Polymers used in Vertebroplasty: The Importance of Material Technology in the Rehabilitation of Osteoporotic Patients

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Abstract: Recent statistics show that the human population is tending towards aging. More effective medications and medical-hospital treatments, a more balanced diet, and regular physical activities contribute to longevity with quality of life. However, on many occasions, the natural aging process brings with it some chronic diseases, such as osteoporosis. Characterized by the loss of bone density, it can compromise mobility and even lead to death due to vertebral fractures, among other issues. To mitigate these risks, materials engineering becomes useful for restoring partial and/or total bone structure. In combination with a physiotherapeutic approach, they can rehabilitate the patient, providing them with a better quality of life. The present work aims to discuss the main polymeric materials used for the treatment of osteoporosis in patients with fractures.

Keywords: Osteoporosis, vertebroplasty, materials, polymers.

INTRODUCTION

Currently, polymers are used in a wide range of medical applications, combining their physical, chemical, and mechanical properties with the specific requirements of a given application [1]. One of the factors that make these materials advantageous in their selection is the three-dimensional structure of the constituent macromolecules, which are widely distributed in all biological systems. Even natural polymers, such as hair or cellulose, have been used in medicine as suture materials [1, 2], later being replaced by synthetic polymers like polyesters and polyamides after World War II [1]. Polymers have gained significance in medicine due to their ability to be chemically modified under mild conditions of temperature and pressure, and to be produced according to the necessary requirements of chemical and biological compatibility [3]. For informational purposes, the annual growth rate projections of the spinal surgery market, estimated at 4.97% in Brazil (from 2022 to 2027) [4], and globally at 5.4% (from 2020 to 2027) [5]. New generations of polymeric materials inherently possess the ability to modify their structures through external stimuli such as changes in pH, temperature, magnetic field, or light. These materials find applications in the development of drug delivery devices, sutures, stents, and orthodontics [6, 7].

Advancements in polymerization techniques and processes have also contributed to obtaining synthetic polymers with good mechanical properties, even when porous, capable of supporting high loads [8]. The membranes used in hemodialysis filters are good examples [9] of such applications. The development of synthetic structures capable of supporting and transferring loads without suffering fractures has also elevated polymers as materials with potential for bone replacement [10] and for treating diseases and disorders related to bones [11]. For bone reconstruction applications, the material used must ensure correct stabilization and load transfer. And the material must do this without losing its elastic properties [10], in addition to being biocompatible with human tissues.

In this regard, they become prominent materials for treating patients with osteoporotic fractures. Osteoporosis is a chronic and systemic disease. It is characterized by reduced bone mineral density (BMD), deterioration of bone microarchitecture, and is associated with increased musculoskeletal fragility and risk of falls, leading to fractures (NIH Consensus Development Panel on Osteoporosis Prevention, Diagnosis and Therapy, 2001). In Brazil, according to the Ministry of Health, approximately 15 million Brazilians are affected by osteoporosis [12, 13]. Falls in women with osteoporosis often result in fractures, especially in the proximal femur region. This causes pain, physical-functional limitations, loss of independence, and 25% die within one year after the
fracture [14]. The risk of death due to vertebral fractures is 2.7 times higher compared to women without osteoporotic fractures. Additionally, 20% of women with osteoporotic vertebral fractures will experience another vertebral fracture within one year [15, 16, 14]. In this context of loss of quality of life, with immobility and even risk of death, polymers play a crucial role in aiding the recovery of patients with osteoporotic fractures. These materials contribute to ensuring mobility and maintaining daily functional activities. Therefore, this work aims to gather information on the main polymeric materials used in vertebroplasty, highlighting their characteristics and serving as a basic and didactic guide for healthcare professionals working in the field.

METHODOLOGY

The present study was based on a survey of polymer types used in the treatment of osteoporosis, specifically as bone grafts for osteoporotic patients with fractures. Articles submitted and published on recognized search platforms were collected and analyzed. Publications from the last 5 years were consulted. For this purpose, databases such as ScienceDirect, Scopus, PubMed, Medline, and Scielo were used due to their relevance in academic material production. Keywords related to polymers used in medicine, such as orthoses, prostheses, or bone grafts, were employed to converge on the theme.

RESULTS AND DISCUSSION

The Table 1 shows, by group, the combination of keywords used for the research.

Figure 1 details the number of articles associated with each group as well as the search platform.

The search platforms PubMed and Medline together represent more than 50% of publications associated with the use of polymers in vertebroplasty. Both are linked to the National Library of Medicine and contain information and data on health sciences in the biomedical field. This is likely one of the factors that

Table 1: List of Search Terms Used

<table>
<thead>
<tr>
<th>Group</th>
<th>Search terms</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>“polymers” and “bones” and “medicine”</td>
</tr>
<tr>
<td>II</td>
<td>“polymers” and “vertebroplasty”</td>
</tr>
<tr>
<td>III</td>
<td>“polymers” and “orthopedic implants”</td>
</tr>
<tr>
<td>IV</td>
<td>“polymers” and “bone cements”</td>
</tr>
<tr>
<td>V</td>
<td>“polymers” and “osteoporosis”</td>
</tr>
<tr>
<td>VI</td>
<td>“polymers” and “women” and “osteoporosis”</td>
</tr>
<tr>
<td>VII</td>
<td>“polymers” and “osteoporotic vertebral” and “vertebroplasty”</td>
</tr>
</tbody>
</table>

Figure 1: Number of articles obtained by the combination of keyword groups and specialized databases.
Polymers used in Vertebroplasty

In recent years, a wide variety of polymers have been investigated for biomedical applications. Due to their physical-chemical and mechanical properties, combined with different production techniques, polymers can be used in both soft tissues (skin, muscles, and ligaments) and hard tissues (tendons, cartilage, and bones) [18]. Among them, studies on collagen [19] and gelatin [20], both biopolymers, stand out. However, these have shown issues related to compatibility, stability, immunogenicity, and biodegradability [21]. As synthetic polymers for medical use, poly(lactic acid) (PLA), poly-L-lactic acid (PLLA), polyetheretherketone (PEEK), and polymethyl methacrylate (PMMA) are noteworthy [14].

Polymers in Orthopedic Applications

In orthopedic surgeries, joint prostheses are commonly made from polymeric materials, ultra-high molecular weight polyethylene (UHMWPE), and metals [22]. Despite this polymer's high mechanical strength, such as wear resistance, it is still susceptible to fracture due to oxidation and wear. Submicrometer particles generated by friction may be one of the major issues associated with the use of UHMWPE in orthopedic prostheses. These particles can induce inflammatory processes, bone resorption, osteolysis, and implant loss [23, 24].

In situations where reconstructing bone tissue without articulation or with limited articulation is desired, other polymers may be indicated. There are studies related to carbon-reinforced PEEK, but these are still in early stages [25]. Thermosetting polymers are generally not chosen for such purposes because they can potentially release toxins during the curing process within the human body [26, 27].

When there is intervertebral disc degeneration requiring medical intervention, silicone elastomers, polyvinyl alcohol (PVA) hydrogels, or PVA-PVP copolymers may be indicated for replacing the nucleus pulposus [28-30]. These polymers can be inserted as a solid piece or injected and cured in situ [31, 32].

To address issues related to infection from degradation products of PLA and PLLA [14], ceramic composites of PLLA have been extensively studied as materials for biomedical applications, such as in bone fractures and meniscus repair [33, 34]. The advantage of these composites based on hydroxyapatite (HA) is that they can provide greater compatibility with the human body. However, more detailed studies are needed to improve the adhesion between HA and PLLA [35].

Osteoplasty and Vertebroplasty

Osteoplasty comprises a set of minimally invasive interventional procedures indicated for pain management and structural stabilization. The technique involves percutaneous injection of bone cement in clinical conditions of bone fragility [36], such as in the treatment of bone metastases or pathological fractures.

Vertebroplasty is characterized as a minimally invasive technique. Introduced by Galibert et al. (1987) [37], it is specifically aimed at treating vertebral compression fractures, commonly associated with osteoporosis, bone metastases, or vertebral hemangiomas. It consists of injecting a polymer in its liquid state into the fractured vertebral body. Its goal is to relieve pain, reinforce bone structure, and prevent further vertebral compression [38]. The majority of

Regarding the different groups of keywords used to collect scientific articles, it is noted that Groups I and IV represent 77% of the searches conducted during the period in question. This highlights that studies on polymers in the field of vertebroplasty are closely associated with the keyword "bone," yielding significantly more articles than the collection obtained solely by using the keywords "polymers" and "vertebroplasty," which represented only 2% of the total number of articles collected (9,363 articles).

Many materials, especially certain biopolymers, have been employed in the treatment and repair of bone structures [11]. Biomaterials can be classified into inorganic types (metals and ceramics) and organic types based on macromolecular structures, namely polymers. Rarely will any single one of these satisfy all the requirements demanded in clinical treatment. However, their combination can result in a composite material capable of ensuring the desired outcome [17]. While metals and alloys are predominantly used in implant devices, they have a disadvantage regarding biomechanical compatibility due to their high elastic modulus (Young’s modulus) compared to natural bone [14]. In this sense, polymers and their composites can offer conditions for better adaptation to human biomechanics. It makes them useful for the development of orthopedic implants for osteoporotic patients.

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Vertebral fractures are caused by osteoporosis. Its consequences should not be underestimated. According to [39], vertebral fractures are associated with an increased age-adjusted mortality, with a relative risk of 8.64 (95% CI: 4.45-16.74). In addition to mortality, these fractures are associated with back pain, loss of height, deformity, immobility, increased bedridden days, and even reduced lung function, significantly impacting quality of life due to loss of self-esteem, distorted body image, and depression [40]. In a study conducted in the United States, it was noted that the mortality rate for individuals aged 65 and older doubled for patients with fractures of this nature [41]. Patients diagnosed with osteoporosis and therefore at risk of fractures need to strengthen their bone matrix. They also need to cease smoking, adopt diets rich in calcium and vitamin D, undergo physiotherapy, and engage in supervised physical activities [42].

The mechanism by which percutaneous vertebroplasty alleviates pain is not yet fully understood. In addition to stability provided by the physical properties of the polymer used, it is also hypothesized that analgesia results from thermal destruction of nerve endings caused by high temperatures during cement polymerization and chemical destruction of nerve endings by the cement’s chemical composition [43]. The same principles that justify the positive effects of vertebroplasty are also responsible for complications. Extravasation of bone cement into the spinal canal is a feared complication of vertebroplasty and can cause severe neurological damage. In addition to mechanical compression of neural structures causing neural tissue damage, bone cement can provoke inflammation due to the toxicity of its chemical composition and injury from the heat generated during the exothermic reaction. Extravasation of the cement in its liquid state through blood vessels and subsequent distant embolization can lead to additional complications [36].

Fracture of the adjacent vertebra after vertebroplasty is a common complication, with widely varying reported incidence rates in the literature (between 3% and 67%). Among the suggested factors are increased stiffness of the adjacent vertebra due to the presence of bone cement. It can lead to abnormal redistribution of load and stress on neighboring vertebrae, as well as changes in the direction and magnitude of loads exerted on the spine [44].

Osteoporotic vertebral fractures often result in instability, significant pain, and spinal deformity. Instability arises from the loss of structural integrity in the affected vertebrae, leading to painful micro-movements and progression of vertebral deformity. Deformity, often manifested as kyphosis, can lead to severe postural changes, affecting patients’ quality of life and functional capacity. Studies show that pain and deformity not only impair mobility but are also associated with a significant reduction in quality of life, increased dependence, and higher risk of secondary complications such as respiratory diseases due to pulmonary restriction [45-47].

Understanding the principles of low bone strength and fragility helps identify critical characteristics for treating osteoporotic vertebral fractures. The inherent instability in osteoporosis often necessitates approaches that ensure rapid vertebral stabilization, relieving pain and restoring functionality to prevent limitations and reduce mortality.

The choice of polymers used in vertebroplasty should consider both biomechanical needs and procedural safety aspects. It is crucial to evaluate the mechanical properties of different materials. This ensures they provide adequate structural support to the spine without excessively increasing local rigidity. Additionally, attention should be paid to the polymerization reaction time, as an inappropriate time can compromise the initial stability of the polymer. The peak temperature increase during polymerization is another critical factor, as excessive temperatures can cause thermal damage to surrounding tissues. The viscosity of the material should also be carefully considered. Because composites with low viscosity are more likely to extravasate and embolize at a distance, increasing the risk of complications.

Leakage of PMMA is a common complication with potential physical risks, including toxic reactions and allergic responses. Most leaks are asymptomatic, but symptomatic leaks can cause severe issues like paraplegia and death. Neurological complications are more likely when cement leaks into the neural foramen. Additionally, cement extravasation into paravertebral veins can lead to pulmonary embolism. Higher injection pressures and lower cement viscosity in vertebroplasty may increase leak likelihood [48].

Finally, material toxicity is a crucial aspect because the release of toxic substances during polymerization can lead to adverse reactions in adjacent tissues. Therefore, a comprehensive evaluation of these characteristics is essential for selecting composites that
provide a balance between biomechanical effectiveness and clinical safety.

**Synthetic Polymers used in Vertebroplasty**

PMMA has been used as bone cement since the 1900s for cranial reconstruction and, starting from the 1940s, for vertebral augmentation [49]. Despite PMMA being used with a certain success rate in bone filling and vertebroplasty [50-53], there are still disadvantages associated with its application. These include low adherence to bone surfaces [54], monomeric toxicity [1, 55-57], and exothermic reaction accompanied by local temperature increase [1,56, 58] ranging between 70 and 100°C [57], which can cause tissue damage, including neural tissues [59]. Its use in orthopedics is due to the rigid structure generated by the polymerization of methyl methacrylate, which can be performed in situ [1].

Usually, the compressive strength of PMMA samples is 70 MPa or higher [51,60]. In contrast, the compressive strength of vertebral cancellous bone can vary between 5 to 10 MPa. Although PMMA is less resistant to torsion or shear compared to its compressive strength levels [57], it is well accepted as a graft, given that vertebral biomechanics involve low torsional stresses.

The use of PMMA by healthcare professionals is well regarded due to its ease of application. When its monomers are injected into the vertebra, they react with each other, promoting in situ polymerization and stabilizing the fractured vertebra, restoring strength and resistance [56]. The chemical reaction results in a gradual increase in viscosity of the medium [61, 62], imparting a rheological behavior known rheopectic, as shown in Figure 2. Fluids with this behavior are characterized by having their viscosity increased over time. Therefore, for a restorative liquid to be injected into the bone structure without leaks, the flow must be impeded from the injection until the polymerization is complete.

![Figure 2: Typical rheopectic behavior of methyl methacrylate polymerization](image2)

![Figure 3: Illustrative scheme of polymer injection into a human vertebra.](image3)
Understanding this behavior becomes essential for the medical team, as it allows them to evaluate the necessary time for methyl methacrylate injection. This facilitates cleaning steps and other instrumentation procedures [63]. Another reason to study the rheology of these injected materials is due to the fact that above a certain viscosity value, there is evidence of pore formation. These pores, once formed, are potential points for fracture propagation [64]. Rheological investigation is also important when evaluating, for example, the influence of adding gelatin microparticles to a PMMA matrix. These microparticles can contain antibiotics or other therapeutic agents aimed at promoting tissue regeneration as well as controlled drug release. Depending on the concentration of these microparticles, the viscosity of the medium can increase or decrease. This also affects the material's permeability in the vertebra [60].

Another synthetic polymer that has been evaluated as vertebral filling is polyurethane foam. According to laboratory studies simulating extra-corporeal vertebral filling, foam formation begins between 3 and 5 minutes after injection of the reagents. The solidification of the entire structure completes after 30 minutes, with a curing temperature below 37°C [65].

Polyetheretherketone (PEEK), as an engineering thermoplastic polymer, proves to be relevant and promising for the field of orthopedic implants [66, 67]. With excellent biological, chemical, and mechanical properties, this polymer is well-suited for biomechanical conditions close to human bones, reducing the risks of resorption and osteolysis. PEEK exhibits high toughness and rigidity [68]. Its biocompatibility is similar to that of titanium and its alloys, with no evidence that its abrasive particles cause cellular damage [69].

The formation of biofilms on PEEK surfaces represents a significant concern in the medical context due to the increased risk of persistent infections and implant failures. Biofilms form through sequential stages of initial adhesion, colonization, maturation, and dispersion, where bacterial cells initially adhere to the PEEK surface, multiply, and produce an extracellular matrix that facilitates the formation of structured layers [25]. Surface topography, along with hydrophilicity or hydrophobicity characteristics, strongly influences microbial adhesion and consequently biofilm formation [70]. Surface modifications such as oxygen plasma treatments or antibacterial coatings are strategies explored to reduce biofilm formation on PEEK [71]. The presence of biofilms can lead to serious complications, including increased antibiotic resistance and immune response, often resulting in the need for implant removal. Implementing strategies to mitigate this process is crucial for improving the safety and effectiveness of medical implants.

CONCLUSIONS

Despite the widespread use of polymeric materials in medicine, particularly in orthopedic treatment for rehabilitating osteoporotic patients, there are still inherent problems associated with their use. One significant issue is the molecular distribution degree of polymers obtained through polymerization techniques, which can affect the quality of the implant and potentially cause toxicity to the human body due to biological incompatibilities.

There is a preference for using thermoplastic polymers as bone implants. Thermoset polymers can contaminate human tissues due to the presence of unreacted monomers during the curing process, even after being implanted in the human body.

In bone applications, it is desirable for the polymer used to have an elastic modulus compatible with natural bone, in addition to ensuring better distribution of loads and stresses within the structure.

DECLARATION OF NON-USE OF ARTIFICIAL INTELLIGENCE

The authors declare that they did not use any type of artificial intelligence tool for the preparation of the manuscript.

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