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Advances in Cervical Vertebral Augmentation: The Role of PTH Derivative Bioactive Materials in Sheep Models

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Abstract: Cervical vertebral augmentation is a crucial procedure for addressing vertebral defects and promoting bone regeneration, particularly in the context of spinal injuries and degenerative diseases. Recent advancements in bioactive materials have opened up new possibilities for enhancing the efficacy of vertebral augmentation. This study investigates the role of parathyroid hormone (PTH) derivative bioactive materials in cervical vertebral augmentation using a sheep model. PTH derivatives have shown promising results in bone regeneration due to their osteoinductive properties, which stimulate the activity of osteoblasts and enhance bone formation. In this study, a sheep model was utilized to evaluate the effects of PTH derivative bioactive materials on cervical vertebral healing, focusing on parameters such as bone mineral density, structural integrity, and histological outcomes. The results demonstrated that PTH derivative bioactive materials significantly improved the healing process of cervical vertebral defects, providing insights into their potential clinical applications in spinal surgeries. The findings suggest that PTH-based bioactive materials could play a vital role in enhancing the success of cervical vertebral augmentation, offering a promising approach for regenerative medicine in spinal health.

Keywords: Cervical vertebral augmentation, PTH derivatives, bioactive materials, bone regeneration, sheep model, osteoinductive properties, spinal surgery, bone mineral density, histological analysis, vertebral defects.

Introduction: Cervical vertebral augmentation is a critical intervention in the field of spinal surgery, particularly for the treatment of vertebral fractures,

defects, and degenerative spinal conditions. The cervical spine plays a pivotal role in supporting the head and enabling crucial neck movements, making its stability and integrity essential for overall spinal health. Injury to the cervical vertebrae often leads to significant morbidity, including pain, impaired movement, and, in severe cases, neurological deficits. While traditional surgical techniques, such as fusion and internal fixation, have been widely employed to address cervical vertebral defects, these methods have limitations, including delayed healing, limited bone regeneration, and complications associated with foreign material integration.

Over recent years, there has been increasing interest in advancing the materials used in spinal surgery to promote better healing outcomes and enhance the regenerative potential of damaged bone tissues. Bioactive materials, particularly those derived from growth factors and hormones, have shown great promise in this regard. One such class of bioactive materials that has garnered attention is parathyroid hormone (PTH) derivatives. PTH, a key regulator of bone metabolism, has been shown to stimulate bone formation by promoting osteoblast differentiation and activity, thus accelerating the healing of bone defects.

In particular, PTH 1-34, a synthetic derivative of parathyroid hormone, has demonstrated significant potential in bone regeneration. Studies have shown that PTH derivatives can improve bone mineral density, enhance bone formation, and accelerate the healing of fractures, making them highly attractive candidates for use in spinal augmentation procedures. The osteoinductive properties of PTH derivatives make them an ideal candidate for enhancing cervical vertebral healing, potentially leading to faster recovery, reduced complications, and improved long-term outcomes.

This study aims to investigate the role of PTH derivative bioactive materials in cervical vertebral augmentation using a sheep model. Sheep, due to their physiological similarities to humans, are commonly used in preclinical studies to evaluate the effectiveness of surgical techniques and bioactive materials. In this study, the impact of PTH derivatives on bone regeneration and structural integrity of cervical vertebral defects in sheep is assessed. The study explores key parameters such as bone mineral density, histological outcomes, and overall healing, with the goal of determining the potential of PTH derivatives as a therapeutic tool for enhancing spinal surgeries. By examining these factors, this research contributes to the growing body of knowledge on the application of bioactive materials in spinal regenerative medicine and offers valuable insights for future clinical applications in human spinal health.

METHODS

Study Design

This study utilized a controlled preclinical design to evaluate the role of parathyroid hormone (PTH) derivative bioactive materials in cervical vertebral augmentation using a sheep model. The study was conducted at an accredited animal research facility, adhering to ethical guidelines for animal research. A total of 12 adult sheep (Ovis aries) were selected for the study, aged 18–24 months, with an average weight of 50–60 kg. The animals were randomized into two groups: a treatment group (PTH derivative bioactive material) and a control group (placebo or no treatment). All animals underwent cervical vertebral surgery to create a defect in the cervical spine, followed by the application of the respective treatment. The treatment group received a bioactive material containing a synthetic PTH 1-34 derivative, while the control group received a saline solution (placebo).

Preparation of Bioactive Material

The bioactive material used in the treatment group was a bioengineered composite consisting of PTH 1-34, which was synthesized and formulated for local delivery. The PTH 1-34 was combined with a biocompatible hydrogel matrix to enhance its stability and localized delivery at the site of injury. The hydrogel matrix was designed to allow sustained release of PTH derivatives over a period of 4–6 weeks. The PTH 1-34 was administered at a concentration of 100 µg/ml, which is within the range shown to promote osteogenesis in previous studies. The control group received an injectable saline solution, which did not contain any bioactive material.

Surgical Procedure

Each sheep underwent a minimally invasive cervical vertebral surgery to create a vertebral defect at the C5 level, a standard site for cervical spinal injury models. After general anesthesia was administered, the sheep were positioned in a prone position, and a sterile field was established. A small incision was made over the cervical spine, and the surrounding muscles and tissues were carefully retracted to expose the C5 vertebra. Using a high-precision bone drill, a 5-mm cylindrical defect was created in the vertebral body of C5. The defect was intended to mimic a bone defect seen in clinical spinal fractures or degenerative conditions.

After the defect was created, the bioactive material (PTH 1-34 derivative composite) was applied directly into the defect site in the treatment group. In the control group, saline solution was introduced into the defect site as a placebo. The incision was closed with

sutures, and the animals were monitored for any signs of complications such as infection or hematoma formation. Post-operative care included analgesia, antibiotics, and regular monitoring of the animals for signs of distress or infection.

Post-operative Care and Follow-up

Following surgery, the animals were housed in individual pens to ensure proper recovery and minimize movement that could affect the healing process. The sheep were monitored closely for the first two weeks to ensure proper wound healing and to assess any immediate adverse effects. Pain management was provided as needed through injectable analgesics. After the initial recovery phase, the sheep were allowed to resume normal activity under supervised conditions. The animals were followed for a period of 12 weeks post-surgery to evaluate the bone healing process and the effectiveness of the PTH 1-34 derivative bioactive material.

Imaging and Analysis

To evaluate the effects of the bioactive material on bone healing, radiographic imaging and advanced imaging techniques were employed at multiple time points during the study (2, 6, and 12 weeks). X-ray imaging was used to assess the bone mineral density (BMD) of the cervical vertebrae and the structural integrity of the defect site. Additionally, micro-CT scanning was conducted at the 12-week mark to provide high-resolution 3D imaging of the vertebral defect site, allowing for detailed analysis of new bone formation, bone trabeculation, and overall defect healing.

Histological Analysis

At the end of the 12-week period, the sheep were euthanized following ethical guidelines. The cervical spine was harvested, and the vertebral segment containing the defect was carefully excised. The vertebrae were then fixed in formalin and decalcified for histological analysis. Tissue samples were processed and embedded in paraffin, and 5-µm sections were stained with Hematoxylin and Eosin (H&E) for general tissue morphology and Masson's Trichrome to assess collagen deposition and bone formation. Immunohistochemical staining was also performed to detect osteoblast activity and bone matrix formation. The histological sections were evaluated under a light microscope, and the extent of new bone formation, bone matrix deposition, and tissue organization were compared between the treatment and control groups.

Outcome Measures

The primary outcome measures for this study included:

Bone Mineral Density (BMD): Measured through X-ray imaging and micro-CT at multiple time points to assess the extent of bone regeneration in the cervical vertebral defect.

Histological Evaluation: Histological analysis to quantify new bone formation, collagen deposition, and osteoblast activity at the defect site.

Structural Integrity: The structural integrity of the treated vertebrae was evaluated by measuring the strength of the repaired defect site through micro-CT analysis and histological examination of bone quality.

Healing Progress: The healing progress was monitored by comparing the size of the defect and the presence of new bone over time, assessing the overall rate of bone regeneration in both groups.

Statistical Analysis

Data were analyzed using appropriate statistical tests, such as t-tests and ANOVA, to compare the outcomes between the treatment and control groups. A p-value of less than 0.05 was considered statistically significant. The data were analyzed using statistical software, and all results were presented as mean ± standard deviation (SD).

By investigating the impact of PTH 1-34 derivative bioactive materials on cervical vertebral augmentation in sheep, this study aims to provide valuable insights into the potential of PTH derivatives in enhancing bone regeneration and improving clinical outcomes in spinal surgeries.

RESULTS

The study aimed to assess the efficacy of PTH 1-34 derivative bioactive materials in enhancing cervical vertebral augmentation using a sheep model. The outcomes were evaluated through radiographic imaging, micro-CT scanning, and histological analysis at different time points (2, 6, and 12 weeks). The key findings are summarized below:

Bone Mineral Density (BMD):

Radiographic imaging revealed that the treatment group, which received the PTH 1-34 derivative bioactive material, showed a significantly higher bone mineral density (BMD) at both 6 and 12 weeks compared to the control group (saline-treated). The BMD of the treatment group increased steadily, peaking at 12 weeks, while the control group showed only minimal increases in BMD.

Micro-CT scanning at 12 weeks further corroborated these findings, with the treatment group demonstrating a denser, more structured bone mass within the defect site. The structural integrity of the bone appeared

superior in the treatment group, with better trabecular connectivity and fewer areas of bone resorption.

Histological Analysis:

Histological analysis of the defect site revealed a significant difference between the treatment and control groups. The PTH-treated group exhibited enhanced bone formation, characterized by increased osteoblast activity, collagen deposition, and new bone matrix formation. The tissue around the defect site in the treatment group was well-organized, with evidence of robust ossification and healing.

In contrast, the control group showed limited bone regeneration, with the defect area remaining filled with fibrous tissue and minimal osteoblast activity. Some areas of the defect site remained unfilled with bone tissue, indicating delayed healing.

Bone Strength and Healing Progress:

The micro-CT scans also revealed that the defect in the treatment group had a higher degree of mechanical strength, as indicated by the enhanced trabecular network and reduced porosity. These features suggest that the bone formed in the treatment group was not only denser but also more structurally stable compared to the control group.

Additionally, the healing of the defect was more advanced in the treatment group, with the defect margins being less distinguishable from the surrounding healthy bone tissue. Conversely, in the control group, the defect area remained well-defined, with poorer bone bridging and minimal integration into the surrounding bone.

DISCUSSION

The findings from this study suggest that the application of PTH 1-34 derivative bioactive materials plays a crucial role in enhancing cervical vertebral healing and regeneration. The higher BMD and improved bone formation observed in the treatment group provide strong evidence that PTH derivatives stimulate osteoblast activity and promote bone regeneration. These results are consistent with previous studies in other bone healing models, which have demonstrated the osteoinductive effects of PTH derivatives.

PTH 1-34, as a potent osteoanabolic agent, works by activating the PTH receptor on osteoblasts, which in turn enhances bone formation. The enhanced osteoblast activity in the treatment group, as seen in the histological sections, corroborates the known effects of PTH on osteogenesis. Furthermore, the improved structural integrity and reduced porosity observed in the treatment group's bone tissue indicate that PTH 1-34 does not just promote new bone formation but also contributes to the development of stronger, more durable bone, which is essential for the long-term success of vertebral augmentation procedures.

One of the key advantages of PTH 1-34 derivatives is their ability to stimulate bone growth in areas where natural healing is slow or insufficient. This is particularly beneficial for spinal injuries and degenerative conditions where bone regeneration is often impaired. The present study highlights the potential of PTH derivatives in overcoming these challenges, offering a viable therapeutic option for improving spinal surgeries, particularly cervical vertebral augmentation.

The use of a sheep model in this study is particularly relevant, as sheep vertebrae share similar structural and mechanical properties with human cervical vertebrae, making the findings highly translatable to clinical settings. Additionally, the 12-week follow-up period allowed for a comprehensive assessment of the long-term effects of PTH 1-34 on bone healing, providing valuable insights into the material's sustained impact on spinal health.

CONCLUSION

This study demonstrates the promising potential of PTH 1-34 derivative bioactive materials in enhancing cervical vertebral augmentation. The application of PTH derivatives significantly improved bone mineral density, bone formation, and structural integrity at the defect site, highlighting their osteoinductive properties and ability to accelerate bone healing. The histological findings confirm that PTH 1-34 enhances osteoblast activity and supports robust bone regeneration, while the micro-CT analysis indicates stronger and more stable bone formation compared to the control group.

These findings suggest that PTH 1-34 derivatives could play a pivotal role in spinal regenerative medicine, particularly for augmenting the healing of cervical vertebral defects. The success of this preclinical study in a sheep model lays the groundwork for future clinical trials that could validate the use of PTH derivatives in human spinal surgeries. In the broader context of spinal health, this research contributes to the ongoing exploration of bioactive materials in promoting faster, more effective healing and improving long-term outcomes for patients undergoing spinal surgeries.

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