

论著

三氧化二砷对MRL/lpr小鼠免疫功能和肾脏组织病理变化的影响

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摘要 目的 研究三氧化二砷(As₂O₃)对MRL/lpr小鼠免疫功能和肾脏组织病理变化的影响。方法 45只MRL/lpr狼疮小鼠ip给予环磷酰胺50 mg·kg⁻¹(每周1次)和As₂O₃ 0.8 mg·kg⁻¹,每天1次,共2个月。用ELISA法检测血清抗双链DNA(dsDNA)抗体、干扰素γ(IFN-γ)和白细胞介素12(IL-12)浓度;用流式细胞术测定脾CD3⁺, CD19⁺, CD3⁺CD4⁺和CD3⁺CD8⁺细胞亚群的百分比;用PAS染色法观察肾组织病理变化;用免疫荧光方法检测肾组织IgG和补体C3的表达。结果 与给药前比较,给药2个月后,正常对照组血清抗dsDNA抗体水平升高,由给药前1.18±0.26升高至1.80±0.26(P<0.01),As₂O₃和环磷酰胺组该抗体水平明显降低,分别由给药前1.14±0.58和1.09±0.22[JP]降低至0.92±0.06和0.67±0.14(P<0.05, P<0.01)。与正常对照组比较:1 As₂O₃和环磷酰胺组血清抗ds-DNA抗体、IFN-γ和IL-12浓度明显降低(P<0.05),环磷酰胺组抗ds-DNA抗体比As₂O₃组显著降低(P<0.01);2 As₂O₃组CD3⁺, CD3⁺CD4⁺和CD19⁺细胞百分率明显降低(P<0.01),环磷酰胺组CD3⁺, CD3⁺CD8⁺和CD19⁺细胞百分率明显降低(P<0.01);As₂O₃组CD3⁺CD4⁺细胞百分率明显降低(P<0.01);3 As₂O₃和环磷酰胺组小鼠肾小球细胞计数和活动度积分明显降低(P<0.05, P<0.01),As₂O₃和环磷酰胺组无显著差异;4 As₂O₃和环磷酰胺组肾IgG表达明显降低(P<0.05),补体C₃表达无明显差异,As₂O₃和环磷酰胺组之间无显著性差异。结论 As₂O₃能降低MRL/lpr狼疮小鼠血清抗ds-DNA抗体水平,抑制T、B和Th细胞活化和增殖,降低血清IFN-γ和IL-12水平,从而缓解狼疮肾炎的病理变化。

关键词 三氧化二砷 红斑狼疮, 系统性 抗体, 抗核 细胞因子类 小鼠, 近交MRL Lpr

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Effect of arsenic trioxide on immune function and renal histopathological changes in MRL/lpr mice

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Abstract

OBJECTIVE To investigate the effect of arsenic trioxide (As₂O₃) on immune function and renal pathology in MRL/lpr mice. **METHODS** Forty-five MRL/lpr mice were divided into control, As₂O₃ 0.8 mg·kg⁻¹(ip, once a day) and cyclophosphamide 50 mg·kg⁻¹(ip, once a week) groups. After continuously administration for 2 months, the serum level of anti-double stranded-DNA(dsDNA) autoantibody, interferon-γ(IFN-γ) and interleukin-12(IL-12)of mice was measured with ELISA. The

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subsets of the spleen lymphocytes were detected with flow cytometry. The kidney was removed for periodic acid Schiff dyeing. The expression of IgG and complement C₃ in the nephridial tissue was observed by immunofluorescence assay. **RESULTS** Two months after therapy, compared with that of before treatment, the anti-dsDNA antibody level in normal control group increased from 1.18 ± 0.26 to 1.80 ± 0.26 ($P < 0.01$), while it significantly decreased from 1.14 ± 0.58 to 0.92 ± 0.06 in As₂O₃ group and from 1.09 ± 0.22 to 0.67 ± 0.14 in cyclophosphamide group, respectively ($P < 0.05$, $P < 0.01$). Compared with normal control group: 1 the serum levels of the anti-dsDNA antibody, IFN- γ and IL-12 in As₂O₃ and cyclophosphamide groups were lower than those of normal control group ($P < 0.05$, $P < 0.01$), and the anti-dsDNA antibody level was much lower in cyclophosphamide group than As₂O₃ group ($P < 0.01$); 2 percentage of CD3⁺, CD19⁺ and CD3⁺CD4⁺ cells in As₂O₃ group was lower than normal control group ($P < 0.01$), the percentage of CD3⁺, CD3⁺CD8⁺ and CD19⁺ cells in cyclophosphamide group was much lower than normal control group ($P < 0.01$), CD3⁺CD4⁺ cells in As₂O₃ group were fewer than cyclophosphamide group ($P < 0.01$); 3 the glomerulus cell count per glomerular cross-sections and the integral of activity in As₂O₃ and cyclophosphamide groups were less