doi: 10.13241/j.cnki.pmb.2019.24.028

注射用丹参多酚酸盐联合丙戊酸钠治疗脑卒中后癫痫患者的疗效分析 *

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摘要 目的：研究注射用丹参多酚酸盐联合丙戊酸钠对脑卒中后癫痫的临床疗效和安全性。**方法：**选择 2016 年 1 月～2019 年 4 月东南大学附属中大医院江北院区神经内科住院的 80 例脑卒中后癫痫患者，将其随机分为两组。对照组的 40 例患者仅给予丙戊酸钠治疗，观察组的 40 例患者给予丹参多酚酸盐联合丙戊酸钠治疗。比较两组治疗后的脑电图检查结果、癫痫症状控制情况。**结果：**治疗后，观察组总有效率为明显高于对照组(97.50 % vs. 80 %，P<0.05)；两组的累及导联数、痫样放电、发作持续时间、发作次数较治疗前以及血清神经元特异性烯醇化酶(Neuron specific enolase,NSE)水平均较治疗前明显降低(P<0.05)，且观察组以上指标均明显低于对照组(P<0.05)。两组的嗜睡、皮疹、头痛、感觉异常、恶心呕吐的发生率比较差异无明显统计学意义(P>0.05)。**结论：**注射用丹参多酚酸盐联合丙戊酸钠治疗脑卒中后癫痫的疗效明显优于单用丙戊酸钠治疗，其可更有效控制癫痫症状，且安全性较高。

关键词：注射用丹参多酚酸盐；丙戊酸钠；脑卒中后癫痫；疗效

中图分类号：R743；R742.1 **文献标识码：**A **文章编号：**1673-6273(2019)24-4723-04

Efficacy of Salvia Miltiorrhiza Polyphenolate Injection Combined with Sodium Valproate in the Treatment of Post-stroke Epilepsy*

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ABSTRACT Objective: To study the clinical efficacy and safety of salvia miltiorrhiza polyphenolate combined with sodium valproate for post-stroke epilepsy. **Methods:** Selected 80 patients with post-stroke epilepsy who were treated in Jiangbei Campus, Zhongda Hospital Affiliated to Southeast University from January 2016 to April 2019, divided into the two groups randomly. In the control group, 40 patients with post-stroke epilepsy were treated with sodium valproate alone, and 40 patients with post-stroke epilepsy in the observation group were treated with salvia miltiorrhiza polyphenolate and sodium valproate. Comparison of EEG findings and outcomes of epileptic symptoms after treatment in both groups. **Results:** After treatment, the total effective rate of the observation group was significantly higher than that of the control group (97.50 % vs. 80 %, P<0.05). The number of involved leads, epileptiform discharge, duration of seizures, number of seizures, and in serum neuron specific enolase (NSE) levelsin the two groups were significantly lower than those before treatment (P<0.05). And the above indicators in the observation group were significantly lower than the control group (P<0.05). There was no significant difference in the incidence of sleepiness, rash, headache, abnormal sensation and nausea and vomiting between the two groups (P>0.05). **Conclusion:** The treatment of Danshen polyphenolate combined with sodium valproate for injection is better than the treatment with sodium valproate alone, which can control epileptic symptoms more effectively and has higher safety.

Key words: Salvia Miltiorrhiza Polyphenolate For Injection; Sodium Valproate; Post-Stroke Epilepsy; Efficacy

Chinese Library Classification(CLC): R743; R742.1 Document code: A

Article ID: 1673-6273(2019)24-4723-04

前言

脑卒中会使患者的大脑出现局灶性的神经功能缺损，引发肢体偏瘫，吞咽、言语以及心理等多种功能障碍，对患者的日常生活能力和社会功能造成严重的影响[1-3]。脑卒中是危害中老年人身体健康的多发病及常见病，大约有 60 %~70 %的中风患者经抢救治疗后可恢复神志，但常常会伴有不同程度的后遗症[4,5]。有资料显示，大于 60 岁的癫痫患者中，脑卒中后癫痫有比较高的比例，大约占 40 %[6]。机体的神经系统一旦受到损伤，免疫系统极易处于活化状态，炎症细胞因子的分泌失去平衡，导致局部的神经组织出现异常性放电。脑卒中后癫痫可能会使神经功能及脑组织损伤程度加重，从而不利于其预后[7-9]。

目前，治疗脑卒中后癫痫的手段包含药物治疗、神经调控治疗和手术治疗，药物保守治疗是最为常用的治疗方式。虽然现阶段对于脑卒中后癫痫的治疗药物多种多样，但是并没有形成统一的治疗标准[10,11]。注射用丹参多酚酸能加速血液循环，抑

* 基金项目：江苏省青年科学基金项目(BK20180555)

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(收稿日期：2019-06-05 接受日期：2019-06-29)

制血小板聚集，且对血管硬化具有恢复效果，尚未见其治疗脑卒中后癫痫的报道。故本研究对注射用丹参多酚酸盐治疗脑卒中后癫痫的效果进行了分析，结果如下。

1 资料与方法

1.1 一般资料

选择 2016 年 1 月～2019 年 4 月东南大学附属中大医院江北院区神经内科住院的 80 例脑卒中后癫痫患者，均符合脑卒中以及癫痫的诊断标准。排除既往有脑外伤、癫痫史、严重感染、肿瘤以及颅脑手术所致的继发性癫痫者；原发性癫痫者；认知功能障碍者；合并神经功能缺陷或者脑肿瘤者；不能坚持随访者；对注射用丹参多酚酸盐、丙戊酸钠过敏者。采用抽签法将患者随机分为两组。观察组 40 例，男 20 例，女 20 例；年龄 54~79 岁，平均 (64.39± 7.25) 岁；病程 1~16 个月，平均 (4.97± 0.74) 个月；全身强直阵挛发作 20 例，单纯发作 16 例，混合性发作 2 例，复杂发作 2 例。对照组 40 例，男 20 例，女 20 例；年龄 55~79 岁，平均 (65.14± 8.39) 岁；病程 1~17 个月，平均 (4.85± 0.63) 个月；全身强直阵挛发作 22 例，单纯发作 14 例，混合性发作 3 例，复杂发作 1 例。两组的基线资料比较差异均无统计学意义(P>0.05)，具有可比性。

1.2 治疗方法

两组均采用降血脂、改善微循环、降血压、降低颅内压、保护脑神经和抗凝治疗。对照组：口服丙戊酸钠，剂量为 15～20 mg/(kg·d)，每天 3 次，连用 1 周后，如果症状没有得到控制，则将给药剂量增加至 20～30 mg/(kg·d)，每天 3 次；如果症状得到有效的控制，则维持此给药剂量，共治疗 6 个月。观察组：联合静脉滴注注射用丹参多酚酸盐，每次 100 mg，每天 1 次，共治疗 2 周。

1.3 观察指标

参考 Graham 等[12]判断治疗效果：① 完全控制：患者在治疗的过程中未发生癫痫；② 显效：患者在治疗的过程中发生癫痫的次数显著降低，与治疗前相比降低超过 50 %；③ 有效：患者在治疗的过程中发生癫痫的次数有所降低，与治疗前相比降低 25 %～50 %；④ 无效：患者在治疗的过程中发生癫痫的次数无改变。

治疗前后，采取 NATION9128W(20 导)数字脑电图仪检测患者的累及导联数以及痫样放电；记录癫痫发作持续时间以及癫痫发作次数；抽取 4 mL 肘静脉血，用 ELISA 法检测血清神经元特异性烯醇化酶(NSE)水平。

记录治疗期间嗜睡、皮疹、头痛、感觉异常、恶心呕吐等的发生情况。

1.4 统计学分析

采用 SPSS 22.0 软件进行统计学分析，计量资料以($\bar{x}$± s)表示，组间比较行 t 检验，计数资料以%表示，组间比较采用 x^2 检验，以 P<0.05 为差异有统计学意义。

2 结果

2.1 两组治疗后的临床效果比较

治疗后，观察组总有效率为明显高于对照组 (97.50 % vs. 80 %，P<0.05)，见表 1。

表 1 两组治疗后的效果比较[例(%)]

Table 1 Comparison of the effects between two groups after treatment [n(%)]

Groups	n	Complete control	Effective	Valid	Invalid	The total effect rate
Control group	40	8(20.00)	13(32.50)	11(27.50)	8(20.00)	32(80.00)
Observation group	40	12(30.00)	17(42.50)	10(25.00)	1(2.50)	39(97.50)*

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

2.2 两组治疗前后脑电图结果比较

两组治疗后累及导联数以及痫样放电较治疗前明显降低(P<0.05)，且观察组的累及导联数以及痫样放电明显低于对照组(P<0.05)，见表 2。

表 2 两组治疗前后脑电图结果的比较($\bar{x}$± s)

Table 2 Comparison of the EEG results between two groups before and after treatment($\bar{x}$± s)

Groups	n	Cumulative derivation /(180s)		Epileptiform discharges /(t/180s)	
		Before treatment	After treatment	Before treatment	After treatment
Control group	40	7.63± 1.14	6.27± 1.05*	14.97± 1.23	10.38± 1.19*
Observation group	40	7.65± 1.09	5.43± 0.97*#	15.12± 1.34	8.64± 0.87*#

Note: Compared with the control group, *P<0.05; compared with before treatment, #P<0.05, the same below.

2.3 两组治疗前后癫痫控制情况对比

两组治疗后的发作持续时间、发作次数较治疗前明显降低(P<0.05)，观察组的发作持续时间以及发作次数明显低于对照组(P<0.05)，见表 3。

2.4 两组治疗前后血清 NSE 水平对比

治疗后，两组的血清 NSE 水平较治疗前明显降低(P<0.05)，且观察组明显更低(P<0.05)，见表 4。

2.5 两组不良反应发生情况的比较

两组的嗜睡、皮疹、头痛、感觉异常、恶心呕吐发生率比较均无明显统计学差异(P>0.05)，见表 5。

3 讨论

脑卒中患者由于神经元受到损伤而导致细胞膜的稳定性降低，促进细胞内外离子和神经递质流出，显著增加神经细胞

表 3 两组治疗前后癫痫控制结果对比($\bar{x}\pm s$)

Table 3 Comparison of the control results of epilepsy between two groups before and after treatment($\bar{x}\pm s$)

Groups	n	Seizure duration(min/ number of times)		Episodes(number of times /year)	
		Before treatment	Aftert treatment	Before treatment	Aftert treatment
Control group	40	4.63± 0.31	3.17± 0.24*	2.65± 0.14	1.34± 0.11*
Observation group	40	4.62± 0.33	2.26± 0.25*	2.66± 0.13	0.89± 0.03*

表 4 两组治疗前后血清 NSE 水平对比($\bar{x}\pm s$, μg/L)

Table 4 Comparison of the serum NSE level between two groups before and after treatment ($\bar{x}\pm s$, μg/L)

Groups	n	Before treatment	After treatment
Control group	40	19.37± 2.45	14.65± 1.73*
Observation group	40	19.64± 2.83	10.13± 1.26*

表 5 两组不良反应发生情况的比较[例(%)]

Table 5 Comparison of the incidence of adverse reactions between the two groups [n(%)]

Groups	n	Drowsiness	Rash	Headache	Paresthesia	Nausea and vomiting	Total incidence rate
Control group	40	2(5.0)	2(5.0)	0(0.0)	1(2.5)	2(5.0)	7(17.5)
Observation group	40	2(5.0)	1(2.5)	1(2.5)	1(2.5)	1(2.5)	6(15.0)

的兴奋性,而且同步放电,诱导癫痫发作,进一步导致脑组织缺氧和缺血,神经元细胞发生坏死,上述病变又会促进癫痫再一次发作,从而形成恶性循环[13]。丙戊酸钠不但能有效改善全身强直痉挛发作以及失神发作,而且具有较好的抗癫痫效果,特别是对于全面性癫痫、良性中央颞区灶性痫发作以及局灶性癫痫发作均具有显著的效果[14-17],其能明显降低 γ- 氨基丁酸水平,降低神经元异常放电,促进神经突触间的传递,提高治疗效果[18-21]。丙戊酸钠能影响钠、钙离子通道,抑制神经元的持续性放电,并有效抑制丘脑皮质环路的构成[22,23]。

中医认为癫痫是由于"赤巴"、"培根"以及"隆"等能有效维持机体正常功能的"三因"丧失平衡后导致的病变[24]。丹参多酚酸具有化瘀通络和行气活血的功效,且其药物用量易控制、成分明确、疗效稳定、毒副作用较小[25,26]。丹参多酚酸具有抗血栓形成及抑制抗血小板聚集的作用,可以拮抗动脉粥样硬化,从而改善动脉粥样硬化所造成的血管硬化,促进血管功能的恢复。同时,丹参多酚酸能降低纤维蛋白原水平和血液黏度,加速血液循环,改善血液流变学,抑制红细胞沉降、聚集。丹参多酚酸可以通过抗缺氧以及抗氧化作用而对血管内皮和缺血心肌发挥保护效果[27]。丹参多酚酸可以有效减轻脑缺血损伤,通过明显抑制脂质过氧化反应,维持机体自由基清除以及生成之间的动态平衡,保护细胞膜,从而增强患者的抗氧化能力。本研究结果显示注射用丹参多酚酸盐联合丙戊酸钠对脑卒中后癫痫的疗效明显优于单用丙戊酸钠,而且可以明显降低累及导联数以及痫样放电明显降低,缩短发作持续时间,减少发作次数,证实了其临床疗效。

NSE 在机体细胞的糖代谢过程中具有重要的作用,有助于满足神经细胞的营养需求。当神经细胞受到损伤时,大量的 NSE 会从细胞内释放到机体的血液中,因而检测血清 NSE 含量可以有效评估神经细胞的受损程度[28-30]。一旦癫痫发作,谷氨酸会产生兴奋毒性效果,导致巨噬细胞释放出大量的自由基,对神经细胞造成破坏,促使 NSE 进入到血液循环中[31-33]。本研究中,两组治疗后的血清 NSE 水平均明显降低,且观察组明显更低,提示丙戊酸钠联合注射用丹参多酚酸盐的作用机制与清除自由基以及促进神经细胞修复相关。此外,两组的嗜睡、皮疹、头痛、感觉异常、恶心呕吐发生率无明显差异,表明注射用丹参多酚酸盐联合丙戊酸钠治疗的安全性。

综上所述,注射用丹参多酚酸盐联合丙戊酸钠治疗脑卒中后癫痫的疗效明显优于单用丙戊酸钠治疗,其可更有效控制癫痫症状,且安全性较高。

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