Higher-dose pneumococcal vaccines improve immune response in ANCA-associated vasculitis patients receiving rituximab

November 8 2022

Credit: Pixabay/CC0 Public Domain

New research presented this week at ACR Convergence 2022, the American College of Rheumatology's annual meeting, showed that a higher dose of pneumococcal vaccine safely and effectively improved antibody response in patients receiving rituximab for ANCA-associated

vasculitis.

Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis is a group of disorders characterized by inflammation and destruction of blood vessels, often accompanied by the production of antibodies that target neutrophil antigens. The standard induction therapy is glucocorticoids plus rituximab. Yet rituximab increases infection risk, especially pneumococcal infection, while weakening response to the pneumococcal vaccine. Researchers undertook this randomized phase 2 trial to develop pneumococcal vaccine strategies that would increase immune response in ANCA-associated vasculitis patients and autoimmune patients in general.

Study participants included 95 adults from the French Vasculitis Study Group, a multidisciplinary network of centers throughout France involved in the management of systemic vasculitis. Patients with newly diagnosed or relapsing ANCA-associated vasculitis with active disease and planned rituximab induction therapy were randomized in a 1:1:1 ratio to one of three parallel arms:

- A standard regimen consisting of an initial dose of pneumococcal conjugate vaccine (PCV13) followed by a dose of pneumococcal polysaccharide vaccine (PPV23) five months later (arm 1);
- A double dose of PCV13 at both day zero and day seven followed by a dose of PPV23 at month five (arm 2);
- Or four doses of PCV13 at day zero followed by a dose of PPV23 at month five (arm 3).

Age is a known factor in poor immune response, so all study arms were balanced for age.

The primary endpoint was the immune response at six months against 12 serotypes of Streptococcus pneumoniae common to the PCV13 and

PPV23 vaccines: 0-3, 4-6, 7-9 or 10-12 serotypes. Secondary endpoints were local and systemic reactions seven days after each vaccination as well as any adverse events possibly related to immunization.

Overall, patients in arm 2 were more likely to be in higher response categories (56.3%, 28.1%, 15.6% and 0%, respectively) compared to the standard regimen after adjustment for age. The second high-dose regimen—arm 3—tended to improve vaccine response only (60.6%, 33.3%, 6.1% and 0%, respectively).

Local and systemic reactions were higher seven days after each dose of high-dose vaccine as were adverse events related to vaccination at six months, though none were severe. Six patients experienced vasculitis flares about 90 days after vaccination: one patient in arm 1, two patients in arm 2 and three patients in arm 3.

"Our study highly suggests that patients receiving rituximab to treat an inflammatory disease could receive a higher dose of vaccine, especially two doses of PCV13 seven days apart, then PPV23 five months later, to induce a better vaccine response," says Benjamin Terrier, MD, a professor of medicine at Cochin Hospital, Paris Cité University and the study's lead author. He adds that the results weren't surprising.

"Since these patients received a high dose of glucocorticoids and rituximab, it was expected that a higher dose of vaccine was required to induce a sufficient response, but it was very important to confirm and demonstrate that."

Dr. Terrier says that since rituximab targets B cells, he and his colleagues chose to increase the dose of T-cell dependent PCV13 rather than T-cell independent PPV23. But he thinks the data suggest using higher doses of any vaccine "could improve antibody response in patients treated with immunosuppressive agents, especially for the current COVID-19

pandemic."

Although the study was open-label and not double-blind, "the primary outcome—the level of antibodies—was a strong endpoint that does not seem to be impacted by the lack of a double-blind [design]," Dr. Terrier says. "Our study shows that using a higher dose of vaccine is safe and effective for improving the protection of patients treated with rituximab against pneumococcal pneumonia."

More information: Conference abstract

Conference: www.rheumatology.org/Annual-Meeting

Provided by American College of Rheumatology