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肾上腺皮质激素在重型乙型脑炎中的作用

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摘要:目的 探讨地塞米松对乙型脑炎患儿的病情、预后及脑脊液 α -肿瘤坏死因子(TNF- α)与干扰素(IFN)的影响。方法 把33例重型极期乙脑患儿随机分为两组,地塞米松组18例给予静脉地塞米松针4~5d;对照组15例则不用地塞米松。观察比较两组的临床过程和脑脊液 TNF- α 与 IFN的变化。结果 入院时两组的主要临床特点和脑脊液 TNF- α 与 IFN的水平相似,4~5d后地塞米松组的临床症状改善情况优于对照组,但两组的脑脊液 TNF- α 与 IFN的水平却无明显改变,并经过一个月的观察地塞米松组的恢复期症状发生率也低于对照组。结论 对重型极期乙脑患儿给予静脉地塞米松可以改善病情,减轻症状,减少恢复期症状的发生。

关键词:乙脑;地塞米松;病情;预后;TNF- α ;IFN

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Effect of adrenal cortical hormone on the severe type of patients with epidemic encephalitis B in children

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ABSTRACT: To investigate the influence of adrenal cortical hormone on the patient's condition, prognosis and the levels of TNF- α and TNF- γ in cerebrospinal fluid in children with epidemic encephalitis B, 33 cases of severe type of patients with epidemic encephalitis B were divided into two groups randomly, i.e. dexamethasone-treated group (18) and the control group (15). In the treated group, patients were treated with intravenous injection of dexamethasone at a dosage of 8 mg/kg/day for 0.4~0.8 or 5 days, while in the control, no dexamethasone was given. The clinical courses and the changes on levels of TNF- α and IFN- γ in cerebrospinal fluid were compared between these two groups of patients. It was demonstrated that the clinical courses and the levels of cytokines in cerebrospinal fluid at time of admission appeared to be similar, however, the improvement of clinical course in the -treated group was better than those of the control group. As to the levels of cytokines in cerebrospinal fluid, there were no significant difference between these two groups. In addition, after one month observation, the rate of symptom development in the convalescence of the treated group was lower than that of the control group. From the above observations, it is evident that treatment with intravenous injection of dexamethasone in severe cases with epidemic encephalitis B can improve the clinical course, lessen the clinical symptoms and reduce the rate of development of symptoms in convalescence.

KEY WORDS: epidemic encephalitis B; dexamethasone; patient's condition; prognosis; tumor necrosis factor- α ; interferon

流行性乙型脑炎(epidemic encephalitis B,简称乙脑)由乙型脑炎病毒引起的以脑实质炎症为主要病变的人兽共患的急性传染病;重型患儿病死率仍在10%左右,并且多数发生在极期。由于乙脑没有特效的治疗方法,主要是积极对症治疗和护理。目前激素在乙脑中的作用仍有不同看法,Hoke等^[1]报道使用大剂量激素没有满意疗效;而何时军等^[2]报道大剂量激素能抑制颅内炎症反应水平,阻止病情恶化。因此激素的应用及其作用机制有待进一步探讨。

1 材料与方法

1.1 一般资料 33例重型乙脑患儿均来自2006年7-10月泸州医学院附属医院感染科住院病例。患儿血清乙脑特异性IgM抗体均阳性,符合乙脑诊断及分型标准^[3]。将33

例随机分为地塞米松组18例,男10例,女8例;对照组15例,男9例,女6例;年龄2~11岁。

1.2 方法 两组年龄、最高体温、GCS评分及脑脊液 TNF- α 与 IFN水平均具可比性,见表1。地塞米松组给予静脉地塞米松针0.4mg-0.8mg/(kg·d),2次/d×4~5d;对照组则不用地塞米松;其余治疗相同。停用地塞米松后比较两组最高体温、GCS评分及脑脊液 TNF- α 与 IFN水平;极期后经过1个月观察比较恢复期症状的发生率。TNF- α 与 IFN检测采用ELISA法,试剂盒购自深圳晶美生物工程有限公司,按说明书操作。

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1.3 统计学方法 采用 SPSS 14.0 软件包进行统计学分析, 计量资料用 t 检验, 计数资料用 χ^2 检验。

2 结果

经治后, 地塞米松组的最高体温明显低于对照组, GCS

评分则明显高于对照组, 均有统计学意义, 地塞米松组恢复期症状发生率要低于对照组, 但无统计学意义, 两组的脑脊液 TNF- α 与 IFN 的水平却无明显改变, 无统计学意义, 见表 2.3。

表 1 入院时两组患儿的年龄、最高体温、GCS 评分及脑脊液 TNF- α 与 IFN 比较 ($\bar{x} \pm s$)

Table 1 Comparison of age, temperature, score of Glasgow, the level of TNF- α and IFN in cerebrospinal fluid on admission between 2 groups ($\bar{x} \pm s$)

组别	年龄(岁)	最高体温(°C)	GCS 评分(分)	TNF- α (ng/l)	IFN (ng/l)
地塞米松组	5.78 ± 1.87	40.26 ± 0.52	4.11 ± 1.02	123.61 ± 10.42	132.33 ± 14.79
对照组	5.73 ± 2.03	40.20 ± 0.65	4.27 ± 1.03	119.93 ± 10.30	129.60 ± 14.44
t	0.065	0.298	0.433	1.015	0.534
P	0.948 > 0.05	0.768 > 0.05	0.668 > 0.05	0.318 > 0.05	0.597 > 0.05

表 2 应用地塞米松与否最高体温、GCS 评分及脑脊液 TNF- α 与 IFN 比较 ($\bar{x} \pm s$)

Table 2 Comparison of temperature, score of Glasgow, the level of TNF- α and IFN in cerebrospinal fluid after treatment with Dexamethasone between 2 groups ($\bar{x} \pm s$)

组别	最高体温(°C)	GCS 评分(分)	TNF- α (ng/l)	IFN (ng/l)
地塞米松组	37.97 ± 0.89	5.39 ± 1.46	117.17 ± 12.28	132.72 ± 11.25
对照组	38.84 ± 0.92	4.40 ± 0.99	125.93 ± 18.30	135.20 ± 13.79
t	2.739	2.230	1.639	0.569
P	0.010 < 0.05	0.033 < 0.05	0.111 > 0.05	0.574 > 0.05

表 3 两组恢复期症状发生率的比较 [% (发生数/治疗数)]

Table 3 Comparison of incidence rate of symptom in convalescent period between 2 groups [% (n/N)]

组别	中枢性低热	神经功能紊乱	肢体瘫痪	癫痫样发作
地塞米松组	27.78% (5/18)	66.67% (12/18)	33.33% (6/18)	22.22% (4/18)
对照组	53.33% (8/15)	73.33% (11/15)	60% (9/15)	26.67% (4/15)
χ^2	2.238	0.172	2.347	0.088
P	0.135 > 0.05	0.678 > 0.05	0.126 > 0.05	0.767 > 0.05

3 讨论

乙脑的病情、预后同脑实质的损害程度直接相关, 目前认为通过免疫病理反应引起脑实质的损害是本病重要的发病机制之一, 而细胞因子与宿主的免疫反应密切相关, 因此调节乙脑患儿的免疫状态, 提高机体的免疫保护作用而又尽量抑制免疫病理损伤是有效的治疗途径之一。

TNF- α 是由激活的单核巨噬细胞产生和分泌, 其次星型胶质细胞、小胶质细胞及激活的 T 细胞也可产生。它是一种具有多种生物学活性的细胞因子, 能直接损伤血管内皮细胞, 增加血管通透性, 并诱导内皮细胞表达粘附分子, 刺激星型细胞分泌白细胞介素, 因而可以加重炎症反应和脑实质的损害。许多报道在中枢神经系统感染疾病中均可见 TNF- α 和 TNF 非特异性的明显增高^[4-6]。乙脑病毒可以激发单核细胞及星型细胞产生大量 TNF^[3], 提示 TNF- α 参与了乙脑的免疫病理过程。IFN 是由病毒或其他 IFN 诱生剂刺激机体产生的一种特殊糖蛋白, 它不仅通过作用于细胞产生抗病毒蛋白酶而进入抗病毒状态, 还有各种生物活性, 如

抑制细胞增殖、抗体产生及迟发性变态反应, 提高细胞抗原提呈能力, 活化多种免疫细胞, 在急性病毒感染初期起着重要作用。本文结果也显示重型乙脑患儿的脑脊液中 TNF- α 与 IFN 水平也明显增高, 同时也说明了乙脑患儿颅内局部的免疫病理反应在乙脑的发病过程中起了重要的作用。

肾上腺皮质激素具有抗炎、抗毒素、抗过敏和免疫抑制等作用。不少文献报道了应用肾上腺皮质激素治疗细菌性脑膜炎, 它可减少死亡率和各种神经系统后遗症的发生^[7-9]。但 Van 等^[10]报道在发展中国家的儿童急性细菌性脑膜炎中使用激素却没有获得有益的效果; Simmons 等^[11]报道了地塞米松在治疗结核性脑膜炎中所起的作用与抑制外周和局部的免疫反应无关。本文结果显示肾上腺皮质激素能有效控制病情, 并可减少部分恢复期症状的发生, 病程中也没有发现明显的激素副作用; 同时我们也发现激素治疗后两组的脑脊液 TNF- α 与 IFN 水平也相似, 故推测其作用与抑制颅内局部的免疫反应关系不大, 其它的机制可能更重要: 1. 退热作用: 糖皮质激素能降低体温调节中枢对内源性和外源性

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致热原的敏感性而使体温下降;2. 改善微循环,增强机体对缺氧的耐受性等;3. 通过降低毛细血管的通透性,改善血脑屏障并维持其完整性,减少脑脊液的产生,增加肾脏的血流量和肾小球滤过率等降低颅内压。激素在乙脑中所起的作用有待进一步探讨。

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