

• 临床经验 •

# 肝病患者 IgA 和 sIgA 含量变化的临床意义

刘冬妍, 刘沛

刘冬妍, 刘沛, 中国医科大学附属第二医院传染科 辽宁省沈阳市 110004

通讯作者: 刘沛, 110004, 辽宁省沈阳市三好街36号, 中国医科大学附属第二医院传染科. sylvupei2003@yahoo.com.cn

电话: 024-83956962

收稿日期: 2005-06-30 接受日期: 2005-07-15

## Changes of IgA and sIgA and its clinical significant in hepatic diseases

Dong-Yan Liu, Pei Liu

Dong-Yan Liu, Pei Liu, Department of Infectious Diseases, the Second Affiliated of China Medical University, Shenyang 110004, Liaoning Province, China

Correspondence to: Pei Liu, Department of Infectious Diseases, the Second Affiliated Hospital of China Medical University, 36 Sanhao Street, Shenyang 110004, Liaoning Province, China. sylvupei2003@yahoo.com.cn

Received: 2005-06-30 Accepted: 2005-07-15

### Abstract

**AIM:** To investigate the values of IgA and sIgA detection in the clinical diagnosis of hepatic diseases.

**METHODS:** Patients with acute hepatitis (AH,  $n = 35$ ), chronic severe hepatitis (CSH,  $n = 9$ ), chronic hepatitis (CH,  $n = 67$ ) and liver cirrhosis (LC,  $n = 57$ ) were involved. The level of IgA was assayed by rate nephelometry, and the level of sIgA was detected by radioimmunoassay.

**RESULTS:** The levels of fecal IgA and sIgA were notably elevated in patients with AH, CSH, CH and LC as compared with those in the controls (IgA:  $100 \pm 47$ ,  $251 \pm 178$ ,  $80 \pm 24$ ,  $145 \pm 164$  mg/L vs  $< 67$  mg/L,  $P < 0.01$ ; sIgA:  $88 \pm 96$ ,  $326 \pm 237$ ,  $88 \pm 121$ ,  $104 \pm 109$  mg/L vs  $13 \pm 10$  mg/L,  $P < 0.01$ ). IgA was positively correlated with sIgA ( $r = 0.4371$ ,  $P < 0.01$ ). The levels of serum IgA and sIgA were markedly increased in patients with AH, CSH, CH and LC as compared with those in the controls (IgA:  $3.1 \pm 1.1$ ,  $3.4 \pm 1.8$ ,  $3.3 \pm 1.7$ ,  $4.9 \pm 3.3$  g/L vs  $1.6 \pm 0.2$  g/L,  $P < 0.01$ ; sIgA:  $31.1 \pm 25.8$ ,  $80.3 \pm 25.4$ ,  $30.5 \pm 24.1$ ,  $50.0 \pm 20.5$   $\mu$ g/L vs  $23.4 \pm 8.2$   $\mu$ g/L,  $P < 0.01$  or  $P < 0.05$ ). The fecal IgA and sIgA were not correlated with serum IgA and sIgA, and serum IgA was not correlated with serum sIgA ( $P > 0.05$ ). In patients with CH, CSH and LC, serum sIgA was significantly correlated with alkaline phosphatase ( $r = 0.523$ ,  $P < 0.01$ )

and total bilirubin ( $r = 0.4581$ ,  $P < 0.01$ ). In patients with AH, serum sIgA level was correlated with alanine aminotransferase ( $r = 0.4692$ ,  $P < 0.01$ ), total bilirubin ( $r = 0.4265$ ,  $P < 0.01$ ).

**CONCLUSION:** The detection of IgA and sIgA can be used in the clinical diagnosis of hepatic diseases.

**Key Words:** IgA; sIgA; Hepatic disease

Liu DY, Liu P. Changes of IgA and sIgA and its clinical significant in hepatic diseases. *Shijie Huaren Xiaohua Zazhi* 2005;13(18):2275-2277

### 摘要

**目的:** 探讨肝脏病变时IgA和sIgA对临床诊断的意义。

**方法:** 肝病患者共168例, 包括急性肝炎35例, 慢性重症肝炎9例, 慢性肝炎67例, 肝硬化57例, 用免疫速率比浊法检测IgA, 用放射免疫分析法检测sIgA。

**结果:** 肝脏患者粪便IgA, sIgA均显著高于正常对照组 (IgA:  $100 \pm 47$ ,  $251 \pm 178$ ,  $80 \pm 24$ ,  $145 \pm 164$  mg/L vs  $< 67$  mg/L,  $P < 0.01$ ; sIgA:  $88 \pm 96$ ,  $326 \pm 237$ ,  $88 \pm 121$ ,  $104 \pm 109$  mg/L vs  $13 \pm 10$  mg/L,  $P < 0.01$ ), IgA和sIgA呈显著正相关 ( $r = 0.4371$ ,  $P < 0.01$ )。血清中IgA和sIgA显著高于正常对照组 (IgA:  $3.1 \pm 1.1$ ,  $3.4 \pm 1.8$ ,  $3.3 \pm 1.7$ ,  $4.9 \pm 3.3$  g/L vs  $1.6 \pm 0.2$  g/L,  $P < 0.01$ ; sIgA:  $31.1 \pm 25.8$ ,  $80.3 \pm 25.4$ ,  $30.5 \pm 24.1$ ,  $50.0 \pm 20.5$  g/L vs  $23.4 \pm 8.2$  g/L,  $P < 0.01$  或  $P < 0.05$ ), 粪便IgA和sIgA与血清中IgA, sIgA含量无相关性, 血清中IgA与血清中sIgA亦无相关性。慢性肝炎、慢性重症肝炎、肝硬化患者血清sIgA与碱性磷酸酶 ( $r = 0.523$ ,  $P < 0.01$ )、总胆红素 ( $r = 0.4581$ ,  $P < 0.01$ )有相关性; 急性肝炎血清sIgA与ALT ( $r = 0.4692$ ,  $P < 0.01$ )、总胆红素 ( $r = 0.4265$ ,  $P < 0.01$ )有相关性。

**结论:** 检测粪便中和血清中IgA和sIgA对肝脏的临床诊断有重要的临床意义。

**关键词:** IgA; sIgA; 肝病

刘冬妍, 刘沛. 肝病患者IgA和sIgA含量变化的临床意义. *世界华人消化杂志* 2005;13(18):2275-2277

<http://www.wjgnet.com/1009-3079/18/2275.asp>

### 0 引言

肠黏膜 sIgA 是肠道主要的免疫球蛋白, 是肠道的第一线的免疫防御, 对黏膜固有的和入侵的病原体具有抵抗作用. 我们检测 168 例各型肝炎和肝硬化患者血清和粪

表1 肝病患者粪便IgA、sIgA含量及血清肝功的变化 (mean ± SD)

分组	n	IgA(mg/L)	sIgA(mg/L)	ALT(nkat/L)	ALP(nkat)	D-BIL(μmol/L)
对照组	30	<67	13 ± 10	260 ± 20	528 ± 43	18 ± 1
重症肝炎	9	251 ± 178 <sup>b</sup>	326 ± 237 <sup>b</sup>	8 098 ± 438	3 492 ± 510	588 ± 107
肝硬化	57	145 ± 164 <sup>b</sup>	104 ± 109 <sup>b</sup>	5 748 ± 342	3 151 ± 423	496 ± 189
慢性肝炎	67	80 ± 24 <sup>b</sup>	88 ± 121 <sup>b</sup>	5 133 ± 363	2 924 ± 445	451 ± 116
急性肝炎	35	100 ± 47 <sup>b</sup>	88 ± 96 <sup>b</sup>	5 613 ± 377	3 744 ± 362	489 ± 100

<sup>b</sup>P<0.01 vs 对照组.

表2 肝病患者血清IgA, IgM, IgG, sIgA含量的变化 (mean ± SD)

分组	n	IgA(g/L)	IgM(g/L)	IgG(g/L)	sIgA(μg/L)
对照组	50	1.6 ± 0.2	0.8 ± 0.2	8.2 ± 2.4	23.4 ± 8.2
重症肝炎	9	3.4 ± 1.8 <sup>b</sup>	2.0 ± 1.5 <sup>b</sup>	18.7 ± 6.5 <sup>b</sup>	80.3 ± 25.4 <sup>b</sup>
肝硬化	57	4.9 ± 3.3 <sup>b</sup>	1.9 ± 1.2 <sup>b</sup>	19.4 ± 6.7 <sup>b</sup>	50.0 ± 20.5 <sup>b</sup>
慢性肝炎	67	3.3 ± 1.7 <sup>b</sup>	1.5 ± 0.7 <sup>b</sup>	16.3 ± 5.1 <sup>b</sup>	30.5 ± 24.1 <sup>a</sup>
急性肝炎	35	3.1 ± 1.1 <sup>b</sup>	2.1 ± 1.2 <sup>b</sup>	13.1 ± 3.4 <sup>b</sup>	31.1 ± 25.8 <sup>a</sup>

<sup>b</sup>P<0.01, <sup>a</sup>P<0.05 vs 对照组.

便中 IgA 和 sIgA 的含量, 以探讨在各种肝病患者肠道免疫防御的变化情况.

## 1 材料和方法

1.1 材料 住院肝病患者168例, 男123例, 女45例, 年龄17-94岁, 急性肝炎(包括甲、乙、丙、戊)35例, 慢性重症肝炎9例, 慢性肝炎(包括乙、丙)67例, 肝硬化(包括肝炎后肝硬化和酒精性肝硬化)57例. 粪便正常对照组为我院五官科住院患者(肝功能正常, HBV和HCV血清标志物阴性)30例, 血清正常对照组为我院体检中心健康者(肝功能正常, HBV和HCV血清标志物阴性)50例. 取患者清晨第一次新鲜粪便称质重, 按1:10(m/m)加入0.01 mol/L pH7.4 PBS, 对照组粪便按1:2加入0.01 mol/L pH7.4 PBS, 混匀, 漩涡振荡器充分震荡5 min, 以10 000 g低温离心30 min, 取上清-30℃冰冻保存待用. 全部受检者于清晨空腹抽血, 分离血清-30℃冰冻保存.

1.2 方法 IgA, IgG, IgM用免疫散射比浊法检测, 仪器和试剂为库尔特公司提供, 血清正常参考值分别为 IgA 1.0-3.2 g/L, IgG 7.0-15.2 g/L, IgM 0.4-1.6 g/L; sIgA用中国原子能科学院提供 sIgA放射免疫分析药盒, 检测仪器为美国德普 γ 计数器, 按说明书操作; 碱性磷酸酶(ALP)、丙氨酸氨基转移酶(ALT)、总胆红素(T-BIL)分别用优化速率法、连续监测法和亚硝酸盐法, 采用日本日立公司生产7600全自动生化分析仪操作, 正常参考值分别为 ALP 750-2 200 nkat/L、ALT 83-667 nkat/L、T-BIL 1.7-20.5 μmol/L.

统计学处理 采用SPSS10.0进行统计学分析, 以P<0.05时有显著性差异.

## 2 结果

肝病患者粪中IgA和sIgA含量均明显高于正常对照组

(P<0.01), 其增高幅度随病变严重程度而增高(表1), 总IgA和sIgA呈显著正相关( $r = 0.4371$ ,  $P<0.01$ ). 肝病患者血清中IgA和sIgA含量均明显高于正常对照组(P<0.01)(表2). 粪中IgA和sIgA与血清中IgA, sIgA含量无相关性( $r = 0.1547$ ,  $r = 0.1593$ ,  $r = 0.1210$ ,  $r = 0.1135$ ), 血清中IgA与血清中sIgA亦无相关性( $r = 0.1983$ ). 慢性肝炎、慢性重症肝炎、肝硬化患者血清sIgA与ALP( $r = 0.5230$ ,  $P<0.01$ )、D-BIL( $r = 0.458$ ,  $P<0.01$ )有相关性; 急性肝炎患者血清sIgA与ALT( $r = 0.4692$ ,  $P<0.01$ )、D-BIL( $r = 0.4265$ ,  $P<0.01$ )有相关性.

## 3 讨论

肠道 sIgA 主要由肠黏膜中的 IgA 浆细胞分泌出聚合 IgA, 然后与上皮细胞分泌的 SC 结合, 继之被上皮细胞以内化的方式携入胞内形成吞饮小泡, 在小泡内被转运至上皮细胞的顶端, 并以 IgA-SC 复合物的形式被胞吐释放入肠腔. 血清 sIgA 的来源有: 一是 sIgA 直接由胆汁反流入血; 二是肝内膜相 SC 游离入血后迅速与血中 pIgA 结合而成. 一般而言, 黏膜病变如炎症、肿瘤只引起局部 SC 改变, 极少引起大量 SC 入血, 故血清 sIgA 多代表肝胆疾病. 人体存在聚和 IgA 的肠肝循环, 即入血的聚合 IgA 经肝脏重回肠腔, 因此肝脏是肠道黏膜免疫系统的组成部分. sIgA 在肠道免疫中起重要作用, 它能与细菌<sup>[1]</sup>和病毒<sup>[2-4]</sup>的特异性抗原相结合或结合在其他毒性分子上, 阻止他们粘附在黏膜表面. 还能排除已穿透上皮细胞层的感染因子, 并与细菌过度生长、细菌易位和肠道渗透性增高呈反比关系<sup>[5]</sup>, 它在抗感染中起重要作用<sup>[6,7]</sup>.

我们发现肝病患者 IgA, sIgA 显著升高, 随病变严重程度增幅顺序依次为: 重症肝炎、肝硬化、急性肝炎、慢性肝炎, 粪中 IgA 和 sIgA 呈显著正相关. 肝硬化等

严重肝病时,内毒素(LPS)产生和吸收增多,引起内毒素血症,LPS能刺激机体产生抗LPS的抗体<sup>[8,9]</sup>,用伤寒沙门氏菌通过口腔、鼻腔、直肠和阴道免疫机体发现直肠免疫后,在结肠分泌液和粪便内能诱导大量抗LPS-IgA抗体,此学者认为此菌能进攻不同的黏膜组织,诱导长期的局部抗LPS的IgA反应<sup>[10]</sup>.有学者发现服用适量的LPS后肺合成sIgA以45%增加,没有任何毒性作用或致热作用<sup>[11]</sup>,这可能是IgA,sIgA升高的一个原因.另外活动性肝病时常伴有炎症性肠病、自身免疫性肠病和感染性肠病,在感染过程中sIgA可升高,炎症性肠病时B淋巴细胞激活,IgA,IgM,IgG较正常肠黏膜产生更多.再有在重症肝炎时有抗肝炎病毒的特异性抗体和自身抗体产生,以及肝库氏细胞功能失调,失去对肠道抗原的处理能力,由肠道吸收的细菌抗原及病毒抗原形成的抗体增多.肝病患者血中IgA,IgG,IgM,sIgA亦显著增高,血清中sIgA与IgA无相关性,有学者发现HIV感染者血清中升高的sIgA与血清中的IgA及多聚IgA无相关性,认为血清中sIgA可能由黏膜部位产生<sup>[12]</sup>.本研究结果患者粪中IgA和sIgA与血清中IgA,sIgA也无相关性,提示血清sIgA与肠道sIgA的合成是相互独立的<sup>[13]</sup>.到底血清中sIgA来源于何处有待于进一步探讨.尽管血清sIgA与IgA无相关性,但是sIgA与碱性磷酸酶、丙氨酸氨基转移酶、总胆红素呈正相关,说明sIgA与病变程度有一定的关系,检测sIgA有助于临床对肝脏病变的鉴别诊断.由上可知,检测肝病患者IgA,sIgA对临床诊断有重要意义,尤其粪便的检测,由于取材简便,方便患者,减少抽血的麻烦,易于临床应用.

#### 4 参考文献

- 1 Kudsk KA. Current aspects of mucosal immunology and its influence by nutrition. *Am J Surg* 2002;183:390-398
- 2 Mantis NJ, Farrant SA, Mehta S. Oligosaccharide side chains on human secretory IgA serve as receptors for ricin. *J Immunol* 2004;172:6838-6845
- 3 Mazanec MB, Nedrud JG, Kaetzel CS, Lamm ME. A three-tiered view of the role of IgA in mucosal defense. *Immunol Today* 1993;14:430-435
- 4 Bomsel M. Transcytosis of infectious human immunodeficiency virus across a tight human epithelial cell line barrier. *Nat Med* 1997;3:42-47
- 5 Deitch EA, Xu D, Qi L, Berg R. Elemental diet-induced immune suppression is caused by both bacterial and dietary factors. *JPEN J Parenter Enteral Nutr* 1993;17:332-336
- 6 Mayer L. Review article: Local and systemic regulation of mucosal immunity. *Aliment Pharmacol Ther* 1997;11:81-85
- 7 Mayer L. The role of the epithelium in mucosal immunity. *Res Immunol* 1997;148:498-504
- 8 Parlesak A, Schafer C, Bode C. IgA against gut-derived endotoxins: does it contribute to suppression of hepatic inflammation in alcohol-induced liver disease? *Dig Dis Sci* 2002;47:760-766
- 9 Vindurampulle CJ, Attridge SR. Impact of vector priming on the immunogenicity of recombinant Salmonella vaccines. *Infect Immun* 2003;71:287-297
- 10 Hopkins S, Kraehenbuhl JP, Schodel F, Potts A, Peterson D, de Grandi P, Nardelli-Haeffliger D. A recombinant Salmonella typhimurium vaccine induces local immunity by four different routes of immunization. *Infect Immun* 1995;63:3279-3286
- 11 Kofler N, Wolf H. [Stimulation of synthesis of secretory immunoglobulin A in the lung by oral immunization: an approach with therapeutic relevance?] *Wien Klin Wochenschr* 1996;108:432-437
- 12 Vincent C, Cozon G, Zittoun M, Mellquist M, Kazatchkine MD, Czerkinsky C, Revillard JP. Secretory immunoglobulins in serum from human immunodeficiency virus (HIV)-infected patients. *J Clin Immunol* 1992;12:381-388
- 13 Bartholomeusz RC, Forrest BD, Labrooy JT, Ey PL, Pyle D, Shearman DJ, Rowley D. The serum polymeric IgA antibody response to typhoid vaccination; its relationship to the intestinal IgA response. *Immunology* 1990;69:190-194

电编 张勇 编辑 潘伯荣 审读 张海宁