT	0.582	0.059	>0.05	0.467	0.698
Log10 of serum HB VDL	0.355	0.056	=0.011	0.246	0.464
Log10 of serumHBsAg level	0.411	0.059	>0.05	0.297	0.526

Correlation coefficient "r" between HBeAg positivity and fibrosis on liver biopsy and constitutional and laboratory data

	HBeAg-positivity		Liver fibrosis score	
	r	P	r	P
HBeAg-positivity			0.242	=0.010
Liver fibrosis score	0.242	=0.010		
Liver necrosis score	0.175	>0.05	0.149	>0.05
Serum ALT	0.199	=0.035	0.120	>0.05
Serum HBV DNA load	0.258	=0.006	0.223	=0.017
Serum HBsAg level	0.402	<0.001	0.258	=0.006
DNA load/HBsAg ratio	0.205	=0.029	0.101	>0.05
Age	0.099	>0.05	0.152	>0.05
Male gender	-0.268	=0.004	0.185	=0.050
BMI	-0.185	=0.049	0.120	>0.05
Duration of disease	0.240	=0.011	0.163	>0.05

ROC curve analysis of parameters differentiating IT from IR cases

	AUC	Std. Error	Sig.	CI	
				Lower	Upper
Log10 of serum HBsAg level	0.755	0.079	=0.017	0.601	0.910
Liver necrosis score	0.312	0.089	>0.05	0.137	0.487
Serum ALT	0.682	0.075	>0.05	0.535	0.829
DVL/HBsAg log10 ratio	0.191	0.058	=0.004	0.077	0.304

Regression analysis of laboratory parameters use d for diagnosis of liver fibrosis, irrespective of histopathological examination of liver biopsy

Parameter	Standardized coefficient	t	Sig.
Log10 of serum HBsAg level	0.258	2.815	=0.006
Positive HBeAg	0.165	1.658	>0.05
Serum ALT	0.141	1.537	>0.05
Log10 of serum HB VDL	0.161	1.686	>0.05

Conclusion

Quantitative estimation of serum level of HBsAg and HBV DNA load could differentiate between phases of CHB disease and predict histopathological status of the liver, so could spare liver biopsy with its inherent complications.

References

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