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Abstract

The effect of intravenous mannitol in combination with normal saline on the prevention of cisplatin-induced nephrotoxicity: A randomized, double-blind, placebo-controlled trial

Panot Sainamthip and Naiyarat Prasongsook

Background: Nephrotoxicity is the major dose-limiting toxicity in cancer patients who were treated with cisplatin. Although there is no standard approach for prevention of cisplatin induced nephrotoxicity, however administration of intravenous (IV) isotonic saline to induce a diuresis before and after cisplatin administration is recommended. Additionally, several agents, including mannitol in combination with hydration have been evaluated, but none has been established yet. Our study aimed to determine the efficacy of mannitol in combination of hydration to prevent cisplatin-induced nephrotoxicity.

Methods: This study was phase II, randomized, placebo-controlled study. All solid cancer patients who were treated with cisplatin at Phramongkutklao Hospital (N = 48) were randomized into 2 groups to receive either placebo or mannitol (20 g in 100 ml of normal saline solution) after completing 2 L of pre-hydration and received cisplatin. Serum Creatinine, BUN, Electrolyte and GFR were measured at baseline and on day 2 and 7. Moreover, 24-hour urine were collected to measure urine creatinine and calculated to urine GFR both prior and 48 hours after treated with cisplatin. Severity of nausea, vomiting was evaluated with Common Terminology Criteria for Adverse Events.

Results: Forty-eight patients were randomized into two groups, 25 patients received placebo and 23 patients received mannitol in combination with hydration. There was no difference in baseline characteristic between two group. Seven out of 23 patients (37.4%) in mannitol group, and 10 out of 25 patients (40%) in placebo group had increased serum creatinine of ≥0.3 mg/dL at 48 hours after (p-value = 0.48). Patients receiving mannitol had significantly lower incidence of 24-hour urine GFR below 60 mL/min/1.73 m2 than placebo group (13.6% vs 48.0% in placebo; p-value =0.012). Univariate analysis showed the greatest benefit in patients receiving cisplatin >80 mg/m2, or patients receiving concomitant radiation.

Conclusions: Intravenous hydration with isotonic solution and avoidance of co-administration with nephrotoxic agents are mainstay of treatment in preventing cisplatin-induced nephrotoxicity. In addition, mannitol in combination with hydration significantly prevented cisplatin-induced nephrotoxicity. Therefore, mannitol should be considered in cancer patients who are treated with cisplatin, especially in patients receiving cisplatin >80 mg/m2, or patients receiving concomitant radiation.