



RESEARCH NEWS

Hydroxychloroquine should not be used for hand osteoarthritis, say researchers

Jacqui Wise

London

Hydroxychloroquine is no more effective than placebo in reducing the symptoms of hand osteoarthritis, a study published in the *Annals of Internal Medicine* has found.¹ The UK researchers said that their findings do not support the current practice of off-label use of hydroxychloroquine in patients with hand osteoarthritis.

Symptomatic hand osteoarthritis affects 4–31% of adults over 70. It can cause significant pain and make it hard to perform basic activities such as eating, cooking, and dressing.

No current therapies modify the progression of damage to cartilage and bone, and treatment is focused on symptom relief. Some studies have suggested that low levels of inflammation cause symptoms in osteoarthritis. Hydroxychloroquine is an established treatment for inflammatory conditions such as rheumatoid arthritis. It is sometimes used off label for hand osteoarthritis, but very few data exist on its effectiveness.

The study,¹ which was funded by Arthritis Research UK, took place in 13 primary and secondary care centres in England. Researchers randomly assigned 248 patients with symptomatic and nodal hand osteoarthritis to receive either hydroxychloroquine (200–400 mg) or placebo, in addition to their usual care. The study participants had an average age of 62.7 years, and 82% were women. They had had symptoms of hand osteoarthritis for about five years, and their average pain level was 7 out of 10 at baseline.

The researchers found no meaningful differences in pain relief between participants treated with hydroxychloroquine and those taking a placebo. At six months the mean hand pain was 5.49 points in the placebo group and 5.66 points in the hydroxychloroquine group, with a treatment difference of –0.16 points (95% confidence interval –0.73 to +0.40); $P=0.57$). No significant treatment difference was found in grip strength, function, or quality of life. The researchers carried out ultrasonography at baseline to determine whether patients with synovitis had a greater response to treatment than patients with less evidence of inflammation, but they found no evidence of this.

A previous study found that early osteoarthritis may be more inflammatory than established osteoarthritis. Accordingly, one

possible limitation of the new study is that it selected adults with longstanding osteoarthritis symptoms and so may have missed an early window of opportunity for the hydroxychloroquine to have a therapeutic benefit.

Another possible limitation is the restriction of the dose to the maximum recommended by the *British National Formulary* of 6.5 mg/kg a day, with most patients receiving 300 mg daily. In clinical rheumatoid arthritis practice, patients may start hydroxychloroquine treatment at a higher dose of 400 mg with a reduction to a lower maintenance dose after three to six months. However, the authors said that only 5.6% of those in the hydroxychloroquine group were receiving the lowest dose of 200 mg and that they saw no evidence of dose-response in relation to a treatment effect.

Osteoarthritis is characterised by flare-ups and periods of relief, which can confuse the results of osteoarthritis drug trials. This study found a substantial placebo effect, with a 20% pain reduction in the placebo group.

In an accompanying editorial Elena Losina and Jeffrey Katz, from Brigham and Women's Hospital and Harvard Medical School in Boston, Massachusetts, wrote that the hypothesis that synovitis plays an important role in the pathogenesis of hand osteoarthritis should not be dismissed on the basis of these trial results.²

“Although hydroxychloroquine is safe, it is also a weak anti-inflammatory agent seldom used in contemporary practice as a solo disease-modifying therapy for rheumatoid arthritis and other inflammatory conditions,” they wrote.

They added that future studies will need to use more potent agents or compounds, developed to target more specifically the inflammatory pathways documented in osteoarthritis.

1 Kingsbury S, Tharmanathan P, Keding A. Hydroxychloroquine effectiveness in reducing symptoms of hand osteoarthritis. *Ann Intern Med* 2018;(Feb). 10.7326/M17-1430. <http://annals.org/aim/article-abstract/2672940/hydroxychloroquine-effectiveness-reducing-symptoms-hand-osteoarthritis-randomized-trial>.

2 Losina E, Katz J. Hydroxychloroquine: another battle lost in the campaign to find effective therapies for hand osteoarthritis. *Ann Intern Med* 2018;(Feb). 10.7326/M18-0035.

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