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 osteoarthritis1-5. 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 (CRD420221261052 and CRD420221261060).

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 (n=5) of the osteoarthritis disease process. For human studies, metformin was assessed for the effect on structural progression (n=3); pain (n=1); and immunomodulation (n=1). Overall, 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: Further high-quality clinical trials are needed to confirm these findings as metformin could be a novel therapeutic drug for the treatment of osteoarthritis.

REFERENCES:


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