Medical Xpress

Steroids prevent protein changes seen in the joints of people with rheumatoid arthritis

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Rheumatoid arthritis (RA) is a chronic inflammatory disease where the body begins to attack the joints and organs of the body. Proteins within inflamed joints are often modified by citrullination, a process that converts the protein building block arginine into citrulline. These two amino acids have very different physical properties and consequently conversion can result in aberrant changes in the three-dimensional structure of an affected protein. New research published in BioMed Central's open access journal *Arthritis Research & Therapy* shows that glucocorticoid therapy can reduce the amount of citrullination and the amount of the enzyme peptidylargininedeiminase 4 (PAD4) responsible for citrullination in the joints of people with RA.

People with RA have excessive amounts of protein citrullination in their inflamed joints. It is thought that these proteins are involved in initiating and maintaining the joint inflammation seen in people with RA. Researchers from three countries, Sweden, America, and the Netherlands collaborated to look at the levels of citrullinated proteins in the joints of people with RA, and compared the before and after effect of current treatments – methotrexate and glucocorticoids.

As expected elevated levels of citrullinated proteins (CP) were found in the knees of people with RA, compared to the joints of the control group. The new research also discovered enhanced levels of the enzymes (PAD2 and 4), responsible for these aberrant proteins, in the biopsies of people with RA. Additionally both the level of CP and of PAD correlated with the extent of inflammation – the more CP and PAD the

worse the inflammation.

Treatment with methotrexate, an anti rheumatic drug, used to treat RA, had no effect on the levels of CP or PAD. However a single injection of glucocorticoid was able to reduce both the level of protein citrullination and PAD4, and this was matched by a decrease in visible signs of inflammation.

The beneficial effect of glucocorticoids was limited to cells from the inflamed joints. A synthetic glucocortioid (DEX) was tested in on both synovial fluid and blood from people with RA, but only the cells from the synovial fluid responded with a decrease in CP and PAD2 or PAD4.

Dr Anca Catrina from the Karolinska Institute and University Hospital who led the research explained that future tailoring of RA management and the development of new treatments is dependent on a better knowledge of the disease. She said, "Our work has been able to establish for the first time that different treatments have different effects on protein citrullination, an important process in the progression of RA."

More information: Local administration of glucocorticoids decrease synovial citrullination in rheumatoid arthritis, Dimtrios Makrygiannakis, Shankar Revu, Marianne Engström, Erik afKlint, Anthony P Nicholas, Ger JM Pruijn and Anca I Catrina, *Arthritis Research & Therapy* (in press)

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