膝痹宁Ⅱ方经JAK2/STAT3通路缓解KOA大鼠滑膜炎症及纤维化的机制研究Δ

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摘　要　目的　基于Janus激酶2(JAK2)/信号转导及转录激活因子3(STAT3)通路,探讨膝痹宁Ⅱ方缓解膝骨关节炎(KOA)大鼠滑膜炎症及纤维化的作用机制。**方法**　将75只雄性SD大鼠随机分为假手术组(Sham组)、KOA组、膝痹宁Ⅱ低剂量组(XBNⅡ-L组,4 g/kg)、高剂量组(XBNⅡ-H组,8 g/kg)、膝痹宁Ⅱ高剂量联合STAT3激活剂Colivelin三氟乙酸盐(C-TFA)组[C-TFA组,8 g/kg膝痹宁Ⅱ+1.0 mg/(kg·d) C-TFA],每组15只。除Sham组外,其余各组采用前交叉韧带离断法建立KOA模型。造模成功后,各药物组分别给予相应药物灌胃和(或)腹腔注射,每日1次,持续28 d。末次给药后,评估各组大鼠膝关节滑膜组织病理改变并进行指标计算;检测血清炎症因子水平,检测膝关节滑膜组织中磷酸化JAK2(p-JAK2)、磷酸化STAT3(p-STAT3)蛋白阳性表达,滑膜组织JAK2/STAT3通路相关蛋白及mRNA表达。**结果**　与Sham组相比,KOA组大鼠滑膜衬里细胞显著增生且排列紊乱,Krenn评分,纤维化占比,p-JAK2、p-STAT3阳性面积百分比,p-JAK2/JAK2、p-STAT3/STAT3和Ⅰ型胶原蛋白、α-平滑肌肌动蛋白的表达水平,JAK2、STAT3、Ⅰ型胶原蛋白、α-平滑肌肌动蛋白mRNA的表达水平,以及血清白细胞介素1β、白细胞介素18水平均显著升高($P<0.05$)。与KOA组相比,XBNⅡ-L组、XBNⅡ-H组大鼠上述病理改变明显改善,各指标均显著下降($P<0.05$),且XBNⅡ-H组的改善效果显著优于XBNⅡ-L组($P<0.05$)。与XBNⅡ-H组相比,C-TFA组上述病理损伤加重,各指标均显著恶化($P<0.05$)。**结论**　膝痹宁Ⅱ方可减轻KOA大鼠滑膜炎症与纤维化,其机制可能与抑制JAK2/STAT3通路激活有关。

关键词　膝痹宁Ⅱ方;膝骨关节炎;滑膜纤维化;滑膜炎症;JAK2/STAT3通路

Mechanism study of Xibining Ⅱ formula in alleviating synovial inflammation and fibrosis in KOA rats via JAK2/STAT3 pathway

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ABSTRACT　OBJECTIVE To investigate the mechanism of Xibining Ⅱ formula in alleviating synovial inflammation and fibrosis in knee osteoarthritis (KOA) rats based on Janus kinase 2 (JAK2)/signal transducer and activator of transcription 3 (STAT3) pathway. **METHODS** Seventy-five male SD rats were randomly divided into sham operation group (Sham group), KOA group, Xibining Ⅱ low-dose group (XBNⅡ-L group, 4 g/kg), Xibining Ⅱ high-dose group (XBNⅡ-H group, 8 g/kg), and Xibining Ⅱ high-dose combined with STAT3 activator Colivelin trifluoroacetate (C-TFA) group [C-TFA group, 8 g/kg Xibining Ⅱ+1.0 mg/(kg·d) C-TFA], with 15 rats in each group. Except for the Sham group, the KOA model was established by anterior cruciate ligament transection in the other groups. After successful modeling, each group was given corresponding drugs by intragastric administration and (or) intraperitoneal injection once daily for 28 consecutive days. After the last medication, the pathological changes of synovial tissue of knee joint in each group were evaluated and the indicators were calculated. The levels of serum inflammatory factors were detected. The positive expressions of phosphorylated JAK2 (p-JAK2) and phosphorylated STAT3 (p-STAT3) in synovial tissue of the knee joint were detected. The expressions of JAK2/STAT3 pathway-related proteins and mRNAs in synovial tissue were detected. **RESULTS** Compared with the Sham group, the synovial lining cells in the KOA group showed significant proliferation and disordered arrangement; the Krenn score, fibrosis ratio, positive area percentage of p-JAK2 and p-STAT3, p-JAK2/JAK2 and p-STAT3/STAT3, protein expression of Collagen-Ⅰ and α-smooth

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