Optimized intrapleural cisplatin chemotherapy with a fibrin carrier after extrapleural pneumonectomy: a preclinical study.

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Abstract:

OBJECTIVE: Our objective was to evaluate whether platinum concentrations in chest wall tissue and in serum are optimized by intracavitary application of cisplatin loaded to a fibrin carrier compared with cisplatin solution in a randomized setting of a pig model.

METHODS: After left-sided pneumonectomy including parietal pleurectomy, pigs were randomly assigned to receive either 90 mg/m(2) cisplatin intracavitary solution (n = 6) or to receive 5 mg cisplatin-fibrin (n = 5) applied on a predefined area of the chest wall. Platinum concentration in serum as well as in chest wall tissue was determined at several early time points until day 5 after treatment. Platinum levels were measured by inductively coupled plasma sector field mass spectrometric detection with a matrix-matched calibration procedure.

RESULTS: The dose- and surface-corrected (geometric) mean concentration of cisplatin in chest wall tissue 2 hours but also at day 5 after the application was doubled in animals treated with cisplatin-fibrin compared with the animals treated with cisplatin-solution. In serum, the dose- and surface-corrected exposure toward cisplatin (area under the curve(0-5d)) was significantly lower with cisplatin-fibrin than with cisplatin-solution ($P < .0005$). This is also reflected by significantly reduced serum creatinine and urea values in the cisplatin-fibrin group ($P < .0001$). Animals treated with cisplatin-fibrin additionally had a significantly better postoperative course as assessed by a well-being score ($P < .001$).

CONCLUSIONS: After cisplatin-fibrin treatment, cisplatin tissue concentration was increased whereas systemic cisplatin concentrations were significantly reduced in comparison with cisplatin-solution treatment. This finding offers a clear advantage inasmuch as rate and severity of systemic adverse events can be reduced while local cytotoxic concentrations are at least maintained.