Response to "In Response to “Diphenhydramine may be a Preventive Medicine Against Cisplatin-Induced Kidney Toxicity"

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To the Editor: We thank Drs. Gupta and Leaf[1] for their comments on the propensity scores, differences in cisplatin dose between the two groups, and statistical analysis by crossover studies in reference to our original publication[2].

We performed propensity score matching with logistic regression for diphenhydramine (DPH) using the parameters of 12 risk factors for acute kidney injury[3]. The model showed a 0.84 concordance index. We conducted one-to-one matching using nearest neighbor matching without replacement with a caliper width set to 0.25 times the standard deviation of the logit of the propensity score (described in detail in the supplemental Materials and methods file).

For the lower cisplatin-induced nephrotoxicity (CIN) rate, the median dose seemed to be lower in DPH users than in non-DPH users, although no statistical significance was noted. In basic experiments, preventive effect of DPH against CIN was seen in cultured cells or mice receiving similar cisplatin dose, suggesting that DPH's preventive effects against CIN are present, regardless of cisplatin dose.

Moreover, the fragility index may be low in the present study. This index is generally used in randomized controlled trials, not in cohort studies[4]. Our cohort study was performed by a retrospective review of medical charts of patients receiving the first course of chemotherapy with cisplatin; thus, the statistical analysis of the retrospective clinical study is thought to be reasonable and appropriate.

A prospective study is required to confirm our conclusions.

References:

1. Gupta S and Leaf DE. In Response to "Diphenhydramine may be a Preventive Medicine Against Cisplatin- Induced Kidney Toxicity" Kidney Int. 2020
2. Hamano H, Ikeda Y, Goda M, et al. Diphenhydramine may be a preventive medicine against

cisplatin-induced kidney toxicity. Kidney Int. 2020; Epub ahead of print.

3. Motwani SS, McMahon GM, Humphreys BD, et al. Development and Validation of a Risk Prediction Model for Acute Kidney Injury After the First Course of Cisplatin. J Clin Oncol 2018; 36: 682-688.

4. Shochet LR, Kerr PG, Polkinghorne KR. The fragility of significant results underscores the need of larger randomized controlled trials in nephrology. Kidney Int 2017;92:1469-1475.