Osteogenic Effect of Ti02 Nanotube BMP2 / BMP7 Composite Layer on Titanium Implant Surface

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Abstract: As we all know, titanium is a metal with many advantages. Titanium and titanium alloys have been widely used in medical artificial joint prosthesis materials because of their excellent mechanical properties, biocompatibility and corrosion resistance. However, due to the inertia of titanium, titanium can not directly combine with bone. The surface modification of titanium implants is one of the research hotspots of implant materials. In this paper, the osteogenic effect of Ti02 nanotube BMP2 / BMP7 composite layer on titanium implant surface was studied. In this study, we prepared TiO2 nanotubes by anodic oxidation method. Eight rats were selected as the research animals, and they were randomly divided into the control group and the experimental group. The femoral implants of rats were implanted into the model for in vivo research. The control group used the general titanium implant, and the experimental group used the modified surface with Ti02 nanotube BMP2 / BMP7 composite layer Titanium implants. We compared and analyzed the histological morphology, bone mineral density, bone implant contact area and bone tensile strength. In this study, we found that the average BMD of the femur of the control group was 124.28mg/cm^2, and that of the experimental group was 375.36mg/cm^2. It can be seen that the femoral density of the experimental group is much higher than that of the control group. The experimental results show that the composite layer of Ti02 nanotube BMP2 / BMP7 on the surface of titanium implant has good osteogenic effect.

1. Introduction

Traditional implant surface coating has some problems, such as insufficient bonding strength, easy to fall off, insufficient comprehensive biological characteristics and unknown long-term stability. Researchers are trying to solve these problems by adding rare metals and bioactive materials. Generally speaking, titanium has good biocompatibility, not only high mechanical strength, but also stable chemical properties, which can form good bone fusion with normal bone tissue, which is a kind of commonly used implant material [1-2]. However, due to the biological inertia of titanium, they can not be directly combined with bone, and can not stimulate bone formation on the surface of implanted materials in the early stage. As a result, there will be a series of problems in the clinical application of pure titanium implants, such as poor osseointegration, long healing time and so on. Good osseointegration between implant and bone tissue is the basis of implant function [3-4]. In order to achieve better and faster osseointegration, some scholars have optimized the chemical composition and physical properties of titanium implant surface in various ways [5-6].

There are many growth factors in the microenvironment of bone cells, which stimulate the cell proliferation of the same kind of cells, play a regulatory role and promote the regeneration and repair of bone tissue. Among them, BMP2 / BMP7 is one of the most studied growth factors in recent years [7-8]. Some studies have shown that BMP 2 / BMP 7 plays an important role in the process of bone defect repair. However, due to the slow synthesis of BMP, the degradation rate is faster, and there are some side effects. Therefore, some scholars have compounded it with corresponding scaffold materials to provide certain support, promote the growth of bone tissue, and reduce the effect of some cytokines and reduce the side effects [9-10]. Adding Ti02 nanotube BMP2 / BMP7 composite layer on the surface of titanium implant is of great significance for promoting

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osteogenesis.

In this paper, eight rats were selected as the research animals, and the control experiment was set up. In the experiment, the rats were randomly divided into two groups, the control group and the experimental group. Then, we implanted the femoral implant model in rats for in vivo research, and then compared the histological morphology, bone density, bone implant contact area and bone tensile strength analysis. The results of this study show that the titanium implant with the surface of Ti02 nanotube BMP2 / BMP7 composite layer can make the bone formation density higher, the contact area between bone and implant is more, and the bone tensile strength is better, that is to say, the effect of titanium implant surface with Ti02 nanotube BMP2 / BMP7 composite layer is better.

2. Surface Modification of TiO2 Nanotubes and Titanium Implants

2.1 Ti02 Nanotubes

Titanium dioxide nanotube is an important inorganic functional material. It has good physical and chemical properties, such as regular electron channel, high specific surface area, low cost, stable chemical properties and good light absorption. TiO2 is a kind of n-type semiconductor with wide band gap. Due to its unique optical, electrical, photochemical and biological properties, TiO2 nanomaterials are a new functional material developed in recent years and have been widely used in many fields.

There are many ways to synthesize TiO2 nanotubes. Generally speaking, there are three methods: hydrothermal method, template method and anodic oxidation method. The results show that the diameter and length of TiO2 nanotubes prepared by hydrothermal method are heterogeneous and disordered; the diameter and length of TiO2 nanotubes prepared by template method are limited by template size, and the morphology of TiO2 nanotubes may be damaged by removing the template; while the diameter and length of TiO2 nanotubes prepared by anodic oxidation method are uniform and orderly, and the quality of TiO2 nanotube film is good, the morphology of TiO2 nanotubes will not be damaged during the preparation process. Based on the above advantages, TiO2 nanotubes were prepared by anodic oxidation method.

2.2 Surface Modification of Titanium Implants

Titanium and titanium alloys have been widely used in implant field because of their excellent physical and chemical properties, biological properties and biocompatibility. However, titanium and titanium alloys are metal materials, which have poor wear resistance, easy corrosion in vivo and biological inertia. Therefore, it is not easy to form good early osseointegration and lead to early loosening and shedding of implants. Therefore, it has been the focus of domestic and foreign scholars to improve the osseointegration of implants by surface modification of titanium implants. Some researchers improve the characteristics of implants by surface modification of titanium implants.

In recent decades, researchers have modified the surface of titanium implant mainly from three aspects: physical modification, chemical modification and biological modification. There are many methods of chemical modification, including sol-gel, electrochemical deposition, acid extraction, anodization, micro arc oxidation and so on. There are many physical modification methods, including ion implantation, sand blasting, plasma spraying, thermal spraying, surface ceramics, laser treatment and so on. There are many methods of biological modification, which are usually achieved by loading active molecules, including proteins, active peptides, biological agents, etc.

3. Experimental Design

In this paper, TiO2 nanotubes were prepared by anodic oxidation method, and titanium implants were modified by biological method. The TiO2 nanotubes BMP2 / BMP7 composite layer was formed on the surface of titanium implants.

(1) Research animals

Eight 4-month-old male Sprague Dawley (SD) rats, weighing between 440 and 470g, were

selected as research animals. These rats were randomly divided into two groups, the experimental group and the control group. There was no significant difference in the weight between the two groups. The rats were reared in a suitable environment.

(2) Preparation of animal model and observation index

In order to verify the osteogenic effect of Ti02 nanotube BMP2 / BMP7 composite layer on the surface of titanium implant, the rat femoral implant model was used for in vivo study. We implanted titanium implants on the surface of femur of rats and titanium implants with Ti02 nanotube BMP2 / BMP7 composite layer on the surface of femur. After 4 weeks, we extracted samples containing implants, made decalcified tissue sections, and carried out Masson staining to observe and analyze the osteogenic effect.

In addition, we compared the histological morphology, bone mineral density, bone implant contact area and bone tensile strength.

4. Experimental Results and Analysis

The natural TiO2 oxide layer formed on the surface of titanium has biological inertia, which can not be chemically bonded with bone tissue after implanting into human body, which protects titanium from being corroded by body fluid after implantation, but also affects the osteogenic effect of titanium and the body. Therefore, some researchers improve the characteristics of titanium implants by modifying the surface of titanium implants.The modification of titanium surface physical properties mainly includes the optimization of surface morphology, roughness, hydrophilicity, crystal form and charge. More and more studies have shown that the surface morphology of materials plays a very important role in regulating the biological reactions of tissues and cells. Compared with the changes of chemical composition of materials, the optimized surface morphology has better strength and stability. It can control and optimize the surface roughness, wettability and surface energy of materials. As the premise of clinical successful implantation, titanium and alloy should have good osseointegration at the bone implant interface.

In the past few years, a large number of studies have been carried out on the optimal surface morphology for biological applications. The research and application of biomedical materials has shifted the focus from micromorphology to nano morphology. To improve the biocompatibility, biocompatibility and biocompatibility of titanium alloy and implant surface, and to improve the biocompatibility and biocompatibility of implants, It is the focus of current research.

The formation of nanostructures on the implant surface contributes to osseointegration. Compared with other surface treatments for titanium implants, it is a simple and cost-effective surface engineering method.

In this paper, titanium was modified to produce nano tubular TiO2 on its surface, and the titanium was modified by biological methods. BMP2 / BMP7 was added to the surface of titanium implant to form a composite layer with TiO2 nanotube, and the osteogenic effect was studied.

In addition, in order to make the data in this paper more convincing, we have carried on certain processing to the experimental data. In the process of data processing, we used some statistical software as auxiliary means to process the data. Then, we analyze the experimental results as follows:

4.1 Analysis of Histological and Morphological Results

After staining, the histological morphology of the femurs of the two groups were compared and analyzed. The results are shown in Table 1.

Table 1. Analysis of histological and morphological results of the two groups

Control group	The continuity of newly formed braided bone was poor, and there were more fibrous tissue around the implant
Experience group	Around the implant, there were a significant increase of dense new bone formation and scattered fibrous tissue.

It can be seen from Table 1 that in the control group, the continuity of the newly formed braided

bone was poor, and there was more fibrous tissue around the implant. In the experimental group, the formation of new bone with dense structure around the implant was significantly increased, and a few fibrous tissue remained. It can be seen that the effect of Ti02 nanotube BMP2 / BMP7 composite layer on titanium implant surface is better, that is to say, adding Ti02 nanotube BMP2 / BMP7 composite layer on the surface of titanium implant can make the osteogenic effect better.

4.2 Bone Mineral Density Analysis

The femoral bone mineral density of the two groups was analyzed, and the results are shown in Figure 1.

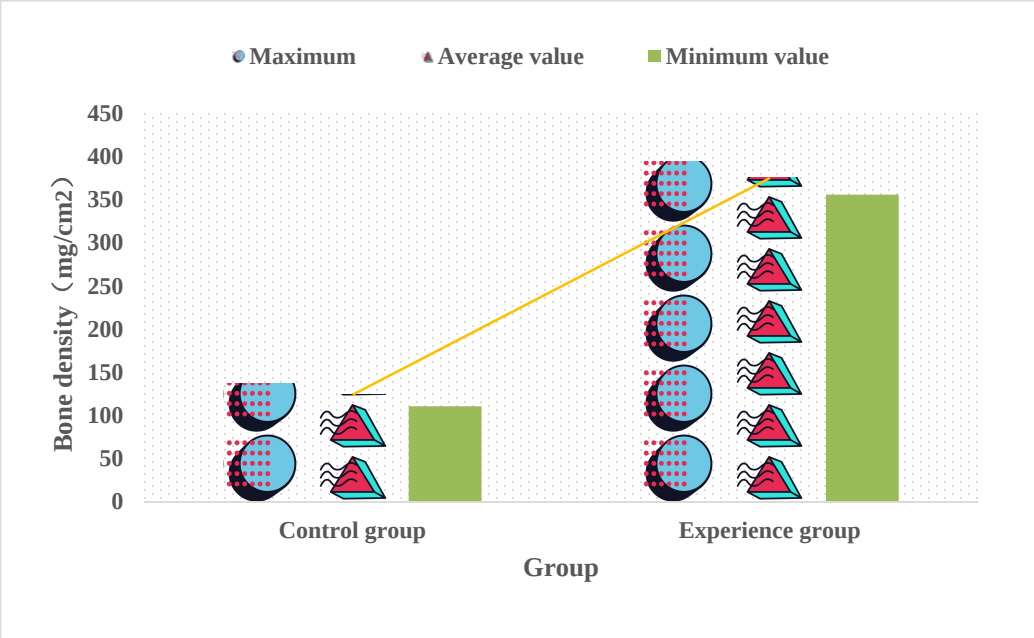

Figure 1. Results of bone mineral density analysis between the two groups

It can be seen from Figure 1 that the maximum bone mineral density of femur of rats in the control group is 137.73mg/cm^2, the minimum value is 110.83mg/cm^2, the average value is 124.28mg/cm^2, while the maximum bone mineral density of femur of experimental group is 394.64mg/cm2, the minimum is 356.08mg/cm^2, and the average value is 375.36mg/cm^2. From this, we can know that the bone mineral density of the control group is far less than that of the experimental group. It can be seen that the osteogenic effect of Ti02 nanotube BMP2 / BMP7 composite layer on the surface of titanium implant is better, that is, adding Ti02 nanotube BMP2 / BMP7 composite layer on the surface of titanium implant can make the osteogenic effect better.

4.3 Bone Implant Contact Area and Bone Tensile Strength Analysis

We analyzed the bone implant contact area and bone tensile strength in the femur of the two groups, and the results are shown in Figure 2. The contact area between the bone and the implant and the tensile strength of the bone are expressed as percentages.

It can be seen from Figure 2 that in the femur of the control group, the contact area between bone and implant reached 25.66%, while in the experimental group, the contact area between bone and implant reached 73.28%, which was much larger in the experimental group than in the control group. In addition, in the bone tensile strength, the bone tensile strength of the control group was 45.32%, and that of the experimental group was 86.26%, which was much higher than that of the control group. Therefore, adding Ti02 nanotube BMP2 / BMP7 composite layer on the surface of titanium implant can make the effect of osteogenesis better.

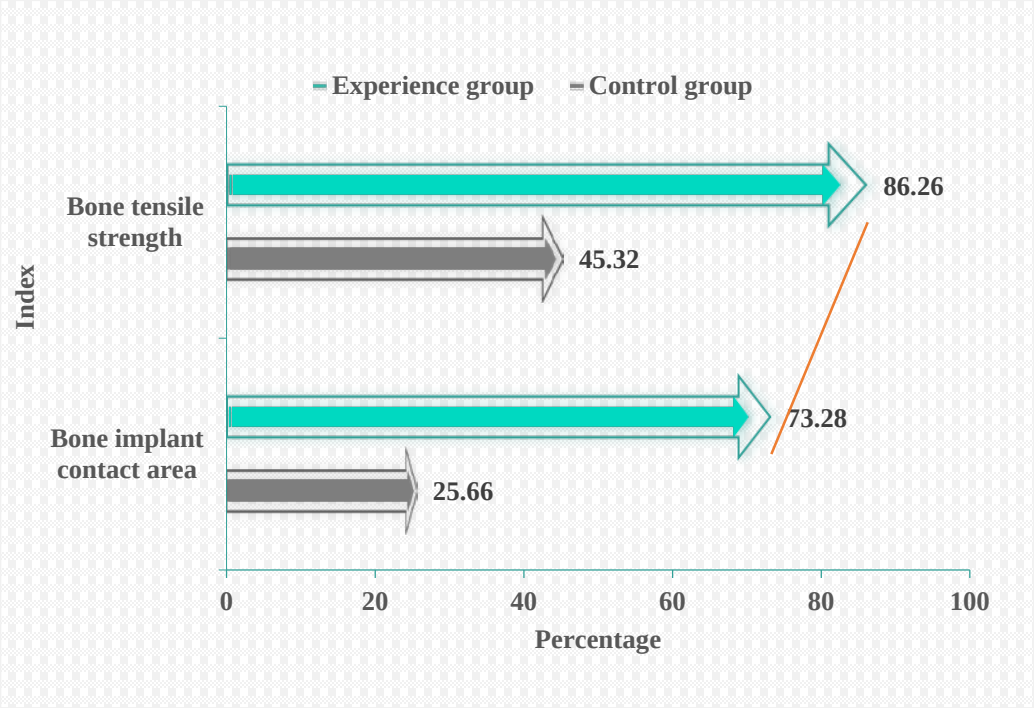

Figure 2. Bone implant contact area and bone tensile strength analysis

5. Conclusions

Titanium has many advantages, not only good biocompatibility, but also high mechanical strength, chemical stability, because of these advantages, titanium can be combined with bone tissue, widely used in medicine. However, pure titanium as an inert metal, it has some disadvantages, for example, it does not have the ability to stimulate the proliferation of bone fibers and bone cells, so pure titanium as bone graft material treatment effect is not good. In order to improve these defects, strengthen the combination of implant and bone, so as to avoid the absorption of bone tissue around the implant and ensure the long-term stability of the implant, some scholars have tested the surface modification technology of multiple implants. Based on this, the osteogenic effect of Ti02 nanotube BMP2 / BMP7 composite layer on titanium implant surface was studied. The results of this study show that adding titanium nanotubes to the surface of BMP2 can promote the bone formation of the implant.

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