Does Cumulative Topical Antibiotic Powder Use Increase the Risk of Nephrotoxicity?

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Purpose: Topical antibiotic powders are increasingly used in an effort to reduce surgical site infections. Although prior research suggests a minimal risk of nephrotoxicity with a single 1.0-g dose of vancomycin powder, patients often have multiple procedures providing additional doses of vancomycin powder and other topical antibiotics, such as tobramycin. The study's primary aim was to determine if cumulative doses of vancomycin or tobramycin powder prophylaxis increase the risk of nephrotoxicity among fracture patients.

Methods: The study was a secondary analysis of single-center data from the PREP-IT trial. We included patients with one or more surgically treated appendicular fractures who received intrawound vancomycin or tobramycin powder. The primary outcome was nephrotoxicity, previously defined as a rise in serum creatinine up to 7 days post-surgery that is at least twice the lowest preoperative value. We used Bayesian logistic regression models to calculate the odds of nephrotoxicity per gram of powder after adjusting for age, sex, and ISS and accounted for the interactive effects of vancomycin and tobramycin.

Results: The study included 782 patients with a median age of 47 years, a median ISS of 9, and 59% were male. 83% of patients received at least one vancomycin dose, with the cumulative vancomycin dose per patient ranging from 0 to 12 g (median, 1 g). 45% of the sample received at least one tobramycin dose, and the cumulative tobramycin dose varied from 0 to 9.4 g. The mean number of surgeries for each patient was 1.4 (23% had more than one surgery). Nephrotoxicity occurred in 10 patients (1.3%). There was no association between the cumulative dose of vancomycin and nephrotoxicity (odds ratio [OR]: 1.16, 95% credible interval [CrI]: 0.60-2.12). However, additional doses of tobramycin were associated with a 2.92 increase in the adjusted odds of nephrotoxicity (95% CrI: 1.47-6.34). Specifically, patients who did not receive tobramycin powder had a nephrotoxicity risk of 0.1% (95% CrI: 0.0%-0.5%). Patients with a cumulative tobramycin dose of 3.6 g had a 3.6% risk of nephrotoxicity (95% CrI: 0.8% to 12.7%), and a 4.8-g cumulative dose was associated with an 11.1% (95% CrI: 1.6%-46.1%) nephrotoxicity risk.

Conclusion: The findings are reassuring, especially regarding vancomycin, and suggest cumulative doses do not increase the risk of nephrotoxicity among fracture patients. The nephrotoxicity risk also remains low after three cumulative 1.2-g doses of tobramycin. However, our data suggest that 4.8 g or more cumulative doses of tobramycin powder was associated with some increased risk of nephrotoxicity. Unlike the typical doses of vancomycin powder, the typical dose of tobramycin powder (1.2 g) is much higher than a standard IV dose; therefore, it seems plausible that transient rises in creatinine are more likely to be associated with higher tobramycin than vancomycin powder doses even if this level of creatinine increase is of unknown clinical importance.