

## CHICKEN COLLAGEN FOR RA

Researchers from Anhui Medical University in Hefei, China have shown that an orally administered form of type II collagen (CII) extracted from chicken breast cartilage is considerably safer, but less effective, than low-dose methotrexate for the treatment of rheumatoid arthritis (RA).

Administration of chicken CII is thought to induce peripheral immunological tolerance to CII, the main constituent of human cartilage and a potential autoantigen involved in the pathogenesis and/or progression of RA. The precise mechanisms underlying the induction of immunological tolerance are unknown, but are thought to involve clonal deletion, suppression of type 1 T helper cells and induction of regulatory T cells.

Prior success with oral chicken CII in small studies of RA prompted Wei and colleagues to conduct a large multicenter, double-blind, randomized trial, comparing the effects of 0.1 mg per day chicken CII ( $n=326$ ) with 10 mg per week methotrexate ( $n=177$ ) on the progression of RA symptoms. Patients enrolled in the study had a disease duration of 6–24 months, at least six painful or tender joints, three or more swollen joints, and morning stiffness lasting at least 45 min in the week prior to the study. In addition, patients were permitted to continue taking the NSAID diclofenac throughout the study period, as required.

After 24 weeks of treatment, patients in the chicken CII group reported vast improvements in pain (measured on a 0–10 visual analog scale), duration of morning stiffness, and tender and swollen joint counts compared with baseline. The improvements observed in the methotrexate group, however, were far better than those seen with chicken CII. Specifically, almost 42% of patients who took chicken CII achieved American College of Rheumatology criteria for 20% improvement compared with nearly 58% of methotrexate users ( $P<0.05$ ). In addition, reductions in erythrocyte sedimentation rate and C-reactive protein level were seen only patients receiving methotrexate.

Importantly, the rate of adverse events was significantly lower in the CII group compared with the methotrexate group (5.52% versus 9.60%,  $P=0.036$ ). Abdominal pain and epigastric discomfort were the most frequently reported adverse events, occurring in 17 of 326 patients receiving chicken CII and 11 of 177 patients taking methotrexate. As the authors note, the relatively high frequency of gastrointestinal problems could have been related to the continued use of diclofenac, which has been associated with adverse gastrointestinal effects.

One weakness of this study was the lack of comparison with a placebo group, which might have affected the results in favor of chicken CII. Furthermore, the dose of methotrexate used was low, and higher doses might have widened the efficacy gap between methotrexate and chicken CII.

Wei and colleagues acknowledge that larger, controlled trials of chicken CII for the treatment of RA are required. Nonetheless, the researchers remain optimistic about the future of immunological tolerance as a future therapeutic strategy. “These results are encouraging and imply that RA can be effectively treated with oral CII, and partly support the mechanisms of immune tolerance.”

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**Original article** Wei, W. *et al.* A multicenter, double-blind, randomized, controlled phase III clinical trial of chicken type II collagen in rheumatoid arthritis. *Arthritis Res. Ther.* **11**, R180 (2009)