

Do Some Patients Benefit More from Vanco Powder? Heterogenous Treatment Effects in the VANCO Trial

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INTRODUCTION: A recent study concluded that topical vancomycin powder was effective in preventing deep surgical site infections (SSI) in lower extremity trauma patients. Characterizing treatment heterogeneity may help identify patient subgroups who benefit differentially from this intervention, help prioritize receipt of this treatment, and guide future research.

METHODS: This study was a preplanned secondary aim of a recently completed multicenter, randomized clinical trial, which enrolled 980 patients comparing topical vancomycin powder to controls in high-risk tibia fractures. A two-step sequential approach was used to examine Heterogenous Treatment Effects (HTE) while controlling for both type 1 and type 2 error. Since no widely accepted risk model for infection is currently available, a formal effect model using interaction terms was constructed. Type 1 error was controlled using the Benjamini and Hochberg method.

RESULTS: The risk difference (RD) in the overall study was -3.4%, and deep SSI were observed in 29 of 481 patients in the treatment group and 46 of 499 patients in the control group. Overall, three patient subgroups met criteria to be tested showing significant effects for both the treatment arm and the infection risk factor. Patients with AO/OTA Fracture Type C had 10.2% and 6.9% deep infection rates in the control and treatment groups, respectively (RD: -3.3%). However, neither the main effect nor interaction term were statistically significant in the interaction model. Patients with severe soft tissue injury (defined as open fracture or Tscherne 3) had 16% and 10% deep infection rates in the control and treatment groups, respectively (RD: -6%), and the main effect term had a p value <0.0001. Patients 40 and older had 6.3% and 11.1% deep infection rates in the control and treatment groups, respectively (RD: -4.9%), and the main effect term had a p-value of 0.012. Neither of these last two subgroups had a statistically significant interaction term in those models.

DISCUSSION AND CONCLUSION:

None of the three subgroups tested in this analysis showed statistically significant evidence of HTE. Patients with severe soft tissue injury and older age may benefit more from local antibiotic powder in this setting, though it did not reach statistical significance. A larger study would be needed to rule out such effects.