

Cisplatin-induced hearing loss: mechanisms, recovery and protection

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Cisplatin continues to be a widely used cytostatic drug. Unfortunately, the compound evokes serious side effects of which hearing loss is a prominent one. In a longitudinal guinea-pig model, we have shown that cisplatin-induced hearing loss, measured by electrocochleography, is partly reversible, a characteristic which has also been anecdotically reported in patients. The recovery was not attributable to regeneration or recovery of hair cells, but it appeared that one of the first effects of cisplatin was a collapse of the endocochlear potential (EP) and that the sensitivity of the cochlea recovered in parallel with recovery of the EP. In the present work we are further characterising recovery by refining the time resolution of the measurements. Albino guinea pigs, equipped with permanent round-window electrodes, were treated daily with an i.p. injection of 1.5 mg/kg cisplatin until the compound action potential threshold (3 μ V criterion) shifted by 40 dB or more. Electrocochleography was continued and after 0, 2, 3, 5 or 7 days the EP was measured. Moreover, the cisplatin concentration was determined in blood and perilymph with atomic absorption spectrometry. Preliminary results show parallel recovery in the EP and the electrocochleographic thresholds with possibly the exception of the first couple of days. This might suggest an additional factor responsible for initial recovery. Pt concentrations were around 80 μ g/L in perilymph at day 0 and dropped below the detection limit afterwards. In blood, the Pt concentration dropped gradually, but slowly from around 1300 μ g/L at day 0 to 400 μ g/L after 7 days. Pharmacological treatment with melanocortins like α -MSH could enhance recovery or even protect against cisplatin. Though the exact mechanism for this melanocortin effect is unknown, we would like to suggest involvement of the melanocytes in the stria vascularis, because this structure is mainly responsible for EP generation.

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