Fewer steroids, no plasma exchange: A change in treatment for vasculitis

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A decade-spanning trial found that for patients with antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis, two common methods of treatment actually do not have an impact on their long-term survival. The study, called PEXIVAS, was co-led by Peter A. Merkel, MD, MPH, chief of Rheumatology in the Perelman School of Medicine

at the University of Pennsylvania, and was the largest ever conducted in vasculitis. It demonstrated that survival and progression to kidney failure (with the need for dialysis) for patients with ANCA-associated vasculitis remained virtually unchanged whether or not they underwent plasma exchange or if they took approximately half the typically prescribed dosage of oral glucocorticoids—which are commonly referred to as "steroids." The study was published today in the *New England Journal of Medicine*.

"This work should be the basis for a significant change in the standard of care for this type of vasculitis," said Merkel, a professor of Medicine at Penn and the principal investigator of the NIH-sponsored Vasculitis Clinical Research Consortium. "Adopting the changes in treatment we studied will greatly reduce our patients' discomfort and their risk of developing several serious side effects from the current therapies."

In ANCA-associated vasculitis, a person's immune system attacks their small- and medium-sized blood vessels, resulting in inflammation and destruction. It is an organ- and life-threatening condition. The kidney is especially vulnerable, and the majority of patients with ANCA-associated vasculitis are at major risk of developing kidney failure.

The researchers examined ways to reduce both kidney failure and overall mortality by carefully studying two types of treatments. They looked into different dosages of glucocorticoids, a treatment known to be effective against ANCA-associated vasculitis but associated with substantial side-effects such as weight gain, infection, and the development of diabetes or osteoporosis. The team also studied plasma exchange (called plasmapheresis, a procedure that removes antibodies from the blood) because while it is used regularly to treat vasculitis, research has never proven it is effective.

Patient recruitment began in 2010 and led to the inclusion of 704

patients with ANCA-associated vasculitis spread across 95 medical centers internationally, making this the largest-ever trial of vasculitis. Patients were randomly assigned twice: once into a group for studying different glucocorticoid doses and another time to study plasma exchange.

To analyze glucocorticoid dosage, one group of patients took the regular dosage of steroids, while the other section was prescribed roughly half the dosage. To study the effectiveness of plasma exchange, half of the study population received plasma exchanges—performed seven times over 14 days (the standard) after enrollment—while the other half didn't receive any exchanges. Every patient was followed for up to seven years.

At the outset, the researchers believed that performing plasma exchanges would be beneficial for patients and that lowering the dose of glucocorticoids would not reduce the overall benefit for patients but would be safer, but data showed no significant difference in either comparison in terms of death or progression to kidney failure resulting in the need for hemodialysis. However, patients who received the lower doses of glucocorticoids had fewer serious infections compared to the patients receiving the higher-dose of glucocorticoids.

Researchers said these findings will likely lead to big changes in how this form of vasculitis is treated and set new standards of care for ANCA-associated vasculitis. That could benefit patients, particularly in reducing the cumbersome nature of their treatment.

"This means we may not have to do plasma exchanges, which involve a catheter, can be uncomfortable, and are expensive," Merkel said. "It's also a big story when it comes to the glucocorticoids because the ability to use less will reduce their toxicity and cut down on the chance for side effects. These are major results."

More information: *New England Journal of Medicine* (2020). DOI: 10.1056/NEJMoa1803537