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急性脑梗死患者血清 H-FABP、干扰素- γ 、半胱氨酸和 Ang-1 联合检测及其临床意义*

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摘要 目的:探讨急性脑梗死患者血清心型脂肪酸结合蛋白(H-FABP)、干扰素- γ (IFN- γ)、同型半胱氨酸(Hcy)、血管生成素-1(Ang-1)联合检测及其临床意义。**方法:**选取本院自2018年4月-2021年4月收治的66例急性脑梗死患者的临床资料,将其作为研究组。同时选取同期来院体检的健康者66例为对照组,均通过酶联免疫吸附试验试剂盒检测H-FABP、IFN- γ 、Hcy、Ang-1水平,比较各组检测水平,分析联合检测意义。**结果:**研究组患者的H-FABP、IFN- γ 、Hcy水平均高于对照组相应指标,Ang-1水平低于对照组水平,差异均具有统计学意义($P<0.05$);H-FABP、IFN- γ 、Hcy、Ang-1水平在不同病情间差异具有统计学意义($P<0.05$),其中与轻度、中度相比,重度患者的H-FABP、IFN- γ 、Hcy水平更高,Ang-1水平更低,差异具有统计学意义($P<0.05$);急性脑梗死患者病情与H-FABP、IFN- γ 、Hcy呈正相关,与Ang-1呈负相关,有统计学意义($P<0.05$);急性脑梗死患者H-FABP与IFN- γ 、Hcy指标相互间呈现正相关关系,与Ang-1呈现负相关关系($P<0.05$)。**结论:**急性脑梗死患者联合检测H-FABP、IFN- γ 、Hcy、Ang-1水平具有重要意义,可作为疾病早期诊断的重要指标。

关键词:急性脑梗死;H-FABP;干扰素- γ ;同型半胱氨酸;血管生成素-1;诊断

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Combined Detection of Serum H-FABP, Interferon- γ , Cysteine and Ang-1 in Patients with Acute Cerebral Infarction and Its Clinical Significance*

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ABSTRACT Objective: To investigate the serum heart-shaped fatty acid binding protein (H-FABP), interferon- γ (IFN- γ), homocysteine (Hcy), and angiopoietin-1 (Ang-1) in patients with acute cerebral infarction Combined detection and its clinical significance. **Methods:** The clinical data of 66 patients with acute cerebral infarction admitted to our hospital from April 2018 to April 2021 were selected as the research group. At the same time, 66 healthy people who came to the hospital for physical examination during the same period were selected as the control group. The levels of H-FABP, IFN- γ , Hcy, and Ang-1 were detected by enzyme-linked immunosorbent assay kits. The detection levels of each group were compared, and the significance of combined detection was analyzed. **Results:** The levels of H-FABP, IFN- γ , and Hcy in the study group were higher than the corresponding indicators in the control group, and the Ang-1 level was lower than that in the control group; H-FABP, The levels of IFN- γ , Hcy, and Ang-1 are statistically significant in different conditions ($P<0.05$). Compared with mild and moderate, severe patients have higher levels of H-FABP, IFN- γ , and Hcy. Ang-1 level was lower($P<0.05$); the condition of patients with acute cerebral infarction was positively correlated with H-FABP, IFN- γ , and Hcy, and negatively correlated with Ang-1, which was statistically significant ($P<0.05$); In patients with acute cerebral infarction, H-FABP, IFN- γ , and Hcy are positively correlated with each other, and negatively correlated with Ang-1 ($P<0.05$). **Conclusion:** The combined detection of H-FABP, IFN- γ , Hcy and Ang-1 levels in patients with acute cerebral infarction is of great significance and can be used as an important indicator for early diagnosis of the disease.

Key words: Acute cerebral infarction; H-FABP; Interferon- γ ; Homocysteine; Angiopoietin-1; Diagnosis

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前言

急性脑梗死指脑血供突然中断后导致的脑组织坏死,通常主要是由于供应脑部血液的动脉出现粥样硬化和血栓形成,使管腔狭窄甚至闭塞,导致局灶性急性脑供血不足而发病;而血小板活化、凝血系统和纤溶系统失衡是脑血栓形成的主要原因^[1,2]。随着老龄社会的到来,急性脑梗死发病率逐年增加,因此对脑梗死高危患者进行早期预测,积极抢救脑梗死后早期缺血半暗带,恢复脑细胞供血,减缓脑细胞损伤,从而可改善患者的临床治疗率^[3,4]。当前,临床诊断急性脑梗死者多以影像学检查为主,在缺氧缺血条件下,患者可在5分钟内出现脑梗死,但影像学检查仅仅在发病24小时后才能诊断疾病,直接影响临床治疗^[5,6]。随着临床技术的发展,生物学标志物在临床疾病诊断中得到应用,因此本文对H-FABP、IFN- γ 、Hcy、Ang-1在急性脑梗死患者联合检测中的意义进行分析。

1 资料与方法

1.1 一般资料

66例急性脑梗死患者来源于本院自2018年4月-2021年4月收治的患者。将其作为研究组,其中男32例,女34例,年龄50~70岁,平均(64.78 $\pm$ 4.34)岁,同时选取同期来院体检的健康体检者66例为对照组,其中男35例,女31例,年龄49~68岁,平均(64.45 $\pm$ 4.64)岁,两组基本资料间差异无统计学意义($P>0.05$),具有可比性($P>0.05$)。所有患者经医学伦理委员会批准且自愿参与此次研究。

纳入标准:(1)发病时间<24小时;(2)经头颅CT、MRI确

诊为急性脑梗死;(3)患者均经过明确治疗、病情控制;(4)临床资料完整。

排除标准:(1)脑外伤者;(2)病前半个月有感染史、自身免疫性疾病者;(3)心肝肾功能性疾病者;(4)1个月内有特殊治疗史;(5)3个月内发生过脑卒中者;(6)短暂性脑缺血者;(7)精神系统疾病及意识障碍性疾病者,无法有效配合研究者。

1.2 指标检测及标准评估

1.2.1 血清 H-FABP、IFN- γ 、Hcy、Ang-1 水平检测^[7,8] 所有受试者均清晨空腹抽取5 mL静脉血,按照3000 r/min的速度离心15 min,取血清,置于零下20℃的环境下待测。严格按照试剂盒中的说明书检测。采用酶联免疫吸附法测定血清H-FABP、Hcy、Ang-1水平,采用双抗体夹心法检测IFN- γ 水平,根据对应试剂盒说明书实施操作。

1.2.2 病情严重程度评估 根据美国国立卫生研究院卒中量表评估病情,分为重度、中度、轻度,重度:其评分为31-42分,中度:16-30分;轻度:0-15分,并进行记录。

1.3 统计学方法

采用SPSS25.0分析,计量资料以($\bar{x}\pm s$)表示,两组间比较采用t检验,三组间比较采用单因素方差分析;采用Pearson进行相关性分析;检验水准 $\alpha=0.05$ 。

2 结果

2.1 两组患者各项指标比较

研究组患者的H-FABP、IFN- γ 、Hcy水平均高于对照组相应指标,Ang-1水平低于对照组水平($P<0.05$),详见表1。

表1 两组患者 H-FABP、IFN- γ 、Hcy、Ang-1 水平比较($\bar{x}\pm s$)

Table 1 Comparison of the levels of H-FABP, IFN- γ , Hcy, and Ang-1 in the two patient groups($\bar{x}\pm s$)

Group	H-FABP(ng/mL)	IFN- γ (pg/mL)	Hcy(μ mol/L)	Ang-1(ng/mL)
Control group(n=66)	2.17 $\pm$ 0.67	56.27 $\pm$ 15.37	9.57 $\pm$ 2.15	1.67 $\pm$ 0.35
Study Group(n=66)	10.16 $\pm$ 4.27	106.73 $\pm$ 14.16	18.93 $\pm$ 2.78	1.05 $\pm$ 0.26
t	11.015	9.366	8.155	0.563
P	<0.001	<0.001	<0.001	0.154

2.2 研究组不同病情的各项指标比较

H-FABP、IFN- γ 、Hcy、Ang-1水平在不同病情间差异具有统计学意义($P<0.05$),其中与轻度、中度相比,重度患者的

H-FABP、IFN- γ 、Hcy水平更高,Ang-1水平更低($P<0.05$),详见下表2所示。

表2 研究组不同病情的各项指标比较($\bar{x}\pm s$)

Table 2 Comparison of for different conditions in the study group($\bar{x}\pm s$)

Groups	H-FABP(ng/ml)	IFN- γ (pg/mL)	Hcy(μ mol/L)	Ang-1(ng/mL)
Mild degree group(n=20)	5.63 $\pm$ 1.14	62.15 $\pm$ 7.15	13.15 $\pm$ 4.25	1.35 $\pm$ 0.98
Moderate degree group (n=22)	8.36 $\pm$ 1.76*	78.35 $\pm$ 7.09*	17.36 $\pm$ 4.11*	1.04 $\pm$ 0.28*
Severe degree group(n=18)	12.04 $\pm$ 1.89*#	110.15 $\pm$ 7.84*#	21.15 $\pm$ 4.26*#	0.76 $\pm$ 0.15*#
F	9.235	20.209	13.451	9.234
P	<0.001	<0.001	<0.001	<0.001

注:*表示与轻度相比, $P<0.05$;#表示与中度相比, $P<0.05$ 。

Note: Compared with mild $P<0.05$, compared with moderate, $P<0.05$.

2.3 急性脑梗死患者病情与各项指标的关系分析

Ang-1 呈负相关($P<0.05$)。详见下表 3 所示。

急性脑梗死患者病情与 H-FABP、IFN- γ 、Hcy 呈正相关,与

表 3 急性脑梗死患者病情与各项指标的关系分析(%)

Table 3 Analysis of the relationship between conditions and various indicators in patients with acute cerebral infarction (%)

Index	H-FABP		IFN- γ		Hcy		Ang-1	
	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>
The severity of the condition	0.782	<0.001	0.735	<0.001	0.734	<0.001	-0.922	<0.001

2.4 急性脑梗死患者各指标相关关系

正相关关系,与 Ang-1 呈现负相关关系($P<0.05$)。详见下表 4

急性脑梗死患者 H-FABP 与 IFN- γ 、Hcy 指标相互间呈现 所示。

表 4 急性脑梗死患者各指标相关关系(*r/P*)

Table 4 Association of various indexes (*r/P*)

Index	H-FABP	IFN- γ	Hcy	Ang-1
H-FABP	-	0.567/0.023	0.601/0.011	-0.364/0.041
IFN- γ	-	-	0.456/0.032	-0.206/0.034
Hcy	-	-	-	-0.412/0.026
Ang-1	-	-	-	-

3 讨论

近年来,脑血管疾病已成为中老年者常见病及多发病,具有较高死亡率、发病率及致残率,不仅影响患者身体健康,而且给患者家庭及社会带来较大负担。脑梗死约占所有脑卒中的 70%,且发病率呈现上升趋势,直接影响患者的生活质量^[9,10]。因此,探讨急性脑梗死患者的发病机制及预防治疗手段尤为重要。当前,临床对脑梗死的病理生理过程等机制尚不明确。其诊断主要通过临床表现、影像学检查显示的梗死面积、梗死部位等,来判断脑梗死的严重程度^[11,12]。然而,脑梗死患者在发病的 24 小时内其 CT 上并无显著的影像学改变,在发病的 24 小时后期梗死区可能会出现低密度灶^[13,14]。因此,脑 CT 仅仅能排查脑出血,对于病情程度、梗死面积存在一定限制。已有学者指出:生物学指标在急性脑梗死患者诊断中有重要意义^[15,16]。

脂肪酸结合蛋白(FABP)存在机体多种组织细胞的胞浆中,承担着结合脂肪酸及调节细胞内代谢的功能的小分子蛋白质,根据组织特异性可分为心肌型 FABP(H-FABP)、小肠型 FABP(I-FABP)、脂肪细胞型 FABP(A-FABP)、脑细胞型 FABP(B-FABP)等^[17,18]。由于以上类型在结构上具有相似性,在功能上具有同源性。其中 H-FABP 是近年来临床学者所推出的心肌标志物^[19,20]。临床已有学者认为 H-FABP 可识别急性期急性脑梗死,尤其是胸痛发病 6 小时内的患者,在决定患者是否住院、冠状动脉造影上具有较大帮助,且在急性脑梗死患者发病早期可作为早期诊断心肌梗死者的有效标志物^[21-23]。本研究分析结果显示:研究组患者的 H-FABP 水平明显高于对照组,且重度急性脑梗死患者的 H-FABP 水平高于轻度、中度,表明检测 H-FABP 可在一定程度上反映急性脑梗死患者的病情程度,能够为其诊治提供重要的分子生物学证据,从而支持以上研究结果。

干扰素- γ (IFN- γ)是一种调节细胞功能的小分子多肽,来源于活化的自然杀伤细胞、T 辅助淋巴细胞 TH1 及 CD8 细胞毒细胞活化的 Tc1 亚型^[24,25]。可介导 T 细胞对巨噬细胞的激活,所激活的巨噬细胞可分泌细胞因子,促进 T 细胞的分化。此外 IFN- γ 有调节免疫活性的作用,也可促进抗原的加工与递呈,抑制 TH2 细胞增值,活化巨噬细胞,直接调节 B 细胞的发育与增值。临床已有学者^[26,27]通过研究发现急性脑梗死患者的 IFN- γ 水平明显高于健康者,且血管中 IFN- γ 的水平与血管内皮生长因子(VEGF)呈负相关,表明 IFN- γ 与急性脑梗死患者的病情有密切关系,且参与了急性脑梗死患者的炎症反应过程,本研究数据分析结果显示:研究组患者的 IFN- γ 水平明显高于对照组,且随着急性脑梗死患者病情的加重,IFN- γ 浓度增高,两者呈正相关,由此表明 IFN- γ 表达参与急性脑梗死患者大脑损伤后期反应中。

同型半胱氨酸(Hcy)是一种含硫氨基酸,是半胱氨酸及蛋氨酸的中间产物,以二硫化物的形式与机体的血浆蛋白结合,形成同型半胱氨酸聚体^[28,29]。Hcy 可导致机体内胆固醇及脂蛋白在血管壁内的沉积,也可通过促进机体前列腺素、血栓素的形成,进而影响凝血因子的活性。Hcy 水平的升高可加快动脉粥样硬化,形成动静脉血栓,诱发心脑血管疾病^[30]。此次数据调查显示研究组患者的 Hcy 水平高于对照组,且随着患者病情的加重,Hcy 浓度也随之而升高。能是由于 Hcy 结合脂蛋白形成复合物,该复合物被动脉壁吞噬细胞吞噬,形成泡沫细胞,分解后分泌胆固醇及脂肪,最终促进动脉粥样硬化,参与急性脑梗死患者疾病发展中。

血管生成素-1(Ang-1)属于血管生长素家族成员,可促进内皮细胞与细胞外基质、内皮细胞间的连接,有效维持新生血管正常功能,也可重塑新生血管,增加分支,促进其成熟。此外,Ang-1 也可促进内皮细胞间及内皮细胞与细胞外基质的连接,

维持新生血管的正常结构及其稳定性。已有学者通过动物实验表明^[6]：脑缺血患者的早期 Ang-1 水平呈现下降趋势，在缺血后的 72 小时则开始升高，且持续升高 2 周，可能参与到血管生成的晚期发展中，而此次研究发现研究组患者的 Ang-1 水平低于对照组，且随着疾病的发展，Ang-1 水平不断下降，表明 Ang-1 参与到急性脑梗死患者发病、疾病发展中，与上述研究结果一致。

综上所述，联合检测 H-FABP、IFN- γ 、Hcy、Ang-1 水平，利于急性脑梗死患者疾病的诊断，可为临床治疗与预后评估提供参考依据。

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(上接第 3332 页)

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