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论著

疡愈涂剂对糖尿病大鼠创面Ⅰ、Ⅲ胶原合成及MMPs、TIMP-1表达的影响

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摘要 目的：观察疡愈涂剂促进糖尿病迟缓愈合伤口的修复作用及其分子机制。 方法： 实验分为对照组、模型组、疡愈涂剂高、中、低剂量组。除对照组外，大鼠腹腔注射链脲佐菌素(STZ)55 mg/kg，造成实验性高血糖。30 d后，各组动物复合背部全厚皮切除直径为1.6 cm的伤口。分别观察疡愈涂剂对创面愈合时间、愈合率的影响；天狼星红染色法以及免疫组化法观察Ⅰ、Ⅲ型胶原含量及Ⅰ、Ⅲ型胶原比值，并观察金属蛋白酶-1、-13(MMP-1、-13)、金属蛋白酶抑制剂-1(TIMP-1)水平及MMP-1、-13 与TIMP-1比值。 结果： 疡愈涂剂各剂量组创面愈合时间明显短于模型组(P<0.01)，愈合率明显高于模型组(P<0.01,P<0.05)。在伤口用药的第3、7、11 d，高、中剂量组创面Ⅰ型胶原含量以及Ⅰ、Ⅲ型胶原比值显著高于模型组(P<0.01)。在伤口用药第3 d疡愈涂剂中剂量、第7、11 d各剂量组创面Ⅲ型胶原显著高于模型组(P<0.01)。各剂量组在第7 d创面MMP-1、-13均高于模型组(P<0.01,P<0.05)，而MMP-1 在第11 d与模型组趋于一致且MMP-13明显低于模型组(P<0.01,P<0.05)。各剂量组在3、7、11 d创面TIMP-1均明显高于模型组(P<0.01,P<0.05)，在第11 d各剂量组MMP-1、TIMP-1比值明显低于模型组(P<0.01)，在第3、7 d高、中剂量组创面MMP-13、TIMP-1比值高于模型组(P<0.01)，而到第11 d高、中、低各剂量组均明显低于模型组(P<0.01)；第11 d高、中剂量组MMP-13、TIMP-1比值低于低剂量组(P<0.05)。 结论： 疡愈涂剂可能通过调节影响胶原代谢的MMPs、TIMPs表达平衡，促进胶原的合成和沉积，从而加速创面的愈合。

关键词 胶原Ⅰ型； 胶原Ⅲ型； 基质金属蛋白酶； 糖尿病； 金属蛋白酶1组织抑制剂

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Effect of Yangyu Tuji on content of type Ⅰ, Ⅲ collagen and the expression of MMPs and TIMP-1 in wound caused by streptozotocin in rats

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Abstract

<FONT face=Verdana>AIM: To study the effects of Yangyu Tuji (YYTJ) on delayed healing wound of diabetic rats caused by streptozotocin (STZ). METHODS: SD male rats were randomly divided into control group (control), model group (model); and 3 different dose groups of YYTJ. 55 mg/kg STZ were given by intraperitoneal injection except for control group. After 30 days, a round skin of 1.6 cm diametre was excised on all dorsal back of rats. The healing time and healing rate were observed according to re-epithelization. The content of collagen Ⅰ and Ⅲ was observed by Picric acid-Sirius red staining , Matrix metalloproteinase-1, 13 (MMP-1, -13), tissue inhibitor of metalloproteinases-1 (TIMP-1) by immuno-histochemistry assay. All data were analyzed by IPP software. RESULTS: The healing time in each group treated with YYTJ was shorter than that in model group (P<0.01), and the healing rate was increased (P<0.01, P<0.05). Content of type I collagen, ratio of type Ⅰ and Ⅲ collagen of high and mid dose group were significantly higher than that in model group (P<0.01) at 3rd, 7th, 11th day. The expression of MMP-1, -13 of each groups were higher than that in model group at 7th day (P<0.01, P<0.05), and MMP-1 trend to equal with model group at 11th day. MMP-13 was significantly lower than that in model group at 11th day (P<0.01, P<0.05). TIMP-1 of each group of wound was higher than that in model group at 3rd, 7th, 11th day (P<0.01, P<0.05). The ratio of type Ⅰ and Ⅲ collagens in each group was lower than that in model group

at 11th day (P<0.01). Ratio of MMP-13 and TIMP-1 of high dose group and mid dose group were higher than that in model group at 3rd and 7th day (P<0.01). The ratio of each group was lower than that in model group at 11th day (P<0.01). Meanwhile, ratio of MMP-13 and TIMP-1 of high dose group and mid dose group were lower than that of lower dose group (P<0.05). CONCLUSION: It is possible that YYTJ accelerates wound healing by increasing collagen content of type Ⅰ and Ⅲ, especially type Ⅰ, as well as improves collagen deposition by regulating the balance of MMP and TIMP.</FONT>

Key words Collagen type Ⅰ Collagen type Ⅲ Matrix metalloproteinases Diabetes mellitus Tissue inhibitor of metalloproteinases-1

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