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口服普萘洛尔对婴幼儿血管瘤MMP-2、MMP-9、TIMP-1、TIMP-2表达水平的影响(PDF)

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Title: Effect of propranolol on expression of MMP-2, MMP-9, TIMP-1 and TIMP-2 in infantile hemangioma

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摘要: 目的 研究口服普萘洛尔前后婴幼儿血管瘤病灶内MMP-2、MMP-9、TIMP-1、TIMP-2表达水平的影响。方法 选择2010年5月至2011年12月来我院就诊、年龄≤3个月、血管瘤病灶位于肢体或隐蔽部位、家属要求手术治疗却具备单独口服普萘洛尔治疗条件、排除口服普萘洛尔禁忌证、先前未接受过其他任何相关治疗的病例作为研究对象,共39例。经过与家属沟通并征得其书面同意,先按口服普萘洛尔诊疗常规,口服用药前在局麻下夹取血管瘤体组织活检,后口服8周普萘洛尔[剂量: 2 mg/(kg·d),分2次,每12小时用药],继而手术切除瘤体。采用免疫组化、实时荧光定量RT-PCR的方法,检测口服用药前后病灶组织内MMP-2、MMP-9、TIMP-1、TIMP-2表达水平的变化,计算口服用药前后病灶微血管密度(MVD)。结果 免疫组化与实时荧光定量RT-PCR结果均提示,口服普萘洛尔后血管瘤病灶内MVD值明显减低且具有统计学意义($t=18.458, P<0.01$),MMP-2、MMP-9表达水平较用药前明显减少($P<0.01$),TIMP-1、TIMP-2表达水平明显增高($P<0.01$)。且口服用药后上述4个因子免疫组化平均积分光密度、mRNA相对表达量变化与MVD值变化密切相关。结论 普萘洛尔可下调血管瘤病灶内MMP-2、MMP-9的表达,上调TIMP-1、TIMP-2的表达,从而抑制新生血管的形成。

Abstract: Objective To investigate the effect of propranolol on the expression of

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matrix metalloproteinase 2 (MMP-2), matrix metalloproteinase 9 (MMP-9), tissue inhibitor of metalloproteinase 1 (TIMP-1) and tissue inhibitor of metalloproteinase 2 (TIMP-2) in infantile hemangioma. **Methods** Thirty-nine patients (age \leq 3 months) with proliferative phase of hemangioma in our hospital from May, 2010 to December, 2010 were enrolled. The patients were treated with propranolol for 8 weeks after hemangioma biopsy, and then underwent surgery for hemangioma resection. The mRNA and protein expression levels of MMP-2, MMP-9, TIMP-1 and TIMP-2 in hemangioma tissues were examined by quantitative real-time RT-PCR and immunohistochemical method, respectively, and the microvessel density (MVD) was calculated before and after propranolol treatment. **Results** The MVD in the hemangioma tissues decreased significantly after propranolol treatment ($P<0.01$). The protein and mRNA expressions of MMP-2 and MMP-9 decreased significantly ($P<0.01$), but the protein and mRNA expressions of TIMP-1 and TIMP-2 increased significantly after propranolol treatment ($P<0.01$). The changes of MVD were closely correlated with the protein and mRNA expression levels of MMP-2, MMP-9, TIMP-1 and TIMP-2. **Conclusion** Propranolol can reduce proliferative hemangioma through down-regulating MMP-2 and MMP-9 expression and up-regulating TIMP-1 and TIMP-2 expression.

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