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rmh TNF协同顺铂抗小鼠Lewis肺癌血管生成的作用 点此下载全文

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摘要：

目的: 观察重组改构人肿瘤坏死因子（recombinant mutant human tumor necrosis factor，rmh TNF）协同顺铂（cisplatin，又称DDP）抗小鼠Lewis肺癌血管生成的作用。方法: 建立C57BL/6小鼠Lewis肺癌模型，随机分为4个治疗组：生理盐水对照组、rmh TNF（150万U/kg）组、DDP（6.15 mg/kg）组、联合用药组（DDP+ rmh TNF）。接种肿瘤细胞后12 d开始瘤内注射药物3 d，RT PCR法测定瘤组织中HIF 1α的表达，免疫组化法检测肿瘤组织血管内皮生长因子（vascular endothelial growth factor，VEGF）、激酶结构域受体（kinase domain region receptor，KDR）、微血管密度（microvascular density receptor，MVD）的表达，流式细胞术测定基质金属蛋白酶2（matrix metalloproteinase 2， MMP 2）的表达。〖HT5W〗结果: 〖HT5"SS〗对照组、rmh TNF组、DDP组和联合用药组小鼠肿瘤组织中的MVD数分别为（24.76±1.28）、（18.95±1.22）、（19.53±1.15）、（10.43±1.05）,两单药组的MVD数明显低于对照组（P<0.05）；联合用药组低于两单药组（P<0.05）。 HIF—1α mRNA相对表达水平分别为（0.171±0.004）、（0.138±0.006）、（0.134±0.006）、（0.095±0.006）,两单药组较对照组明显下降（P<0.05），联合用药组明显低于两单药组（ P< 0.05）。肿瘤组织中MMP 2蛋白的荧光指数FI值依次为（1.000±0.000）、（0.875±0.020）、（0.848±0.127）、（0.545±0.107），单药组的MMP 2蛋白的(FI)值较对照组明显下降（P<0.05），联合用药组明显低于两单药组（P<0.05）。单药组VEGF、KDR表达均明显低于对照组（P<0.05），联合用药组的表达均低于各单药组（ P< 0.05）。结论: rmh TNF能够增强DDP抗小鼠Lewis肺癌血管生成的作用。

关键词：重组改构人肿瘤坏死因子 顺铂 Lewis肺癌 抗血管生成 协同作用

Recombinant mutant human tumor necrosis factor enhances anti angiogenesis effect of cisplatin on Lewis lung carcinoma in mice Download Fulltext

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Abstract:

Abstract Objective: To observe the role of rmh TNF in enhancing the anti angiogenesis effect of cisplatin on Lewis lung carcinoma in the mice. Methods: Lewis lung carcinoma model was established in C57BL/6 mice. Sixty model mice were randomly divided into 4 groups: control group, rmh TNF group（1 500 000 U/kg）, cisplatin group（6.15 mg/kg）, and rmh TNF plus cisplatin group. Twelve days after implantation of cancer cells, different drugs were injected intra tumorally for 3 d. The expression of hypoxia inducible factor 1α(HIF 1α) gene in the tumor was identified by RT PCR. Immunohistochemistry (IHC) image analysis was performed to determine the vascular endothelial growth factor (VEGF) and kinase domain region receptor (KDR) expression and the microvessel density(MVD). Expression of matrix metalloproteinase 2(MMP 2) was detected by flow cytometry. 〖WTHZ〗Results: 〖WTBZ〗The MVD values in the control group, the rmh TNF group, the DDP group and the combination group were（24.76±1.28）, （18.95±1.22）, （19.53±1.15）, （10.43±1 05）, respectively , with those of the rmh TNF and DDP groups significantly lower than that of the control group and higher than that of the combination group (all P<0.05）. The relative levels of HIF-1α mRNA in the control group, rmh TNF group, DDP group and the combination group were （0.171±0.004）, （0.138±0.006）, （0.134±0 006）, （0.095±0.006）, respectively, with the levels in the single drug groups significantly lower than that in the control group（P<0.05）and higher than that of the combination group (P<0.05). The relative levels of MMP 2 in the control group, rmh TNF group, DDP group and combination group were （1.000±0 000）, （0.875±0.020）, （0.848±0.127）, and （0.545±0.107）, respectively, with those of the single drug groups significantly lower than that of the control group and higher than that of the combination group (respectively P<0.05）. VEGF, KDR expression levels in the single drug groups were significantly higher than that in the combination group and lower than that in the control group (P<0.05). Conclusion: rmh TNF can enhance the anti angiogenesis effect of DDP on Lewis lung cancer in mice and improve their immunological function.

Keywords:recombinant mutant human tumor necrosis factor cisplatin Lewis lung carcinoma synergism anti agniogenesis

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