

Knee osteoarthritis and bisphosphonates: Could BCP crystals be the missing link?

I read with interest your article regarding the potential of bisphosphonates for osteoarthritis (OA).¹ Since OA affects the entire joint, it is unsurprising that there has been great difficulty developing an effective targeted treatment. The lifetime risk of symptomatic knee OA has been estimated to be as high as 44.7%,² and therefore, we are in urgent need of finding a disease-modifying OA drug.³

Basic calcium phosphate (BCP) crystals have been found in 100% of OA knee and hip cartilages removed at joint replacement and therefore might represent a potential therapeutic target in OA.⁴ BCP crystals include various calcium phosphates, including partially carbonate-substituted hydroxyapatite, octacalcium phosphate, tricalcium phosphate and magnesium whitlockite.⁵ BCP crystals have multiple biologic effects in vitro. They have the ability to stimulate prostaglandins, cytokines and matrix metalloproteinase synthesis in various cells including macrophages, synovial fibroblasts and chondrocytes.⁶ BCP crystals also contribute to inflammation in OA via the innate immune system.

Bisphosphonates are well-known analogues of endogenous pyrophosphate. They have a strong affinity for bone mineral and therefore tightly bind to hydroxyapatite crystals.⁷ This may be the reason behind the potential therapeutic effect of bisphosphonates in knee OA. With OA being the most prevalent rheumatic disease, affecting millions of patients worldwide, it is essential we urgently find a treatment for this much neglected disease. There is ample evidence that BCP crystals are a pathogenic mediator of OA and bisphosphonates as a potential OA treatment should be explored further.

Claire-Louise M Murphy,¹ Geraldine McCarthy²

¹Department of Rheumatology, Homerton University Hospital NHS Foundation Trust, London, UK

²Department of Rheumatology, Mater Misericordiae University Hospital, Dublin, Ireland

Correspondence to Dr Claire-Louise M Murphy, Department of Rheumatology, Homerton University Hospital NHS Foundation Trust, London E9 6SR, UK; claire-louise.murphy@nhs.net

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