A new treatment for osteoarthritis in horses and potentially humans

June 27 2023

Credit: Pixabay/CC0 Public Domain

For the first time, an intervention has emerged that seems competent in slowing down osteoarthritis (OA) progression. In a clinical study from SLU and University of Gothenburg, OA horses treated with a novel drug combination became completely free from lameness with a simultaneous

impediment of the joint tissue degradation. It could be worth exploring this drug for human OA intervention as well. The findings are published in the journal *Osteoarthritis and Cartilage Open*.

OA is an inflammatory-whole joint disease which affects both animals and humans. It is the most common cause of lameness and pain in horses . Racehorses often become lame early in their careers, and every year a large number of horses retire due to the disease.

A new drug with potential cure

The new potential treatment for OA is a product of a long-term collaboration of researchers and at SLU and the University of Gothenburg, resulting in a series of basic science publications. Through an extensive cell culture studies, the researchers were able devaluate and present a drug combination consisting of a local anesthetic drug, and an anti-inflammatory drug (sildenafil), in extremely low concentrations when combined with glucose can restore the derailed cartilage cells (i.e., chondrocytes) in OA.

"We have successfully reported the drugs' potential in receding inflammation and restoration of the derailed chondrocytes in OA. Such restored cartilage cells began to produce more matrix molecules, which are important building blocks of cartilage tissue. This further strengthens the drug combinations' potential to cure osteoarthritis," says Elisabeth Hansson, professor at Sahlgrenska Academy, University of Gothenburg, who is one of the research leaders in the collaboration.

New method for diagnosis

The research team has developed assays to screen horses' synovial fluid from the joints and diagnose OA much earlier i.e., even before the

clinical indications of OA. This was indispensable for clinically testing the drug in horses. The current study, published in the journal Osteoarthritis and Cartilage Open, uses these assay methods both to diagnose the disease and to measure the efficacy of the new drug treatment.

Two biomarkers are elevated in both synovial fluid and blood, in the horses with OA. These biomarkers are by-products of OA associated degradation of extracellular matrix molecules in the joint namely: $COMP^{156}$, a fragment of cartilage extracellular matrix component i.e., cartilage oligomeric matrix protein and BGN^{262}, a fragment of bone extracellular matrix component biglycan (BGN^{262}). These biomarkers have been crucial in the development of the new drug treatment presented.

"With the aid of these biomarkers, we can now diagnose the disease in an early stage (which was not possible previously), measure the efficacy of drug and also screen for the drugs side effects," says Eva Skiöldebrand, professor at the Swedish University of Agricultural Sciences.

Randomized clinical trial

In this study, the new drug combination was tested in a randomized triple-blinded controlled clinical trial. The study was conducted at Hallands Djursjukhus (Kungsbacka Hästklinik). The clinic manager Kristin Abrahamsson-Aurell was responsible for the study with veterinarian Cecilia Grahn as the treating veterinarian. Twenty lame trotters with mild radiological changes in the carpal joint were included in the study. The horses were randomized into groups for treatment with the drug combination or the treatment widely in use (the drug Celeston bifas). The horses were followed thereafter for 60 days.

"The horses treated with the new drug combination became free from lameness. The treatment efficiently lowered the analyzed biomarkers' levels in the synovial fluid when compared to the horses that received the control substance. The drug intervention did not cause any side effects in this study. Moreover, several of the treated horses remained sound for a long time following the treatment, which gives great hope for the future of the drug as a disease-modifying agent. This will have a tremendous positive impact on horse welfare," says Eva Skiöldebrand.

Potential for treatment in humans

In Sweden, OA is also the most common joint disease in humans, especially among the elderly. About one in four people over the age of 45 develop osteoarthritis. Currently there is no cure for this. Moreover, the available drugs on the market can only reduce pain and limit inflammation in the joint.

"Horses and humans are genetically very similar. Horses develop OA spontaneously, thus making it an excellent study and translation to explore and develop therapeutics for human OA. Additionally, the biomarkers identified and evaluated in the clinical trial are identical in horses and humans. Therefore the biomarkers and the analytical methods are equally relevant in human OA," says Eva Skiöldebrand.

The research team has a patent for the new drug combination and aims to commercialize it as a licensed drug for horses with OA, starting in Sweden. They will now also seek authorization to conduct a clinical trial of the drug in humans.

More information: E. Skiöldebrand et al, A randomized, triple-blinded controlled clinical study with a novel disease-modifying drug combination in equine lameness-associated osteoarthritis, *Osteoarthritis and Cartilage Open* (2023). DOI: 10.1016/j.ocarto.2023.100381

Provided by University of Gothenburg