

doi: 10.13241/j.cnki.pmb.2020.04.037

乙型肝炎患者体液免疫功能、肝纤维化指标及 $\alpha 1$ -MG、TGF- $\beta 1$ 水平分析 *

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摘要 目的: 探讨乙型肝炎患者体液免疫功能、肝纤维化程度及血清中 $\alpha 1$ -MG、TGF- $\beta 1$ 水平的变化。**方法:** 选取 2016 年 1 月~2018 年 10 月我院收治的轻度乙型肝炎患者 60 例为轻度组,重度乙型肝炎患者 60 例为重度组及同期来我院体检的健康志愿者 60 例为对照组。检测并比较三组患者血清中补体 C3、补体 C4、肝纤维化指标及 $\alpha 1$ -微球蛋白 ($\alpha 1$ -MG)、转化生长因子- $\beta 1$ (TGF- $\beta 1$) 水平。**结果:** 乙型肝炎患者血清中补体 C3 及补体 C4 水平明显低于对照组;重度组患者血清中补体 C3 及补体 C4 水平明显低于轻度组患者 ($P < 0.05$)。乙型肝炎患者血清中各肝纤维化指标水平明显高于对照组;重度组患者血清中各肝纤维化指标水平明显高于轻度组患者 ($P < 0.05$)。乙型肝炎患者血清中 $\alpha 1$ -MG 水平明显低于对照组, TGF- $\beta 1$ 水平明显高于对照组;重度组患者血清中 $\alpha 1$ -MG 水平明显低于轻度组, TGF- $\beta 1$ 水平明显高于轻度组 ($P < 0.05$)。**结论:** 乙型肝炎病毒感染可导致患者免疫功能水平下降, 肝脏纤维化及细胞因子水平紊乱, 且上述指标水平的变化与疾病进展程度密切相关, 临床治疗时需加强对上述指标的监测。

关键词: 乙型肝炎; 免疫功能; 肝纤维化; $\alpha 1$ -微球蛋白; 转化生长因子- $\beta 1$

中图分类号: R512.6+2 文献标识码: A 文章编号: 1673-6273(2020)04-772-04

Analysis of the Humoral Immune Function, Hepatic Fibrosis Index and Levels of $\alpha 1$ -MG and TGF- $\beta 1$ in Patients with Hepatitis B*

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ABSTRACT Objective: To investigate the changes of humoral immune function, degree of liver fibrosis and serum levels of $\alpha 1$ -MG and TGF- $\beta 1$ in patients with hepatitis B. **Methods:** 60 patients with mild hepatitis B were selected as mild group and 60 patients with severe hepatitis B were selected as severe group from January 2016 to October 2018. During the same period, 60 healthy volunteers in our hospital were selected as control group. The levels of complement C3, complement C4, liver fibrosis index, $\alpha 1$ -microglobulin ($\alpha 1$ -MG) and transforming growth factor- $\beta 1$ (TGF- $\beta 1$) of patients in the three groups were detected and compared. **Results:** The serum levels of complement C3 and complement C4 in patients with hepatitis B were significantly lower than those in the control group. The serum levels of complement C3 and complement C4 of patients in severe group were significantly lower than those in mild group ($P < 0.05$). The serum levels of liver fibrosis indexes in patients with hepatitis B were significantly higher than those in the control group. The serum levels of liver fibrosis indexes of patients in severe group were significantly higher than those in mild group ($P < 0.05$). The serum levels of $\alpha 1$ -MG in patients with hepatitis B was significantly lower than those in the control group, and the levels of TGF- $\beta 1$ was significantly higher than that in the control group. The serum levels of $\alpha 1$ -MG in severe group were significantly lower than those in mild group, and the level of TGF- $\beta 1$ were significantly higher than those in mild group ($P < 0.05$). **Conclusion:** Hepatitis B virus infection can lead to the decline of immune function, liver fibrosis and cytokine disorders, and the changes of these indicators are closely related to the degree of disease progression. The monitoring and intervention of the above indicators should be strengthened in clinical treatment.

Key words: Hepatitis B; Immune function; Liver fibrosis; $\alpha 1$ -microglobulin; Transforming growth factor- $\beta 1$

Chinese Library Classification(CLC): R512.6+2 **Document code:** A

Article ID: 1673-6273(2020)04-772-04

前言

乙型病毒性肝炎(viral hepatitis type B)简称乙型肝炎,是由

于感染乙型肝炎病毒而导致的以肝脏病变为主的传染性疾病,临床上以食欲减退、上腹部不适、肝区痛、乏力为主要表现^[1-3]。研究显示部分乙型肝炎患者伴有黄疸发热及肝功能损害,严重

* 基金项目:广东省医学科学技术研究基金项目(A20181502)

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(收稿日期:2019-05-07 接受日期:2019-05-31)

者甚至发展成肝硬化,少数可发展为肝癌,严重威胁患者生命健康^[4-6]。乙型肝炎治疗前需对患者的免疫功能状况进行评估,以便制定适宜的治疗方案^[7-10]。本研究观察了不同程度乙型肝炎患者的免疫功能、肝纤维化程度及血清中细胞因子的水平,旨在探讨上述指标与乙型肝炎疾病进展的关系,现将研究结果报道如下。

1 资料与方法

1.1 一般资料

选取2016年1月~2018年10月我院收治的乙型肝炎患者120例。所有入选患者均符合中华医学会肝病学会发布的《慢性乙型肝炎防治指南》^[11]中关于乙型肝炎的诊断标准。其中,轻度乙型肝炎患者60例为轻度组,男性36例,女性24例,年龄11~84岁。重度乙型肝炎患者60例为重度组,男性28例,女性32例,年龄11~84岁。纳入标准:①符合乙型肝炎诊断标准者;②病程已超过6个月者;③无糖尿病及甲状腺功能亢进者。排除标准:①合并免疫缺陷型疾病者;②1个月内服用抗生素等损肝药物者;③病毒性肝炎、酒精性肝病等导致的肝损伤者;④处于妊娠期及哺乳期女性。另选同期来我院体检的健康志愿者60例为对照组,男性27例,女性33例,年龄11~84岁。三组入选患者一般临床资料比较差异无统计学意义($P>0.05$),具有可比性。

表1 各组患者补体蛋白水平的比较(g/L, $\bar{x} \pm s$)

Table 1 Comparison of the serum complement protein levels among different groups(g/L, $\bar{x} \pm s$)

Groups	Cases	C3	C4
Control group	60	1.07 $\pm$ 0.21	0.39 $\pm$ 0.06
Mild group	60	0.74 $\pm$ 0.08*	0.25 $\pm$ 0.04*
Severe group	60	0.52 $\pm$ 0.05* [△]	0.11 $\pm$ 0.02* [△]

注:与对照组比较,* $P<0.05$;与轻度组比较,[△] $P<0.05$ 。

Note: Compared with the control group, * $P<0.05$; compared with the mild group, [△] $P<0.05$.

2.2 各组肝纤维化水平比较

乙型肝炎患者血清中各肝纤维化指标水平明显高于对照

1.2 检测指标及方法

所有研究对象均于空腹8h后,采集静脉血5mL。4000 r/min离心10 min,取上层血清备用。免疫功能水平检测:利用罗氏Cobas8000全自动生化分析仪,采用速率散射免疫比浊法检测待测血清中C3及C4水平;肝纤维化程度水平检测:采用酶联免疫吸附法(ELISA)检测待测血清中前胶原蛋白III(PCIII)、IV型胶原(CIV)、层黏连蛋白(LN)及透明质酸(HA)水平; α 1-MG及TGF- β 1水平检测:采用免疫比浊法检测待测血清中 α 1-MG水平;采用酶联免疫吸附法(ELISA)检测待测血清中TGF- β 1水平。所有操作均严格按照仪器及试剂盒说明书进行。

1.3 统计学分析

本次研究采用SPSS17.0统计学软件分析处理,所得数据均为计量资料,以均数 $\pm$ 标准差($\bar{x} \pm s$)表示,多组间比较采用单因素方差分析,两组间比较采用t检验,以 $P<0.05$ 表示差异有统计学意义。

2 结果

2.1 各组血清补体蛋白水平的比较

乙型肝炎患者血清中补体C3及补体C4水平明显低于对照组;重度组患者血清中补体C3及补体C4水平明显低于轻度组患者,差异均有统计学意义($P<0.05$)。见表1。

组;重度组患者血清中各肝纤维化指标水平明显高于轻度组患者,差异均有统计学意义($P<0.05$)。见表2。

表2 各组患者肝纤维化水平的比较(μ g/L, $\bar{x} \pm s$)

Table 2 Comparison of liver fibrosis levels in each group(μ g/L, $\bar{x} \pm s$)

Groups	Cases	PCIII	CIV	LN	HA
Control group	60	82.45 $\pm$ 8.33	51.65 $\pm$ 5.24	53.18 $\pm$ 5.51	67.18 $\pm$ 7.02
Mild group	60	107.68 $\pm$ 10.22*	73.08 $\pm$ 7.59*	72.63 $\pm$ 7.14*	159.63 $\pm$ 16.38*
Severe group	60	159.16 $\pm$ 16.35* [△]	112.58 $\pm$ 11.38* [△]	125.32 $\pm$ 12.39* [△]	321.32 $\pm$ 30.15* [△]

注:与对照组比较,* $P<0.05$;与轻度组比较,[△] $P<0.05$ 。

Note: Compared with the control group, * $P<0.05$; compared with the mild group, [△] $P<0.05$.

2.3 各组血清 α 1-MG及TGF- β 1水平的比较

乙型肝炎患者血清中 α 1-MG水平明显低于对照组,TGF- β 1水平明显高于对照组,差异有统计学意义($P<0.05$)。重度组患者血清中 α 1-MG水平明显低于轻度组;TGF- β 1水平明显高于轻度组,差异有统计学意义($P<0.05$)。见表3。

3 讨论

慢性乙型肝炎是严重威胁人类生命健康的传染性疾病之一,乙型肝炎病毒可通过医源性、母婴、血液等多种途径传播,不仅可以改变患者肝脏功能及结构,还可引起肝外多种脏器损伤^[12-15]。研究表明乙型肝炎病程进展过程中,患者体内免疫功能状态及相关因子水平变化较大^[16-19]。因此,本次研究观察并比较了轻度乙型肝炎患者及重度乙型肝炎患者的免疫功能状态。研

究结果显示乙型肝炎患者血清中补体 C3 及补体 C4 水平明显低于对照组;重度组患者血清中补体 C3 及补体 C4 水平明显低于轻度组患者,表明乙型肝炎病毒感染可导致机体免疫系统紊乱,且疾病程度愈重,免疫功能水平愈低。补体 C3 及补

体 C4 主要由巨噬细胞和肝脏合成,在补体经典激活途径和旁路激活途径中均发挥重要作用,共同调节机体的免疫功能。如果机体肝细胞受损,其合成补体蛋白的能力就会下降^[20-22]。因此,肝脏功能损伤可能是患者补体蛋白水平下降的主要原因。

表 3 各组患者 $\alpha 1$ -MG 及 TGF- $\beta 1$ 水平比较($\bar{x} \pm s$)
Table 3 Comparison of $\alpha 1$ -MG and TGF- $\beta 1$ levels in each group($\bar{x} \pm s$)

Groups	Cases	$\alpha 1$ -MG(mg/L)	TGF- $\beta 1$ (ng/mL)
Control group	60	20.69 $\pm$ 2.12	12.39 $\pm$ 1.21
Mild group	60	17.84 $\pm$ 1.85*	23.28 $\pm$ 2.37*
Severe group	60	14.37 $\pm$ 1.49* [△]	36.45 $\pm$ 3.68* [△]

注:与对照组比较,* $P < 0.05$;与轻度组比较,[△] $P < 0.05$ 。

Note: Compared with the control group, * $P < 0.05$; compared with the mild group, [△] $P < 0.05$.

乙型肝炎患者肝损伤的主要表现为肝脏纤维化。肝脏纤维化是一个病理生理过程,是指由各种致病因子所致肝内结缔组织异常增生^[23,24]。任何肝脏损伤在肝脏修复愈合的过程中均会引起肝纤维化,如果损伤持续加重,则会导致肝脏由纤维化发展为肝硬化^[25-28]。本次研究结果显示乙型肝炎患者血清中 PCII、CIV、LN 及 HA 水平明显高于对照组,重度组患者血清中 PCIII、CIV、LN 及 HA 水平明显高于轻度组患者,表明随着乙型肝炎病情加重,上述肝脏纤维化指标水平明显升高,肝脏纤维化程度加重。研究显示 TGF- $\beta 1$ 具有调节细胞生长和分化的作用,可通过促进肝纤维化细胞生长及诱导肝细胞坏死等途径,加重肝脏纤维化^[29]。

$\alpha 1$ -MG 是由肝细胞特异性合成的糖蛋白,在人体内分布广泛。既往研究显示血清中 $\alpha 1$ -MG 水平可作为检测乙型肝炎患者肝功能的重要指标^[30,31]。因此,本研究进一步比较了两组患者血清中 $\alpha 1$ -MG 及 TGF- $\beta 1$ 水平。结果显示乙型肝炎患者血清中 $\alpha 1$ -MG 水平明显低于对照组;TGF- $\beta 1$ 水平明显高于对照组,重度组患者血清中 $\alpha 1$ -MG 水平明显低于轻度组;TGF- $\beta 1$ 水平明显高于轻度组,表明随着疾病程度加深,患者血清中相关因子水平异常愈加明显,其作用机制可能与患者肝细胞增殖受到影响导致的肝功能受损有关。

综上所述,乙型肝炎病毒感染会导致患者免疫功能水平下降,肝脏纤维化及体内细胞因子水平紊乱,上述指标随着疾病程度的加重的变化愈加明显。其作用机制可能为乙型肝炎病毒感染后导致肝细胞功能受损,影响血清相关因子水平,致使肝脏纤维化加重,免疫功能愈加紊乱。因此,临床治疗时需加强对上述指标的监测及干预。

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