Investigational Vaccine Not Effective In Reducing Post-Operative Staph Infections

Use of a vaccine to prevent *Staphylococcus aureus* infections among patients undergoing cardiothoracic surgery did not reduce the rate of serious postoperative *S aureus* infections compared with placebo and was associated with increased mortality among patients who developed *S aureus* infections, according to a study in the April 3 issue of *JAMA*.

Infections with *S aureus* following median sternotomy (incision through the midline of the sternum) cause substantial illness and death. "A safe vaccine that provides protection against a majority of *S aureus* strains during the postoperative period would address an important unmet medical need," according to background information in the article. A novel vaccine candidate (V710) is immunogenic and generally well tolerated in volunteers, with elevated antibody responses persisting for at least 1 year after vaccination in most patients.

Vance G. Fowler Jr., M.D., M.H.S., of Duke University Medical Center, Durham, N.C., and colleagues conducted a phase 2b/3 study to evaluate the efficacy and safety of preoperative V710 vaccination in preventing serious postoperative *S aureus* infection in patients undergoing cardiothoracic surgery. The randomized trial was conducted between December 2007 and August 2011 among 8,031 patients 18 years of age or older who were scheduled for full median sternotomy within 14 to 60 days of vaccination at 165 sites in 26 countries. Participants were randomly assigned to receive a single intramuscular injection of either V710 vaccine (n=4,015) or placebo (n=4,016).

The independent data monitoring committee recommended termination of the study after the second interim analysis because of safety concerns and low efficacy. In the primary modified intention-to-treat analysis, V710 vaccine was not significantly more efficacious than placebo in preventing the prespecified primary end point (*S aureus* bacteremia and/or deep sternal wound infection through postoperative day 90) (22 adjudicated cases in 3,528 evaluable V710 recipients vs. 27 adjudicated cases in 3,517 evaluable placebo recipients). No significant differences in efficacy between the vaccine and placebo groups were observed at any point during the study.

The researchers also found that the V710 vaccine was not significantly more efficacious than placebo in preventing the secondary end points (all *S aureus* surgical site and invasive infections through postoperative day 90).

Compared with placebo, the V710 vaccine was associated with more adverse experiences during the first 14 days after vaccination (30.8 percent vs. 21.8 percent), including injection site reactions (20.1 percent vs. 9.5 percent) and serious adverse events (1.7 percent vs. 1.3 percent), and a significantly higher rate

of multiorgan failure during the entire study (31 vs. 17 events).

Although the overall incidence of vaccine-related serious adverse events (1 in each group) and the all-cause mortality rate (201/3,958 vs. 177/3,967) were not statistically different between groups, the mortality rate in patients with staphylococcal infections was significantly higher among V710 vaccine than placebo recipients (15/73 vs. 4/96).

"In our study of adult patients undergoing cardiothoracic surgery, preoperative vaccination with V710 did not significantly reduce the composite incidence of *S aureus* bacteremia and deep sternal wound infection," the authors write. "These findings do not support the use of the V710 vaccine for patients undergoing surgical interventions."

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