Tanezumab: best pain treatment yet?

Recent research has been published on a new class of pain relievers that may alleviate osteoarthritis pain better than any drug that is currently on the market.

Osteoarthritis sufferers often use nonsteroidal anti-inflammatory drugs, such as ibuprofen, to deal with the pain caused by the disease. As the disease develops and the pain gets worse, patients may start using opioids, such as oxycodone. Nonsteroidal anti-inflammatory drugs inhibit an enzyme that causes inflammation and opioids target receptors in the central nervous system. These drugs can cause side effects, such as internal bleeding, liver damage and, with opioids, a danger of addiction.

The new treatment, called tanezumab, works in a different way to the other drugs. It targets musculoskeletal pain receptors and avoids the side effects caused by other drugs. It is the first in a new class of pain relievers. The drug works by preventing nerve growth factor from attaching to sensory neurons and stopping them from signaling to the brain. The pathway is specific to muscle and bone pain and allows the possibility of targeted pain relief.

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In the recent study, it was found that patients experience up to a 62% reduction in pain – 40% better than the placebo. Patrick Mantyh from the University of Arizona (AZ, USA) described the impact of the research, "This really represents a new class of drugs, and it's been many decades since we've introduced a new class of agents for treating osteoarthritis. It's an outstanding paper, very thorough, and a beautiful case of coming up with a really novel approach for treating pain and showing a clinically significant result."

However, the US FDA has suspended Phase II and III trials on tanezumab, owing to the fact that some participants in the trials experienced such a great amount of tissue damage that they required joint replacement surgery, and not always for the joint that they were undergoing treatment for.

Further work is required to determine the reason for this damage. It could be that tanezumab was affecting the bone; however, Nancy Lane, lead author of the study, believes there is another reason for the joint damage. She believes that the treatment is so effective that patients do not feel pain that warns them of their injury and, therefore, become more active than usual. "It works so well that people are going to need to be counseled. Just because they don't feel pain doesn't mean their disease is gone," she says. "Pain is good; it keeps us from doing too much. And this medication is very good, so good that it allows people to do more than they should."

According to Mantyh, even if tanezumab is found to cause damage by acting on the bone, the research is no less important. It shows that NGF is an important target for pain relief.

Sources: Lane NE, Schnitzer TJ, Birbara CA et al.*: Tanezumab for the treatment of pain from osteoarthritis of the knee.* N. Engl. J. Med. *doi: 10.1056/NEJMoa0901510 (2010) (Epub ahead of print); Technology Review: www.technologyreview.com/biomedicine/26406/?p1=A2&a=f*

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Genetic factors may have a role in the progression of osteoarthritis

Research at the University of North Carolina (NC, USA) at Chapel Hill School of Medicine and Interleukin Genetics, Inc. (NC, USA) evaluates the link between certain genetic factors and a worse progression of osteoarthritis (OA).

In the recent work, patients who had evidence of knee osteoarthritis, determined by x-ray, and who had inherited a certain pattern of genetic variation in the IL-1 receptor antagonist (*IL-1Ra*) gene were twofold more likely to reach a severe form of the disease compared with other patients.

The study, led by Joanne Jordan, the Herman & Louise Smith Distinguished Professor of Medicine and Chief of the Division of Rheumatology, Allergy, and Immunology at the Thurston Arthritis Research Center at the University of North Carolina, followed 1154 patients for up to 11 **years**. It is the only research, to date, that includes Caucasians and African–Americans, in addition to carrying out genetic, radiographic, serologic, physical and functional examinations on its participants.

"The strong association shown in this study between progressive OA and the *IL-1Ra* gene variations, as well as the body of previous related published research, might suggest that this *IL-1Ra* genetic information could be tested as a tool to identify high-risk patients for participation in clinical trials for the development of a much-needed disease modifying OA drug," hinted Jordan.

Currently, there are no approved drugs for the modification of disease progression in OA, despite the fact that it is the greatest cause of disability in the USA. In order to develop new drugs, there needs to be methods for predicting which patients are more likely to progress to severe disease.

"Drug development for OA has been challenging, in part due to the difficulty of enrolling patients who are likely to exhibit disease progression during the study. There appears to be strong potential to use the *IL-1Ra* genetic patterns to select for clinical trials patients who are more likely to benefit from an effective drug," explained Ken Kornman, Chief Scientific Officer, Interleukin Genetics. "A genetic test also would have strong clinical utility for physicians to better manage patients who will more likely progress to a severe form of the disease and require surgery."

This study was part of the Johnston County Osteoarthritis Project, directed by Jordan, which monitored 1154 **individuals** between 4 and 11 **years** to analyze the initiation and progression of OA. At the beginning of the study, the participants were examined for genetic markers predicting whether they would remain stable or progress to severe disease, confirmed radiographically. A total of nine genes were discovered to be associated to osteoarthritis progression, the strongest predictor being the variations found in *IL-1Ra*.

Source: University of North Carolina School of Medicine: www.med.unc.edu

"There appears to be strong potential to use the IL-1Ra genetic patterns to select for clinical trials patients who are more likely to benefit from an effective drug..."

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Study suggests that supplements to combat joint pain are taken by millions but do not work

Glucosamine and chondroitin are supplements that are taken together or alone to minimize the pain caused by osteoarthritis. A group of scientists, led by Peter Jüni at the University of Bern in Switzerland, warn that, "health authorities and health insurers should not cover the costs for these preparations, and new prescriptions to patients who have not received treatment should be discouraged."

However, as the supplements are not dangerous, they see no harm in allowing people to continue to use them as long as they perceive a benefit and that the cost is covered by the patient.

The authors expressed a desire for treatments that reduce pain and also slow the progression of disease since the most common treatments – pain-killers and anti-inflammatory drugs – can cause stomach and heart problems when used for long periods of time.

Glucosamine and chondroitin have been increasingly prescribed by GPs and rheumatologists over the last 10 **year**s, and many osteoarthritis sufferers have purchased the supplements over the counter. By 2008, global sales of glucosamine had accomplished nearly $2bn, an increase of 60% since 2003.

There are conflicting results presented by previous trials on the effectiveness of glucosamine and chondroitin and a review of these studies was required on a large scale, in order to determine whether or not the supplements work.

In the recent work, Juni and coworkers evaluated data from ten published trials, including 3803 **patient**s with knee or hip OA. Changes in pain levels were analyzed after patients had taken glucosamine, chondroitin or a combination (with placebo or head-to-head). The results of this evaluation was that there is no relevant effect of chondroitin, glucosamine, or their combination, on perceived joint narrowing or joint pain.

However, regardless of this conclusion, some patients appear to be persuaded that these preparations are beneficial. The authors suggest that this is owing to the natural cause of osteoarthritis or the placebo effect.

The authors conclude, "Compared with placebo, glucosamine, chondroitin, and their combination do not reduce joint pain or have an impact on narrowing of joint space. Health authorities and health insurers should be discouraged from funding glucosamine and chondroitin treatment."

Sources: Wandel S, Jüni P, Tendal B et al.: Effects of glucosamine, chondroitin, or placebo in patients with osteoarthritis of the hip or knee: network meta-analysis. BMJ doi: 10.1136/bmj.c4675 (2010) (Epub ahead of print).

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