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Advancements in Engineering for the Treatment of Joint Diseases

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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Review Article

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ABSTRACT

Joint diseases such as osteoarthritis are a significant burden on healthcare systems worldwide, and current treatments have numerous limitations in terms of efficacy and side effects. However, advancements in engineering treatments, including tissue engineering and stem cell therapy, have shown promise in providing better solutions for joint disease treatment. Biomaterials, growth factors, and synthetic polymers are being explored to create new tissues and organs, and genetic engineering and 3D printing have shown potential benefits in the field of engineering treatments. Nevertheless, developing new treatments is a complex and time-consuming process, and further clinical trials and improved infrastructure are needed to translate in vitro and preclinical data into clinical applications. Future directions for joint disease treatment engineering include the development of more biomimetic scaffolds and incorporation of stem cells to improve tissue regeneration.

Keywords: Joint diseases; tissue engineering; stem cell therapy; biomaterials; 3D printing.

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1. INTRODUCTION

1.1 Current Treatments and Limitations for Joint Diseases

Despite the high prevalence and morbidity of these diseases, andthe wide range of treatment options available for joint diseases, there are significant limitations to their effectiveness. Current treatments primarily focus on relieving symptoms such as pain and swelling, but they do not address the underlying disease process that leads to joint degeneration. Furthermore, “all existing treatments have relatively short-term effects, and they do not specifically prevent the later development of osteoarthritis. Pharmacological treatments have limited effects on early symptoms and structural disease modification, and are associated with inappropriate polypharmacy and an increased risk of dangerous side effects” [1]. “While joint reconstruction is an effective approach for treating joint diseases, it is also limited by donor variations and the challenges associated with maintaining a stable cartilage phenotype in differentiated MSCs and preventing them from progressing towards osteogenesis” [1]. “For example, many reparative techniques result in the formation of fibrocartilage that lacks clinical durability, thereby failing to address the underlying issue at hand” [1]. “Cell-based strategies such as autologous chondrocyte implantation (ACI) have very limited shelf-life and face problems of graft delamination and insufficient cartilage regeneration” [1]. “Restorative techniques are also hampered by limitations in donor tissue availability, as well as morbidity at donor sites” [1].

“Current surgery options for joint diseases, such as total knee arthroplasty (TKA) and unicompartmental knee arthroplasty (UKA), have varying levels of success rates. A study compared the cumulative revision rate of components in patients older than 60 years and those younger than 60 years treated with TKA or UKA for osteoarthritis or similar conditions” [2]. “It was observed that the risk for revision decreased for both groups when considering the year of surgery, likely due to better implant components and surgical techniques” [2]. “However, younger patients treated for osteoarthritis using TKA and UKA have a lower implant survival rate when compared with older patients” [2]. “In terms of minimally invasive procedures, arthrocentesis and arthroscopy have a documented long-term high success rate of over 80% for managing temporomandibular joint internal derangement” [3]. “The clinical impact of these minimally invasive procedures is comparable to non-surgical options and open joint surgery such as discectomy” [3]. Unfortunately, current treatments for osteoarthritis are only moderately effective, and disease-modifying efficacy has not been demonstrated for any of the drugs used to treat it [4]. Chronic administration of these drugs often leads to gastrointestinal side effects, leaving patients with a substantial pain burden even after taking them [4].

“Pharmacological treatment includes non-steroidal anti-inflammatory drugs (NSAIDs), analgesics, intraarticular corticosteroids, glucosamine sulfate, chondroitin sulfate, diacerein, unsaponifiables extract of soybean and avocado administered orally and intrarticular hyaluronic acid” [5]. “However, the standard pharmacological treatment for joint diseases comes with side effects. For example, NSAIDs are frequently accompanied by renal-, hepatic-, gastrointestinal-, and cardiovascular side-effects” [6]. “Aspirin and other NSAIDs have been shown to have adverse effects on the stomach and kidney, particularly in elderly patients” [7]. “In the meantime, the COX-2 inhibitors celecoxib (Celebrex) and rofecoxib (Vioxx) cause fewer gastrointestinal side effects than traditional NSAIDs” [7]. “However, there is accumulating data about the side effects of the COX-2 inhibitors” [7]. “Furthermore, the COX-2 inhibitors have not been shown to be safer than acetaminophen” [7]. “There is also evidence that hydroxychloroquine may be efficacious in OA treatment, but the results are conflicting” [5]. “Classic disease-modifying drugs used in inflammatory arthritides and antiresoptive agents are being investigated as potential future therapies” [5]. While pharmacological treatment remains a standard approach for joint diseases, the associated side effects should be taken into account when determining treatment options.

1.2 Advancements in Engineering for Joint Disease Treatment

Joint disease has been a significant challenge in the medical field, and various approaches are being explored to tackle this issue. One of the latest advances in joint disease treatment engineering is the use of biomaterials to deliver stem cells and growth factors for joint repair, which is a promising technique [8]. “Researchers are also investigating the use of stem cell engineering to treat joint diseases, particularly

using mesenchymal stem cells (MSCs) for cartilage repair and regeneration" [8]. "Tissue engineering approaches are being developed to create functional bone and cartilage for joint repair, including meniscus tissue engineering, which has gained particular interest from the orthopedic and bioengineering communities" [8,9]. "Innovative scaffold and scaffoldless approaches are being used to engineer the meniscus, and various biochemical agents and mechanical bioreactors may enhance meniscus tissue" [9]. "The use of growth factors as the most prominent biochemical stimuli for tissue engineering of the knee meniscus has also been explored" [9]. "Effective therapies based on tissue engineering approaches are required for joint disease treatment, as existing methods such as partial meniscectomy commonly result in the progressive development of osteoarthritis" [9]. In conclusion, numerous new approaches are being investigated to tackle joint disease, including tissue engineering, stem cell therapy, and the use of biomaterials. However, further clinical trials and improved infrastructure are needed to translate in vitro and preclinical data into clinical applications [9].

"A variety of tissue engineering approaches have been explored to address the limitations of traditional reparative techniques. One promising method is the use of hydrogels, such as the hyaluronate-alginate hybrid hydrogel (HAH)" [10]. "HAH has shown great potential as a scaffold for cartilage regeneration with its tunable mechanical properties and ability to promote cell-cell interactions" [10]. "Double network (DN) hydrogels represent another promising approach, combining highly crosslinked polyelectrolyte networks with lowly crosslinked or non-crosslinked neutral network structures to achieve high strength for cartilage tissue engineering" [10]. "Several different methods have been employed to enhance the mechanical strength of hydrogels, including increasing crosslink density, reducing gel swelling degree, introducing fibrous reinforcing agents, and preparing interpenetrating networks" [10]. "To further improve the mechanical properties of hydrogels, researchers have also explored the use of combination natural hydrogels and the addition of functional components, such as chondroitin sulfate or TGF-β3" [10]. "Despite these advancements, further improvement is needed in forming cartilage and simulating its function" [10]. "Overall, tissue engineering has emerged as a promising therapeutic strategy for cartilage tissue reconstruction, with a range of approaches being explored to optimize scaffold properties and promote effective cartilage regeneration" [10].

2. POTENTIAL BENEFITS OF NEW ENGINEERING TREATMENTS

The field of regenerative medicine has seen rapid growth in recent years, with regenerative biomaterials potentially opening a new frontier in this field [11]. Synthetic biomaterials can incorporate biologically active components to create an artificial in vivo environment that fosters and regulates stem cells, similar to the processes that occur in a natural cellular microenvironment [11]. "Tissue engineering, a multidisciplinary approach to creating new tissues and organs, seeks to create new tissues and organs that are similar to the original ones" [12]. "New synthetic polymer formulations have facilitated tissue replacement and could represent alternatives to tissue regeneration in certain conditions" [12]. "Biotechnology and biomaterials offer exciting possibilities for repairing or regenerating tissue lost to injury, disease, or aging" [12]. Genetic engineering and 3D printing have shown potential benefits in the field of engineering treatments, as they can potentially form biomimetic neotissues [13,14]. They can also avoid the limited biocompatibility associated with scaffold use, as well as the release of degradation byproducts [14]. Recent advances in stem cell research, cellular and molecular biology, tissue engineering, and materials science have led to the development of new engineering treatments with the potential to provide better solutions for oral health issues than traditional restorative solutions [13]. Regenerative dentistry, which uses biomaterials, genes, stem cells, and growth factors to apply tissue engineering approaches to dentition, may help re-establish the functionality of disrupted teeth [13]. Additionally, advancements have been made in cartilage tissue engineering, with promising results from cell-based tissue engineering techniques such as autologous chondrocyte implantation and matrix-assisted chondrocyte implantation, which support chondrogenesis and provide mechanical stability.

3. CHALLENGES IN DEVELOPING NEW ENGINEERING TREATMENTS FOR JOINT DISEASES

The field of bone-tissue engineering has seen significant advances in recent years. Despite the amount of research that goes into developing new drugs for joint diseases, the success rate of

these drugs upon reaching clinical trials is quite low. In fact, approximately 90% of drugs that make it past animal studies fail in clinical trials [15]. While there have been advancements in tissue engineering, not all information is made public, as many details remain proprietary, leading to a lack of transparency in the field [15]. A major challenge in cartilage tissue engineering is the ability to move promising technologies from the lab into the clinic. This requires overcoming numerous regulatory and technical hurdles, such as scaling up production and ensuring quality control [15]. However, despite these challenges, advancements to tissue engineered products are continuously being made. Researchers are exploring new materials and methods to improve the effectiveness and longevity of these treatments, and there is hope that they will eventually become a viable option for patients suffering from joint diseases [15]. Nonetheless, it is important to remain cautious and realistic when examining the progress of tissue engineering.

"Researchers have made progress in understanding the molecular and cellular level of bone healing, leading to numerous animal and pilot clinical studies using tissue-engineered constructs for local bone regeneration" [16]. "Seven human studies have been conducted using culture-expanded, non-genetically modified MSCs for regeneration of bone defects" [16]. "However, there are still important areas that need to be addressed in this approach" [17]. For instance, the optimum dosage and sustained, biologically appropriate concentration of BMPs at the bone regeneration site needs to be further examined [16]. Inhibitory molecules are also being researched to mimic normal growth-factor production [16]. Additionally, the use of three-dimensional porous scaffolds with specific architectures is continually being evaluated [16]. Bioreactor technologies are also being investigated as an approach to optimize cell growth and differentiation [16]. The field of tribocorrosion studies has focused on the wear and erosion of materials in corrosive environments, and research has shown that recent insights combining wear and corrosion have led to further understanding of the tribo-corrosion process [17]. Significant advances have been made in the study of wear and corrosion mapping in the past 50 years, although many tribological situations in aqueous conditions have been neglected [17]. The mapping approach enables a mechanistic description to be linked to a wastage rate, leading to an improvement in materials selection and process parameter optimization [17]. Furthermore, novel approaches in cell harvesting, in vitro expansion, and subsequent implantation are being investigated as alternatives or adjuncts to standard methods used for bone regeneration. Alternative sources of cells such as peripheral blood and mesenchymal progenitor cells from fat or muscle tissue are also under research [16]. Overall, ongoing research in all related fields has led to the development of novel therapies for bone regeneration and the optimization of tribocorrosion processes.

4. FUTURE DIRECTIONS FOR JOINT DISEASE TREATMENT ENGINEERING

Tissue engineering is a promising alternative to limited clinical options for end-stage disc disorders in the temporomandibular joint (TMJ) [18]. However, tissue engineering is far from complete for TMJ disc regeneration, and future directions include addressing the hurdles in tissue engineering of the disc and its application in translation to clinical practice [18]. Incorporation of advanced fabrication techniques like 3D printing and electrospinning is expected to enhance scaffold design and production [18]. Future directions for joint disease treatment engineering include the development of more biomimetic scaffolds and incorporation of stem cells to improve tissue regeneration [18]. Research is ongoing to improve the mechanical properties and biocompatibility of scaffolds for joint disease treatment engineering [16]. Novel approaches using nanotechnology, such as magnetic biohybrid porous scaffolds and injectable scaffolds, are being explored for joint disease treatment engineering [16]. Improved biodegradable and bioactive three-dimensional porous scaffolds are being investigated [16]. Natural materials with enhanced mechanical support and biodegradability are favorable for cell adhesion, while synthetic materials allow for artificial adjustment of pore size and stiffness of the structure [19]. A TGF-β1-immobilized PLGA-gelatin scaffold seeded with ADSCs enhances the quality of tissue-engineered cartilage [19]. Hydrogel-based scaffolding systems can create high-quality engineered cartilage but may exhibit inferior mechanical properties [19]. 3D collagen scaffold culture combined with PDGF and insulin promotes chondrogenic differentiation [19]. Type I collagen is an appropriate scaffold due to low inflammatory response and cell compatibility, while smaller pore sizes (90-250 μm) are better

for preserving cell adhesion and proliferation and allow for higher expression levels of collagen, aggrecan, and type II collagen [19]. Materials, pore size, and rigidity of the scaffold must be considered in joint disease treatment engineering, as scaffold pore size affects stem cell proliferation and chondrogenic differentiation, and the 3D structure of loaded ADSCs is important for promoting cartilage recovery [19].

5. CONCLUSION

In conclusion, while current treatments for joint diseases have numerous limitations, advancements in engineering treatments, including tissue engineering and stem cell therapy, have shown promise in providing better solutions for joint disease treatment. The use of biomaterials, growth factors, and synthetic polymers are being explored to create new tissues and organs, and genetic engineering and 3D printing have shown potential benefits in the field of engineering treatments. However, developing new treatments is a complex and time-consuming process, and further clinical trials and improved infrastructure are needed to translate in vitro and preclinical data into clinical applications. Future directions for joint disease treatment engineering include the development of more biomimetic scaffolds and incorporation of stem cells to improve tissue regeneration. Overall, ongoing research in all related fields has led to the development of novel therapies for joint disease treatment and the optimization of tribocorrosion processes.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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