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甲泼尼龙琥珀酸钠对外伤性脑水肿患者血清 NO、ET、LPO 和 SOD 水平的影响 *

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摘要 目的：观察甲泼尼龙琥珀酸钠用于治疗外伤性脑水肿的疗效及对患者血清一氧化氮(NO)、内皮素(ET)、过氧化脂质(LPO)、超氧化物歧化酶(SOD)水平的影响。**方法**：选择我院 2014 年 11 月 ~2016 年 11 月收治的 104 例外伤性脑水肿患者，按治疗方式分为对照组与研究组，每组 52 例。对照组采用常规治疗，研究组在对照组基础上联合甲泼尼龙琥珀酸钠治疗，两组均持续治疗 7 天。观察并比较两组临床疗效，治疗前后血清 NO、ET、LPO、SOD 水平、脑水肿体积、神经功能缺损程度评分(NIHSS)、格拉斯哥昏迷评分(GCS)的变化及并发症的发生情况。**结果**：治疗后，研究组的治疗总有效率高于对照组(P<0.05)；两组血清 NO、SOD、GCS 水平均较治疗前显著上升，且研究组明显高于对照组；两组血清 ET、LPO、NIHSS、脑水肿体积均较治疗前明显降低，且研究组显著低于对照组，差异均有统计学意义(P<0.05)。两组并发症的发生情况比较差异无统计学意义(P>0.05)。**结论**：甲泼尼龙琥珀酸钠可显著提高外伤性脑水肿的临床疗效，可能与其能够有效调节血清 NO、ET、LPO、SOD 水平有关。

关键词：外伤性脑水肿；甲泼尼龙琥珀酸钠；疗效；一氧化氮；内皮素；过氧化脂质；超氧化物歧化酶
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Efficacy of Methylprednisolone Sodium Succinate in the Treatment of Traumatic Brain Edema and effects on the Serum NO, ET, LPO, SOD Levels*

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ABSTRACT Objective: To observe the efficacy of methylprednisolone sodium succinate in the treatment traumatic brain edema and effect on the serum nitric oxide (NO), endothelin (ET) and lipid peroxide (LPO) and superoxide dismutase (SOD) levels. **Methods:** 104 cases of patients with traumatic brain edema from November 2014 to November 2016 were divided into the control group and the research group according to the treatment mode, both groups were treated for seven days. The control group was treated with conventional treatment, and the research group was treated with methylprednisolone sodium succinate based on control group. The clinical curative effect, changes of serum NO, ET and LPO, SOD, cerebral edema volume, National Institutes of Health Stroke Scale (NIHSS) and Glasgow coma scale (GCS) before and after the treatment, and incidence of complications were observed and compared between two group. **Results:** The total effective rate of research group was higher than that of the control group (P<0.05). Before treatment, no significant difference was found in the serum NO, ET, LPO, SOD levels, cerebral edema volume, NIHSS, GCS NO between two groups (P>0.05). After treatment, the serum NO, SOD, GCS levels of both group were markedly higher than those of the control group, which were significantly higher in the research group than those of the control group, the serum ET and LPO, NIHSS, cerebral edema volume of both groups were significantly lower than those before treatment, which were significantly lower in the the research group than those of the control group (P<0.05). There was no statistically significant difference in the incidence of complications between the two groups (P>0.05). **Conclusion:** Prednisolone sodium succinate could effectively enhance the clinical efficacy of traumatic cerebral edema, which might be related to significant regulation of the serum levels of NO, ET, LPO, SOD.

Key words: Traumatic brain edema; Methylprednisolone sodium succinate; Curative effect; Nitric oxide. Endothelin; Peroxide; Superoxide dismutase
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前言

脑外伤为神经外科一种常见急症，主要是由外界暴力直接作用于头部所致，因损伤部位较为特殊，其致残率及病死率相对较高 [1,2]。临床试验证实脑外伤能够导致细胞膜代谢发生障碍，并引起血脑屏障受损，诱导液体于血管内出现渗出，并于脑

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细胞内外间隙集聚，造成脑水肿，是脑外伤的主要继发性损伤之一[3,4]。且有研究指出外伤性脑水肿能够使颅内压出现上升，降低脑血流量，引起脑疝等并发症，导致神经功能出现进一步损伤，甚者可导致死亡，对患者的预后造成较为显著的影响[5]。国外研究报道外伤性脑水肿多见于血管源性，其中多种细胞因子能够参与，一氧化氮（nitric oxide, NO）及内皮素（Endothelin, ET）是最新发现的一类血管活性物质，能够调节脑血流，二者动态平衡能够确保血管张力的正常[6,7]。同时，脑水肿进展期间氧自由基可发挥较为关键性的作用，过氧化脂质（Superoxide dismutase, SOD）活性较低可使氧自由基的清除能力下降，造成LPO浓度出现相应上升，加剧脑水肿[8]。外伤性脑水肿目前无特定疗法，甲泼尼龙琥珀酸钠能够对细胞膜起到稳定作用，从而防治脑水肿，并且能够发挥抗炎性，但临床关于其报道不一[9]。本研究旨在探讨甲泼尼龙琥珀酸钠对外伤性脑水肿患者血清NO、ET、LPO和SOD水平的影响。

1 资料与方法

1.1 一般资料

104例外伤性脑水肿患者入选标准[10]：脑部外伤史明确；经影像学检查提示脑水肿；损伤至就诊时间在12 h以内，并接受急诊手术治疗。将心、肝肾等主要器官显著病变；多发伤或者复合伤；恶性肿瘤者排除。对照组年龄22~67岁，平均(41.03± 7.45)岁；29例男，23例女；损伤类型：13例脑内血肿，12例硬膜下血肿，17硬膜外血肿，10例其他。研究组年龄20~66岁，平均(40.52± 7.89)岁；27例男，25例女；损伤类型：14例脑内血肿，13例硬膜下血肿，16硬膜外血肿，9例其他。两组一般临床特征比较差异均无统计学意义(P>0.05)，具有可比性。

1.2 方法

对照组予以常规治疗，均接受急性手术，术后进行止血、利尿等治疗。研究组基于对照组接受甲泼尼龙琥珀酸钠治疗，静脉滴注40 mg，tid。两组均持续治疗1周，于治疗结束时评估疗效，并统计两组并发症的发生情况。

1.3 观察指标

1.3.1 临床疗效观察 显效：临床体征及表现显著改善，脑水肿体积缩小超过30%；好转：临床体征及表现有一定缓解，脑水肿体积缩小在25%~30%；无效：临床体征及表现未见缓解，脑水肿体积缩小在25%以下。显效及好转均判定为总有效[11]。

1.3.2 指标测定 于治疗前及结束时抽取2 mL患者晨起静脉血，分离后保存待检。NO及ET按免疫比浊法进行，LPO按抗氧化活性法进行，SOD按黄嘌呤氧化酶法进行。

1.3.3 脑水肿体积测定 选取颅脑CT进行，参照多田氏公司[层数× 短径(cm)× 最大层面长径(cm)× π /6]计算水肿体积。

1.3.4 神经功能缺损程度评分 (NIHSS) 及格拉斯哥昏迷评分 (GCS) NIHSS分数在0~45分，神经功能损伤程度与分数越呈正相关。GCS：评估肢体运动、语言及睁眼3个方面，分数越低提示昏迷程度越重[12]。

1.4 统计学分析

选用SPPS18.0进行数据处理，计量资料用($\bar{x}$± s)表示，组间比较选用t检验，用[(例)%]表示计数资料，组间比较用x^2检验，以P<0.05为差异有统计学意义。

2 结果

2.1 两组临床疗效的比较

治疗后，研究组总有效率为92.3%，明显高于对照组(P<0.05)，见表1。

表1 两组临床疗效的比较[(例)%]

Table 1 Comparison the clinical curative effect between two groups[(n)%]

Groups	n	Effective	Improve	Invalid	Total effective rate
Control group	52	20(38.46)	20(38.46)	12(23.08)	40(76.92)
Research group	52	29(3.63)	19(2.38)	4(7.69)	48(92.30)[a]

Note: Compared with the control group [a]P<0.05.

2.2 两组治疗前后血清NO、ET、LPO、SOD水平的变化比较

两组治疗前血清NO、ET、LPO、SOD水平比较差异无统计学意义(P>0.05)；两组治疗后血清NO、SOD水平均较治疗前上升，且研究组上明显高于对照组；两组治疗后血清ET、LPO水平均较治疗前明显下降，且研究组显著低于对照组，组间差异统计学意义(P<0.05)，见表2。

表2 两组治疗前后血清NO、ET、LPO、SOD水平的比较($\bar{x}$± s)

Table 2 Comparison of the serum NO, ET, LPO, SOD levels between two groups before and after the treatment ($\bar{x}$± s)

Groups	n	Time	NO(μmol/L)	ET(ng/L)	LPO(nmol/L)	SOD(nmol/L)
Control group	52	Before treatment	41.09± 5.11	116.77± 14.56	14.29± 1.76	21.57± 2.69
		After treatment	69.11± 8.50[b]	93.02± 11.90[b]	11.56± 1.45[b]	25.40± 3.11[b]
Research group	52	Before treatment	41.56± 5.76	115.90± 15.20	13.42± 2.11	21.09± 2.90
		After treatment	83.14± 10.34[ab]	81.67± 10.23[ab]	9.79± 1.25[ab]	29.11± 3.65[ab]

Note: Compared with control group [a]P<0.05; Compared with before treatment [b]P<0.05.

2.3 两组治疗前后脑水肿体积的比较

两组治疗前脑水肿体积比较差异无统计学意义(P>0.05)；两组治疗后脑水肿体积均较治疗前明显减少，且研究组下降更明显，组间有统计学差异(P<0.05)，见表3。

表 3 两组治疗前后脑水肿体积的比较($\bar{x}\pm s$)

Table 3 Comparison of the brain edema volume between two groups before and after the treatment ($\bar{x}\pm s$)

Groups	n	Time	Brain edema volume(cm3)
Control group	52	Before treatment	24.79± 3.05
		After treatment	11.05± 1.37[b]
Research group	52	Before treatment	24.11± 3.79
		After treatment	5.20± 0.65[ab]

Note: Compared with control group [a]P<0.05; Compared with before treatment [b]P<0.05.

2.4 两组治疗前后 NIHSS 及 GCS 评分的比较

两组治疗前 NIHSS 及 GCS 评分比较差异无统计学意义(P>0.05);两组 NIHSS 治疗后均显著下降,且研究组下降幅度更显著,两组治疗后 GCS 评分均较治疗前明显上升,且研究组上升更明显(P<0.05),见表 4。

表 4 两组治疗前后 NIHSS 及 GCS 评分比较($\bar{x}\pm s$)

Table 4 Comparison of the NIHSS and GCS scores between two groups before and after the treatment ($\bar{x}\pm s$)

Groups	n	Time	NIHSS(point)	GCS(point)
Control group	52	Before treatment	20.65± 2.54	7.87± 0.98
		After treatment	14.20± 1.76[b]	12.53± 1.56[b]
Research group	52	Before treatment	20.98± 2.99	7.83± 0.90
		After treatment	11.56± 1.43[ab]	14.90± 1.87[ab]

Note: Compared with control group [a]P<0.05; Compared with before treatment [b]P<0.05.

2.5 两组并发症发生情况的比较

研究组并发症发生率为 11.54%，与对照组比较差异无统计学意义,见表 5。

表 5 两组并发症发生情况的比较[(例)%]

Table 5 Comparison of the complication between two groups[(n)%]

Groups	n	Lung infection	Gastrointestinal bleeding	Complication rate
Control group	52	3(5.77)	3(5.77)	6(11.54)
Research group	52	2(3.85)	3(5.77)	5(9.62)

3 讨论

外伤性脑水肿是临床常见继发性损伤,机体正常情况下脑组织含水量为相对平衡状态,多种内外源性等因素刺激能够导致脑组织的水平衡出现变化,增加细胞及组织的含水量,导致水肿[13]。相关研究指出脑外伤预后和受损组织周围水肿程度有着良好的相关性,尽早防治脑水肿是脑外伤临床治疗的关键[14]。

糖皮质激素是外伤性脑水肿的常用药物,其中氢化可的松和泼尼龙的血药浓度相对较低,效果较差[15]。甲泼尼龙琥珀酸钠的亲脂性及组织分布性较好，能够于短时间内发挥效果,且可透过血脑屏障,并对水钠作用几乎不产生影响。临床研究证实,甲泼尼龙琥珀酸钠能够诱导类固醇受体于短时间内快速上升,从而产生显著的消炎、抗感染效果,同时能够增强神经自我保护作用,恢复受损组织的局部微循环,加快血液循环,增加局部灌注,缓解脑水肿[16]。相关研究显示甲泼尼龙琥珀酸钠应用于外伤性脑水肿患者能够取得良好的临床效果,但具体作用机制并不明确。本研究结果也表明甲泼尼龙琥珀酸钠治疗可显著提高外伤性脑水肿的临床疗效。

外伤性脑水肿发生的主要诱因是微血管变化引起的灌注不足,ET 作为一种缩血管物质,生理浓度下能够确保血管的紧张性,脑水肿对周围组织形成压迫,从而引起神经细胞、内皮细胞等表达上调,诱导 ET 的过度生成[17]。ET 可使磷酶 A2 出现激活,诱导氨基酸、花生四烯酸等刺激物质的分泌,引起血管通透性增加,导致脑水肿;同时 ET 能够开放钙离子通道,导致细胞膜受到破坏,使脑水肿加剧[18]。同时,外伤性脑水肿能够使 NO 的合成出现障碍,NO 与 ET 是血管内皮功能的典型标志物,具有拮抗作用,机体正常状态下二者处于一个动态平衡,保持血管正常的张力，若 NO 含量降低诱导血管收缩产生痉挛,导致血管通透性发生增加,造成脑水肿加剧[19]。有研究报道,脑外伤能够诱导自由基的过度生成，导致血管内皮细胞出现损伤,加剧脑水肿[20]。LPO 是机体代表性的活性氧自由基,其浓度过量可引起脂质过氧化。SOD 是一种重要的抗氧化酶,能够使自由基清除,避免细胞损伤。本研究显示,两组治疗后 ET、LPO 均有下降,NO、SOD 均有上升，但甲泼尼龙琥珀酸钠治疗后变化更明显，说明其更有利于缓解受损脑组织缺氧缺血状态,缓解血管通透性，考虑与其能够使系列炎性因子的释放受到抑制,对细胞膜发挥保护作用,缓解脑部血供,并减轻局部的过氧化作用,从而缓解脑水肿有关[21,22]。本研究结果显示:甲泼尼龙琥珀酸钠治疗后脑水肿体积下降更明显,进一步提示其可利于脑水肿的吸收。同时,甲泼尼龙琥珀酸钠治疗后 NIHSS 及 GCS

评分改善更明显，提示其对神经功能可起到一定的保护作用，可能与其能够确保脑组织的血供，从而利于神经细胞发生有氧代谢有关[23]。但甲泼尼龙琥珀酸钠仍存在一定程度的副反应，本研究显示甲泼尼龙琥珀酸钠治疗期间有少数患者出现副反应，但与常规治疗组比较未见差异，说明其并未增加不良反应，易于患者耐受，安全性高[24]。但本研究由于纳入样本量较小，且观察时间较短，因此结果可能存在一定的偏差，有待于临床进一步考察。

综上，甲泼尼龙琥珀酸钠可显著提高外伤性脑水肿的临床疗效，可能与其能够有效调节血清 NO、ET、LPO、SOD 水平有关。

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