EXPERIMENTAL STUDY

The potential use of tetracalcium phosphate in vertebral augmentation: A study in a sheep model

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ABSTRACT

BACKGROUND: Percutaneous vertebroplasty (PVP) and percutaneous kyphoplasty (PKP) are widely used to treat vertebral fractures. However, the standard filler material, polymethylmethacrylate (PMMA), presents significant drawbacks, including thermal damage, allergic reactions, and poor biocompatibility. Tetracalcium phosphate (TTCP), a calcium phosphate cement (CPC), has emerged as a promising alternative due to its superior biocompatibility, osteoconductivity, and ability to integrate with natural bone. This study aimed to evaluate the feasibility of TTCP for vertebral augmentation in a preclinical sheep model, focusing on biomechanical stability, biocompatibility, and osteogenic potential.

METHODS: Five Akkaraman sheep underwent PKP with TTCP at three lumbar vertebral levels (L2–L4). Under general anesthesia, TTCP cement was injected into cavities prepared according to the standard PKP procedure. Postoperative care included analgesia and antibiotics. Four animals were followed for 12–14 weeks, and one for 25 weeks. At the end of the study period, the animals were euthanized and vertebrae were harvested for biomechanical testing using a Shimadzu AG-IS 100 kN machine. Histological evaluation was performed to assess ossification stages according to Shapiro's classification. Statistical analysis was conducted using paired t-tests ($p<0.05$).

RESULTS: One animal was euthanized prematurely due to infection, while four completed the study without complications. Biomechanical analysis demonstrated no significant difference in compressive strength between treated and untreated vertebrae ($p>0.05$). Histological examination revealed osteoblastic activity, progressive mineralization, and successful bone integration.

CONCLUSION: TTCP demonstrated promising biomechanical and biophysiological properties for vertebral augmentation. However, its use in infected sites and in the presence of metabolic bone disorders may be limited. Further clinical studies are required to validate its long-term efficacy.

Keywords: Percutaneous vertebroplasty; percutaneous kyphoplasty; tetracalcium phosphate; calcium phosphate cements; polymethylmethacrylate.

INTRODUCTION

Percutaneous vertebroplasty (PVP) and percutaneous kyphoplasty (PKP) are minimally invasive procedures designed to reinforce weakened vertebrae caused by osteoporosis, tumors, or trauma.[1] These interventions involve the percutaneous injection of polymethylmethacrylate (PMMA) into the affected vertebrae to restore structural integrity.[1] First introduced in 1987 by Galibert and Deramond, PVP was initially performed to stabilize a collapsed C2 vertebra affected by a hemangioma through the percutaneous administration of PMMA.[1]

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Over the years, PVP and PKP techniques have been refined to achieve near-optimal clinical outcomes; however, the search for more advanced biomaterials remains ongoing.[2] Numerous studies, including our own,[2] have aimed to develop bone replacement materials that are not only biophysiologically compatible but also capable of overcoming the limitations of existing materials.[3-5] Despite its widespread use, PMMA continues to present several challenges, including the risk of allergic reactions, excessive heat generation during polymerization, biomechanical properties that differ from those of spinal bone, and difficulties in processing.[6] Most notably, the lack of intrinsic biocompatibility of PMMA has prompted continued exploration of alternative materials.[6]

Among the candidate materials under investigation, calcium phosphate cements (CPCs) have emerged as a promising class of biomaterials due to their exceptional biocompatibility and osteoinductive properties.[7-11] These attributes make CPCs particularly suitable for bone repair and replacement applications.[7-11] One of the most extensively studied types of CPC is tetracalcium phosphate (TTCP), which combines a basic TTCP component with an acidic counterpart, such as brushite or monetite.[12] This formulation exhibits a self-setting mechanism in which an acid-base reaction, triggered by the addition of a hardening liquid, results in the formation of calcium-deficient hydroxyapatite.[12] CPCs possess several advantageous properties, including high bioactivity, non-cytotoxicity, and osteoconductivity.[13] Furthermore, their biodegradability allows gradual replacement by newly formed bone tissue following implantation.[13] These characteristics have led to their widespread application in dental implantology, where they have been used to reinforce implant sites and stabilize implants in cases of insufficient bone volume.[13-15]

Given the favorable properties of TTCP and its potential role in bone repair, the present study was designed to evaluate its applicability for vertebral augmentation in a preclinical sheep model. The objective was to determine whether TTCP could serve as a viable alternative to currently used materials for vertebral stabilization, leveraging its superior biocompatibility and osteogenic potential.

MATERIALS AND METHODS

Ethical Approval and Funding

All experimental procedures were approved by the Animal Research Ethics Committee of our university (Decision No: 2023/12) and were conducted in strict accordance with the European Communities Council Directive (86/609/EEC) on animal welfare. Funding was provided by the Scientific Research Projects Fund of Niğde Ömer Halisdemir University (Project No: 2024/4). The study was conducted in compliance with the principles of the Declaration of Helsinki.

Animal Selection and Surgical Preparation

The study included five Akkaraman sheep (2 years of age; 60–70 kg) obtained from the Ayhan Şahenk Agricultural Research and Application Center of Niğde Ömer Halisdemir University (Fig. 1). The animals were fasted for 24 hours prior to surgery. Rectal temperature was monitored to maintain a stable body temperature of 37°C throughout the procedure. All experiments were conducted in a controlled environment under veterinary supervision (H.K.) and surgical supervision (İ.K.) (Fig. 1). General anesthesia was induced intravenously with xylazine hydrochloride (Rompun®, Bayer, İstanbul, Türkiye; 0.1 mg/kg) and ketamine hydrochloride (Ketalar®, Bayer, İstanbul, Türkiye; 2.2 mg/kg). The animals were positioned on their right side to minimize the risk of hypoxia (Fig. 1). Surgical readiness was confirmed by the absence of palpebral and pinch reflexes. Standard aseptic and antiseptic protocols were followed. The surgical field was disinfected with povidone-iodine (Dermosept®, Algilaç, İstanbul, Türkiye) and sterile draping was applied (Fig. 1).

PKP Procedure

For the PKP procedure, the L2–L4 vertebral landmarks (transverse and spinous processes) were identified by palpation. A sterile Jamshidi cannula needle was inserted percutaneously at a 45° angle, 3 cm lateral to the midline, advancing into the cancellous bone of the vertebral body. A drilling device was used to create a 1 cm-deep cavity, which was verified with a probe. Subsequently, 3 mL of TTCP compound, comprising alpha-tricalcium phosphate, dicalcium phosphate, tetracalcium phosphate, and calcium silicate powder mixed with a sodium citrate solution (Grandus® B-One, Permed Health Products, Çanakkale, Türkiye), was injected into the cavity. Each animal underwent PKP at vertebral levels L2–L4 (a total of 15 treated vertebrae). The entry points were closed using sharp-needle 0/0 polypropylene sutures.

Postoperative Care and Follow-up Period

Postoperative pain and inflammation were managed with meloxicam (Maxicam®, Sanovel, İstanbul, Türkiye; 0.5 mg/kg/day for three days). Infection control included oxytetracycline hydrochloride spray (NEO CAF®; Merck Sharp & Dohme [MSD], İstanbul, Türkiye) and antibiotic injections (Reptopen S®, Ceva, İstanbul, Türkiye; 3 mL/day for five days). Animals recovered under close observation and were housed individually for five days before being returned to the flock. They

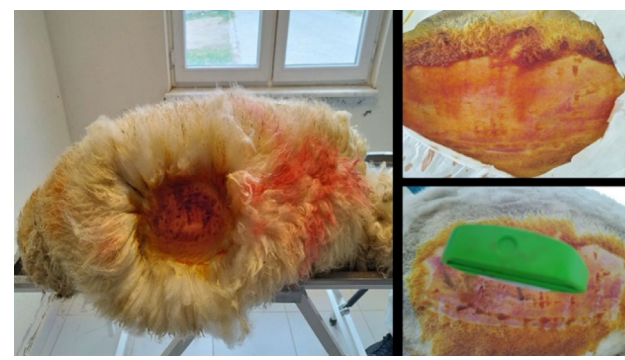

Figure 1. Study phases.

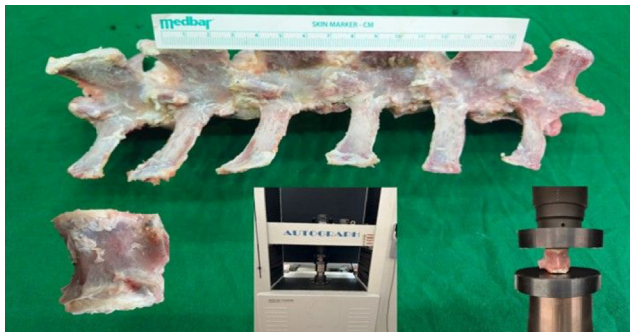

Figure 2. Appearance of the isolated vertebra and the treated vertebra, along with the biomechanical force-impact testing procedure performed using the Shimadzu Autograph AG-IS 100 machine.

were maintained at the Ayhan Şahenk Agricultural Research and Application Center of Niğde Ömer Halisdemir University with unrestricted access to food and water. One animal was euthanized on postoperative day 10 due to systemic infection secondary to wound contamination, likely resulting from the inability to protect the surgical site from contact with surrounding structures during movement. This animal was excluded from the final analysis. The remaining four animals were followed longitudinally: three were observed for 12–14 weeks, and one for 25 weeks. Sutures were removed two weeks postoperatively. No additional complications or adverse effects were observed, and all remaining animals resumed normal flock activity. At the end of the study period, euthanasia was performed using an overdose of xylazine hydrochloride (Rompun®; Bayer, İstanbul, Türkiye) and ketamine hydrochloride (Ketalar®; Bayer, İstanbul, Türkiye). Vertebrae L1–L5 were dissected for analysis (Fig. 2).

Biomechanical Testing

Biomechanical compressive testing of vertebrae L1, L2, L4, and L5 was performed using a Shimadzu Autograph AG-IS 100 kN testing machine (Shimadzu, Kyoto, Japan). Testing was conducted with a compressive tool at a crosshead displacement rate of 1 mm/min to generate force-stroke curve data in the Hydraulic and Pneumatic Laboratory, Faculty of Engineering, Department of Mechanical Engineering, Niğde Ömer Halisdemir University (Fig. 2). Force-stroke data for each specimen were recorded using the Trapezium software integrated with the Shimadzu testing system. Data analysis was conducted on a computer equipped with an Intel Xeon 2.2 GHz processor, 28 GB RAM, and a 16 GB NVIDIA Tesla P100 GPU. All tests were conducted in air at 20°C under an atmospheric pressure of 656 mmHg. Further biomechanical evaluation of TTCP was considered infeasible due to ethical constraints, limited animal availability, financial limitations, and fundamental anatomical and postural differences inherent to the species.

Histological Processing and Evaluation

The L3 vertebrae were fixed immediately in 10% formalin following dissection of L1-5 for histological analysis. After completion of biomechanical testing, L2 and L4 vertebrae were also fixed in formalin and processed histologically together with L3 at the Department of Pathology, Faculty of Medicine, Niğde Ömer Halisdemir University. Bone specimens underwent decalcification in 3% nitric acid, followed by paraffin embedding, sectioning at 4 µm thickness, and hematoxylin-eosin (H&E) staining. All histological evaluations were performed in a blinded manner by a professional histopathologist (C.Ö.). Microscopic findings related to bone formation were assessed according to the "Classification of Stages of Woven Bone Formation" described by Shapiro et al.[16] (Table 1).

Table 1. "Classification of Stages of Woven Bone Formation" by Shapiro et al.[16]

Stage 1	Highly cellular, densely packed accumulations of differentiating pre-osteoblasts present de novo at sites with no evidence of pre-existing bone tissue. These pre-osteoblasts are derived from the undifferentiated mesenchymal cell pool.
Stage 2	Mesenchymal osteoblasts surround themselves in a 360° arc with randomly oriented matrix fibers: a. The cell area is greater than the matrix area. b. The cell area is equal to the matrix area. c. The matrix area is greater than the cell area.
Stage 3	The matrix is sufficient to act as a scaffold upon which surface osteoblasts begin to synthesize bone in a lamellar configuration.
Stage 4	There is progressive reduction of woven bone within the woven bone/lamellar bone complex. This reduction is relative due to increased synthesis of lamellar bone and absolute due to osteoclastic resorption: a. Woven bone exceeds lamellar bone. b. Woven bone equals lamellar bone. c. Lamellar bone exceeds woven bone.
Stage 5	When the entire bone tissue developmental sequence from undifferentiated mesenchymal cells to exclusively lamellar bone is considered, stage 0 is defined as mesenchymal cell development from undifferentiated elongated cells to progressively differentiating oval cells, whereas Stage V represents the stage at which all bone observed in a region is lamellar.

Table 2. Key parameters of the force-impact curve data obtained using a Shimadzu Autograph AG-IS 100 kN testing machine (Shimadzu, Kyoto, Japan) at a constant test speed of 1 mm/min

Study Groups	Treated Vertebrae (L2, L4)	Control Vertebrae (L1, L5)
Minimum load	10,726.9 N*	10,342.5 N
Maximum load	9,920 N	10,713.8 N
Average maximum load	10,210.4 N	10,528.2 N
Standard deviation	448.436 N	262.549 N

*Newton

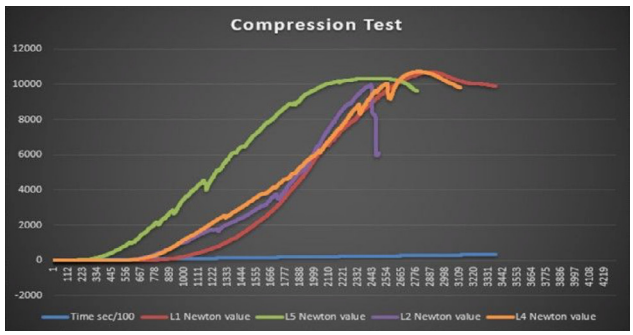

Figure 3. Force-impact test results.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics version 23 (IBM Corp., Armonk, NY, USA) and Microsoft Excel (version 17). Paired-sample t-tests and percentage analyses were conducted. Statistical significance was defined as $p<0.05$.

RESULTS

Macroscopically, no abnormalities were observed in the vertebrae. The entry points were located within 1–4 mm of the intended target regions (Fig. 2), and a penetration depth of at least 1 cm was achieved in all treated vertebrae.

Regarding mechanical resistance, no statistically significant differences were detected between treated and untreated vertebrae ($p>0.05$) (Table 2, Fig. 3). Despite the anatomical proximity of the vertebrae assigned to the treatment (L2, L4) and control (L1, L5) groups, as well as the inclusion of craniocaudally mixed levels, the comparable force–impact curve profiles observed in both groups suggest that TTCP effectively replicates the load-bearing characteristics of a healthy spine (Table 2, Fig. 3).

Microscopic examination demonstrated osteoblastic activity and mineralization within the bone specimens. The margins of the treated regions were interwoven with native bone tissue, rendering the distinction between treated and untreated areas difficult. Additionally, the material used for ossification appeared as a crystal-like foreign body in certain regions (Figs. 4, 5). Early ossification foci were also observed (Fig. 6). According to Shapiro et al.'s [16] "Classification of Stages of Woven Bone Formation" (Table 1), ossification at three months was classified as Stage 2c, whereas ossification at six months corresponded to Stage 4a (Figs. 4-6). These findings indicate that TTCP undergoes progressive replacement by newly formed bone over time.

DISCUSSION

Since its introduction in 1987 by Galibert and Deramond,[1] PVP and PKP techniques have undergone substantial refinement.[2] Despite numerous advancements, ranging from improvements in Jamshidi cannulas to the development of stent-assisted systems, progress in filler materials has remained largely confined to experimental trials, with PMMA continuing to be the only universally accepted material in clinical practice to date.[2-5] Considering its widespread use, PMMA has several notable limitations, including thermal injury, allergic reactions, difficulties in revision procedures when used in conjunction with implants, incompatibility with subsequent implant placement at treated sites, and, most critically, its lack of biocompatibility.[6,17]

In this context, TTCP, a member of the CPC family, has emerged as a promising alternative for PVP and PKP applications. Its unique properties make it particularly suitable for vertebral augmentation. TTCP hardens through an exothermic reaction at temperatures below 30°C, a process reported to be non-cytotoxic.[18] It achieves 50% of its ultimate compressive strength within one hour and 80% within four hours, thereby providing early mechanical stability and adhesive support in bone defects.[18] A key characteristic of TTCP is its higher calcium-to-phosphorus (Ca/P) ratio compared to hydroxyapatite, the principal mineral component of bone. Specifically, TTCP has a Ca/P ratio of 2.0, whereas hydroxyapatite has a ratio of 1.67.[19] This composition enables TTCP to form hydroxyapatite during the setting process.[19,20] The resulting structure is approximately 50–60% porous and negatively charged, creating an environment conducive to protein binding.[19,20] This, in turn, facilitates the attachment of circulating endogenous growth factors, thereby support-

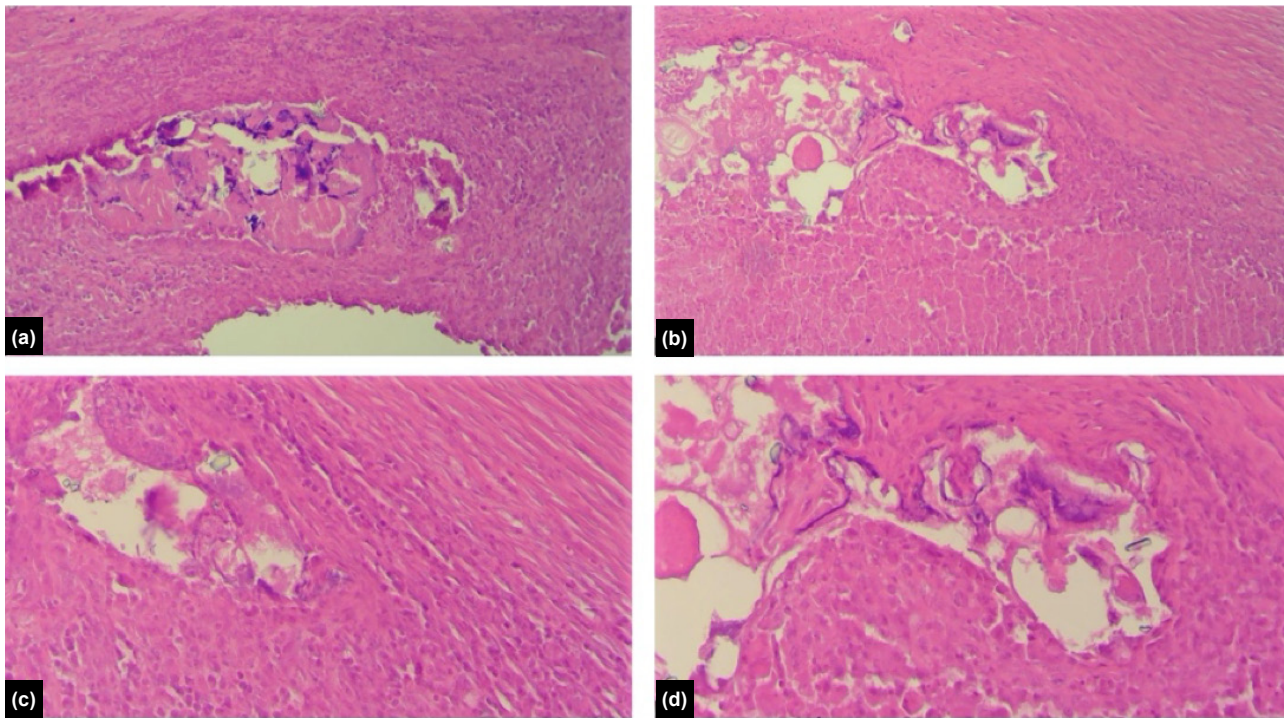

Figure 4. Representative images of microscopic ossification from the 14-week sample (A-B: Hematoxylin and eosin staining, ×100; C-D: Hematoxylin and eosin staining, ×200).

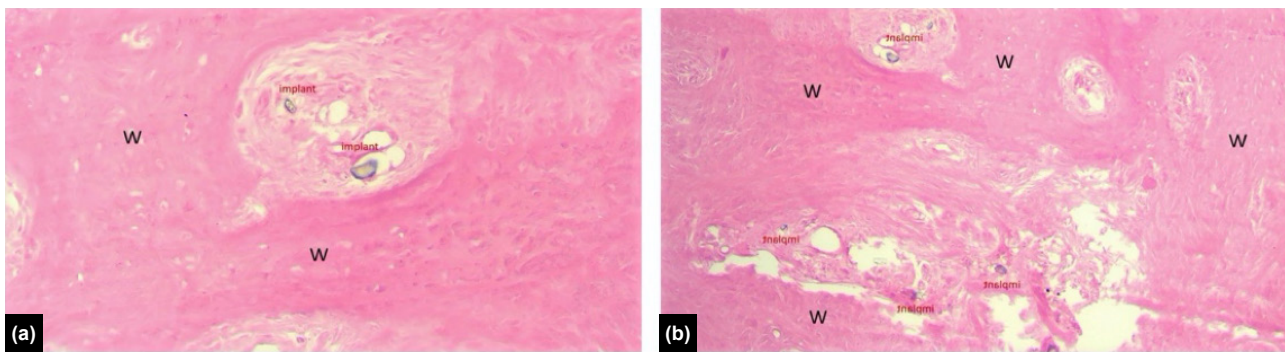

Figure 5. Representative images of woven bone formation with tetracalcium phosphate (TTCP) from the 25-week sample (A: Hematoxylin and eosin staining, ×100; B: Hematoxylin and eosin staining, ×200).

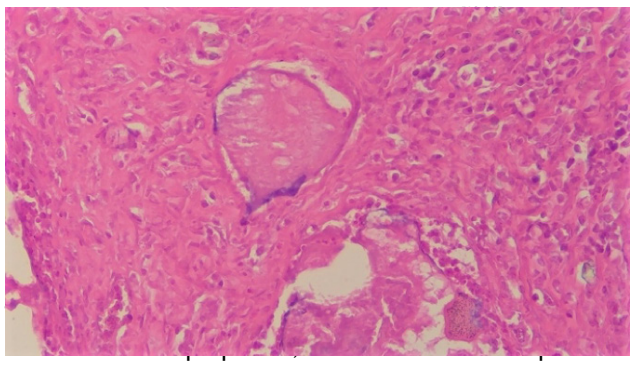

Figure 6. Representative image of an early ossification focus (Hematoxylin and eosin staining, ×200).

advantages and clinical applications. Unlike PMMA,[6] TTCP does not hinder implant placement or removal, as it gradually converts into native bone tissue over time. Additionally, TTCP demonstrates adhesive strength to both metal and bone that is comparable to that of native bone, as evidenced by long-term applications.[21,23] A significant advantage of TTCP cements is their potential to reduce the need for bone grafting, thereby eliminating donor-site morbidity associated with traditional graft materials.[22] Another noteworthy feature of TTCP is the absence of bone-inductive growth factors or osteogenesis-stimulating hormonal components in its formulation, which may render it suitable for use in tumorous pathologies.[24] Furthermore, TTCP is compatible

Table 3. Comparative biophysical properties of grafts[26-28]

Graft Type	TTCP (Tetracalcium Phosphate) Used in the Study	Autograft	Allograft
Hardening time	10 minutes	6 months	6 months
Time to full load-bearing capacity	4 hours (hardens in 10 minutes)	6 months	6 months
Graft resorption time	4-8 months	4-8 months	4-8 months
Volume loss	2%	10%	10%

with the instruments and devices currently used for PVP and PKP procedures with PMMA.[21,25] In our study, TTCP was successfully applied using these techniques in a sheep model characterized predominantly by cancellous vertebral bone, demonstrating its effectiveness. Tomita et al.[26] reported that, in cadaveric vertebral models subjected to PVP and PKP, no statistically significant differences were observed between preliminary tricalcium phosphate cement and PMMA under biomechanical testing conditions identical to those employed in our study, even in the absence of osteoregeneration. These findings suggest that, from a purely mechanical standpoint, advanced TTCP formulations may provide immediate load-bearing capacity comparable to that of PMMA following augmentation procedures.[26] Similarly, our short- and long-term microscopic and biomechanical analyses demonstrated findings comparable to those of normal bone, consistent with previous reports (Table 3).[17,19,21,22,25,27-33]

Despite its advantages, certain limitations of TTCP must be acknowledged. Unlike PMMA, TTCP does not generate high temperatures during polymerization, thereby preventing thermal damage to vascular lesions. Also, in such regions, the presence of blood may alter the liquid-to-powder ratio of the mixture, interfering with its activation.[18-20] Similarly, the use of TTCP is not recommended in infected sites.[34] This limitation is related to its organic composition, which may compromise infection control when implanted into contaminated tissues.[34] Additionally, alterations in the activator ratio may also occur in infected environments, further complicating the clinical use of TTCP under such conditions.[18-20] In these cases, alternative materials may be more appropriate, and research into antibiotic-containing materials is ongoing.[34] Another limitation of TTCP is its inability to achieve bone-level resistance to shear forces until complete replacement by native bone has occurred.[30] Although this limitation is not critical for PVP or PKP procedures, it presents challenges in long-bone reconstruction, where prolonged immobilization may be necessary.[30] Furthermore, TTCP is unsuitable in cases of severe degenerative bone disease (Z-scores below -3), as its primary mechanism relies on remodeling into functional bone tissue.[6] Similarly, conditions that impair osteoblastic activity, such as uncontrolled diabetes, pregnancy, substance or alcohol abuse, and renal failure, may compromise treatment outcomes with TTCP.[35] Conversely, in patients with hypercalcemia, the osteoinductive properties of TTCP may promote excessive deposition, making it unsuitable for use in such conditions.[35] Lastly, TTCP requires a bony scaffold for effective application, rendering it inappropriate for environments involving purely soft-tissue environments.[36]

CONCLUSION

Tetracalcium phosphate emerges as a highly suitable material for PVP and PKP procedures in modern medical practice due to its strong biomechanical and microscopic resemblance to natural bone, along with its faster ossification compared to autografts. However, TTCP has certain limitations, particularly its unsuitability for use in infected tissues or areas containing bodily fluids. Additionally, its effectiveness may be reduced in cases of severe degenerative bone disease, uncontrolled diabetes, hypercalcemia, or other conditions that impair normal bone metabolism. Further large-scale clinical studies are needed to validate its long-term efficacy and safety.

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Ethics Committee Approval: This study was approved by the Niğde Ömer Halisdemir University Animal Research Ethics Committee (Date: 16.10.2023, Decision No: 2023/12).

Peer-review: Externally peer-reviewed.

Authorship Contributions: Concept: İ.K., H.Y., H.K.; Design: İ.K.; Supervision: İ.K., H.Y., H.K., C.Ö.; Resource: İ.K., H.Y., H.K., C.Ö.; Materials: İ.K., H.Y., H.K., C.Ö.; Data collection and/or processing: İ.K., H.Y., H.K.; Analysis and/or interpretation: İ.K., H.Y., H.K., C.Ö.; Literature review: İ.K.; Writing: İ.K.; Critical review: İ.K.

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REFERENCES

1. Galibert P, Deramond H, Rosat P, Le Gars D. Preliminary note on the treatment of vertebral angioma by percutaneous acrylic vertebroplasty. Neurochirurgie 1987;33:166–8.

2. Kaya İ, Yakar H, Kesen E. Low-cost 3-D-printer-assisted personalized cranioplasty treatment: A case series of 14 consecutive patients. World Neurosurg 2023;175:e1197–e1209. [CrossRef]
3. Askari M, Afzali Naniz M, Kouhi M, Saberi A, Zolfagharian A, Bodaghi M. Recent progress in extrusion 3D bioprinting of hydrogel biomaterials for tissue regeneration: A comprehensive review with focus on advanced fabrication techniques. Biomater Sci 2021;9:535–73. [CrossRef]
4. Bodaghi M, Liao WH. 4D printed tunable mechanical metamaterials with shape memory operations. Smart Mater Struct 2019;28:045019. [CrossRef]
5. De Santis R, Russo T, Rau JV, Papallo I. Design of 3D additively manufactured hybrid structures for cranioplasty. Materials (Basel) 2021;14:181. [CrossRef]
6. Gaetti-Jardim EC, Santiago-Junior JF, Goiato MC, Pellizer EP, Magro-Filho O, Jardim Junior EG. Dental implants in patients with osteoporosis: A clinical reality? J Craniofac Surg 2011;22:1111–3. [CrossRef]
7. Chow LC. The centennial memorial issue of the Ceramic Society of Japan. J Ceram Soc Jpn 1991;99:954–64. [CrossRef]
8. Costantino PD, Friedman CD, Jones K, Chow LC, Pelzer HJ, Sisson GA Sr. Hydroxyapatite cement: I. Basic chemistry and histologic properties. Arch Otolaryngol Head Neck Surg 1991;117:379–84. [CrossRef]
9. Friedman CD, Costantino PD, Takagi S, Chow LC. BoneSource™ hydroxyapatite cement: A novel biomaterial for craniofacial skeletal tissue engineering and reconstruction. J Biomed Mater Res B Appl Biomater 1998;43:428–32. [CrossRef]
10. Liu CS, Shen W, Gu YF. Mechanism of hardening process for a hydroxyapatite cement. J Biomed Mater Res 1997;35:75–80. [CrossRef]
11. Shindo ML, Costantino PD, Friedman CD, Chow LC. Facial skeletal augmentation using hydroxyapatite cement. Arch Otolaryngol Head Neck Surg 1993;119:185–90. [CrossRef]
12. Brown WE, Chow LC. Dental restorative cement pastes. US Patent 4518430. 1985.
13. Carey LE, Xu HHK, Simon CG, Takagi S, Chow LC. Premixed rapid-setting calcium phosphate composites for bone repair. Biomaterials 2005;26:5002–14. [CrossRef]
14. Kawsar M, Sahadat Hossain M, Alam MK, Bahadur MN, Shaikh AA, Ahmed S. Synthesis of pure and doped nano-calcium phosphates using different conventional methods for biomedical applications: A review. J Mater Chem B 2024;12:3376–91. [CrossRef]
15. Nakamura T, Hayashi M, Tamura M, Kaketani M, Ito T, Takamizawa T, Suzuki Y, et al. Utility of biphasic calcium phosphate cement as a seal for root-end filling. Dent Mater J 2023;42:412–7. [CrossRef]
16. Shapiro F, Wu JY. Woven bone overview: structural classification based on its integral role in developmental, repair and pathological bone formation throughout vertebrate groups. Eur Cell Mater 2019;38:137–67. [CrossRef]
17. Blum KS, Schneider SJ, Rosenthal AD. Methylmethacrylate cranioplasty in children: long-term results. Pediatr Neurosurg 1997;26:33–5. [CrossRef]
18. Cohen MS, Whitman K. Calcium phosphate bone cement--the Norian skeletal repair system in orthopedic surgery. AORN J 1997;65:958–62. [CrossRef]
19. Moseke C, Gbureck U. Tetracalcium phosphate: Synthesis, properties and biomedical applications. Acta Biomater 2010;6:3815–23. [CrossRef]
20. Permed Health Products. Grandus brand B-ONE bone adhesive containing tetra calcium phosphate. Available at: https://grandusbone.com/. Accessed 2025 Feb 2.
21. Kaymaz B, Yılmaz O, Taşova AO, Anapa D. Tetracalcium phosphate treatment on experimental fracture model in rats. Jt Dis Relat Surg 2022;33:172–9. [CrossRef]
22. Larsson S, Bauer TW. Use of injectable calcium phosphate cement for fracture fixation: A review. Clin Orthop Relat Res 2002;395:23–32. [CrossRef]
23. Ko CL, Chang YY, Liou CH, Chen WC. Characterization of the aspects of osteoprogenitor cell interactions with physical tetracalcium phosphate anchorage on titanium implant surfaces. Mater Sci Eng C Mater Biol Appl 2015;49:7–13. [CrossRef]
24. Ogino I, Kitagawa M, Watanabe S, Yoshida H, Hata M. Calcium phosphate cement paste injection as a fiducial marker of cervical cancer. In Vivo 2018;32:1609–15. [CrossRef]
25. Foley KT, Woodard EJ, Slotkin JR, Mayotte CK, Baldwin AC, Brown MC, et al. Cranial flap fixation in sheep using a resorbable bone adhesive. J Neurosurg 2020;134:621–9. [CrossRef]
26. Tomita S, Kin A, Yazu M, Abe M. Biomechanical evaluation of kyphoplasty and vertebroplasty with calcium phosphate cement in a simulated osteoporotic compression fracture. J Orthop Sci 2003;8:192–7. [CrossRef]
27. Baldwin P, Li DJ, Auston DA, Mir HS, Yoon RS, Koval KJ. Autograft, allograft, and bone graft substitutes: Clinical evidence and indications for use in the setting of orthopaedic trauma surgery. J Orthop Trauma 2019;33:203–13. [CrossRef]
28. Greenberg MS. Handbook of Neurosurgery. 7th ed. New York: Thieme; 2010, p.197–200.
29. Ishiguro S, Kasai Y, Sudo A, Iida K, Uchida A. Percutaneous vertebroplasty for osteoporotic compression fractures using calcium phosphate cement. J Orthop Surg (Hong Kong) 2010;18:346–51. [CrossRef]
30. Lim TH, Brebach GT, Renner SM, Kim WJ, Kim JG, Lee RE, et al. Biomechanical evaluation of an injectable calcium phosphate cement for vertebroplasty. Spine (Phila Pa 1976) 2002;27:1297–302. [CrossRef]
31. Nakano M, Hirano N, Matsuura K, Watanabe H, Kitagawa H, Ishihara H, et al. Percutaneous transpedicular vertebroplasty with calcium phosphate cement in the treatment of osteoporotic vertebral compression and burst fractures. J Neurosurg 2002;97:287–93. [CrossRef]
32. Nakano M, Hirano N, Zukawa M, Suzuki K, Hirose J, Kimura T, et al. Vertebroplasty using calcium phosphate cement for osteoporotic vertebral fractures: Study of outcomes at a minimum follow-up of two years. Asian Spine J 2012;6:34–42. [CrossRef]
33. Welch RD, Zhang H, Bronson DG. Experimental tibial plateau fractures augmented with calcium phosphate cement or autologous bone graft. J Bone Joint Surg Am 2003;85:222–31. [CrossRef]
34. Joosten U, Joist A, Frebel T, Brandt B, Diederichs S, von Eiff C. Evaluation of an in situ setting injectable calcium phosphate as a new carrier material for gentamicin in the treatment of chronic osteomyelitis: Studies in vitro and in vivo. Biomaterials 2004;25:4287–95. [CrossRef]
35. Hou X, Zhang L, Zhou Z, Luo X, Wang T, Zhao X, et al. Calcium phosphate-based biomaterials for bone repair. J Funct Biomater 2022;13:187. [CrossRef]
36. Kim Y, Lee EJ, Kotula AP, Takagi S, Chow L, Alimperti S. Engineering 3D printed scaffolds with tunable hydroxyapatite. J Funct Biomater 2022;13:34. [CrossRef]

DENEYSEL ÇALIŞMA - *ÖZ*

Omurga augmentasyonunda tetrakalsiyum fosfatın olası kullanımı: Koyun modeli ile deneysel bir çalışma

AMAÇ: Perkütan vertebroplasti (PVP) ve perkütan kifoplasti (PKP), vertebra kırıklarının tedavisinde yaygın olarak kullanılan minimal invaziv yöntemlerdir. Ancak bu işlemlerde standart dolgu materyali olan polimetilmetakrilatın (PMMA) termal hasar, alerjik reaksiyonlar ve düşük biyouyumluluk gibi önemli dezavantajları bulunmaktadır. Kalsiyum fosfat esaslı bir çimento olan tetrakalsiyum fosfat (TTCP), üstün biyouyumluluğu, osteokondüktivitesi ve doğal kemikle entegrasyon yeteneği sayesinde alternatif bir materyal olarak öne çıkmaktadır. Bu çalışmanın amacı, TTCP'nin vertebra augmentasyonu amacıyla bir koyun modelinde biyomekanik stabilite, biyouyumluluk ve osteojenik potansiyel açısından değerlendirilmesidir.

GEREÇ VE YÖNTEM: Beş Akkaraman koyununda, L2–L4 lomber vertebra seviyelerinde standart PKP prosedürüyle hazırlanmış boşluklara TTCP enjeksiyonu yapıldı. Genel anestezi altında uygulanan işlem sonrasında analjezik ve antibiyotik tedavileri sağlandı. Dört hayvan 12-14 hafta, bir hayvan ise 25 hafta boyunca gözlemlendi. Takip sonunda ötenazi uygulanan hayvanlardan elde edilen vertebralar, Shimadzu AG-IS 100 kN cihazı ile biyomekanik testlere tabi tutuldu. Histolojik değerlendirme ise Shapiro sınıflamasına göre ossifikasyon evrelerini inceledi. Veriler, eşleştirilmiş t-testi ile analiz edildi ($p<0.05$).

BULGULAR: Bir hayvan enfeksiyon nedeniyle çalışmadan çıkarılırken, diğer dört hayvanda komplikasyon gözlenmedi. Biyomekanik analizler, tedavi edilen ve edilmeyen vertebralar arasında basma dayanımı açısından anlamlı fark olmadığını gösterdi ($p>0.05$). Histolojik incelemeler osteoblastik aktivite, ilerleyici mineralizasyon ve kemik entegrasyonu varlığını doğruladı.

SONUÇ: TTCP, vertebra augmentasyonu için umut verici biyomekanik ve biyofizyolojik özellikler sergilemiştir. Bununla birlikte, enfekte bölgelerde ve metabolik kemik hastalıklarında kullanımı sınırlıdır. Uzun dönem etkinliğini değerlendirmek amacıyla ileri klinik çalışmalara ihtiyaç vardır.

Anahtar sözcükler: Kalsiyum fosfat çimentolar; perkütan vertebroplasti; perkütan kifoplasti; polimetilmetakrilat; tetrakalsiyum fosfat.

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