Title: Comparison of Bolus and Continuous Hydration Regimens for the Prevention of Contrast-Associated Acute Kidney Injury in the Emergency Department: A Randomized Controlled Non-InferiorityTrial

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Comparison of Bolus and Continuous Hydration Regimens for the Prevention of Contrast-Associated Acute Kidney Injury in the Emergency Department: A Randomized Controlled Non-Inferiority Trial

Yunus Emre Gemici, Furkan Ay, Alper Görkem Cimen, İbrahim Sarbay, Mustafa Calik

Study Protocol

Study Design and Settings

A single-center, prospective, open-label, non-inferiority randomized controlled clinical trial was conducted at the ED of a tertiary hospital. The ED staff consisted of a mix of emergency medicine specialists, emergency medicine residents, and general practitioners. The ED admits all trauma patients regardless of age, as well as non-trauma patients aged 18 years and older. An average of 385000 patients are admitted annually, and imaging with contrast media is performed on an average of 12250 patients.

The study was approved by the Clinical Research Ethics Committee of xxx (Decision No: E-66291034-202.3.02-4819, Date: 07/08/2024) and was conducted in accordance with the principles of the Helsinki Declaration. This study has been reported in accordance with the CONSORT statement. Informed written consent was obtained from all patients participating in the study.

Study Enrollment

Between August 10, 2024, and March 26, 2025, patients aged 18 and over who presented to the ED with creatinine levels above the reference range (1.2 mg/dl in men and 1.1 mg/dl in women) and underwent contrast-enhanced tomography were deemed eligible for inclusion in the study. Exclusion criteria were as follows: (1) Pregnancy, (2) known allergy history to contrast agents, (3) exposure to contrast agents within the last 72 hours, (4) being on dialysis due to end-stage kidney disease, (5) presenting with decompensated heart failure, (6) patients who were unable to provide informed consent.

Eligible patients were randomly allocated in a 1:1 ratio to receive either bolus hydration or continuous hydration therapy. Permuted block randomization was employed at each

participating site to distribute patients, stratified by age groups (18–44, 45–59, 60–74, and 75 years and older) and gender. This study did not use blinding. Both the implementers of the intervention and the researchers evaluating the outcome measures are aware of the intervention groups.

Interventions

After the patients were divided into two groups, one group received bolus hydration therapy while the other group received continuous hydration therapy.

In the Bolus hydration therapy group, 500 ml of 0.9% saline treatment was started half an hour before the procedure and after the procedure, 1000 ml of 0.9% saline treatment was continued at a rate of 500 ml/h to be completed in 2 hours. A total of 1500 ml 0.9% saline hydration therapy was administered over 2.5 hours.

In the Continuous hydration therapy group, saline treatment started 2 hours before the intravenous (IV) contrast agent application at a rate of 150 ml/h, and hydration was applied for 8 more hours after the procedure at the same rate. A total of 1500 ml 0.9% saline hydration therapy was administered over 10 hours.

According to the literature, individuals with an ejection fraction of less than 40% got a half-dose hydration protocol[12,13]. In the bolus hydration group, 250 ml of treatment was administered half an hour before the procedure, and hydration was continued at a rate of 250 ml/h for 2 hours after the procedure. In the continuous hydration group, 75 ml/h of hydration was administered for 2 hours before the procedure and for 8 hours after the procedure.

The IV contrast agent used in the study was iohexol, which belongs to the non-ionic low osmolar contrast agent group. 300 mgI/ml 100 ml solutions were used, and the dose was adjusted between 80 and 100 ml depending on the imaging and the patient. In the majority of patients, 100 ml of contrast was administered, with an average of 98 ml of solution given in the bolus hydration group and an average of 96 ml of solution given in the continuous hydration group.

Patients were given control forms to provide follow-up blood samples 48-72 hours later and were asked to present to the ED with the form on the specified date. To inquire about the development of dialysis needs and mortality status, patients were contacted 30 days later to gather information.

Outcomes

The primary outcome of our study was the development of CA-AKI, defined as an increase in serum creatinine value by ≥25% compared to baseline or an absolute increase in serum creatinine value by ≥0.5 mg/dL within 48-72 hours after contrast administration.

The secondary outcomes of the study are the need for dialysis and all-cause mortality within 30 days.

Statistical Analysis

Categorical variables are presented as frequencies and percentages. Continuous variables were assessed for normality using the Kolmogorov-Smirnov and Shapiro-Wilk tests; non-normally distributed variables are reported as median (25th–75th percentiles). Between-group comparisons of categorical variables were performed using Pearson's Chi-square or Fisher's Exact test, as appropriate. Continuous variables were compared using the Mann-Whitney U test for independent groups and the Wilcoxon signed-rank test for paired groups. The incidence of contrast-associated acute kidney injury (CA-AKI) between hydration protocols was compared using risk differences (RDs) with 95% confidence intervals (CIs). Non-inferiority of the bolus hydration protocol was assessed using a pre-specified margin; the protocol was considered non-inferior if the upper bound of the 95% CI was below this margin. All other statistical tests were two-sided, and statistical significance was set at $p < 0.05$. Analyses were conducted using IBM SPSS Statistics.

Power Calculation

The sample size calculation aims to establish the non-inferiority of bolus prophylaxis relative to routine prophylaxis concerning the primary outcome, CA-AKI. The anticipated incidence of CA-AKI patients following conventional prophylaxis is 6.2%[6], while the non-inferiority margin, derived from clinical consensus and literature, is 8%[14]. A one-tailed hypothesis was established, with a Type I error rate (α) of 0.05 and a statistical power ($1-\beta$) of 0.80. In light of clinical settings, the dropout rate was established at 15%, resulting in a total inclusion of 266 individuals, with 133 assigned to the regular prophylaxis group and 133 to the bolus prophylaxis group[15]. The computation employed the complimentary website sealedenvelope.com[16].

At conclusion of the study, a total of 257 patients were included into the final analysis. While 113 individuals in the bolus and continuous prophylaxis groups sufficed for the study, a total of 257 patients were recruited, adhering to dropout limitations and ensuring an adequate sample size.