

# 慢性肝炎肝硬化患者中医证型与血清肝纤维化指标的关系

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**摘要** 测定 160 例慢性肝炎肝硬化患者的血清肝纤维化标志物透明质酸(HA)、Ⅲ型前胶原(hPC Ⅲ)和Ⅳ型胶原(Ⅳ-C)3 项,以探讨中医证型与上述指标的关系。结果显示,各中医证型组的肝纤 3 项指标均较对照组升高,但改变有各自的特点,其中肝郁脾虚组的平均升高幅度最小。同时发现,湿热中阻组肝纤 3 项均有显著性升高,肝肾阴虚和瘀血阻络组以 HA、hPC Ⅲ 升高为主,脾肾阳虚组以 HA、Ⅳ-C 升高为主。提示测定上述指标对慢性肝病患者的中医分型有一定指导意义,湿热留恋可能是肝纤维化的启动因素,而血瘀则贯穿于肝纤维化的整个过程。

**主题词** 肝硬化/血液 肝/病理学 辨证分型

为了探讨慢性肝炎肝硬化中医分型与血清肝纤维化标志物之间的关系,认识肝纤维化的中医病因病机本质,我们在 1997 年 4 月~1998 年 9 月间对本院 160 例诊断为慢性肝炎肝硬化的患者和 35 例对照组的血清肝纤维化标志物透明质酸(HA)、Ⅲ型前胶原(PC Ⅲ)和Ⅳ型胶原(Ⅳ-C)3 项指标进行了检测分析,现将结果报告如下。

## 1 临床资料

病例组共 160 例,均为在本院住院和门诊就医的慢性肝炎或肝硬化患者,其中男 128 例,女 32 例;年龄 19~58 岁,平均  $34.5 \pm 12.7$  岁;慢性肝炎 135 例,肝炎后肝硬化 25 例,其中乙型肝炎 137 例,丙型肝炎 11 例,乙型重叠丙型肝炎 5 例,乙型重叠戊型肝炎 7 例。临床诊断和病原学诊断均按 1995 年全国传染病与寄生虫病学术会议修订的病毒性肝炎诊断标准<sup>[1]</sup>。中医辨证分型属肝郁脾虚 49 例,湿热中阻 43 例,肝肾阴虚 31 例,瘀血阻络 29 例,脾肾阳虚 8 例,中医分型符合 1991 年全国中医学会肝病专业委员会肝炎中医辨证分型标准<sup>[2]</sup>。

对照组共 35 例,为同期住院及门诊的其他内科病

人,均经肝功、生化、乙肝病毒血清标志物、丙肝两项、B 超等检查,排除慢性肝炎、肝硬化及结缔组织病变。男 25 例,女 10 例,平均年龄  $36.7 \pm 8.6$  岁。

## 2 检测方法

HA、hPC Ⅲ、Ⅳ-C 均用放射免疫法检测,HA 试剂盒由上海海军医学研究所提供,hPC Ⅲ、Ⅳ-C 试剂盒由重庆肿瘤研究所提供,按说明书由专人严格进行操作。统计资料采用方差分析和 Newman-Keuls 法进行检验,所有数据资料的处理均在微机上进行(采用统计分析专用软件 SPSS7.50 for WINDOWS)。

## 3 结果

附表示,各中医证型慢性肝炎肝硬化患者的 HA、hPC Ⅲ、Ⅳ-C 均明显升高,与对照组比较存在显著性差异( $P < 0.01$ )。以升高的幅度而言,肝郁脾虚组是各型中升高幅度最小的组别,分别为对照组肝纤 3 项指标的 3.2、3 和 2.2 倍。将各中医证型组与肝郁脾虚组分别进行比较,结果发现,湿热中阻组肝 3 项指标均升高,并存在显著性差异( $P < 0.01$ ),分别为肝郁脾虚组的 3.7、3 和 2.9 倍;肝肾阴虚和瘀血阻络组均升高( $P < 0.05$  或  $P < 0.01$ ),分别为 4.2、2.2、1.7 和 5.1、9、1.4 倍;脾肾阳虚组则以 HA 和 Ⅳ-C 的升高为主( $P < 0.01$ ),分别为 5.2、4.6 倍。进一步的两两比较检验表明,除肝郁脾虚组外,其他各中医证型组的 HA 值均较高,且有逐渐升高的趋势,但彼此的组间差异无统计学意义( $P > 0.05$ );肝郁脾虚组的 hPC Ⅲ 与脾肾阳虚组比较差异无显著性( $P > 0.05$ ),两者与湿热中阻、肝肾阴虚、瘀血阻络组比较均存在显著性差异( $P < 0.01$ ),尤其以湿热中阻组 hPC Ⅲ 的升高最明显,肝肾阴虚、瘀血阻络组 Ⅳ-C 的升高与肝郁脾虚组比较差异有显著性( $P < 0.05$  或  $P < 0.01$ ),三者与湿热中阻、脾肾阳虚组比较亦有显著性差异( $P < 0.01$ ),尤其以脾肾阳虚组 Ⅳ-C 的升高最明显。

## 4 讨论

现代医学的研究发现,各种病因引起的慢性肝炎,都具有肝细胞变性、坏死及纤维化的病理特征<sup>[3]</sup>。纤维化是慢性肝炎向肝硬化发展的必经过程,肝纤维化的实质是肝脏细胞外间质的增生,其主要成分有胶原蛋

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附表 各中医证型组与对照组肝纤 3 项指标的比较( $\bar{X} \pm S$ )

| 组 别  | 例数 | HA               | hPC III          | N—C              |
|------|----|------------------|------------------|------------------|
| 对照组  | 35 | 43.90±24.02      | 44.48±15.66      | 36.19±11.22      |
| 肝郁脾虚 | 49 | 141.56±116.50*   | 132.56±66.65*    | 80.81±53.40*     |
| 湿热中阻 | 43 | 527.43±266.61*△△ | 396.22±184.28*△△ | 231.76±135.75*△△ |
| 肝肾阴虚 | 31 | 600.32±255.06*△△ | 286.80±169.00*△△ | 138.08±98.51*△△  |
| 瘀血阻络 | 29 | 703.91±146.97*△△ | 250.87±84.81*△△  | 112.65±60.92*△   |
| 脾肾阳虚 | 8  | 740.00±171.27*△△ | 175.00±94.40*    | 365.00±153.20*△△ |

与对照组比较, \*  $P < 0.01$ ; 与肝郁脾虚组比较,  $\Delta P < 0.05$ ,  $\Delta\Delta P < 0.01$

白、糖蛋白及蛋白多糖等。近年来针对这些成分及其降解产物的血清含量进行了广泛的研究,发现了一些能较好地反映肝纤维化的血清标志物,其中 HA、hPC III 是临床用于肝纤维化诊断的常用指标。研究发现<sup>[4]</sup>, N—C 也是诊断肝纤维化的良好指标,在早期或轻度肝纤维化时血清 N—C 即明显上升,而后其他胶原才随之增多, N—C 与慢性肝病中医分型的关系尚未见报道,由于上述指标均各自反映了肝脏细胞外间质代谢的不同侧面,且存在非特异性的问题,临床上必须联合应用才能较好地反映肝纤维化的病变程度。

慢性病毒性肝炎属于中医“疫毒”、“黄疸”、“胁痛”的范畴,肝硬化属于中医“积聚”、“臌胀”的范畴,两者的病因病机常涉及湿热疫毒和气滞血瘀,临床上常辨证分型为肝郁脾虚、湿热中阻、肝肾阴虚、瘀血阻络、脾肾阳虚等。中医并无肝纤维化的相应病名,临床上通常按照慢性肝炎的辨证方法进行分型治疗,然而肝纤维化的中医病因病机本质及肝纤维化标志物与慢性肝炎肝硬化辨证分型之间的关系如何目前尚不甚清楚,显然对这方面问题的探讨将有助于深化中医对肝纤维化过程的认识。

本组资料显示,各中医证型组肝纤 3 项标志物均较对照组明显升高( $P < 0.01$ ),但各中医证型组间的肝纤 3 项并不呈简单的依次升高顺序,这与张俊富等<sup>[5]</sup>发现慢性肝病患者 HA、hPC III、LN 升高依次为肝郁脾虚型、肝肾阴虚型、脾肾阳虚型、湿热中阻型、瘀血阻络型的结论不同。肝郁脾虚组在各证型组中上升的幅度最小,提示该组患者处于肝纤维化的相对静止期或肝纤维化的程度较轻,与吴婉芬等<sup>[6]</sup>观察发现肝郁脾虚型慢性肝炎患者病理诊断大多呈轻度病理变化,肝纤维化组织学分期亦相对较轻的结论相一致,将各病例组与肝郁脾虚组进行两两比较发现,湿热中阻组是肝纤 3 项标志物同时显著性升高的唯一组别( $P < 0.01$ ),且该组 N—C 明显较其他证型组高( $P < 0.01$ ,脾肾阳虚组除外),提示该组病人处于肝纤维化的活跃期,湿热留恋可能是导致这种情况的重要启动因素。至于脾肾阳虚组的高 N—

C 状态,由于本资料中 8 例均为慢性重症肝炎患者,是否与该组患者病情严重,具有特殊的病理生理过程有关,有待进一步的探讨。认识上述各中医证型组肝纤 3 项标志物改变的不同特点有助于指导临床的辨证分型。值得注意的是,本组资料的 HA 按附表中医证型组顺序呈明显的增高趋势,尤其以瘀血阻络组 HA 的均数较高且代表性好,提示该指标与瘀血阻络密切相关,然而除肝郁脾虚组外,其他中医证型组间的统计学分析无显著性差异( $P > 0.05$ ),其原因可能与肝胆湿热、肝肾阴虚两组 HA 的标准差大,均数代表性差有关。事实上,有研究表明<sup>[7]</sup>,慢性病毒性肝炎兼夹有瘀血阻络表现者可高达 55.0%,临床辨证时不少证型都或多或少地兼有血瘀的表现,这可能是造成肝胆湿热、肝肾阴虚组 HA 标准差大,统计学分析未显示出显著性差异的内在原因。

本组调查结果表明,慢性肝炎肝硬化的中医分型与血清肝纤维化标志物之间存在一定的相关性,因此,在临床上如何清除留滞不去的湿热疫毒,又兼顾整个过程中的活血化瘀方法,这将是提高中医治疗效果的重要环节。

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## ABSTRACTS FROM ORIGINAL ARTICLES

### **Clinical Observation on 30 Cases of Lupus Nephritis Treated with Large — dose Radix Astragali seu Hedysari Concerted with Venous Dripping of Radix Salviae Miltiorrhiza**

*Su Li, Chen Xiangjun, Hu Jiandong, et al.*

Investigation was made on lupus nephritis (type of Qi — deficiency and blood — stasis) treated mainly with large — dose Radix Astragali seu Hedysari (60g/day) concerted with venous dripping of Radix Salviae Miltiorrhiza to probe into its effect and mechanism. Through study on 30 cases, it was shown that the therapeutic effect was definite, being superior to oral cortisone. It not only improved clinical signs and symptoms, but also ameliorated the clinical biochemical and immunological indices.

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**Key words:** Lupus nephritis/TCM therapy Radix Astragali seu Hedysari/drug administration and dosage Injection of Radix Salviae Miltiorrhiza/therapeutic action

(Original article on page 476)

### **Fever of Unknown Origin after Transplantation of Hemopoietic Stem — cells in 15 Cases of Leukemia**

*Li Haiyan, Feng Sizhou, Han Mingzhe, et al.*

Treatment of all the cases were based on differential diagnosis of zheng. Oral medicines were given to the cases in two groups, the damp — heat type and the type of Yin — deficiency blood — heat together with dampness. Of the 15 cases, 14 were markedly effective, a relapsed case was ineffective, the average days of antipyresis was 5 days, demonstrating that the therapy was rather satisfactory and helpful to their convalescence.

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**Key words:** Leukemia/surgical operation hemopoietic stem cell/transplantation

(Original article on page 482)

### **Ten Cases of I — type Diabetes Mellitus Treated by Transplantation of Pancreatic Islands to Acupoints**

*Chen Jianfei, Ling Bing, Zhang Jianhua, et al.*

Cultivated human fetal pancreatic islands were used in the therapy. Of them, 3 cases had completely suspended their insulin for 3 — 12 months, 5 cases decreased the dosage to 33% — 66% of that before the treatment. The conditions were well under control with marked amelioration of capillary and nervous complications, 2 cases were ineffective. The results showed that the effects were definite, and were safe, simple and reliable.

**Authors' address:** Zhuhai City Hospital of TCM, Zhuhai 519015

**Key words:** Diabetes Mellitus/acupoint therapy pancreatic island transplantation/acupoint therapy

(Original article on page 484)

### **Relationship Between the Serum Indices of Liver Fibrosis and TCM Syndromes Types in Liver Cirrhosis due to Chronic Hepatitis**

*Pan Zhiheng, Chen Yanbi, Deng Zide, et al.*

In order to probe into the relationship between the TCM syndrome types and the five indices of fibrotic markers of liver in serum, the HA, hPC III, IV — C in 160 of liver cirrhosis patients induced by chronic hepatitis were examined. Results showed that the 5 indices in all TCM syndrome types were all higher than the control group, each with its specificity. The increased amplitude in the group of liver — stagnant, spleen — deficiency was the least one. It was also found that the 3 indices of liver fibrosis in the group of internal blockade of damp — heat were markedly increased; it was mainly the increase of HA, hPC III in the group of yin — deficiency of both liver — kidney and obstruction of collaterals by static blood; but it was mainly the increase of HA, IV — C in the group of Yang — deficiency of spleen and kidney. This demonstrated that the above indices were of significance in TCM syndrome typing for chronic hepatic victims. Lingering of damp — heat may be the trigger factor for liver fibrosis in which blood stasis was present during the whole course of liver fibrosis.

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**Key words:** Liver cirrhosis/blood liver/pathology typing based on differential diagnosis of syndromes

(Original article on page 494)