A Prospective, Randomized, Double-blind Study of Pre-chemotherapy Hydration with or without Mannitol to Prevent Renal Toxicity in Non-small Cell Lung Cancer (NSCLC) Patients Receiving Cisplatin-gemcitabine Chemotherapy

Nattiya Thavornpattanapon¹, Preeyaporn Kaewmanee², Supaporn Rungruangbaiyok², Cholticha Panbo³, Ketsaree Maneekrong³, Sarayut L. Geater¹

¹Department of Internal Medicine, Faculty of Medicine, Prince of Songkla University, ²Pharmaceutical Compounding center, Faculty of Medicine, Prince of Songkla University, ³Chemotherapy Center, Faculty of Medicine, Prince of Songkla University, Songkla 90110, Thailand

Background: Cisplatin-induced renal toxicity is the most serious adverse event in cisplatin-gemcitabine treated NSCLC patients. Nowadays, there is no gold standard of pre-medication regimens that can prevent cisplatin induced nephrotoxicity.

Objective: The primary aim of this study was to compare renal function decline between two pre-medication regimens with saline or saline added to mannitol by using Cockcroft-Gault equation. We also aimed to compare safety profiles between these two premedication regimens by using Common Terminology Criteria for Adverse Events version 4.03.

Methods: We randomized 55 patients who received cisplatin 80 mg/m2 every 3 weeks into two hydration groups. The patients of each group received one liter of 0.9% Sodium Chloride solution pre-hydration and also received a half liter of 0.9% Sodium Chloride solution post hydration. Both groups received Cisplatin (80 mg/m2 IV: d1) plus gemcitabine (1000 mg/m2 IV: d1,8). In the mannitol added group, 40 gm of mannitol was mixed with cisplatin. Chemotherapy was given at 21-day interval for 6 cycles or until developing intolerant toxicity or progressive disease, whichever occurred first. Clinical parameters, renal function, clinical response, and adverse events were recorded. Renal toxicity was defined as more than 20% reduction in creatinine clearance compared with baseline level.

Results: There were 29 patients in the 0.9% Sodium Chloride solution alone group and 26 patients in the mannitol added group. No significant difference was noted between these randomized groups, including age, gender, comorbid disease, and baseline creatinine clearance. For each group, the 20% or more decline in creatinine clearance were 82% in the 0.9% Sodium Chloride solution alone group and 54% in the mannitol added group (p-value = 0.021). The declination rate of creatinine clearance in the 0.9% Sodium Chloride group was faster than the other group (p-value = 0.004). There was no difference in the safety profile.

Conclusion: Hydration with 0.9% Sodium Chloride solution alone appears to be associated with an increasing risk for cisplatin nephrotoxicity, compared to the 0.9% Sodium Chloride solution with mannitol.

Keywords: Cisplatin, Nephrotoxicity, Mannitol, Lung cancer