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论著

甲氧基聚乙二醇-聚乳酸胶束载体对丝裂霉素的抑瘤活性及局部组织损伤的影响

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摘要 目的 探讨甲氧基聚乙二醇 聚乳酸（mPEG-PLA）胶束是否可以提高丝裂霉素（MMC）的抗肿瘤活性及降低MMC的局部组织损伤作用。方法 采用腹腔种植方法分别制备昆明小鼠肉瘤180（S180）实体瘤模型及H22肝癌腹水瘤模型，每个模型小鼠均分为模型组（生理盐水0.1 ml·kg^{-1}）， mPEG-PLA组，MCC 1 mg·kg^{-1}组，胶束MMC 2，6 和18 mg·kg^{-1}组。分别观察S180实体瘤的抑瘤率及H22腹水瘤的生命延长率。BALB/C小鼠分别右后肢im给予生理盐水组（正常对照），mPEG-PLA，胶束MMC 0.02，0.04，0.08，0.1，0.16，0.2和0.4 mg·kg^{-1}组，MMC 0.02，0.04，0.08，0.1，0.16，0.2和0.4 mg·kg^{-1}组，观察小鼠局部组织损伤情况。结果 在S180实体瘤模型上，mPEG-PLA无肿瘤抑制作用；MMC 1 mg·kg^{-1}的肿瘤抑制率为34.8%，胶束MMC 2，6和18 mg·kg^{-1}的肿瘤抑制率分别为31.23%，51.8%，66.8%，胶束MMC 6和18 mg·kg^{-1}的肿瘤抑制率明显高于MMC组（P<0.01）。在H22腹水癌模型上，mPEG-PLA对肿瘤小鼠的生命延长率无影响；MMC 1 mg·kg^{-1}的生命延长率为123.4%，胶束MMC 2，6和18 mg·kg^{-1}的生命延长率分别为76.6%，171.0%和206.5%，胶束MMC 2 mg·kg^{-1}组生命延长率显著低于MMC组（P<0.01），但高于模型组（P<0.01），胶束MMC 6和18 mg·kg^{-1}的生命延长率明显好于MMC组（P<0.05）。在组织损伤模型上，胶束MMC组损伤发生时间和损伤面积明显低于相同剂量的MMC组（P<0.05）。结论 mPEG-PLA胶束能够提高MMC体内抗肿瘤作用，降低MMC的毒性作用。

关键词 丝裂霉素 肉瘤S180 H22腹水瘤 化学修饰 药物毒性 聚乙二醇 聚乳酸

分类号 R979.1，R969

Effect of mitomycin modified with methoxy polyethylene glycol-polylactic acid on tumor inhibition and tissue injury of rats

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Abstract

OBJECTIVE To explore whether methoxy polyethylene glycol-polylactic acid (mPEG-PLA) could affect the anti-cancer effect of mitomycin (MMC) in vivo and reduce the tissue injury. **METHODS** This experiment had two parts: a sarcoma 180 (S180) mice model to observe the tumor weight and tumor inhibition rate as well as an H22 ascitic tumor model to observe survival time and life elongation rate. Mice were divided into the model group, MMC 1 mg·kg^{-1} group, mPEG-PLA-MMC 2, 6 and 18 mg·kg^{-1} group and mPEG- PLA group. BALB/C mice were used in the tissue injury experment. The mice were divided into the normal control group, MMC 0.02, 0.04, 0.08, 0.10, 0.16, 0.20 and 0.40 mg·kg^{-1} group, mPEG-PLA-MMC 0.02, 0.04, 0.08, 0.10, 0.16, 0.20, and 0.40 mg·kg^{-1} groups and mPEG-PLA group. **RESULTS** mPEG-PLA had no anti-cancer effect on tumor weight, tumor inhibition rate and survival time in the two model groups. The tumor inhibition rate of mPEG-PLA-MMC 2, 6 and 18 mg·kg^{-1} was 31.23%, 51.78% and 66.80%, respectively while in MMC 1 mg·kg^{-1} group it was 34.78%. The tumor inhibition rate of mPEG-PLA-MMC 6 and 18 mg·kg^{-1} was significantly increased compared with MMC 1 mg·kg^{-1} (P<0.01). Ascetic tumor H22 results indicated that mPEG-PLA-MMC could lengthen the life of tumor-bearing mice *in vivo*. The life-elongation rates of mPEG-PLA-MMC 2, 6 and 18 mg·kg^{-1} were 76.6%, 171.0% and 206.5%, respectively while the life-elongation rate in MMC 1 mg·kg^{-1} group was 123.4%. Compared with MMC, the life-elongation rate in mPEG-PLA-MMC 2 mg·kg^{-1} was shortened（P<0.01）, but higher than in model group(P<0.01). The life-elongation rates of mPEG-PLA-MMC 6 and 18 mg·kg^{-1} were significantly increased (P＜0.05). Tissue injury showed that there was significant difference between mPEG-PLA-MMC groups and MMC groups (P<0.05, P<0.01). **CONCLUSION** mPEG-PLA could remarkably reinforce the anti-cancer effect of MMC *in vivo* and significantly reduce the tissue injury.

Key words mitomycin sarcoma 180 H22 chemical modification drug toxicity polyethylene glycol-polylactic acid

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