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Changes of P3 potentials after intervention to GABAR subtypes in CA1 region in rabbits

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Abstract Objective: To explore the mechanism for the effects of GABAAR and GABABR on P3 potentials in CA1 region. Methods: P3 potentials at Pz site were recorded in 10 healthy rabbits. After the catheter was implanted, either Bicuculline, a selective antagonist to GABAAR, or Baclofen, an agonist to GABABR, was microinfused into the CA1 region to observe the effects of intervention of GABA subtypes on P3 potentials. Results: P3 amplitude was markedly decreased by Bicuculline in a dose-dependent manner (3, 6, 12 μmol/L) and P3 latency was increased by Baclofen in the same manner (6.25, 12.5, 25 mmol/L). The blocking effects of Bicuculline (12 μmol/L) or Baclofen (25 mmol/L) on P3 potentials could be reversed by microinfusion of GABA (100 mmol/L), but the latency was prolonged. Conclusion: GABAAR inhibitory postsynaptic potential in the CA1 region might be one important component of P3b amplitude and GABAR action can prolong P3b latency through reducing capacity of neurons to form P3b potential.

Key words P3; CA1; GABAR; Bicuculline; Baclofen; rabbit

锌剂对 Wilson氏病患者临床表现和影像学改变的影响

The effects of $ZnSO_4$ on the clinical features and image changes in patients with Wilson's disease

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Wilson病患者长期用硫酸锌治疗后,临床症状和颅脑影像学异常信号获得明显改善,现报告如下。

1 临床资料

1.1 一般资料

患者 5例,均为男性,年龄 18~33岁,病程 2个月至 3年。临床及辅助检查均符合 Wilson氏病诊断。除例 1外,余 4例颅脑 CT均示程度不等的基底节、丘脑低密度影和脑萎缩。例 5又行 MRI检查,示基底节、丘脑、中脑、桥脑和小脑齿状核在 T_1 加权有片状低信号,边缘不清, T_2 加权呈高信号。该例确诊前被误诊为精神分裂症 3年。5例临床症状都很典型。

1.2 治疗结果

5例均予 2%硫酸锌液 15 ml, 3/日 (例 5最初联合服青霉胺 3.0 g/日)。15~30 d后, 5例病情都明显减轻。继续治疗一个月,例 1恢复学习,例 2能生活自理,例 3和例 4均可下床活动,例 5仍有明显肌张力增高和构音障碍。坚持治疗半年后,例 2和例 3亦恢复原工作,例 4仍有轻度构音障碍,能承担小商品销售工作,例 5尚留有轻度肌张力增高和构音障碍,能胜任收发室工作。1年后裂隙灯检查,例 4和例 5原角膜 K-F环颜色变浅,宽度变窄。余 3例原有的 K-F环消退,例 2和例 3复查了颅脑 CT,原双侧基底节和丘脑低密影明显减轻、缩小,例 5MRI复查,原基底节和丘脑的异常信号区明显吸收、缩小,脑干和小脑齿状核在 T_1 加权未见明显异常信号, T_2 加权仅隐约见稍高信号的点、片状影。脑电图复查例 1,由原轻度异常转为正常范围,余 4例均由原中-重度异常转为轻度异常脑电图。5例患者的血清铜和尿铜较治疗前明显改变 (铜蓝蛋白仍低)。随访 2~5年,病情稳定,无加重、恶化。

2 讨论

Wilson氏病系一种常染色体隐性遗传的铜代谢障碍疾病,但又是少数能有效对症治疗的遗传病之一。近年的研究和临床实践证明锌剂 (硫酸锌、醋酸锌、甘草锌等)是治疗 Wilson病安全有效的药物[1,2]。其作用机制有① 锌能竞争性地抑制铜在肠道吸收,使粪铜排出增加。② 锌能通过诱导肠和肝细胞合成金属硫蛋白 (Metallothionein),后者与铜亲和力高,使大部分铜呈

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Effects of recombinant human tumor necrosis factor-α on hypertrophic scars transplanted to nude mice

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Abstract **Objective**: To investigate the effects of recombinant human tumor necrosis factor-α (rhuTNF-α) on the collagen content in and histomorphology of postburn hypertrophic scar tissues. **Methods**: Twelve nude mice with human postburn hypertrophic scar tissues (2 cm × 2 cm) transplanted on to their back and survived were randomized into the experimental group (EG) and the control group (CG). For animals in EG, 0.1 ml (500 g/ml) rhuTNF-α dissolved in normal saline was injected into the hypertrophic scar tissues for 3 times a week. For those in CG, only normal saline was injected in the same manner. The contents of collagen, hydroxyproline and acidic mucopolysaccharide in and the histomorphological changes of the hypertrophic scar tissues were determined 3 weeks later. **Results**: As compared with CG, in EG the contents of collagen, hydroxyproline and acidic mucopolysaccride were significantly decreased. After the injection of rhuTNF-α, the hypertrophic scar tissues became flatter and smaller. Collagenous nodules in hypertrophic scar tissues drastically decreased or disappeared. The number of rough endoplasmic reticulum in fibroblasts was markedly reduced and no dilatation was seen. **Conclusion**: rhuTNF-α can remarkably reduce collagen deposition in hypertrophic scar tissues, which suggests that rhuTNF-α may be of potential value in treating hypertrophic scars.

Key words tumor necrosis factor-α; hypertrophic scar; therapy; nude mouse

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非毒性结合状态或随肠粘膜细胞脱落而排出体外。③ 锌剂对肝和脑中过量的铜尚有解毒作用。④ 锌剂诱导肠、肝细胞产生的金属硫蛋白是一种潜在的羟自由基清除剂。锌剂副作用小,仅见少数病人餐前服发生恶心、呕吐和腹泻。

我们坚持用硫酸锌治疗 5例 Wilson病患者,不仅临床症状和异常生化指标明显改善,而且能消除患者的颅脑影像学异常信号和 K-F环,这和 Huang等[3]报告一致。有报道用青霉胺治疗 Wilson病,3个月内用药者几乎全部缓解,2年后用药者效果差[4]。本组有 4例病程超过 3个月,其中例 4,2年 5个月。例 5,3年。例 2亦有 1年余。但坚持长期服硫酸锌,使病程长、病情危重者的临床症状和颅脑影像学等异常征象均获戏剧性改善;随访 2~5年无复发恶化。表明硫酸锌不仅能干预铜的异常代谢,而且可能逐渐驱除体内多年积蓄的铜,但亦有人认为口服锌剂不能阻止肝铜蓄积或反而使症状恶化[5]。我们推测可能与剂量或其它因素有关;另外肝铜增加可能是由于锌剂诱导肝细胞内金属硫蛋白合成,后者结合多量铜呈无毒性状态存在于肝细胞中,以后才随机体负铜平衡的建立,肝中积蓄铜才逐渐降低。

值得注意的是由于 Wilson氏病患者出生后即开始铜代谢障碍,铜渐进性沉积于脑、肝、角膜等器官,若延误诊断、病程延长,短期内不可能将多年沉积的铜驱出,即存在疗效与药物时间剂量关系。可见 Wilson氏病治疗成功的关键有 3点,首先尽早确诊,坚持长期治疗。其次尽早检出症状前患者,用锌剂长期预防性治疗。另外应避免停药,终生忌食高铜饮食。

关键词　肝豆状核变性;硫酸锌

中图法分类号　R742.4

参考文献

1 Bona I, Broussolle E, Neuschwander P, *et al*. Treatment of Wilson's disease with zinc. 5 cases. Rev Neurol Paris, 1993, 149(6~7): 393

2 陈　嵘,梁秀龄,刘焯霖,等.锌孵育对肝豆状核变性离体培养细胞内铜、锌和金属硫蛋白代谢的影响.中国神经精神疾病杂志, 1996, 22(1): 13

3 Huang C C, Chu N S. Wilson's disease: resolution of MRI lesions following long-term oral zinc therapy. Acta Neurol scand, 1996; 93(2): 215

4 陈芷若,赵翕平,张贞浏.肝豆状核变性的早期诊断和治疗.中华神经精神科杂志, 1985; 18(4): 226

5 李乃忠,姚　莉,吕传真,等.青霉胺及锌剂治疗肝豆状核变性的疗效.临床神经科学, 1996; 4(2): 99

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