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舍曲林辅助治疗对抑郁症合并冠心病患者血清炎症因子水平及预后的影响

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摘要 目的:探讨舍曲林辅助治疗对抑郁症合并冠心病患者血清炎症因子水平及预后的影响。**方法:**选择 2009 年 8 月～2011 年 8 月我院收治的 86 例抑郁症合并冠心病患者,将其随机分入对照组与观察组,40 例对照组患者接受冠心病常规治疗,46 例观察组患者在常规治疗基础上给予舍曲林口服,每次 50～100 mg,每日 1 次,疗程 24 周。比较两组治疗期间心血管事件发生率、治疗前后汉密尔顿抑郁量表(HAMD)评分及血清炎症因子超敏 C- 反应蛋白(hs-CRP)、肿瘤坏死因子 -α(TNF-α)及白介素 -6(IL-6)的变化。**结果:**观察组心血管不良事件发生率显著低于对照组(13.0 % vs 32.5%,P<0.05);观察组治疗后 HAMD 评分、血清 hs-CRP、TNF-α 及 IL-6 水平显著均显著低于对照组(P<0.05)。**结论:**舍曲林辅助治疗可显著改善抑郁症合并冠心病患者的抑郁状态,降低炎症因子水平并改善其预后。

关键词:抑郁症;冠心病;舍曲林;预后;炎症因子

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Effect of Sertraline on the Prognosis and Serum Cytokines of Patients with Depressive Disorder Combined Coronary Heart Disease

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ABSTRACT Objective: To explore the effect of sertraline on the prognosis and serum cytokines of patients with depressive disorder combined coronary heart disease. **Methods:** 86 cases with depressive disorder combined coronary heart disease were randomly divided into the control group and observation group. 40 patients of the control group were given routine treatment and 46 cases in the observation group received sertraline (50～100mg, qd) oral based on routine treatment for 24 weeks. The incidence of cardiovascular events, HAMD and HAMA scores, serum hs-CRP, TNF-α and IL-6 levels were compared between two groups. **Results:** The incidence rate of cardiovascular events in the observation group was much lower than that in the control group (13.0 % vs 32.5%, P<0.05); the HAMD score after treatment in the observation group was less than that in the control group (P<0.05); compared with the control group, serum hs-CRP, TNF-α and IL-6 levels after treatment were greatly decreased (P<0.05). **Conclusion:** Adjuvant therapy by sertraline may greatly decrease the serum cytokines levels and improve the depressive status and prognosis of patients with depressive disorder combined coronary heart disease.

Key words: Depressive; Coronary heart disease; Sertraline; Prognosis; Cytokines

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前言

冠心病患者易出现抑郁、焦虑等不良情绪[1-3],伴有重度抑郁的冠心病患者病死率可升高 3 倍以上。近年来研究认为抑郁症的发生与细胞因子介导的免疫功能失调有关,舍曲林为第 3 代选择性 5- 羟色胺再摄取抑制剂, 目前已被广泛应用于临床抑郁症的治疗。本组研究旨在探讨舍曲林对抑郁症合并冠心病患者血清炎症因子水平及预后的影响,以期为临床合理治疗抑郁症合并冠心病提供更多的理论依据。

1 资料与方法

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1.1 临床资料

选择 2009 年 8 月～2011 年 8 月期间本院收治的 86 例抑郁症合并冠心病患者为研究对象,所有患者均行冠状动脉造影证实为冠心病,汉密尔顿抑郁量表(HAMD)评分≥ 8 分诊断为抑郁。其中男 50 例,女 36 例,年龄 38～79 岁,中位数年龄 56.9 岁。排除标准:①脑血管疾病所致精神障碍者;②严重肝肾功能不全;③自身免疫性疾病;④恶性肿瘤或近期手术者。将 86 例患者随机分入对照组与观察组,其中对照组 40 例,观察组 46 例,两组患者在年龄、性别及 HAMD 评分等临床资料方面差别无统计学意义(P>0.05),具有可比性。

1.2 治疗方法

对照组患者接受冠心病常规治疗, 给予抗血小板药物、β 受体阻滞剂、硝酸酯类、ACEI 及他汀类药物治疗。观察组在常规治疗基础上给予舍曲林口服,每次 50～100 mg,每日 1 次,

治疗 24 周。

1.3 评估指标

比较两组治疗期间心血管事件的发生率、治疗前后汉密尔顿抑郁量表 (HAMD) 评分及血清炎症因子超敏 C- 反应蛋白(hs-CRP)、肿瘤坏死因子 -α(TNF-α)及白介素 -6(IL-6)的差别。采用免疫比浊法检测血清 hs-CRP 水平,采用 ELISA 法检测 TNF-α 及 IL-6 水平。

1.4 统计学指标

采用 SPSS17.0 统计学软件进行数据分析,计量资料用表示,采用 t 检验,计数资料采用 X^2 检验,P<0.05 表示差异具有统计学意义。

2 结果

2.1 两组心血管不良事件发生率的比较

对照组 40 例患者中,7 例发生不稳定心绞痛,3 例发生急性心肌梗死,3 例行支架植入,心血管不良事件的发生率为 32.5%,而观察组 46 例患者中,4 例发生不稳定心绞痛,2 例行支架植入,心血管不良事件的发生率为 13.0%,显著低于对照组,差别具有统计学意义(P<0.05),见表 1。

表 1 两组心血管不良事件发生率比较【例(%)】

Table 1 Comparison of the incidence rate of cardiovascular events between two group cases[n(%)]

Groups	Cases	Sudden cardiac death	Unstable angina	Acute myocardial infarction	Stent implantation	Cardiovascular events
Control group	40	0	7(17.5)	3(7.5)	3(7.5)	13(32.5)
Observation group	46	0	4(8.7)	0	2(4.3)	6(13.0)△

注:与对照组相比,△P<0.05。

Note: Compared with the control group, △P<0.05.

表 2 两组治疗前后 HAMD 评分比较($\bar{x}\pm s$)

Table 2 Comparison of HAMD scores before and after treatment of the two groups($\bar{x}\pm s$)

Groups	Cases	Before treatment	12 week after treatment	24 week after treatment
Control group	40	20.87± 3.28	18.09± 3.18	15.38± 2.75#
Observation group	46	21.05± 3.56	14.87± 2.86△	9.26± 1.36△

注:组内治疗前后相比,#P<0.05; **与对照组相比,**△P<0.05。

Note: Comparison between and within groups #P<0.05; Compared with the control group △P<0.05.

2.2 两组治疗前后 HAMD 评分比较

治疗前,两组 HAMD 评分无显著差别(P>0.05);两组治疗后 HAMD 评分均有所降低,与治疗前相比差别均具有统计学意义(P<0.05);而治疗后 12 周和 24 周,观察组 HAMD 评分均显著低于对照组,差别具有统计学意义(P<0.05),见表 2。

表 3 两组治疗前后血清炎症因子水平比较

Table 3 Comparison of cytokines between two groups

Groups	Hs-CRP(mg/L)		TNF-α(pg/mL)		IL-6(pg/mL)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	13.76± 3.28	10.72± 2.73#	83.29± 12.56	69.63± 10.75#	62.78± 11.28	50.37± 8.95#
Observation group	13.58± 3.12	7.46± 2.17△	82.89± 12.19	48.37± 8.37△	63.08± 11.79	37.69± 6.82△

注:组内治疗前后相比,#P<0.05; **与对照组相比,**△P<0.05。

Note: Comparison between and within groups #P<0.05;Compared with the control group △P<0.05.

2.3 两组治疗前后血清炎症因子水平比较

治疗前,两组血清 hs-CRP、TNF-α 及 IL-6 水平比较均无显著性差异(P>0.05);治疗后 12 周,两组血清炎症因子均显著下降,与治疗前相比差别具有统计学意义(P<0.05),且观察组治疗后血清 hs-CRP、TNF-α 及 IL-6 水平显著低于对照组(P<0.05),见表 3。

3 讨论

抑郁症患者下丘脑垂体肾上腺皮质轴功能亢进,引起血液中儿茶酚胺异常升高、血管收缩,心血管功能失调,与冠心病的发病关系密切[4,5]。伴有抑郁症的心血管疾病患者非勺型血压昼夜节律常见,即夜间血压下降不明显[6-8],患者心脏负荷增加引起左室重塑,更易发生左心功能衰竭。舍曲林是治疗抑郁症的一线用药,是 5- 羟色胺再摄取抑制剂,通过选择性抑制 5- 羟色胺的再摄取,使突触间隙的 5- 羟色胺含量升高[9-11],可激动心脏 4 型受体,增强心脏的兴奋性和心肌收缩力,提高左室射血分数。抑郁症患者心率变异性增加,因而心血管事件的发生率增加[12,13]。传统的三环类抗抑郁药并不适合应用于冠心病患者,这是由于此类药物具有增快心率的不良反应,可能出现心律失常。舍曲林对冠心病心衰患者左室电机械重构不会产生不利影响,有利于减小左室舒张末期容积。舍曲林还通过抑制内皮细胞和血小板激活、延长出血时间等途径,减少心血管事件的发

生率。

本组结果显示:舍曲林治疗的抑郁症合并冠心病患者心血管不良事件发生率显著低于对照组，治疗后患者 HAMD 评分显著低于对照组,表明舍曲林可显著改善此类患者的抑郁状态和预后。

目前研究表明,炎症因子与抑郁症及冠心病的发生均密切相关,炎症因子可诱导下丘脑及垂体等部位的皮质激素受体功能发生改变,使负反馈功能受影响,导致下丘脑 - 垂体 - 肾上腺轴的长期激活,引起抑郁的发生。hs-CRP 是一种急时相蛋白,当机体出现炎症时其血清浓度显著升高,可以激活补体途径参与炎症反应[14,15]。TNF-α 可激活 T 细胞和 B 细胞,参与机体的体液和细胞免疫,使中枢神经递质的释放受到影响[16,17]。IL-6 和 TNF-α 可触发级联反应,通过启动炎症反应等途径,引起血清中其它炎症因子水平的显著升高[18-20]。而本研究结果提示舍曲林治疗的抑郁症合并冠心病患者血清 hs-CRP、TNF-α 及 IL-6 水平显著下降,且明显低于对照组,表明舍曲林可能通过降低炎症因子水平,调节免疫系统,发挥抗抑郁作用。

综上所述,舍曲林辅助治疗可显著改善抑郁症合并冠心病患者的抑郁状态并改善其预后,这可能与其降低患者血清炎症因子水平有关,具体机制尚有待于进一步的研究证实。

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