ScienceDirect

Life Sciences

Volume 147, 15 February 2016, Pages 24-29

Review

Unraveling the role of Mg^{++} in osteoarthritis

Yaqiang Li [1], Jiaji Yue [1], Chunxi Yang

Show more

Share Cite

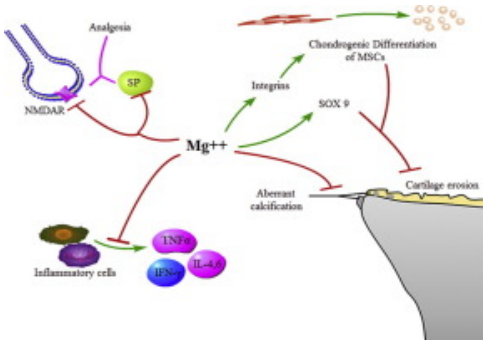
https://doi.org/10.1016/j.lfs.2016.01.029

Get rights and content

Abstract

Mg^{++} is widely involved in human physiological processes that may play key roles in the generation and progression of diseases. Osteoarthritis (OA) is a complex joint disorder characterized by articular cartilage degradation, abnormal mineralization and inflammation. Magnesium deficiency is considered to be a major risk factor for OA development and progression. Magnesium deficiency is active in several pathways that have been implicated in OA, including increased inflammatory mediators, cartilage damage, defective chondrocyte biosynthesis, aberrant calcification and a weakened effect of analgesics. Abundant *in vitro* and *in vivo* evidence in animal models now suggests that the nutritional supplementation or local infiltration of Mg^{++} represent effective therapies for OA. The goal of this review is to summarize the current understanding of the role of Mg^{++} in OA with particular emphasis on the related molecular mechanisms involved in OA progression.

Graphical abstract



Download : Download high-res image (71KB)

Download : Download full-size image

Introduction

Osteoarthritis (OA) is currently one of the most prevalent chronic diseases and is a major source of pain, disability and socioeconomic cost worldwide. Prevalence studies show that OA affects an estimated 10% of men and 18% of women over 60years of age [1]. Joint replacement is the primary means of treatment for arthritis; however, this procedure has substantial adverse outcomes and a finite prosthesis lifespan. Current goals of OA research include reduction of OA morbidity and new prevention and treatment methods.

The pathogenesis of OA is not fully understood; however, the enhanced production of pro-inflammatory cytokines, predominantly interleukin (IL)-1 and tumor necrosis factor (TNF) α, in addition to extracellular matrix mineralization and cartilage degradation, are important features of OA pathophysiology [2]. Clinically, OA is characterized by joint pain, stiffness and limited mobility [3]. New therapeutic strategies for alleviating pain and mitigating early pathological changes have been proposed for the treatment of early osteoarthritis [4], [5].

Mg^{++} is the second most abundant intracellular and fourth most abundant extracellular cation and is a microelement in the human body [6]. The adult human body contains approximately 24g of magnesium—approximately 60%–65% in bones and, teeth and approximately 27% in soft tissues. Magnesium is an essential mineral that is needed for numerous physiological functions. Emerging evidence indicates that magnesium deficiency has a strong relationship with osteoarthritis. The Mg^{++} contents of biological samples (blood, serum, and scalp hair) from rheumatoid arthritis patients are lower than referents in both genders [7]. Numerous studies show that low dietary intake of Mg^{++} is associated with OA [8], [9]. Therapeutically, magnesium salicylate, a magnesium salt applied in the treatment of clinical diseases, is effective in treating osteoarthritis [10]. The role of Mg^{++} in OA is currently being studied in detail, and recent investigations have yielded new and exciting knowledge; this review aims to describe this new knowledge.

Section snippets

Magnesium and the inflammatory response

Several systematic studies have been conducted in recent years to determine the molecular mechanisms and roles played by Mg^{++} in a state of inflammation. Experimental magnesium deficiency in rats induces a series of inflammatory syndromes characterized by macrophage and leukocyte activation, the release of inflammatory cytokines and acute phase proteins, and the excessive production of free radicals. Elevated levels of pro-inflammatory cytokines (such as interleukin (IL)-6 and TNFα) play…

Protective effects of magnesium in cartilage

Extensive studies have revealed that damage to joints induced by a magnesium-deficient diet is identical to that by quinolones [30], [31]. A study on juvenile Wistar rats showed that supplementation with Mg^{++} can decrease joint cartilage lesions; a combination of vitamin E and Mg^{++} produced a better protective effect of cartilage [32]. We reasoned that if magnesium protects joint cartilage, Mg^{++} can directly enhance chondrocyte proliferation and increase growth factor effectiveness by…

Inhibition of aberrant mineralization

Articular chondrocalcinosis is characterized by the deposition of calcium pyrophosphate dehydrate (CPPD) crystals in articular cartilage [46]. Clinical manifestations of CCPD-induced articular diseases can present as acute synovitis, degenerative arthritis, chronic arthritis and certain forms of periarthritis [47], [48], [49]. CCPD-induced diseases commonly occur in elderly people. A cross-sectional study found that hypomagnesemia was associated with chondrocalcinosis [46]. In that study, the…

Analgesic effect

Patients suffering from arthritis ordinarily display joint pain. This joint pain severely impairs the patient's quality of life and significantly inhibits their daily life. Emerging evidence indicates that magnesium is effective in the treatment of arthritis and can significantly decrease a patient's pain [66], [67], [68]. The intra-articular injection of Mg^{++} is effective for postoperative analgesia in patients after arthroscopic knee surgery [69]. Mg^{++}-deficient rats demonstrate mechanical…

Future research directions

Therapies for OA, which are intended only to treat symptoms and alleviate pain or ultimately accept the total knee replacement surgery, do not slow the rate of disease progression. Effective strategies that increase our understanding of OA pathogenesis are essential for the development and evaluation of new disease-modifying therapies. More research is needed to identify the early molecular players in OA pathogenesis.

Abundant *in vivo* and *in vitro* evidence now suggests that Mg^{++} is an important…

Conclusion

Mg^{++} deficiency may influence several of the pathways involved in OA pathology, including the progressive loss of articular cartilage, abnormal bone formation and tissue inflammation, which collectively culminate in pain, loss of joint function and disability (Fig. 2). The evidence presented in this review strongly supports the hypothesis that Mg^{++} deficiency is a factor in OA onset and progression. Furthermore, the nutritional supplementation of Mg^{++} or local infiltration may represent a…

Conflicts of interest

The authors declare no conflicts of interest.…

Acknowledgments

The author's work was supported by Grants from the National Natural Science Foundation of China (81101344/HO604), the outstanding young talent-training plan of Tenth People's Hospital, Shanghai Tongji University School of Medicine (11RQ104), the Climb talent-training plan of Tenth People's Hospital, Shanghai Tong Ji University School of Medicine (04.01.13023) and the Fundamental Research Funds for the Central Universities (1501219095)....

Recommended articles

References (82)

S.L. Volpe
Magnesium in disease prevention and overall health
Adv. Nutr. (2013)

C. Malpuech-Brugere *et al.*
Inflammatory response following acute magnesium deficiency in the rat
Biochim. Biophys. Acta (2000)

M. Kharitonova *et al.*
Comparative angioprotective effects of magnesium compounds
J. Trace Elem. Med. Biol. (2015)

A. Mazur *et al.*
Magnesium and the inflammatory response: potential physiopathological implications
Arch. Biochem. Biophys. (2007)

A.J. Kowaltowski *et al.*
Ca2+-stimulated mitochondrial reactive oxygen species generation and permeability transition are inhibited by dibucaine or Mg2+
Arch. Biochem. Biophys. (1998)

L. Cabal-Hierro *et al.*
Signal transduction by tumor necrosis factor receptors
Cell. Signal. (2012)

N.Y. Su *et al.*
Phosphoinositide 3-kinase/Akt pathway is involved in mediating the anti-inflammation effects of magnesium sulfate
J. Surg. Res. (2013)

F. Gao *et al.*
Magnesium sulfate provides neuroprotection in lipopolysaccharide-activated primary microglia by inhibiting NF-kappaB pathway

J. Surg. Res. (2013)

Q. Li *et al.*

Ofloxacin induces oxidative damage to joint chondrocytes of juvenile rabbits: excessive production of reactive oxygen species, lipid peroxidation and DNA damage

Eur. J. Pharmacol. (2010)

M. Shimaya *et al.*

Magnesium enhances adherence and cartilage formation of synovial mesenchymal stem cells through integrins

Osteoarthr. Cartil. (2010)

View more references

Cited by (23)

Hybrid composites with magnesium-containing glycosaminoglycans as a chondroconducive matrix for osteoarthritic cartilage repair

2022, International Journal of Biological Macromolecules

> *Citation Excerpt :*
>
> ...H. Yao et al. found that injection of magnesium chloride into the joint cavity is beneficial to reduce inflammation and inhibit the progression of OA [20]. It has been reported that magnesium exerts an anti-inflammatory effect by enhancing the activity of PI3K/Akt and magnesium supplementation is beneficial to inhibit OA [21,22]. Moreover, it has been found that the increase in magnesium dietary intake was related to better cartilage structure of the knee joint through a cross-sectional study of cartilage structure [23]....

Show abstract

Research status of biodegradable metals designed for oral and maxillofacial applications: A review

2021, Bioactive Materials

> *Citation Excerpt :*
>
> ...The controlled release of Mg ions from the scaffolds significantly enhanced the proliferation and odontogenic differentiation of hDPSCs in vitro and generated more dentin like mineralized structures in vivo [184]. About 27% of Mg in adults is stored in soft tissues [185]. There is a close relationship between Mg and soft tissue....

Show abstract

Tetraacuo-bis-(N,N-dimethylacetamide-O)magnesium(II) chloride dihydrate. An option to improve magnesium effect on phosphatase stimulation and albumin binding

2021, Journal of Molecular Structure

Citation Excerpt :

...Literature shows that different alkaline phosphatases could be affected by the presence of magnesium. It has also been shown that magnesium compounds may behave as anti-osteoporotic agents. [38] The activation of alkaline phosphatase could be a good strategy to develop a new class of anti-osteoporotic agents....

Show abstract

Synthesis of chondroitin sulfate magnesium for osteoarthritis treatment

2019, Carbohydrate Polymers

Citation Excerpt :

...Numerous studies have proved the symptomatic efficacy of chondroitin sulfate on pain reduction, apoptosis inhibition, and functional ability improvement (Egea, Garcia, Verges, Montell, & Lopez, 2010; Hochberg et al., 2016; Jomphe et al., 2008; Mantovani, Maccari, & Volpi, 2016). Magnesium is the second most common cation in intracellular fluid of the human body and it mainly exists in the bone and soft tissue (Li, Yue, & Yang, 2016). Several studies have suggested that the deficiency of magnesium may cause inflammation (Lin, Tsai, Hung, & Huang, 2010; Malpuech-Brugere et al., 2000)....

Show abstract

A correlation between intestinal microbiota dysbiosis and osteoarthritis

2019, Heliyon

Show abstract

Calcium, magnesium, zinc and lead concentrations in the structures forming knee joint in patients with osteoarthritis

2018, Journal of Trace Elements in Medicine and Biology

Citation Excerpt :

...Furthermore, Mg deficiency is a factor in OA onset and progression. The nutritional supplementation of magnesium may slow the OA progression as well as decrease pain in the affected knee [13,14]. Zinc (Zn) plays a role in the growth and maturation of bone and cartilage, stimulating metallothionein synthesis and regulating the activity of vitamin D [15]....

Show abstract

View all citing articles on Scopus

1 These authors contributed equally to this work.

View full text