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论著

芍药苷对胶原诱导型关节炎大鼠下丘脑-垂体-肾上腺轴的影响

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摘要 目的 探讨芍药苷治疗胶原诱导型关节炎(CIA)是否与调节下丘脑-垂体-肾上腺(HPA)轴有关。方法 Wistar大鼠右足趾皮内注射牛Ⅱ型胶原(CⅡ)和弗氏完全佐剂制备CIA大鼠模型, 7 d后大鼠背部和尾根部皮下注射CⅡ加强免疫1次。初次免疫后第14天ig给予地塞米松2 mg·kg^{-1}或芍药苷25, 50和100 mg·kg^{-1}, 每天1次, 连续28 d。初次免疫后第14, 21, 28, 35和42天观察CIA大鼠的足爪肿胀度和关节炎指数的变化。给药结束后第2天大鼠摘眼球取血, 放射免疫法检测血浆促肾上腺皮质激素释放激素(CRH) 、促肾上腺皮质激素(ACTH)和皮质酮(CS)含量;制备血清, 用ELISA法检测白细胞介素4(IL-4)、干扰素γ(IFN-γ)、IL-1β、肿瘤坏死因子α(TNF-α)和抗CⅡ 抗体含量。结果 与正常对照组相比, 模型对照组大鼠关节红肿, 关节炎指数升高(P<0.01), 血中CRH、CS、抗CⅡ抗体、IFN-γ、IL-1β和TNF-α水平明显升高(P<0.01), IL-4水平下降(P<0.01), ACTH无明显改变。ig给予芍药苷50和100 mg·kg^{-1}可抑制CIA大鼠关节肿胀, 降低关节炎指数(P<0.05), 在第42天关节炎指数由模型对照组的6.4±0.7降至5.6±0.5和5.4±0.7(P<0.05);使模型对照组血清IFN-γ由(21.3±2.5)ng·L^{-1}降至16.6±1.3和(16.1±1.9)ng·L^{-1}(P<0.01), IL-1β由(37.3±4.2)ng·L^{-1}降至32.1±2.9和(31.2±4.1)ng·L^{-1}(P<0.01), TNF-α由(53.9±7.9)ng·L^{-1}降至39.4±6.8和(31.3±6.1)ng·L^{-1}(P<0.01), 抗CⅡ抗体由(2.13±0.32)ng·L^{-1}降至1.35±0.58和(1.10±0.42)ng·L^{-1}(P<0.01), IL-4由(26.6±3.0)ng·L^{-1}升至41.9±3.1和(49.1±4.2)ng·L^{-1}(P<0.01);能使血浆CRH的水平由模型对照组的(2.3±0.5)μg·L^{-1}升高至4.9±1.0和(5.3±1.1)μg·L^{-1}(P<0.01), CS由(33±10)μg·L^{-1}升高至47±9和(51±13)μg·L^{-1}(P<0.01), ACTH水平亦有明显升高(P<0.01)。结论 芍药苷治疗CIA可能与调节PHA轴有关。

关键词 芍药苷 胶原Ⅱ型 关节炎 下丘脑-垂体系统

分类号 R285

扩展功能

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Effect of paeoniflorin on hypothalamic-pituitary-adrenal axis of rats with collagen-induced arthritis

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Abstract

OBJECTIVE To study whether paeoniflorin's effectiveness in treating rheumatoid arthritis is associated with regulating hypothalamic-pituitary-adrenal (HPA) axis in rats with collagen-induced arthritis (CIA). **METHODS** CIA was induced in Wistar rats by an intradermal injection of bovine type Ⅱ collagen(CⅡ) emulsified with complete adjuvant. Seven days later, the rats were repetitively immunized by this emulsion. From the 14th day after primary immunization, the CIA rats were intragastrically administered paeoniflorin 25, 50 and 100 mg·kg^{-1} or dexamethasone 2 mg·kg^{-1}, once a day, for 28 consecutive days. On the 14th, 21st, 28th, 35th and 42nd days after primary immunization, the toe and ankle swelling and the arthritis index(AI) of each rat were observed. After administration, the rat blood was taken by removing the eyeball. The concentration of corticotropin-releasing hormone (CRH), adrenocorticotropic hormone (ACTH) and corticosterone (CS) in plasma was measured by radioimmunoassay. The level of interleukin-4(IL-4), interferon-γ(IFN-γ), IL-1β, tumor necrosis factor-α(TNF-α) and anti-CⅡ antibody in serum was determined by ELISA. **RESULTS** Compared with normal control rats, the level of IFN-γ, IL-1β, TNF-α, CRH, CS and anti-CⅡ antibody in the peripheral blood and AI of CIA rats increased while IL-4 decreased(P<0.01), and ATCH had no significant change. Paeoniflorin was able to inhibit the toe and ankle swelling and reduce AI of CIA rats. In paeoniflorin 50 and 100 mg·kg^{-1} groups, AI on the 42nd day was reduced from 6.4±0.7 in model group to 5.6±0.5 and 5.4±0.7 respectively(P<0.05), the level of IFN-γ in serum was reduced from (21.3±2.5)ng·L^{-1} to 16.6±1.3 and (16.1±1.9)ng·L^{-1}(P<0.01), IL-1β from (37.3±4.2)ng·L^{-1} to 32.1±2.9 and (31.2±4.1)ng·L^{-1}(P<0.01), TNF-α from (53.9±7.9)ng·L^{-1} to 39.4±6.8 and (31.3±6.1)ng·L^{-1}(P<0.01), and anti-CⅡ

antibody from (2.13±0.32)ng • L^{-1} to 1.35±0.58 and (1.10±0.42)ng • L^{-1}(P<0.01), while the level of IL-4 was increased from (26.6±3.0)ng • L^{-1} to 41.9±3.1 and(49.1±4.2)ng • L^{-1}(P<0.01). The content of CRH in plasma was increased from (2.3±0.5)μg • L^{-1} in model group to (4.9±1.0)μg • L^{-1} for paeoniflorin 50 mg • kg^{-1} and (5.3±1.1)μg • L^{-1} for paeoniflorin 100 mg • kg^{-1}(P<0.01), CS was increased from(33±10)μg • L^{-1} to 47±9 and (51±13)μg • L^{-1}(P<0.01), and ACTH was also elevated(P<0.01). **CONCLUSION** The treatment of CIA with paeoniflorin may be related to its regulation of the HPA axis.

Key words paeoniflorin collagen type Ⅱ arthritis hypothalamic-hypophyseal system

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