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论著

# 多种药物联合应用对小鼠顺铂肾毒性的拮抗作用

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摘要 目的 探讨硫酸锌（Zn）、亚硒酸钠(Se)、磷霉素钠(Fos)、乙酰半胱氨酸（NAC）、硫代硫酸钠（STS）、蛋氨酸(Met)和牛磺酸(Tau)等对顺铂肾毒性的联合拮抗作用。方法 采用7因素（7个药物）2水平（给药或不给药）的正交设计，共8个实验组。各组小鼠ig给予不同组合的拮抗药物，每日1次，连续9 d。从第3天起，ig给予拮抗药后6 h，ip顺铂3.5 mg·kg$^{-1}$，连续5 d，分别于给予顺铂前和实验结束前测量小鼠体重。给药结束次日，摘小鼠眼球取血，然后处死。快速取肾组织，并分别测定血清尿素氮（BUN）、肾还原型谷胱甘肽（GSH）含量及谷胱甘肽过氧化物酶（GSH-Px）活性。结果 Zn, Fos和Met可显著改善顺铂引起的体重减轻；Fos和Met可显著降低顺铂引起的肾脏系数升高；Fos, STS和Met可显著抑制顺铂引起的血清BUN和肾GSH含量升高；Met可显著抑制顺铂引起的肾GSH-Px活性升高。单独给予Se, NAC和Tau对以上指标未见明显改善作用。结论 多种药物联合应用可协同拮抗顺铂的肾毒性作用，以Zn（或Se），Fos（或STS）和Met联合应用的拮抗效果最好。

关键词 顺铂 肾/毒性 药物拮抗作用 蛋氨酸 磷霉素 硫酸锌 亚硒酸钠 硫代硫酸钠

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# Combined effects of agents against nephrotoxicity induced by cisplatin in mice

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**Abstract**

**AIM** To explore the protective effects of zinc sulfate (Zn), sodium selenium(Se), fosfomycin(Fos), *N*-acetyl-cysteine (NAC), sodium thiosulfate (STS), methionine(Met) and taurine(Tau) on nephrotoxicity induced by cisplatin. **METHODS** Animal experiment was carried out based on the orthogonal design, and mice were divided into 8 groups according to the orthogonal table of $L_8$ ($2^7$) setting 7 factors with 2 different levels. Mice were supplemented by gavage with various combinations of agents as designed in the orthogonal table once a day for nine days. Three days later, 3.5 mg·kg$^{-1}$ of cisplatin was given intraperitoneally once a day for 5 d simultaneously, and rat weights were measured before cisplatin was given and before experiment finished. Twenty-four hours after cessation of supplementation, blood was taken by removing the eyes, and kidneys were taken rapidly after sacrificing mice. Contents of blood urea nitrogen (BUN) in serum and reduced glutathione (GSH) in kidney and activities of glutathione peroxidase(GSH-Px) in kidney were analyzed. **RESULTS** Zn, Fos and Met could ameliorate obviously the cisplatin-induced weight loss; Fos and Met could ameliorate obviously the cisplatin-induced increase in kidney ratio; Fos, STS and Met could ameliorate obviously the cisplatin-induced increase in BUN levels in serum and GSH levels in kidney; Met could ameliorate obviously the cisplatin-induced increase in GSH-Px activities in kidney. However, supplementation of Se, NAC or Tau alone failed to show any beneficial effects. **CONCLUSION** The potentiated effects for prevention of cisplatin induced nephrotoxicity could be achieved via combined use of the agents. The optimal combination of agents for prevention of cisplatin induced nephrotoxicity was Zn (or Se), Fos (or STS) and Met.

**Key words** cisplatin kidney/toxicity drug antagonism methionine fosfomycin zinc sulfate sodium selenite sodium thiosulfate

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