Reducing corticosteroid use in rheumatoid arthritis

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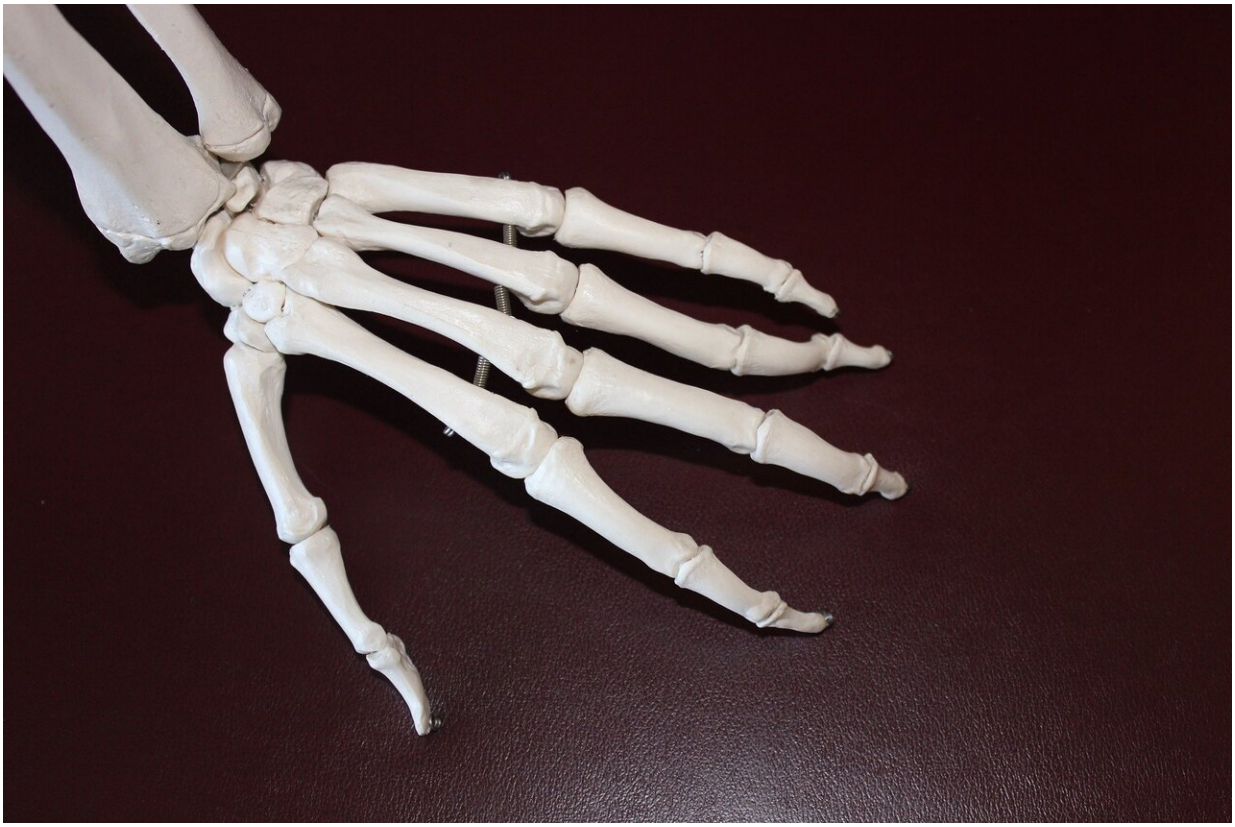

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Is the long-term use of glucocorticoids essential in people with chronic inflammatory diseases such as rheumatoid arthritis, or can early discontinuation prevent characteristic side effects? How can these drugs

be discontinued without giving rise to glucocorticoid withdrawal syndrome? These were the questions addressed by the SEMIRA study, a large European trial led by Charité - Universitätsmedizin Berlin. According to the trial's findings, continuous glucocorticoid regimens were better at controlling disease activity. However, discontinuation also proved successful in the majority of cases, and could be used to prevent the long-term side effects associated with glucocorticoid treatment. Results from this trial have been published in *The Lancet*.

Glucocorticoids, such as cortisone, are highly effective in controlling inflammatory diseases. Their long-term use, however, is associated with severe side effects, including cardiovascular disorders, osteoporosis and infections. These drugs also suppress the adrenal glands, thereby impairing the body's ability to produce its own cortisone. This can lead to fatigue, nausea and low blood pressure, and can even prove life-threatening. An appropriate period of gradual dose reduction—known as tapering—is essential to enable the body to adapt to a reduced supply of this substance and prevent withdrawal syndrome. Tapering glucocorticoids without triggering a recurrence of inflammation is a common challenge faced by many medical specialties.

"We had not previously had access to data from double-blind, randomized, placebo-controlled trials which compared a tapering regimen for low-dose prednisone—the most common glucocorticoid used—with continued use of low-dose prednisone. In the SEMIRA trial, our comparative analysis focused on rheumatoid arthritis, a condition commonly treated with glucocorticoids," explains the article's first author, Prof. Dr. Gerd-Rüdiger Burmester, Head of the Medical Department, Division of Rheumatology and Clinical Immunology on Campus Charité Mitte. He and his Deputy Head of Department, Prof. Dr. Frank Buttgereit, form part of the team responsible for conducting the Steroid Elimination In Rheumatoid Arthritis (SEMIRA) study, a trial including more than 250 participants recruited from close to 40 trial

centers in six different countries.

All recruited patients had been receiving glucocorticoids for a minimum of six months, meaning their disease-related inflammation was well-controlled. Patients in the control group continued to receive prednisone at a similar dose for a duration of six months, while patients on the dose reduction regimen had their treatment tapered down to zero over the course of four months. Both groups received the anti-interleukin-6 receptor antibody tocilizumab as adjunctive therapy. Treatment successfully prevented disease flare-ups in 77 percent of patients on the continued prednisone regimen. The same outcome was achieved in 65 percent of patients on the tapering regimen. Fortunately, neither of the two groups had to contend with clinically relevant changes in their laboratory parameters, disease-related inflammation or other severe problems.

"The fact that glucocorticoid tapering was associated with a treatment success rate of 65 percent is of enormous significance for shared decision-making involving patients. It will now be possible to decide, on a case-by-case basis, whether glucocorticoid treatment should continue or whether tapering should be attempted," says Prof. Burmester. He adds: "Our results also set the scene for studies to investigate glucocorticoid tapering in other clinical settings—for instance in the fields of allergology, neurology and dermatology—where these drugs are also used, and where there is a certain level of uncertainty regarding the risks and benefits of discontinuing treatment."

More information: Burmester GR et al. Continuing versus tapering glucocorticoids after achievement of low disease activity or remission in rheumatoid arthritis (SEMIRA): a double-blind, multicentre, randomised controlled trial. *Lancet* (2020) DOI: 10.1016/S1040-6736(20)30636-X

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