Identification of a candidate drug for the prevention of cisplatin-induced nephrotoxicity by a database analysis-basic research-clinical study

Yasumasa Ikeda¹, Hirofumi Hamano², Mitsuhiro Goda³, Keijo Fukushima³, Seiji Kishi⁴, Masayuki Chuma⁵, Yoshito Zamami⁶, Licht Miyamoto⁷, Keisuke Ishizawa⁶, Hiromichi Fujino³, Ken-ichi Aihara⁸, Koichiro Tsuchiya⁷, Toshiaki Tamaki⁹


Background: Cisplatin is widely used as an anti-tumor drug for the treatment of solid tumors. Unfortunately, it causes nephrotoxicity as a critical side effect, limiting its use, given that no preventive drug against cisplatin-induced nephrotoxicity (CIN) is currently available. In the present study, we searched and identified candidate drugs for preventing CIN.

Methods: We used a database of medical big data for the screening of candidate drugs for the prevention of CIN. Based on the results of the analysis of medical big data, we evaluated the actual efficacy of DPH via in vitro and in vivo experiments in culture cells and a mouse model.

Results: We identified that a previously developed drug, diphenhydramine (DPH), may provide a novel treatment for CIN by the analysis of medical big data. DPH inhibited cisplatin-induced cell death in renal proximal tubular cells. Mice administered cisplatin developed kidney injury with renal dysfunction, augmented oxidative stress, increased apoptosis, and elevated inflammatory cytokines; however, most of these symptoms were suppressed by treatment with DPH. Additionally, the renal concentration of cisplatin was attenuated in DPH-treated mice. Importantly, DPH did not interfere with its anti-tumor effect in any of the in vitro or in vivo experiments. Moreover, a retrospective clinical study showed that patients with malignant cancer who had used DPH before cisplatin treatment exhibited less acute kidney injury.

Conclusion: DPH may be a preventive medicine against CIN.