

Potential role of hydrogen sulfide in osteoarthritis

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Background and aims. Osteoarthritis (OA) is a degenerative joint pathology associated with pain, reduced range of motion, impaired function and reduction in quality of life with a high prevalence among the elderly population. Although its complete etiology is not known, it is characterized by a progressive loss of articular hyaline cartilage in the joints with the involvement of multiple inflammatory mediators. Hydrogen sulfide, traditionally classified as a soluble toxic gas, is now considered the third endogenous gasotransmitter and is emerging as a potential regulator of inflammation. Balneotherapy or bathing in thermal or mineral waters is used as a non-invasive treatment for several conditions and one of the main features of sulfurous water is the presence of hydrogen sulfide which might offer therapeutic value in the treatment of OA.

The purpose of this review is to provide an overview of the potential therapeutic benefits of hydrogen sulfide as an anti-inflammatory approach to osteoarthritis.

Methods. Non-systematic review of the published literature about the subject in the scientific database MEDLINE/PubMed using the following search terms "hydrogen sulfide", "osteoarthritis", "sulfurous water" and "balneotherapy". Data was retrieved from published articles in the last 10 years and selected according to their relevance.

Results. Hydrogen sulfide (H₂S) has been proposed to be a novel mediator of inflammation and is present in the synovial fluid. It has been found an endogenous production and seems to play an important function in physiological processes as a signaling molecule, in particular with vasodilator, anti-inflammatory, antioxidant and anti-nociceptive effects. Reports of possible pro-inflammatory properties regarding the endogenous production were also found and inhibition of H₂S endogenous synthesis also showed benefits, leading to a possible target intervention in human chronic inflammatory diseases with control of H₂S synthesis. Nonetheless, H₂S exogenous sources showed anti-catabolic cartilage effects in vitro cellular models which were maintained over time directly in OA cartilage tissue. The usage of H₂S sources also led to reduction in the activation of NF-κB pathway, PGE-2,

IL-6 and Collagenase-3. Furthermore, H₂S donors was found to elicit anti-inflammatory activity with superior effects than naproxen in a preclinical in vivo study. In addition, the sulphide ion (S²⁻) seems to be beneficial for proteoglycan synthesis in the cartilage tissue. Balneotherapy constitutes an important approach in OA with improvements in pain management, motor function and psychosocial aspects and, in addition to the mechanical and heat effect of water, absorption of minerals may also play a therapeutic role. In fact, evidence for an antioxidant effect of sulfur water in patients with hip OA and an overall clinical improvement was established. These gains were also present in knee OA and patients treated with hot sulfurous water had better outcomes than those treated with heated non-sulfurous water. This same conclusion was established for hand osteoarthritis, with longer lasting improvement, reaffirming the potential role of exogenous hydrogen sulfide as a therapeutic approach.

Conclusions. There is increasing evidence that hydrogen sulfide plays an important role in osteoarthritis joint inflammation in low concentrations of exogenous application. Balneotherapy with sulfurous water might be a good non-invasive approach with benefits other than the H₂S exogenous administration alone. Further studies are needed regarding hydrogen sulfide role in the inflammatory process and exogenous administration properties.

Keywords. osteoarthritis, hydrogen sulfide, sulfurous water, balneotherapy