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Radiologic study of the magnesium oxide nanoparticles effect on growth plate healing in rabbits

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ABSTRACT

Background: The growth plate is important in new bone developing; therefore, its injury may cause closing the plate in premature period and effect on growth of the bone. This injury can lead to deformity of the skeleton, if not treated correctly and not monitored for a long time.

Aim: This study was aimed to evaluate radiographically the role of autogenous cartilage grafts impregnated with Magnesium Oxide Nanoparticles (MgONPs) in growth plate regeneration and in preventing the bone bridge formation at the growth plate defect.

Methods: Ten adult rabbits were divided into two groups: a control group and an MgO group. A 2 mm section of the proximal tibia's growth plate was surgically removed from all rabbits. In the control group, the gap was filled with an autogenous ear cartilage graft soaked in normal saline. While in the MgO group, the gap was filled with an autogenous graft soaked in a 50 µg/ml MgONPs solution.

Results: Post-surgery, both groups showed immediate lameness. However, lameness resolved in the MgO group after 3 days in compared to the control. The radiographic results in 7, 14, 21, and 28 days after surgery showed early growth plate closure in the control group, without limb shortening or angular deformity. In contrast, the MgO group exhibited a small periosteal reaction around the growth plate gap, with no evidence of bone bridge formation.

Conclusion: local application of MgONPs to a growth plate defect may postpone bone bridge formation, potentially preventing bone growth disorders. This finding highlights a promising strategy for managing growth plate injuries.

Keywords: Growth plate, Magnesium oxide nanoparticles, Rabbit, Radiography.

Introduction

Growth plate is a specialized cartilage type hyaline, which is situated at the end of the long immature bone and has a critical role in the growth and development of bones through endochondral ossification process (Long and Ornitz, 2013). Endochondral ossification is the process by which most bones in the vertebrate skeleton are formed and involved systemic replacement of cartilage template by bones (Jassim *et al.,* 2023). Chondrocyte cells attract angiogenesis and the inflow of osteoblasts and osteoclasts while acting as a crucial regulator of this process during its transitions via differentiation, growth, and finally death. Growth plate is under the regulatory control of several hormones and signaling compound and this site of bone is manifested by a high metabolic rate (Ağırdil, 2020). The five stages of chondrocyte maturation in growth plates are resting, proliferative, prehypertrophic, hypertrophic, and terminal phases, which the chondrocytes go through in a synchronized, step-by-step manner (Samsa *et al.,* 2017).

Damage to the development plate may cause growth abnormalities such as axial deviation or length disparities. When a growth plate cartilage tissue is damaged, undesired bone tissue typically forms a bony bar. This can result in issues such as rotational or angular deformity, total development stop, and changed joint mechanics (Guo *et al.,* 2023). Tissue engineering is currently widely employed for bone and cartilage regeneration after being presented as a potential therapeutic technique for achieving tissue regeneration using functional biological materials, seed cells, and biological factors. There were increase applications of nanoparticles come from their nanoscale dimension, which is the most important properties of these materials that enabling them to develop critical

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chemical and physical characteristics that enhance their performance (Poovi, 2017).

Tissue engineering technology used nanoparticles in order to achieve improved biological and mechanical performances. One useful method that simulates the extracellular matrix and facilitates cell-scaffold interaction to produce more functionalized tissue engineering constructs is the incorporation of particles into biomaterials (Barabaschi *et al.,* 2015).

The present study was aimed to evaluate the efficacy of Magnesium oxide Nanoparticles (MgONPs) in regeneration of the growth plate defect and prevention of bone bridge formation.

Materials and Methods

Ten rabbits weighing (1.5–2) kg were utilized in the present study. The rabbits were kept in individual cages, provided free food, and purified tap water. The animals were divided into two groups (five for each one): control group in which growth plate gap was filles by autogenous cartilage graft with local application of normal saline, while in the MgONPs group, the created gap in the growth plat was also filled by autogenous ear cartilage graft but with local application of 50 µg/ml MgONPs (NANOSHEL - US).

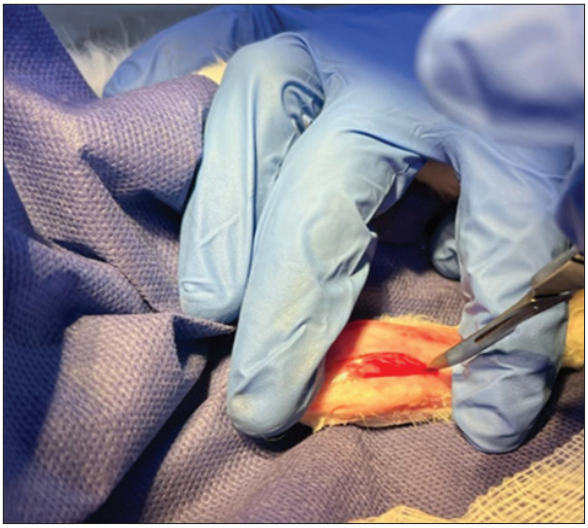

Fig. 1. Show skin incision in the proximal tibia.

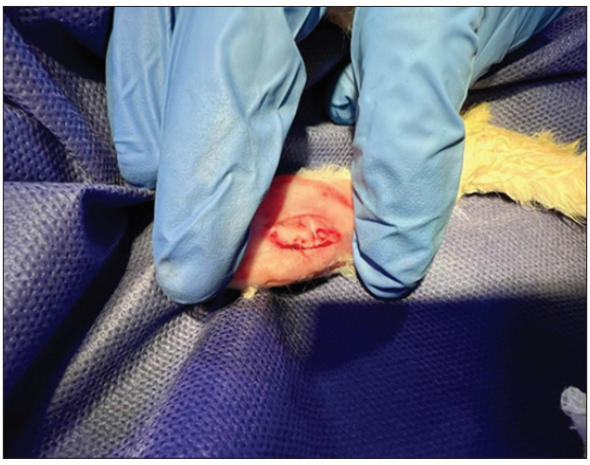

Fig. 2. Show exposure of tibial growth plate.

Xylazine HCL 5 mg/kg and ketamine HCL 13 mg/kg were injected intramuscularly (IM) as part of the anesthetic regimen to put the animals to sleep. In addition, only one-third of the ketamine dose could be used for the maintenance of anesthesia (Abduljaleel, 2024; Jasim *et al.*, 2025).

Surgical procedure

The right proximal tibia area was prepared for aseptic surgery by hair clipping and antiseptic application. The right proximal tibia was exposed by sharp surgical dissection about 3 cm on the medial part of the tibia (Fig. 1). When tibial growth plate is exposed (Fig. 2), 2 mm was removed from the growth plate by using bone drill (Fig. 3). In control group, the growth plate gap was filled by autogenous ear cartilage graft with normal saline, While in MgONPs group; the created gap in the growth plate was filled by autogenous ear cartilage graft with MgO nanoparticles (Fig. 4).

The skin was closed by using a simple interrupted suture pattern with Nylon suture material size 2–0. The rabbits were injected prophylactic antibiotic IM (4–5) days post-surgery to prevent secondary bacterial infection. The rabbits were monitored daily for signs of lameness. In addition, the growth plate healing process was evaluated radiologically for 7, 14, 21, and 28 days postoperatively.

Ethical approval

The Research Ethics Committee at the College of Veterinary Medicine, University of Basrah, granted its approval for the current investigation. All animal procedures were conducted in strict accordance with

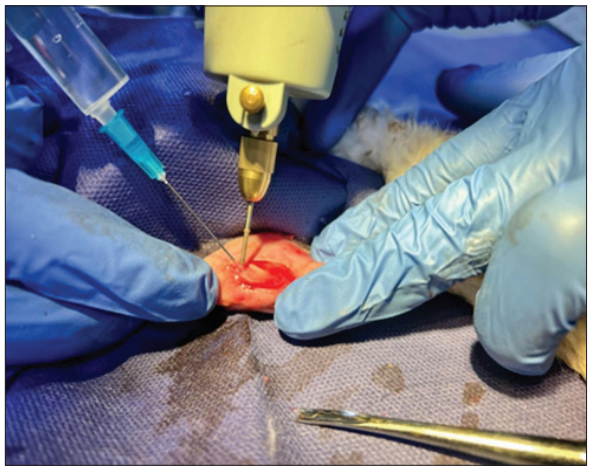

Fig. 3. Show creation of growth plate gap by using bone drill.

the recommendations provided by the committee. The approval number is 119/37/2026.

Results

Immediately after surgery, the clinical examination revealed the same degree of lameness in all animals of experiment (control and MgONPs groups) which was almost due to similarity of lesion. Lameness improvement was obvious at the end of the third day post-surgery in MgONPs group which showed normal weight bearing as a compared with control group in which lameness was disappear at fifth day post-surgery.

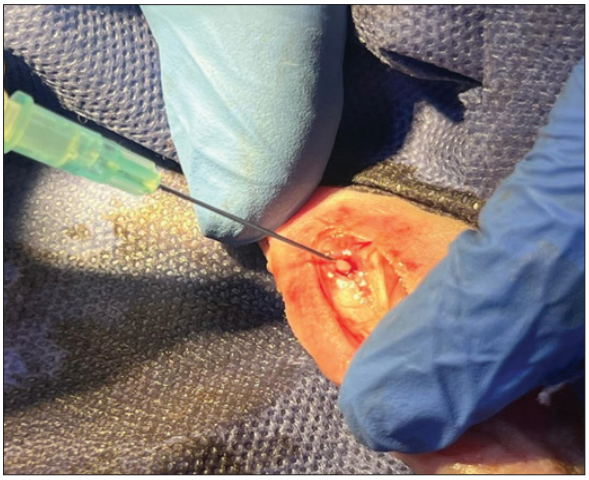

Fig. 4. Show local application of MgONPs on growth plate defect.

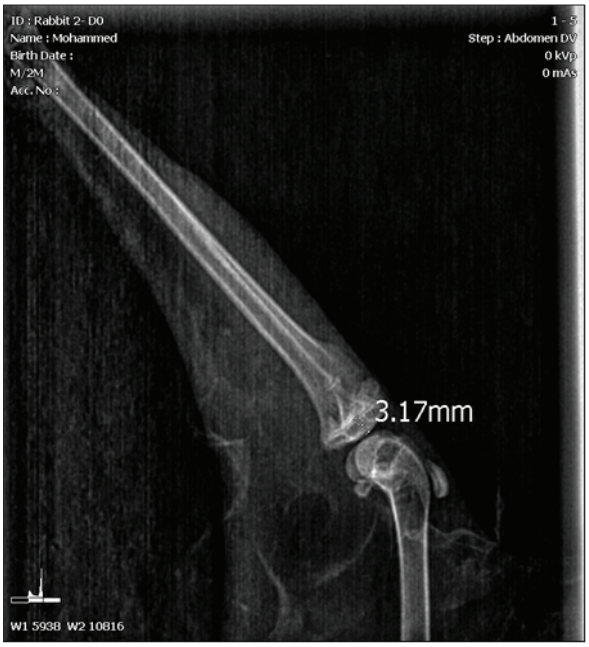

Fig. 5. Radiographic picture showed normal tibial growth plate.

We used X- ray before and after surgery to determine the accurate site of tibia growth plate (Figs. 5 and 6). Radiological findings after 7 days post-surgery showed more tissue reaction around the created gap in control group (Fig. 7). However, the MgO group showed a tiny tissue reaction (Fig. 8). The periosteal reaction was started to happened in the growth plate gap in control group in 14-day post-surgery (Fig. 9) as a compared

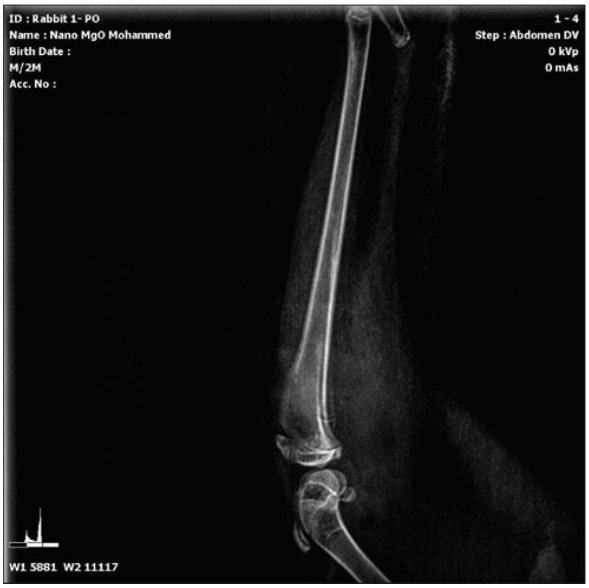

Fig. 6. Immediately post-surgery, radiographic picture showed autogenous ear cartilage in a created gap.

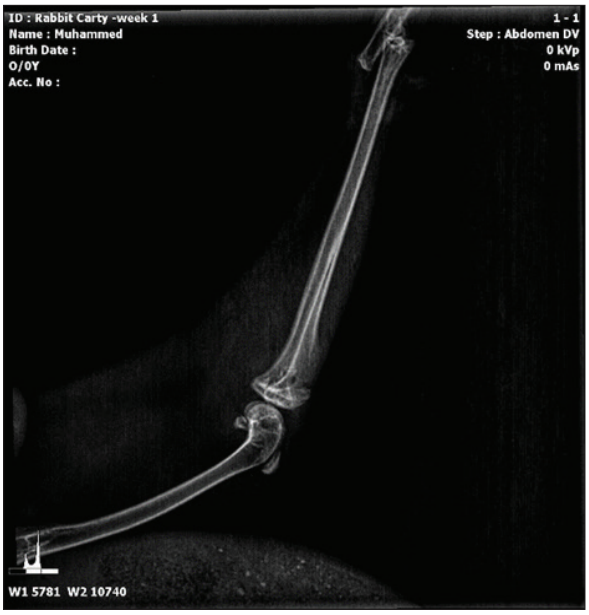

Fig. 7. Seven days post-surgery, control group showed created gap in the growth plate with evidence of tissue reaction.

with MgO group in which indication of periosteal reaction was not evident (Fig. 10).

Three weeks post-surgery, there were massive periosteal reaction at the growth plate in the created gap of the control group (Fig. 11); however, in MgO group the periosteal reaction was tiny (Fig. 12). Bone bridge formation with marked central epiphyseal plate closure were radiologically evidence in control group (Fig. 13) which were not recorded radiologically in MgO group which had just minor periosteal reaction (Fig. 14).

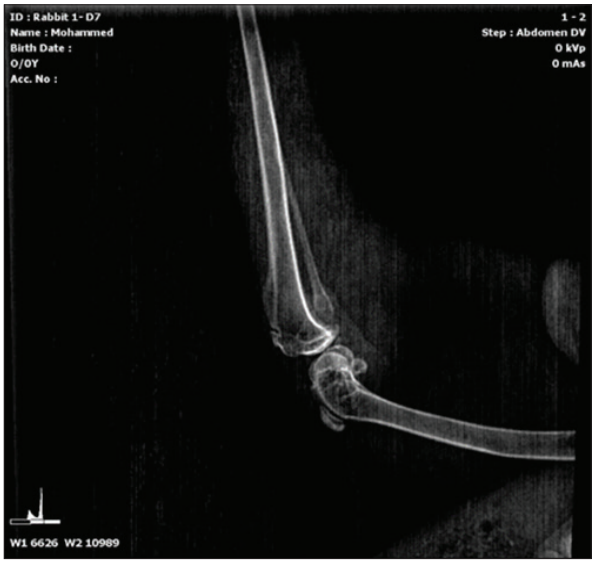

Fig. 8. Seven days post-surgery, MgO group showed the created gap tiny tissue react around the gap ridge.

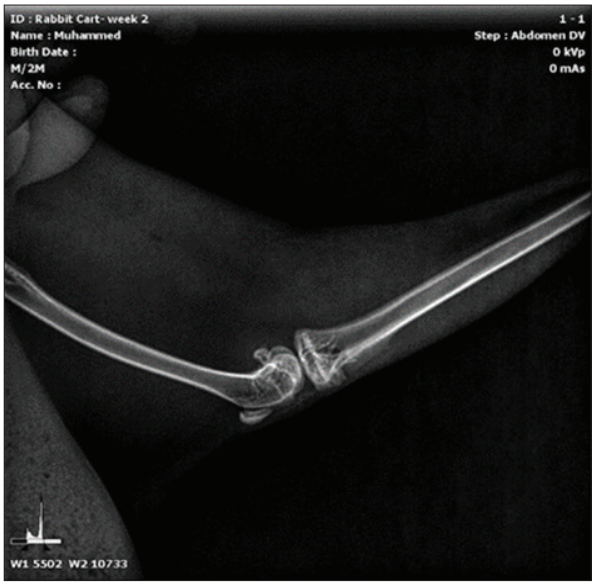

Fig. 9. Fourteen day post-surgery, radiography of control group showed created gap with periosteal reaction 2 weeks post-operation.

Discussion

Since growth plates are a cartilaginous tissue in nature, thus they are avascular and characterized by a limited capacity for regeneration. Since they are also developing tissues, injuries to them require prompt attention to avoid developmental problems and present special difficulties for clinical treatment. Therefore, growth plates present a special opportunity for the study of regenerative medicine, and they can offer insight into tissue engineering techniques not only for growth

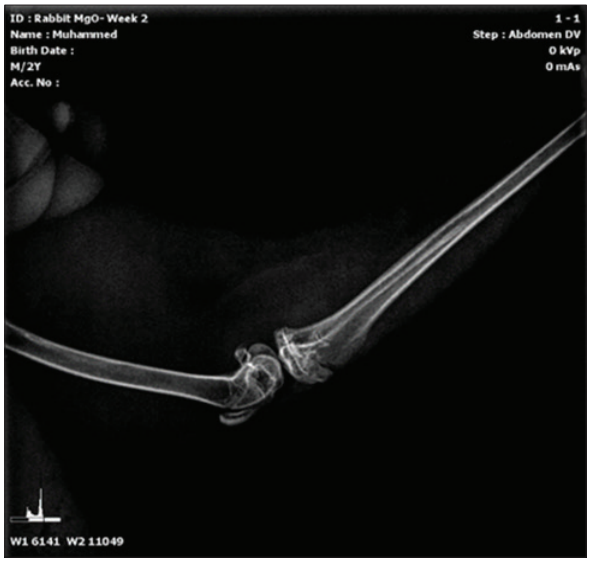

Fig. 10. Fourteen day post-surgery, Radiography of MgO group showed created gap with periosteal reaction 2 weeks post-operation.

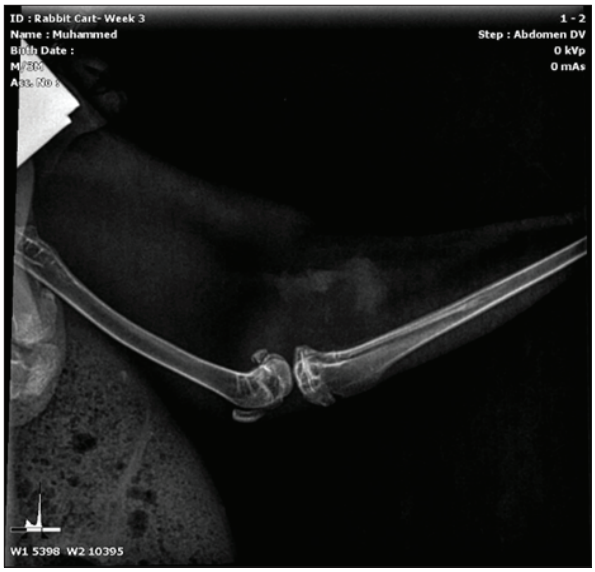

Fig. 11. Three weeks post-surgery, radiography of control group showed massive periosteal reaction with beginning of bone bridge formation after 3 weeks .

plate injuries but possibly for a broader spectrum of musculoskeletal tissues (Tiffany and Harley, 2022). In our present study, we investigated the possibility of using MgONPs with autogenous ear cartilage to accelerate growth plate cartilage healing and to prevent bone bridge formation at the growth plate defect.

Because Mg2+ can enhance proliferation and chondrogenic differentiation and inhibit Bone marrow-derived stem/stromal cells osteogenic differentiation by regulating protein kinase Bphosphorylation, our current study demonstrated that MgO NPs can prevent epiphyseal growth plate closure and prevent the formation of bone bridge at the growth plate defect (Zheng *et al.,* 2024). Our results agreed with those of Mei *et al.* (2024) who demonstrated that MgO NPs may extend the Mg2+ release period from 0.5 to 12 hours and are a safe and effective therapy for osteoarthritis (OA). Cytotoxicity was not detected at values lower than 250 μg/ml. possible ways that MgONPs might be used to treat OA. Nanoparticles of magnesium oxide help cells scavenge reactive oxygen species. In the synovial fluid, MgONPs break down to Mg $(OH)_2$, which releases magnesium ions while counteracting the acidic environment in the joint cavity, encourages the formation of cartilage matrix, and suppresses the expression of genes linked to inflammation and osteogenesis.

Hu *et al.* (2018), Alrafas *et al.* (2023), and Mohsin *et al.* (2025) discovered that magnesium inhibition affected the inflammatory cytokines secreted by activated macrophages triggered by lipopolysaccharide and interferon-γ, which may have contributed to magnesium's anti-inflammatory qualities. Additionally, by preventing the negative consequences of inflammation generated by activated macrophages, magnesium promotes the chondrogenic development of Mesenchymal Stem Cells

In order to treat OA in rabbits, Liu *et al.* (2025)devised a delivery method based on a Controlled Magnesium Ion Release System for Targeted Inhibition of OA Progression ($MgO@SiO_2$) core/shell nanoparticles, which intended as a depot for the regulated release of magnesium ions. They discovered that the ongoing release of Mg2+ from the nanocapsules, which reduces

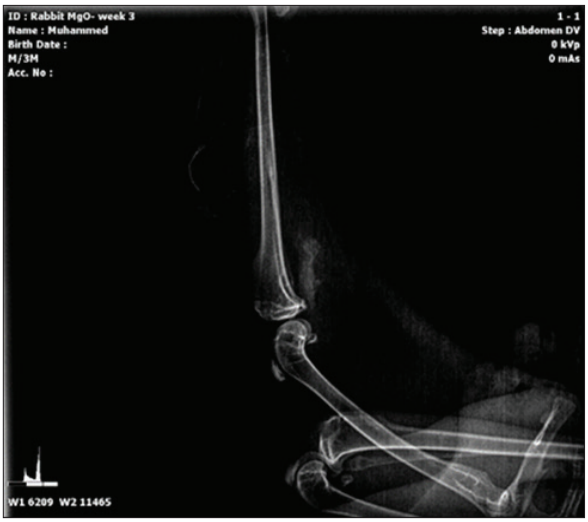

Fig. 12. Three weeks post-surgery, radiography of MgO group showed growth plate created gap with tiny periosteal reaction 3 weeks post-surgery.

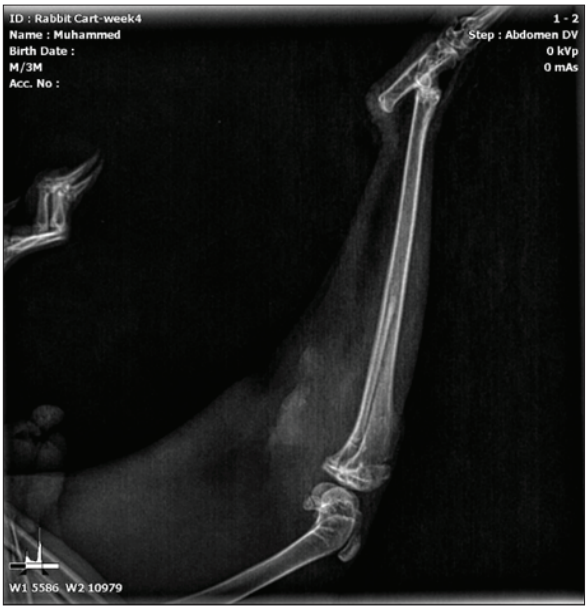

Fig. 13. Three weeks post-surgery, radiography control group showed periosteal reaction with bone bridge formation after 4 weeks.

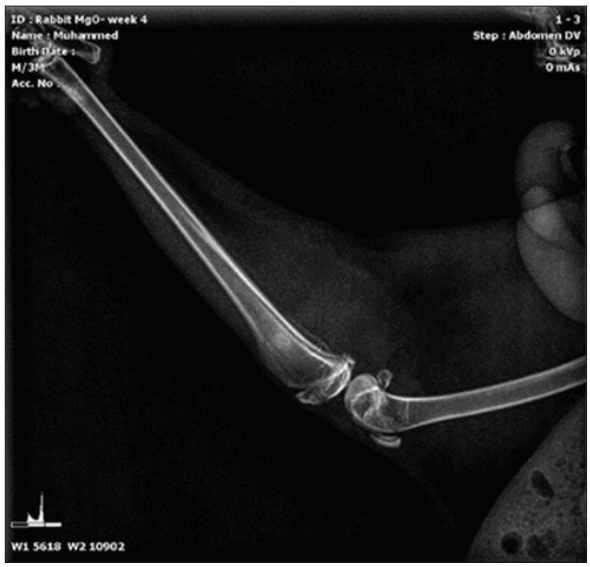

Fig. 14. Three weeks post-surgery, radiography of 2 MgO group showed minor periosteal reaction without evidence of bone bridge formation after 4 weeks.

the synthesis of inflammatory factors linked to the NF-κB/p65 pathway, is probably what suppresses the development of OA.

Conclusion

Our study showed the ability of autogenous ear cartilage impregnated with MgO NPs in preventing bone bridge formation at the site of growth plate defect. Also, the present study showed the efficacy of MgONPs in prevents early closure of epiphyseal plate and thereby improve bone growth disorders.

Acknowledgments

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Conflict of interest

The authors have declared no conflict of interest.

Funding

None.

Novelty statement

This study presents a novel approach to growth plate injury repair by demonstrating that MgONPs, when incorporated into autogenous cartilage grafts, can postpone bone bridge formation at the defect site. This is a significant finding as it suggests a potential mechanism to prevent growth disturbances and angular deformities commonly associated with premature growth plate closure. Unlike conventional methods that often lead to early bridging and subsequent growth issues, our findings highlight the unique ability of MgONPs to modulate the healing process, allowing for more natural growth plate regeneration.

Authors' contributions

R.M. Naeem, A.A. Ibrahim, A.M. Hashim, W.M.M. Saleh and L.A. Naeem, worked in development of the methodology, preparing and writing the initial draft, reviewing, and editing the manuscript, and analyzing the data. In addition, R.M. Naeem, A.A. Ibrahim, A.M. Hashim, M.R. Abduljaleel and M.M. Jassim performed surgical operations, animals' monitoring, and X-ray evaluations. While, W.M.M. Saleh and R.M. Naeem looked over the document, provided feedback, and approved the final version.

Data availability

To obtain any complementary information, please contact the corresponding author.

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