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酒精性肝病患者血清中CA125水平的改变及意义

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Evaluation of serum CA125 levels in alcoholic liver disease

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Abstract

AIM: CA125 is a tumor marker usually used in monitoring of ovarian carcinoma patients. This study was performed to evaluate the behavior of CA125 in 188 patients with different hepatic diseases who underwent thorough clinical and laboratory evaluation and to determine whether CA125 can be a sensitive marker for the diagnosis of alcoholic liver disease

METHODS: A total of 188 patients and 19 health controls were included in the study and the patients were divided into alcoholic and non-alcoholic fatty liver group, post-hepatitis liver cirrhosis and alcoholic liver cirrhosis as well as primary hepatic carcinoma. Serum CA125 levels were determined using a solid-phase immunoassay. Comparisons among the groups were made.

RESULTS: Serum CA-125 in primary hepatic carcinoma group, post-hepatitis liver cirrhosis group, alcoholic liver cirrhosis group and alcoholic fatty liver group were 797±1468 U/L, 327±364 U/L, 210±207 U/L, 77±64 U/L, respectively, significantly higher than that of health control (17±9 U/L) (P <0.05 or P <0.01). But the lever of serum CA-125 in nonalcoholic fatty liver was 38±33 U/L and there was no difference between nonalcoholic fatty liver and health control (P >0.05). In the different stage of liver cirrhosis, the elevated level of CA-125 in the patients caused by alcohol in Child A and B stage were 168±166 U/L and 285±261 U/L, magnificently greater than Child A stage 92±83 U/L and Child B stage 161±71 U/L caused by hepatitis (P <0.01), although there was not much difference between both groups of cirrhosis in Child C stage(P >0.05). In alcoholic cirrhosis patients, the elevated level of serum CA-125 increased significantly in Child C stage than that in Child B stage and Child B's CA125 level was much higher than that of Child A (P <0.01). In the post-hepatitis and alcoholic cirrhosis patients with ascites, the serum levels of CA125 were 306±256 U/L and 400±416 U/L, significantly higher than 122±88 U/L and 228±245 U/L (P <0.01) in patients without ascites. However, in the comparison between two groups of cirrhosis without ascites, the serum of CA125 was higher in alcoholic liver cirrhosis than that in post-hepatitis liver cirrhosis.

CONCLUSION: CA125 is a sensitive marker for diagnosis of alcoholic fatty liver alcoholic liver cirrhosis and alcoholic liver cirrhosis, especially in Child A and B stage, suggesting that it is an earlier marker for diagnosis of alcoholic liver disease.

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摘要

目的: 抗原CA125是一个非特异性肿瘤标记物, 他可以来源于正常组织和肿瘤细胞. 最近有文献报道CA125除在卵巢癌等恶性肿瘤升高外, 许多良性疾病也有升高, 特别是在肝硬化伴腹水的报道较多. 临床上酒精性肝病患者CA125水平常升高, 本研究目的检测酒精性肝病和其他原因引起的肝病CA 125水平的改变, 探讨CA 125是否可用于诊断酒精性肝病的敏感指标.

方法: 收集188例肝病患者和19个正常人的晨起空腹血清. 将这些肝病患者分为原发性肝癌组, 肝炎后肝硬化和酒精性肝硬化组, 酒精性脂肪肝组和非酒精性脂肪肝组. 其中肝硬化组根据Child-Pugh的分级又分为A, B, C三级. 用ELISA法检测受检者血清中CA125水平.

结果: 原发性肝癌组, 肝炎后肝硬化组, 酒精性肝硬化组及脂肪肝组血清CA125水平分别为797±1 468 U/L, 327±364 U/L, 210±207 U/L, 77±64 U/L明显高于健康对照组的17±9 U/L (P <0.05或P <0.01), 但非酒精性脂肪肝组为38±33 U/L, 与正常对照组无明显差异(P >0.05). 在肝硬化Child-Pugh分级中, 酒精性肝硬化A级和B级的CA 125水平为168 ± 166 U/L和285 ± 261 U/L, 明显高于肝炎后肝硬化组的A级92 ± 83U/L和B级161 ± 71 U/L (P <0.01), 在C级为522 ± 496 U/L, 在统计学上与肝炎后肝硬化C级的390±276 U/L没有明显差别(P >0.05). 在酒精性肝硬化患者中, CA 125水平在Child C级明显

高于B级，B级明显高于A级(P<0.01). 在肝炎后肝硬化患者中，Child C级的CA 125水平明显高于A级和B级(P<0.01)，但Child A级和B级在统计学上无明显差异(P>0.05). 酒精性肝硬化和肝炎后肝硬化腹水阳性组CA125水平为400±416 U/L和306±256 U/L，均高于腹水阴性酒精性肝硬化组228±245 U/L和肝炎后肝硬化组122±88 U/L (P<0.01)，在腹水阴性患者中，酒精性肝硬化患者CA125水平明显高于肝炎后肝硬化患者(P<0.05)，但腹水阳性患者中，二者无明显差别(P>0.05).

结论: CA 125不仅在肝癌时升高，在肝脏良性病变肝硬化时也升高，尤其在酒精性脂肪肝及酒精性肝硬化时A级，B级及在腹水阴性时CA125水平较肝炎后肝硬化升高更为明显，但在Child C级和腹水阳性患者中无明显差异，CA125可作为酒精性脂肪肝及酒精性肝硬化的一个敏感性指标和早期诊断指标.

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0 引言

CA-125是一个大分子糖蛋白，MW 220 000[1]，近来报道CA-125水平增高常见于肝硬化、肝癌合并腹水的患者，且与腹水的量有良好的相关性[2-9]，临床上我们发现CA-125在慢性肝病的患者中常升高，特别是酒精性肝病的患者升高尤为明显，目前很少有关于CA-125在酒精性肝病患者中的改变的报道，我们检测并比较不同原因引起的慢性肝病患者CA-125水平的改变，探讨CA-125是否可以用来作为诊断酒精性肝病的一个敏感性指标.

1 材料和方法

1.1 材料 本研究共收集2000-06/2001-11中国医科大学一院消化内科门诊和住院的肝病患者188例，其中酒精性脂肪肝19例，非酒精性脂肪肝各18例，肝炎后肝硬化组57例，Child-Pugh A级20例，B级19例，C级18例，酒精性肝硬化61例，Child-Pugh A级19例，B级22例，C级20例; 原发性肝癌组33例; 肝炎后肝硬化腹水阴性者28例，腹水阳性者27例，酒精性肝硬化腹水阴性者31例，腹水阳性者30例. 所有病例均剔除发热、自发性腹膜炎，肾功能不全及上消化道大出血患者. 正常对照组为本院研究生及献血员共19例(表1).

1.2 方法 所有受试者均清晨空腹抽肘静脉血5 mL，分离血清，-20 ℃保存，CA125的检测由中国医科大学一院中心实验室统一用ELISA法检测.

统计学处理 数据用日本JSTAT统计软件以非配对两组和多组之间的t检验和F检验比较各组之间的差别. 各组年龄与性别无明显差别.

2 结果

与健康对照组相比，原发性肝癌组、肝炎后肝硬化组、酒精性肝硬化组、酒精性脂肪肝组CA125水平均明显升高(P<0.05)，CA125异常(CA125小于35IU/L)的病例数及百分数也高于对照组，但非酒精性脂肪肝组与对照组相比无明显异常(表1). 肝炎后肝硬化患者Child B级患者血清CA125水平(161 ± 71 U/L)与Child A(92 ± 82 U/L)级无明显差别(P >0.05)，C级的血清CA125水平(390 ± 276 U/L)明显高于B级和A级(P<0.01); 酒精性肝硬化患者Child B级患者血清CA125水平(285 ± 261 U/L)高于Child A级(168 ± 166 U/L)(P<0.05)，Child C级(522 ± 496 U/L)明显高于B级(P<0.01). 在酒精性肝硬化患者中，Child A级和B级CA125水平分别较肝炎后肝硬化患者Child A级和B级水平高(P <0.05)，而Child C级的血清CA125水平与肝炎后肝硬化患者Child C级无明显差别(P>0.05). CA125水平在酒精性肝硬化中较肝炎后肝硬化患者升高明显，且随着肝硬化病情加重而升高，但在Child C级，CA125水平与肝炎后肝硬化患者Child C级无明显差别(P>0.05)，提示CA125水平为酒精性肝硬化较早及较敏感的指标，但不能直接作为分级指标. 我们将肝硬化患者按有无腹水分组并分别统计酒精性肝硬化和肝炎后肝硬化两组CA 125水平，结果发现，酒精性肝硬化组和肝炎后肝硬化两组腹水阳性患者均明显高于腹水阴性患者(P<0.01)，在腹水阴性患者，酒精性肝硬化患者CA 125水平明显高于肝炎后肝硬化(228 ± 254 *vs* 122 ± 88 U/L，P<0.01)，而腹水阳性患者酒精性肝硬化患者CA 125水平与肝炎后肝硬化水平无明显差别(401 ± 417 U/L *vs* 307 ± 257 U/L P>0.05).

表1 肝病患者CA125异常的百分比值及CA125检测值

组别	n	男/女	年龄	CA125异常的		CA125(U/L)
				n	%	
健康对照组	19	9/10	38±12	0	0	16±8
非酒精性脂肪肝组	19	10/9	42±18	2	11.77 %	38±33
酒精性脂肪肝组	18	13/5	38±21	12	66.67 %[a]	77±64[a]
肝炎后肝硬化组	57	34/23	47±22	48	84.21 %[a]	210±207[b]
酒精性肝硬化组	61	45/15	41±19	52	86.67 %[b]	327±364[b]
原发性肝癌组	33	27/6	49±16	30	90.01 %[b]	797±1468[b]

[a]P <0.05, [b]P<0.01 *vs* 健康对照组.

3 讨论

酒精性肝病是西方国家最常见的肝病，在我国发病率有增多的趋势，目前认为长期过度饮酒可造成肝细胞中脂肪聚集、变形、坏死和再生[10-12]，最终导致肝纤维化和肝硬化[13-15]，甚至可能引起肝癌的发生[16-19]. 然而人类对酒精的反映个体差异较大，嗜酒程度与肝病的严重程度并无明确的关系[20-23]. 目前酒精性肝病的确诊仍以肝穿刺活检检查为主，但由于肝穿刺是损伤性检查，不易被患者接受，同时受到穿刺部位的局限也

不能对酒精性肝病进行动态观察，因此无创伤性、简单易行的诊断方法十分必要.目前已有研究表明，各种慢性肝病的相关检查既是对病理诊断的补充，也在疾病性质的独立诊断上具有较高的价值[24, 25]，本研究探讨CA-125这一无创性指标是否可以用来作为诊断酒精性肝病的一个敏感性指标.

CA125是很重要的卵巢癌相关抗原[26-30]，肝病中CA125产生来源目前尚不清楚，可能与酒精影响雌激素灭活有关，雌激素灭活障碍可引起雌激素水平升高，既往曾经有报道雌激素和孕激素的改变可引起血清CA125水平改变，特别在男性饮酒患者升高明显[31, 32]，本研究结果表示酒精性脂肪肝时血清CA125水平既有改变，随着酒精性肝病病情的加重，CA125水平升高幅度加大，特别是在Child A级和Child B级的酒精性肝硬化患者，其升高的幅度明显高于酒精性肝硬化的升高幅度，所以CA125水平为酒精性肝病较早及较敏感的诊断指标.以往报道认为CA125升高与腹水的生成有关，我们的结果表示，酒精性和肝炎后肝硬化腹水阳性患者均高于腹水阴性患者，在腹水阴性患者，酒精性肝硬化患者CA125水平明显高于肝炎后肝硬化，但腹水阳性患者酒精性肝硬化患者CA 125水平与肝炎后肝硬化水平无明显差别，此结果也提示CA125为酒精性肝硬化诊断早期且较敏感的指标.但随着病情加重，肝炎后肝硬化与酒精性肝硬化的CA125水平无明显差别，血清CA125水平与酒精性肝病预后具有良好的相关性，监测CA125水平，以此来评价酒精性肝病预后还需更多的临床试验才能得出结论.总之，在酒精性肝病的诊断中，CA125水平这一无创指标，不仅对妇科的癌症及肝癌等具有诊断作用，在肝脏良性病变的诊断中，特别是对酒精性脂肪肝和肝硬化早期的诊断具有较高的价值.

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