EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 7
Issue: 7
13-16
Year: 2020

REASEARCH PROGRESS ON MODIFLED MESOPOROUS BIOACTIVE GLASSES FOR REPAIRING MAXILLOFACIAL BONE DEFECTS

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Article Received on 24/04/2020 **Article Revised on 15/05/2020** **Article Accepted on 05/06/2020**

ABSTRACT
Mesoporous bioactive glasses are a kind of bioactive material that exhibits a bonding effect with bone tissues. They possess high biocompatibility, biodegradability and good bone formation and conduction properties, which are essential for bone tissue engineering applications. With the aim of increasing their clinical value, researchers in recent years have improved the performance of mesoporous bioactive glasses by reforming their structures. This article provides a brief review on the research progress of modified mesoporous bioactive glasses for maxillofacial bone defect repair.

KEYWORDS: Modified mesoporous bioactive glasses; maxillofacial bone defects; repairmen.

Alveolar bone resorption and maxillofacial bone defects caused by inflammation, injury, tumor, congenital malformation, and aging are common clinical manifestations in the field of stomatology. They not only affect chewing, speaking, eating and other functions, but also seriously affect the physical-mental health and quality of life of patients. Therefore, it is a common issue facing scholars today that how to achieve a good repair of bone defects caused by various diseases, to improve the survival rate and life quality of patients.

Mesoporous bioactive glass is a kind of bioactive material with multi-pore structure. It can repair, replace and regenerate tissues, and enable bonding between tissues and materials.[1] In the past, most mesoporous bioactive glass has some defects, including difficulty in dispersing the particles, controlling the micro-nano structure, morphology and size. These defects lead to poor stability of the material and difficult performance of micro - nano effect. In order to solve these problems, the researchers improved the mesoporous bioactive glass by adjusting the composition of elements and improving the development method, optimized their structure, and prepared the improved mesoporous bioactive glass with excellent performance.[2] They are used in bone repair, jaw defect repair, skin wound repair and so on. This paper reviews the application of modified mesoporous bioactive glass in maxillofacial bone defect repair.

1. Composition elements of improved mesoporous bioactive glass

The main components of traditional bioactive glass are calcium (Ca), phosphorus (P) and silicon (Si). To improve the biological properties of the material conducive to osteogenesis, boron (B), diamond (Co), copper (Cu) and titanium (Ti) were added.[3-6] Kaur et al.[2] improved the mineralization rate of mesoporous bioactive glass by adding boron. The addition of boron can form $B_2O_3SiO_2$ and B_2O_3, which are network generator oxides, and their structural units are boron-oxygen triangle and silicon-oxygen tetrahedron, respectively. The structure was easy to fracture, which improves the specific surface area, pore volume, pore diameter and Ca^{2+} precipitation rate of the modified mesoporous bioactive glass. High precipitation rate of Ca^{2+} can promote the deposition of hydroxyapatite and the occurrence of mineralization.[2-3] Recently, some scholars[4] found that incorporation of Co ions could create a low-oxygen environment and induce overexpression of hypoxia inducible factor (HIF) and vascular endothelial growth factor (VEGF). HIF is the key to promote angiogenesis of transcription factors, so that the blood supply for bone defect could be provided and the formation of bone tissue could be promoted.

Resistance to infection is an important part of bone defect repair. Studies have been reported that bioactive glass mixed with Cu or Ti ions has bactericidal effect.[5] At the same time, Cu ions could also effectively promote

angiogenesis and provide blood supply to the bone defect, which was conducive to osteogenesis.[6]

2. Development method of improved mesoporous bioactive glass

In the early 1970s, bioactive glass was prepared by melting and sintering. PerioGlas®, ERMI® and NovaBone™ have been successfully used in clinical therapy. Perio Gias® was used for the repair of periodontal bone defects, the filling of bone defects after the removal of maxillary cyst, the increase of alveolar ridge and the fixation of Artificial implant. ERMI® was used for filling the posterior notch of teeth extraction. NovaBone™ was used to repair limbs and vertebrae. The bioactive glass prepared by this method had poor stability due to the limitation of high temperature.

In the 1990s, bioactive glass was prepared by sol-gel method. This method is easy to operate and the material structure could be designed and cut. But the problem was that the particles of the product were difficult to disperse, and the sizes of the particles were different. As a result, the specific surface area and pore clearance were small, which was not conducive to good osteogenesis.

In the late 1990s, researchers prepared ordered mesoporous bioactive glass by template method. Viglia's research group[7] prepared highly ordered mesoporous bioactive glass by using organic template self-assembly technology, which had a larger specific surface area and osteogenic activity.

With the deepening of the research, in the field of medicine, micro-nano biomaterials had become the direction of development. Hong et al.[8] prepared micronanometer ordered mesoporous bioactive glass using P123 copolymer as template on the basis of electrostatic spinning technology, which had adjustable in vitro biomineralization properties and drug release capacity, and could be used as a drug carrier for the repair and treatment of maxillofacial bone defects.

3. Mechanism of modified mesoporous bioactive glass in maxillofacial bone defect repair

In recent years, the research on the mechanism of modified mesoporous bioactive glass used in the reconstruction of maxillofacial bone defects has been increasingly improved. The reaction mechanism mainly includes the following three aspects.

1. Improved mesoporous bioactive glass was chemically bonded to the surface of bone tissue. Na^+ and Ca^{2+} in the modified mesoporous bioactive glass were rapidly exchanged with H^+ in the body fluid, resulting in the fracture of the Si-O bond in the glass structure and the formation of silicon hydroxyl. Then the Si-OH bond further condenses to form a SiO_2-rich gel layer on the surface of the modified mesoporous bioactive glass. Because H^+ in the body fluid was exchanged with Na^+ and $Ca2^+$ in the glass, the body fluid showed weak alkalinity. In such a weakly alkaline environment, the SiO_2-rich gel layer on the surface of the modified mesoporous bioactive glass was negatively charged and can adsorb Ca^{2+}, followed by the formation of an amorphous apatite layer. With the release of OH^- and CO_3^{2-} from the body fluids, bone-like apatite would be formed[9], which could adsorb collagen and cells and participate in the life process.
2. Improved mesoporous bioactive glass gradually released active ingredients, such as silicon, calcium and phosphorus ions. This process coould enhance the cell reaction at the modified mesoporous bioactive glass interface and promote the proliferation and differentiation of osteoblasts and their precursors. Osteoblast cells in host bone were stimulated for gene expression.[10] The expression of BMP-2, the gene encoding bone morphogenetic protein (BMP), and osteogene-related genes (genes encoding X collagen, osteocalcin, sialoprotein, alkaline phosphatase, etc.) was significantly increased, which accelerated osteoblast division, promoted the generation of growth factors and extracellular matrix, and promoted bone regeneration.
3. Improved mesoporous bioactive glass could promote angiogenesis.[11] For example, the addition of Co^{2+} can promote the adhesion and proliferation of vascular endothelial cells and the generation of endothelial vessels, as well as the secretion of angiogenesis growth factor in fibroblasts, so as to provide blood supply for the formation of bone tissue, prevent the occurrence of sepsis, and facilitate the formation of new bone.

4. Application of modified mesoporous bioactive glass in maxillofacial bone defect repair

Bioactive glass was mainly used for the repair of maxillofacial bone defects in the past, but the repair of maxillofacial bone defects had rarely been reported. In recent years, many scholars devoted themselves to the research in this field. The improved mesoporous bioactive glass has a promising prospect in maxillofacial bone repair.

4.1 Application in the repair of bone defects caused by maxillary cyst

Maxillary cyst is a common lesion leading to bone defects in the department of stomatology. In order to repair the bone defect in such patients, Elgali I[12] combined collagen membrane and modified mesoporous bioactive glass for the treatment of maxillary cyst and obtained satisfactory clinical results. Other studies found that the combined application of guided tissue regeneration and bioactive glass could give play to their respective characteristics and promote the healing of bone tissue in different ways. In addition, no local tissue swelling and other adverse reactions were found after surgery.

4.2 Application of bone reconstruction in maxillofacial fine site

The maxillofacial structure is quite complex, people put forward higher request to the repair effect of fine structure defect. At present, many scholars were engaged in the research of maxillofacial fine site defect repair. Stoor et al.[13] developed a new type of improved mesoporous bioactive glass that could be used for orbital floor reconstruction. No postoperative complications were found in this study, and the material showed excellent biocompatibility. The modified mesoporous bioactive glass could form anatomic droplet shape to maintain orbital volume. Van G. et al.[14] applied this material to the treatment of postoperative bone healing and osteomyelitis in patients with nasal septum perforation and found that the cure rates reached 10/11 and 22/23. The reason for the failure of one case was the complete septal perforation of pituitary gland after operation, and no material absorption was observed in other cases, showing a good effect. Therefore, modified mesoporous bioactive glass was a good choice for repairing nasal septum perforation. In addition, some scholars combined improved mesoporous bioactive glass and autologous bone fragments from the iliac roof in the operation of maxillary sinus floor elevation. Postoperative examination showed that the combination of autologous bone and bioactive glass could form thicker new bone, compared with the use of autologous bone alone. This method could reduce the use of autologous bone and obtained better results. It was believed that through further research, the improved mesoporous bioactive glass was expected to be used for bone reconstruction in other craniofacial fine anatomical sites.

4.3 Application in the treatment of maxillofacial osteomyelitis

Osteomyelitis is a serious bone infection. The conventional treatment is to implant antibacterial materials after surgical debridement. The material had to be removed two weeks after surgery, causing pain in patients undergoing a second operation. The modified mesoporous bioactive glass S53P4 simplifies the whole treatment process because of its inherent antibacterial activity. The researchers[15-17] reported 3 cases of successful treatment of chronic osteomyelitis with modified mesoporous bioactive glass. The X-ray showed that new bone was formed around the lesion and was well combined with the surrounding bone tissue. The material also had the potential to promote angiogenesis. Many clinical trials had confirmed that modified mesoporous bioactive glass was expected to be widely used in the repair of bone defects caused by osteomyelitis.

4.4 Application of bone defect repair after maxillofacial tumor surgery

Patients with maxillofacial tumors often have bone defects after surgery, which makes them very painful and annoying. To improve the life quality of patients, scholars continued to explore the methods of bone repair after maxillofacial tumor surgery. Roohaniesfahani et al.[18] confirmed that bone tissue formed by modified mesoporous bioactive glass as scaffold material had a hard bone with a thicker bone cortex, which was more suitable for autologous bone transplantation, and no abnormal bone was found around soft tissue. The material was expected to be used to repair bone defects after maxillofacial tumor surgery.

4.5 Application of maxillofacial articular cartilage regeneration

With the development of the application of modified mesoporous bioactive glass in bone tissue defect repair, researchers have been working on the application of mesoporous bioactive glass in articular cartilage. The multifunctional bioactive glass prepared by Shanghai institute of ceramics showed bidirectional functional properties of repairing bone and cartilage. It can not only promote the repair of articular subchondral bone, but also promote the healing and regeneration of articular cartilage defects. The main mechanism was that these materials could activate not only the Wnt/β-catenin signaling pathway of bone marrow stromal stem cells, but also the autophagy function of chondrocytes.

5. Defects of modified mesoporous bioactive glass in maxillofacial bone defect repair

Bioactive glass has good bioactivity, biodegradability and the ability to promote the proliferation of bone cells, showing a good application prospect in bone defect repair. However, there are still the same shortcomings as inorganic materials, such as brittleness, bending resistance, anti- damage performance is not ideal. Its mechanical strength was insufficient when it was applied to some large bone tissue defects as a scaffold material for bone tissue engineering. At present, some researchers have integrated the modified mesoporous bioactive glass with organic materials to improve the mechanical properties of the materials. However, their osteogenic behavior, osteogenic mechanism, degradation and metabolism in vivo still need to be further studied. It is believed that in the near future, modified mesoporous bioactive glass will be used as scaffold material in clinic.

Bioactive glass has been studied for nearly 40 years. Due to its simple fabrication process, easy material acquisition and excellent osteogenic properties, it has been used in the repair and treatment of maxillofacial bone defects. With the development of the technology and the innovation of the concept, the bioactivity and osteogenic properties of the maxillofacial bone defect have been improved, and the satisfactory results have been obtained in the reconstruction of maxillofacial bone defects. However, the application of mesoporous bioactive glass in the scaffold materials of bone tissue engineering is still facing great challenges, which need to be further studied.

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