Section: Research Paper

DEVELOPMENT OF TITANIUM IMPLANTS WITH CALCIUM PHOSPHATE COATING FOR ADDRESSING ASEPTIC INSTABILITY IN SPINE STABILIZATION PROCEDURES

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ABSTRACT:
Internal stabilization has become a popular approach for treating spine injuries and diseases, but aseptic instability of stabilizing system components remains a significant concern. This study aims to address this challenge by developing and implementing titanium implants with a novel therapeutic effect, incorporating a calcium phosphate coating for spinal fixation. A comprehensive study involving 1810 stabilizing operations was conducted, and the occurrence of aseptic instability was analyzed. Factors contributing to instability, such as osteopenia and non-compliance with exercise regimens, were identified. The study highlights the importance of specialized surface treatment and the potential of calcium phosphate coatings to improve osseointegration. The fabrication process of the experimental implants with calcium phosphate coatings is described. Clinical trials of these implants are planned to assess their effectiveness and safety. The findings of this research contribute to improving the outcomes of spine stabilization procedures and have implications for domestic implant manufacturers.

KEYWORDS: internal stabilization, aseptic instability, calcium phosphate coating, titanium implants, spine injuries, osteopenia, osseointegration, clinical trials.

INTRODUCTION

In recent years, internal stabilization has emerged as a modern approach for treating spine injuries and diseases, offering improved outcomes for patients [13, 16]. The increasing number of surgeries performed worldwide highlights the need to address associated challenges, especially late complications, despite advancements in surgical techniques and the wide range of available internal stabilization methods [10, 21]. Among these complications, aseptic instability of the stabilizing system components has become a significant concern due to its high frequency and potential dangers [1, 2, 11, 12].

The pathogenesis of aseptic instability is influenced by the phenomenon of metallosis, whereby accumulated wear particles can lead to the loosening of metal screws [8]. In 1994, Harris introduced the concept of "particle disease" to explain this mechanism [20]. One approach to addressing this issue involves the application of coatings on endoprosthesis surfaces that mimic the structure of bone tissue and exhibit enhanced biocompatibility, such as calcium phosphate coatings [5, 14, 17, 19]. Various studies have focused on improving the properties of these coatings through the addition of different components [6, 7].

However, the lack of new inorganic medical materials presents a challenge, as approximately 80% of promising engineering solutions for next-generation medical devices cannot be implemented [3]. In the Republic of Uzbekistan, the domestic production of medical devices and implants falls short of meeting the market demand. In response, the government has initiated import substitution programs to increase the share of domestically produced medical devices and implants.

The objective of this study is to develop, manufacture, and implement titanium implants with a novel therapeutic effect, incorporating a calcium phosphate coating, for spinal fixation in the surgical treatment of severe spinal injuries and diseases. The aim is to improve surgical outcomes and address the challenges associated with aseptic instability in spine stabilization procedures.

MATERIALS AND METHODS

From 2016 to 2022, a comprehensive study was conducted at the spinal department of the RSSPMCN, involving a total of 1810 stabilizing operations. Implants from various manufacturers, namely Medbiotech, Double Medical, Medyssey, ChM, and Medtronic, were utilized in these procedures (Fig. 1). The study population comprised 543 male patients (30%) and 1276 female patients (70%). The mean age of the patients was 58.9 ± 9.9 years, ranging from 26 to 85 years.

The study encompassed a wide range of spinal pathologies, with the majority of cases attributed to degenerative-dystrophic diseases of the spine (57%). Additionally, tumors (31%), aggressive hemangiomas (7.2%), and other pathologies of the spine (4.8%) were represented in the study population. This diverse representation of spinal disorders allowed for a comprehensive evaluation of the effectiveness and outcomes of the stabilizing operations across different clinical scenarios.

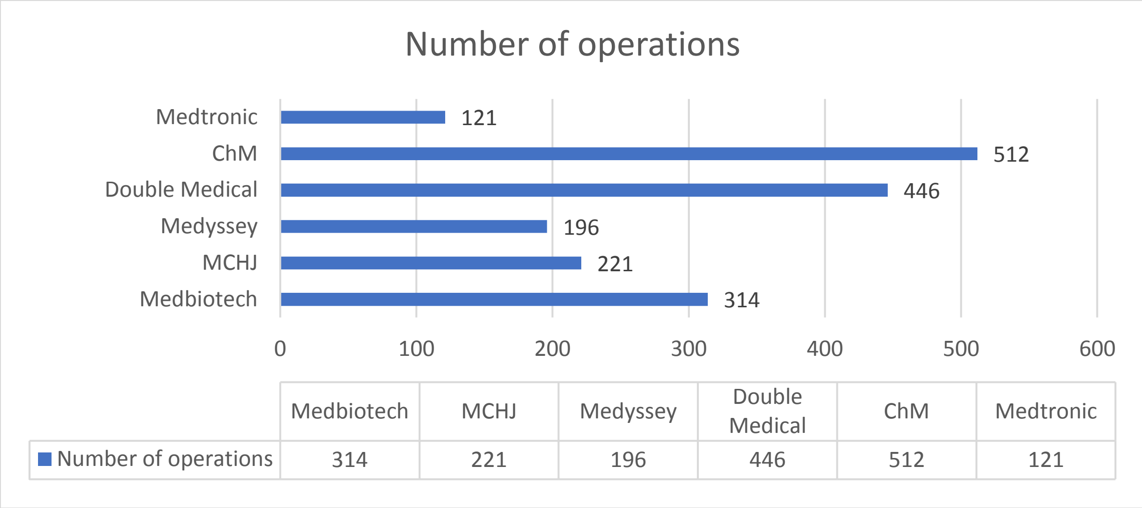

Figure 1. The number of transpedicular stabilizing systems used in the clinic for 2014-2021 (n=1810)

As indicated in Table 1, the majority of the stabilizing operations utilized the ChM endoprosthesis, followed by Double Medical and Medbiotech. It is worth mentioning that in Uzbekistan, transpedicular stabilization initially commenced with the utilization of the Medbiotech and ChM systems, which were the most readily available at that time. These systems were constructed using titanium alloy VT6.

RESULTS AND DISCUSSION

An analysis of the treatment outcomes involving the use of titanium implants demonstrated the occurrence of aseptic instability in a total of 15 cases (0.8%). The development of aseptic instability was observed within a timeframe ranging from 6 months to 7 years, as shown in Figure 2.

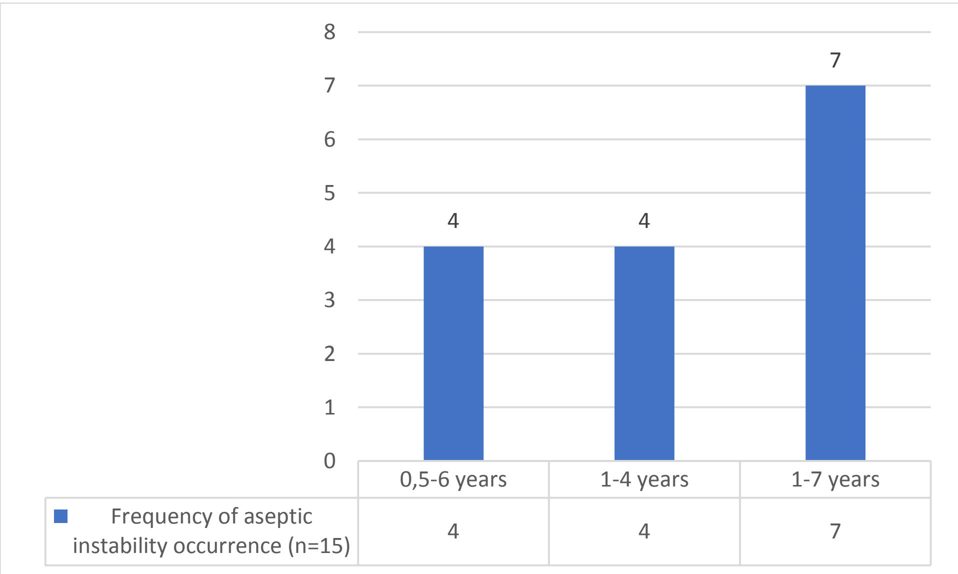

Figure 2. Frequency and timing of aseptic instability occurrence.

The early development of screw instability in the context of osseointegration is an area of particular interest. It appears that the lack of specialized surface treatment, such as coating, could be a contributing factor. To illustrate this point, let's consider a specific clinical case.

Patient G., a 59-year-old individual with case history № 17532, was admitted to our clinic in 2020. Upon examination, the patient was diagnosed with a "Pathological unstable fracture of the body VL4." As part of the treatment plan, a stabilizing operation was performed using a titanium alloy VT6 implant. The postoperative period was uneventful, and the patient was discharged on the 10th day. Regular follow-up examinations were conducted as recommended. However, after 1.5 years, the patient started experiencing pain in the lumbosacral region, which progressed to leg pain and noticeable lameness after 2 years. Radiographic and MSCT imaging revealed significant zones of bone tissue resorption surrounding the screws, which required their removal (Figure 3).

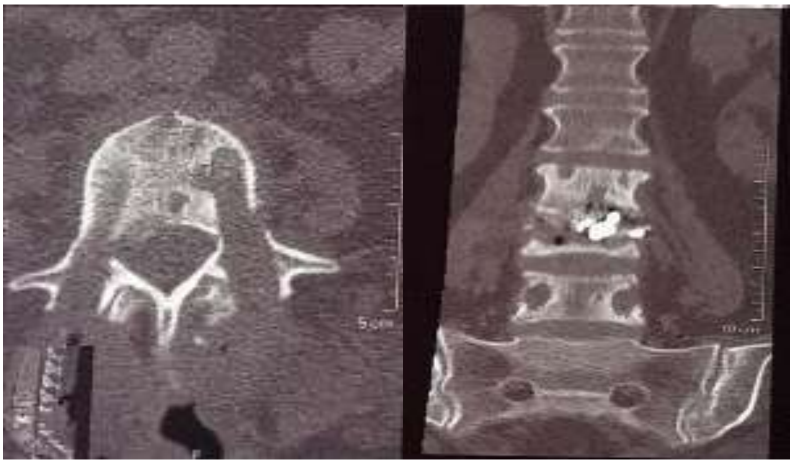

Figure 3. CT scan showing bone resorption around removed transpedicular screws.

In a larger cohort of 512 patients who underwent surgery utilizing implants from a particular manufacturer (ChM), aseptic instability was observed in 7 cases. In our assessment, osteoporosis (osteopenia) was identified as the primary factor in 5 patients, while in the remaining 2 cases, non-compliance with prescribed exercise regimens and calcium supplementation appeared to be the contributing factors. Furthermore, it is worth mentioning that the surgeon's approach might also impact the development of instability, such as the selection of screws with a smaller diameter, particularly when the patient already displayed signs of osteopenia before the surgical intervention.

Additionally, there were 4 instances of aseptic instability observed in patients who underwent surgery utilizing screws from another manufacturer within a 0,5-6-year timeframe. To provide an example, let's examine the case of Patient K, a 62-year-old individual with case history № 2433. This patient presented with degenerative stenosis of the spinal canal at the VL3-VL5 level and underwent decompression and stabilization surgery using a transpedicular titanium system on May 16, 2022. The postoperative period was uneventful, and the patient was discharged on the 10th day with instructions regarding physical activity and calcium supplementation. However, after 1 year, the patient began experiencing intermittent pain in the lumbosacral region with radiation to the left leg. Rest provided temporary relief, but the pain eventually became persistent, accompanied by left leg lameness. Further investigation revealed that the patient had disregarded the recommended load regimen and failed to adhere to calcium supplementation. Additionally, the patient had a history of long-term hormonal medication due to polyarthritis. MSCT of the lumbar spine confirmed the presence of aseptic instability (Figure 4).

Figure 4. Instability of transpedicular screws.

In summary, our analysis suggests that aseptic instability of titanium pedicle screws is more commonly observed when utilizing products without coatings that promote osseointegration, as well as in patients with osteopenia. These findings have prompted our study on the osseointegrative properties of various coatings, which could be of interest to domestic implant manufacturers. To investigate this, we employed the production capabilities of the Medical Manufacture Center MCHJ to create prototypes of titanium implants with a novel calcium phosphate coating.

To fabricate these experimental implants, we subjected titanium screws (VT 6 grade) to a series of pre-treatment procedures. This involved thorough cleaning with concentrated solutions of sulfuric acid or potassium hydroxide, followed by multiple rinses with distilled water. Subsequently, the screws were degreased using ethanol, and the hydrophilicity of the surface was enhanced in a model medium. The application of calcium phosphate coatings

a b c

Figure 3. Titanium screws with calcium phosphate coatings obtained by three methods:

immersion deposition (a), micro-arc oxidation (b), and electrochemical deposition (c).

After obtaining official registration of the product from relevant organizations, we plan to proceed with clinical trials of the implants. This stage is crucial for assessing the effectiveness and safety of the implants in real research conditions. We hope that the clinical trials will confirm the results of preliminary studies and provide valuable information about the performance of the implants in patients. This will serve as a foundation for making decisions regarding the further use of the implants in neurosurgical practice and improving the treatment outcomes for our patients.

CONCLUSION

The conducted research and its analysis lead to the following conclusions:

1. The current level of technological advancement does not allow for the creation of a calcium-phosphate material (CPM) that perfectly mimics the natural bone matrix [6, 7, 9]. As a result, orthopedic CPMs inherently lack certain properties of natural bone tissue and have specific limitations [6, 7, 15].
2. To overcome these limitations, various methods have been proposed and widely utilized for applying calcium phosphate coatings to metallic implants, including titanium. These methods include magnetron sputtering, combined electron-beam evaporation of CaO and thermal evaporation of P2O5, ion-stimulated deposition, laser ablation deposition, chemical vapor deposition, electrophoretic deposition, sol-gel, biomimetic, and other techniques.
3. Analysis of the causes of aseptic instability in titanium transpedicular screws revealed a higher incidence when using uncoated products that do not promote osseointegration, as well as in patients with osteopenia.
4. Prior to applying a calcium-phosphate coating to a titanium product, it is essential to conduct sandblasting treatment. Failure to do so would result in an unstable coating that is susceptible to physical forces.
5. Calcium-phosphate coatings formed through micro-arc oxidation on titanium and its alloys exhibit several advantages, including high corrosion resistance, wear resistance, hardness, and chemical stability in aggressive environments. The parameters of the coating, such as thickness, mass, roughness, spherolite size, and pore size, can be adjusted by modifying the process voltage [4, 5, 18].
6. Preliminary tests involving screwing and unscrewing titanium implants with calcium-phosphate coatings into cortical bone (rabbit iliac bone) demonstrated satisfactory outcomes. A significant portion of the calcium-phosphate coating remained on the surface of the screws after unscrewing.

CONFLICT OF INTEREST

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Institutional Review Board at the Republican Specialized Scientific and Practical Medical Center of Neurosurgery.

AUTHOR CONTRIBUTIONS

R.M. Yuldashev, A.I. Ibragimov: substantial contributions to the conception or design of the work. A.S. Negmatzhonov, S.N. Ishmukhammedov: acquisition, analysis, and interpretation of data for the work. R.M. Yuldashev,S.N. Ishmukhammedov: drafting and critical revision of the manuscript for important intellectual content. All authors contributed to the article and approved the submitted version.

REFERENCES

1. Dryagin, V.G., et al. Aseptic instability after total hip arthroplasty. Ural Traumatology and Orthopedics Bulletin, 2009, 1(1), 25-28.
2. Dryagin, V.G., et al. Biochemical aspects of aseptic instability in total hip arthroplasty for coxarthrosis. Human. Sport. Medicine., 2010, 19(195), 55-59.
3. Buryanov, A.A., et al. Metallic materials for orthopedic and traumatological implants. Orthopedics, Traumatology, and Prosthetics, 2008, 3, 5-10.
4. Legostaeva, E.V., et al. Study of the influence of microarc oxidation voltage on the physicochemical properties of calcium phosphate coatings on titanium. Perspective Materials, 2011, 13, 456-465.
5. Gnedenkov, S.V., et al. Calcium-phosphate bioactive coatings on titanium. Far Eastern Branch of the Russian Academy of Sciences Bulletin, 2010, 5, 47-57.
6. Karlov, A.V. Regulatory mechanisms of optimal biomechanics in external fixation systems. Kurgan, 2003, 335 p.
7. Karlov, A.V., Shakhov, V.P. External fixation systems and regulatory mechanisms of optimal biomechanics. Tomsk: STT, 2001, 480 p.
8. Maximov, A.L., et al. Analysis of causes of aseptic instability of "Altimed" total hip prosthesis. Modern Problems of Science and Education, 2012, 5, 52.
9. Orlovsky, V.P., et al. Synthesis, properties, and application of calcium hydroxyapatite. Dentistry, 1996, 5, 68-73.
10. Sementkovsky, A.V. Revision arthroplasty of the hip joint in aseptic instability of the femoral component of the prosthesis. Traumatology and Orthopedics of Russia, 2011, 1(59), 153-159.
11. Slobodskoy, A.B., et al. Complications after total hip arthroplasty. NN Priorov Traumatology and Orthopedics Bulletin, 2011, 3, 59-63.
12. Prokhorenko, V.M., et al. Comparative analysis of midterm and long-term results of primary hip arthroplasty with cementless and cemented fixation prostheses. NN Priorov Traumatology and Orthopedics Bulletin, 2014, 3, 21-27.
13. Tikhilov, R.M., Shapovalov, V.M. Manual for total hip arthroplasty. St. Petersburg: RNIITO named after R.R. Vreden, 2008, 301 p.
14. Khamchukov, Y.D., et al. Thin coatings of carbonate-hydroxyapatite on the surfaces of metals and monocrystalline dielectrics. Physics and Chemistry of Materials Treatment, 2006, 2, 38-43.
15. Khlusov, I.A., Pichugin, V.F., Ryabtseva, M.A. Fundamentals of biomechanics of biocompatible materials and biological tissues: a textbook. Tomsk: Tomsk Polytechnic University Publishing, 2007, 149 p.
16. Shapiro, K.I., Moskalev, V.P., Grigoriev, A.M. (1997). Incidence of large joint diseases in the adult population and the state of endoprosthetics: a guide for physicians. St. Petersburg, Russia: Publisher. P.14.
17. Shashkina, G.A., Sharkeev, Y.P., Kolobov, Y.R. (2005). Formation of calcium-rich bioceramic coatings on titanium. Prospective Materials, 1, 41-46.
18. Legostaeva, E.V., et al. (2006). Evolution of structure and properties of a nanoscale titanium-based biocomposite with microarc calcium-phosphate coatings under environmental interaction. Physical Mesomechanics, 9(Special Issue), 205-208.

19. Shadmanov, T.T., et al. (2001). Experimental morphological study of local influence of some calcium-containing implants on reparative osteogenesis. Orthopedics, Traumatology and Prosthetics, 3, 77-85.
20. Harris, W.H. (1994). Osteolysis and particle disease in hip replacement: a review. Acta Orthopaedica Scandinavica, 65(1), 113-123.
21. Iorio, R., et al. (2008). Orthopaedic surgeon workforce and volume assessment for total hip and knee replacement in the United States: preparing for an epidemic. Journal of Bone and Joint Surgery, 90-A(7), 1598-1605.