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纳络酮对脑梗塞患者血清降钙素原及叶酸水平及临床疗效的影响*

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摘要 目的:探讨纳络酮对脑梗塞患者血清降钙素原、叶酸水平及临床疗效的影响。**方法:**收集我院收治的 110 例急性脑梗死患者,随机分为实验组和对照组,每组 55 例。两组患者入院后根据实际情况给予抗血小板聚集,保护脑细胞,调控血压,脱水降低颅内压降颅压等对症治疗。对照组患者给予疏血通注射液 6 mL+0.9%氯化钠注射液 250 mL 静脉滴注,1 次/d;实验组患者在对照组基础上给予盐酸纳络酮注射液 3.2 g/d,+0.9%氯化钠注射液 250 mL 静脉滴注,治疗疗程为 14 d。观察并比较两组患者治疗前后血清降钙素原(PCT)、同型半胱氨酸(Hcy)、叶酸水平以及临床治疗有效率。**结果:**与治疗前相比,两组患者治疗后的血清 PCT、Hcy 水平均显著下降,叶酸水平均明显升高,差异均具有统计学意义($P<0.05$);与对照组相比,实验组患者的 PCT、Hcy 水平较低,差异具有统计学意义($P<0.05$);与对照组相比,实验组患者治疗后的血清叶酸水平、临床治疗有效率均较高,差异具有统计学意义($P<0.05$)。**结论:**纳络酮能够显著提高脑梗塞患者的临床疗效,可能与其减轻炎症反应,降血清 Hcy 水平,升高血清叶酸水平有关。

关键词:纳络酮;脑梗塞;降钙素原;叶酸;同型半胱氨酸

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Effect of Naloxone on the Serum Level of Calcitonin, Folic Acid and Clinical Efficacy of Patients with Cerebral Infarction*

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ABSTRACT Objective: To investigate the effect of naloxone on the serum calcitonin, folic acid levels and clinical effect of patients with cerebral infarction. **Methods:** 110 cases of acute cerebral infarction were randomly divided into the experimental group and control group, 55 cases in each group. The patients were given anti platelet aggregation, protection of brain cells, regulation of blood pressure, dehydration and reduction of intracranial pressure drop intracranial pressure and other symptomatic treatment after admission according to the actual situation. The Control group was treated with Shuxuetong injection 6 mL+0.9% chloride sodium injection 250 mL intravenous injection, 1 times/d; patients in the experimental group was given naloxone hydrochloride injection 3.2 g/d +0.9% chloride sodium injection 250 mL intravenous injection based on the control group, treatment lasted for 14 days. The serum calcitonin (PCT), homocysteine (Hcy), folic acid levels and the clinical treatment efficiency of two groups were observed and compared before and after the treatment. **Results:** Compared with before treatment, the serum PCT, Hcy levels of two groups were significantly decreased after treatment ($P<0.05$) the folate levels of two groups were significantly increased after treatment ($P<0.05$); compared with the control group, the PCT, Hcy levels were obviously lower of the patients in experimental group ($P<0.05$), while the serum folic acid level and clinical effective rate were higher of the patients in experimental group ($P<0.05$). **Conclusion:** Naloxone could significantly improve the clinical efficacy of patients with cerebral infarction, which might be related to the decrease of inflammatory reaction, serum Hcy and folic acid levels.

Key words: Naloxone; Cerebral infarction; Calcitonin; Folic acid; Homocysteine

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前言

脑卒中是一种常见的神经系统疾病,脑梗塞是脑卒中的主要类型之一,是目前临床最常见的脑血管病之一,致残率、致死率均较高^[1]。盐酸纳络酮(naloxonehydrochloride, NX)是阿片受

体拮抗剂,于上世纪六十年代起应用于临床^[2],对迟发性的神经元损伤具有较好的治疗作用,且具有较好的催醒作用^[3],对急性脑梗死患者的昏迷、失语等症状具有较好的改善作用,且能够明显减少血小板聚集、降低患者的血黏度,缩小患者的脑梗塞范围^[4,5]。本研究通过观察纳络酮对脑梗塞患者血清降钙素原、

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叶酸水平的变化,旨在探讨纳络酮对脑梗塞的治疗效果及可能机制,现将结果报道如下。

1 资料与方法

1.1 临床资料

收集 2014 年 12 月~2015 年 6 月于我院就诊或住院治疗的 110 例急性脑梗死患者,随机分为实验组和对照组,每组 55 例。实验组组内男性 33 例,女性 22 例,患者平均年龄(46.75±1.03)岁;对照组内男性 31 例,女性 24 例,患者平均年龄(47.59±0.93)岁。所有患者均符合中华医学会制定的《各类脑血管疾病诊断要点》中关于急性脑梗死的诊断标准,并经 CT、MRI 等影像学检查确诊。患者均符合急性脑梗死的诊断标准。所有入选对象年龄在 35~59 岁之间,性别不限;所有患者均心血管病以及肾功能不全;患者入院时脑梗死发病在 1 周至半年之内;患者无恶性肿瘤;患者神志清楚,无脑出血;所有患者对实验药物无过敏反应,所有患者均签署知情同意书同意进行实验措施。两组患者一般资料相比无明显统计学差异,具有可比性(P>0.05)。

1.2 方法

两组患者入院后根据实际情况给予抗血小板聚集,保护脑细胞,调控血压,脱水降低颅内压降颅压等对症治疗。对照组患者给予疏通灌注液(国药准字 Z20010100 牡丹江友搏药业股份有限公司)6 mL+0.9%氯化钠注射液 250 mL 静脉滴注,1 次/d;实验组患者在对照组基础上给予盐酸纳洛酮注射液(国药准字 H20059407 北京市永康药业有限公司)3.2 g/d,+0.9%氯化钠注射液 250 mL 静脉滴注,治疗疗程为 14 d。

1.3 检测指标

1.3.1 血清降钙素原(PCT)水平检测 所有患者治疗前后取外周静脉血 2 mL,采用电化学发光夹心法,检测血清降钙素原(PCT)水平。

1.3.2 血清血清同型半胱氨酸(Hcy)水平检测 所有患者于治疗前后采集外周静脉血 3 mL,采用荧光定量分析法,检测患者血清同型半胱氨酸(Hcy)水平。

1.3.3 血清叶酸水平检测 所有患者于治疗前后采集外周静脉血 3 mL,采用放射免疫法,应用全自动生化分析仪,对患者血清叶酸水平进行检测。

1.4 疗效评价

治疗后对患者的治疗效果进行判定:患者功能缺损的评分(NIHSS)减少在 90%以上为基本痊愈;患者 NIHSS 减少在 46%~90%之间为显著进步;患者 NIHSS 减少在 18%~45%之间为进步;患者 NIHSS 减少量低于 17% 为无效。

1.5 统计学分析

采用 SPSS 19.0 统计软件进行分析。计量数据采用 t 检验,以均数±标准差($\bar{x} \pm s$)表示;计数资料采用卡方检验,以%表示。所有数据比较,以 P<0.05 认为差异有统计学意义。

2 结果

2.1 两组患者治疗前后血清 PCT 水平比较

与治疗前相比,治疗后两组患者的血清 PCT 水平均下降(P<0.05),与对照组相比,实验组患者的血清 PCT 水平较低

(P<0.05),具体见表 1。

表 1 两组患者治疗前后 PCT 水平比较(ng/mL, $\bar{x} \pm s$)

Table 1 Comparison of the serum PCT level between two groups before and after treatment (ng/mL, $\bar{x} \pm s$)

	Before treatment	After treatment
Experimental group	15.94± 1.22	2.37± 0.78* [#]
Control group	16.32± 1.05	5.38± 0.99*

注:与治疗前相比,*P<0.05,与对照组相比,[#]P<0.05。

Note: Compared with before treatment, *P<0.05; Compared with the control group, [#]P<0.05.

2.2 两组患者治疗前后血清 Hcy 水平比较

治疗后,两组患者的血清 Hcy 水平与治疗前相比均下降(P<0.05),与对照组相比,实验组患者的血清 PCT 水平较低(P<0.05),具体见表 2。

表 2 两组患者治疗前后 Hcy 水平比较(μmol/L, $\bar{x} \pm s$)

Table 2 Comparison of the serum Hcy level between two groups before and after treatment (μmol/L, $\bar{x} \pm s$)

	Before treatment	After treatment
Experimental group	23.28± 3.27	10.73± 1.78* [#]
Control group	22.93± 2.69	16.93± 2.01*

注:与治疗前相比,*P<0.05,与对照组相比,[#]P<0.05。

Note: Compared with before treatment, *P<0.05; Compared with the control group, [#]P<0.05.

2.3 两组患者治疗前后血清叶酸水平比较

治疗后,两组患者的血清叶酸水平与治疗前相比均升高(P<0.05),与对照组相比,实验组患者的血清叶酸水平较高(P<0.05),具体见表 3。

表 3 两组患者治疗前后血清叶酸水平比较(nmol/L, $\bar{x} \pm s$)

Table 3 Comparison of the serum folic acid level between two groups before and after treatment (nmol/L, $\bar{x} \pm s$)

	Before treatment	After treatment
Experimental group	7.12± 1.03	16.73± 2.19* [#]
Control group	7.31± 1.68	10.48± 1.66*

注:与治疗前相比,*P<0.05,与对照组相比,[#]P<0.05。

Note: Compared with before treatment, *P<0.05; Compared with the control group, [#]P<0.05.

2.4 两组患者的临床疗效比较

与对照组相比,实验组患者治疗的总有效率较高(P<0.05),具体见表 4。

3 讨论

脑梗塞占全部卒中中类型的约 85%,其中近 10%的患者于急性期内死亡。急性脑梗塞又称为缺血性脑卒中^[6],病理过程较为复杂,大部分学者认为动脉硬化血栓形成是脑梗塞发病的主要原因^[7]。有研究表明脑梗塞的病理过程与炎症关系密切,炎症因子在脑梗塞病情的发展中起到了重要作用^[8]。炎症反应参与了患者体内的血小板活化、聚集过程,是脑梗塞血栓形成的主

要原因^[8]。脑梗塞起病时多伴有意识障碍、反射消失以及尿便障碍等症状,且在治疗期间极易并发一系列感染,加重病情,增加

了患者的死亡率^[15]。盐酸纳络酮除能够缩小脑梗死患者的脑梗塞范围外,对昏迷、失语等症状具有较好的改善作用。

表 4 两组患者的临床疗效比较(% , $\bar{x} \pm s$)

Table 4 Comparison of the clinical curative effect between two groups(% , $\bar{x} \pm s$)

	Recovered fundamentally	Significant progress	Progress	Invalid	Total effective rate
Experimental group	33(60.0)	14(25.45)	7(12.73)	1(1.82)	54(98.19)*
Control group	18(32.73)	19(34.55)	9(16.36)	9(16.36)	46(83.64)

注:与对照组相比,*P<0.05。

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

降钙素原(procalcitonin, PCT)是降钙素的前体糖蛋白,在生理状态下由甲状腺 C 细胞分泌产生,当机体发生炎症反应,早期降钙素原水平会异常升高^[10]。急性脑梗死发生时,患者 G 蛋白被激活,血小板发生聚集,导致血栓的形成^[11]。之前已有研究证实,降钙素原水平与急性脑梗塞病情严重程度相关^[12-14]。我们的实验结果表明:急性脑梗塞患者的血清降钙素原水平显著升高,治疗后降钙素原水平均下降,而与对照组相比,实验组患者的降钙素原水平较低。降钙素原近年研究用以监测患者的感染程度降钙素原由降钙蛋白、降钙素和 N 端残基片段组成,对于细菌感染的敏感度在 95%以上^[16]。因此检测脑梗塞患者的血清降钙素原水平对于了解患者的病情以及预后具有重要意义。

叶酸(Folic acid)是一种水溶性的 B 族维生素,是同型半胱氨酸(Homocysteine, Hcy)合成蛋氨酸的辅酶之一^[17]。既往研究结果显示^[18]叶酸水平与心脑血管疾病的关系较为密切。我们的实验结果表明:脑梗塞患者的血清叶酸水平较低,而同型半胱氨酸水平较高。当体内叶酸水平缺乏时,就会影响患者同型半胱氨酸的代谢,血浆中的同型半胱氨酸水平升高,产生氧自由基,损伤患者血管内皮,影响凝血因子,增加血小板的粘附性,加重患者病情。治疗后患者的叶酸水平均升高,同型半胱氨酸水平均下降,与对照组相比,实验组患者的叶酸水平较高,同型半胱氨酸水平较低。高半胱氨酸血症是引起各种脑血管疾病的危险因素之一。有研究表明^[19]叶酸与神经管发育有关,叶酸水平的升高促进了同型半胱氨酸的甲基化,降低了患者血浆中同型半胱氨酸水平,有效的加快了蛋白质的分解与合成反应,加速有害产物的代谢,使患者病情趋于康复,提高了患者的生存质量^[20]。

综上所述,纳络酮能够显著提高脑梗塞患者的临床疗效,可能与其减轻炎症反应,降低血清 Hcy 水平,升高血清叶酸水平有关。

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