Intrapleural topical application of cisplatin with the surgical carrier Vivostat increases the local drug concentration in an immune-competent rat model with malignant pleuromesothelioma.

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Abstract:

Objective: We sought to investigate whether intrapleural topical application of cisplatin with a surgical carrier has a prolonged local tissue level in comparison with cisplatin solution while reducing systemic toxicity. Methods: Forty immune-competent Fischer rats were inoculated with 10⁶ mesothelioma cells. Ten days later, left pneumonectomy with tumor debulking was performed. Twenty animals underwent local application of cisplatin solution (100 mg/m²), whereas the same quantity of cisplatin was topically applied as a gel with the Vivostat (Vivolution) system in 20 other animals. In each group 5 subgroups of 4 animals were defined according to the harvesting time of blood and tissue samples (2, 4, 24, and 72 hours and 1 week) after local therapy. Platinum concentrations in serum and tissue and systemic toxicity were analyzed. Results: Platinum concentrations in tissue were significantly higher in the gel group (group 1) than in the solution group (group 2) at 1, 3, and 7 days after therapy (1510, 1224, and 1069 pg/mg for group 1 vs 598, 382, and 287 pg/mg for group 2; P = .007, P = .005, and P = .0002, respectively). Laboratory findings showed renal insufficiency in the animals of the solution group at 1 week, with values of 98 mmol/L versus 7.7 mmol/L for urea and 410 mumol/L versus 43 mumol/L for creatinine (P = .02 and P = .01, respectively), which was confirmed by means of pathologic analysis. Conclusions: Intrapleural administration of cisplatin with the carrier Vivostat significantly provides sustained higher platinum concentrations up to 1 week in tissue in comparison with application of

cisplatin solution without conferring systemic toxicity in this model.