Early high-dose intravenous vitamin-C is being investigated as adjuvant therapy in critically ill patients, but the optimal dose and infusion method are unclear” de Grooth et al (2018).

Abstract:

BACKGROUND: Early high-dose intravenous vitamin-C is being investigated as adjuvant therapy in critically ill patients, but the optimal dose and infusion method are unclear. The primary aim of this study was to describe the dose-plasma concentration relationship and safety of four different dosing regimens.

METHODS: Four-group randomized pharmacokinetic trial. Critically ill patients with multiple organ dysfunction were randomized to receive 2g/day or 10g/day vitamin-C as a twice daily bolus infusion or continuous infusion for 48 hours. Endpoints were plasma vitamin-C concentrations during 96-hours, 12-hour urine excretion of vitamin-C and oxalate and base excess. A population pharmacokinetic model was developed using NONMEM.

RESULTS: Twenty patients were included. A two-compartment pharmacokinetic model with creatinine clearance and weight as independent covariates described all four regimens best. With 2g/d bolus, plasma vitamin-C concentrations at T=1h were 29-50 mg/l and trough concentrations were 5.6-16 mg/l. With 2g/d continuous, steady state concentrations were 7-37 mg/l at T=48h. With 10g/d bolus, T=1h concentrations were 186-244 mg/l and trough concentrations were 14-55 mg/l. With 10g/d continuous, steady state concentrations were
40-295 mg/l at T=48h. Oxalate excretion and base excess were increased in the 10g/d dose. Forty-eight hours after discontinuation, plasma concentrations declined to hypovitaminosis levels in 15% of the patients.

CONCLUSIONS: The 2g/d dose was associated with normal plasma concentrations, the 10g/d dose with supra-normal plasma concentrations, increased oxalate excretion and metabolic alkalosis. Sustained therapy is needed to prevent hypovitaminosis.

CLINICAL TRIAL REGISTRATION: The trial protocol was registered at clinicaltrials.gov before inclusion of the first patient (NCT02455180).

Reference:


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