Background: Osteoarthritis causes significant pain and disability with no approved disease-modifying drugs. There is evidence emerging from pre-clinical and human studies suggesting metformin may have disease-modifying properties in osteoarthritis. Given its pleiotropic effects and safety profile, metformin has the potential to be a novel therapy for osteoarthritis.

Objectives: We systematically reviewed the evidence from both pre-clinical and human studies for the potential disease-modifying effect of metformin in osteoarthritis.

Methods: Ovid MEDLINE, Embase and CINAHL were searched between inception and June 2021 using MeSH terms and key words to identify studies examining the association between metformin use and outcome measures related to osteoarthritis. Two reviewers performed the risk of bias assessment and 3 reviewers extracted data independently. Qualitative evidence synthesis was performed. This systematic review is registered on PROSPERO (CRD42021261052 and CRD42021261060).

Results: Fifteen (10 pre-clinical and 5 human) studies were included. Most studies (10 pre-clinical and 3 human) assessed the effect of metformin using knee osteoarthritis models. In pre-clinical studies, metformin was assessed for the effect on structural outcomes (n=10); immunomodulation (n=3); pain (n=4); and molecular pathways of its effect (n=2). For human studies, metformin was evaluated for its chondroprotective effect on structural progression (n=3); pain (n=1); and immunomodulation (n=1). Overall, all pre-clinical studies consistently showed metformin having a chondroprotective, immunomodulatory and analgesic effect in osteoarthritis, predominantly mediated by adenosine monophosphate-activated protein kinase activation. Evidence from human studies, although limited, was consistent with findings in pre-clinical studies.

Conclusion: There was low-certainty evidence for a medium effect of oral corticosteroids on pain relief and small-to-medium effect on functional improvement at 4-6 weeks. Intra-articular corticosteroids showed low-certainty evidence for a medium effect on functional improvement at 4-6 weeks. Corticosteroids had no significant effect on any outcomes over longer term. No trials examined the effect of corticosteroids on disease progression. The role of corticosteroids in hand osteoarthritis is limited.

REFERENCES:

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ASSOCIATION OF ADIPOKINES WITH SEVERITY OF KNEE OSTEOARTHRITIS ASSESSED CLINICALLY AND ON MAGNETIC RESONANCE IMAGING

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Background: Adipokines secreted by adipose tissue create a low grade systemic inflammatory state that could contribute to the pathogenesis of knee OA (KOA). Previous studies of association between adipokines and radiographic KOA represented late-stage disease shown as bony changes. Magnetic Resonance Imaging (MRI) has the advantage of showing early changes of KOA in all joint structures.

Objectives: We aimed to evaluate the association between the adipokines: Leptin, Adiponectin, Resistin, and hs-CRP with clinical, radiographical and MRI assessment of KOA severity.

Methods: We performed a cross-sectional study in participants with early KOA. Demographics, clinical (WOMAC), and MRI (IKOS Score) of KOA severity were assessed. Serum leptin, adipokines, resistin and hs-CRP were measured. Association of adipokines with clinical and MRI severity outcomes were evaluated using regression models with adjustment with age, sex, and body mass index (BMI).

Results: 139 participants with early KOA (82% women, mean ± SD age: 55.5 ± 7.8 years) were included. Participants had moderate KOA symptoms, mean WOMAC pain and function were 31.1 ± 18.4, and 32.0 ± 19.9 respectively. Mean BMI was 26.0 ± 5.9kg/m². After adjustment with age, sex and BMI, Leptin (p=0.001) and hs-CRP (p=0.03) were positively associated, while adiponectin (p=0.02) and resistin (p=0.03) were negatively associated with osteophyte size.