Platelet Gel on Reconstructing Bone Defects and Nonunions

Subjects: Orthopedics
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In ideal circumstances, a fractured bone can heal properly by itself or with the aid of clinical interventions. However, around 5% to 10% of bone fractures fail to heal properly within the expected time even with the aid of clinical interventions, resulting in nonunions. Platelet gel is a blood-derived biomaterial used in regenerative medicine aiming to promote wound healing and regeneration of damaged tissues. Most of the studies applied the combination of platelet gel and bone graft to reconstruct bone defects and nonunions, and most of the results were positive, suggesting that this treatment strategy could promote successful reconstruction of bone defects and nonunions. In conclusion, the application of platelet gel could be a promising and useful treatment method for reconstructing bone defects and nonunions, and more future clinical studies are encouraged to further investigate the effectiveness of this promising treatment method.

bone fractures orthopedics surgery

1. Introduction

Bone is a specialized tissue rich in cells including osteoblasts, osteoclasts, and osteocytes responsible for remodeling [1]. Because of its remarkable remodeling ability, bone is a type of tissue that has high potential for regeneration (i.e., self-healing or self-repair) [2][3]. In ideal circumstances, such as the healing of a simple bone fracture or a tooth extraction socket, a fractured bone can heal properly by itself or with the aid of standard conservative or surgical clinical interventions [1][3]. However, it has been reported that around 5% to 10% of bone fractures fail to heal properly within the expected time even with the aid of clinical interventions, resulting in delayed union or nonunion [4][5][6][7][8][9][10][11][12][13]. Delayed union or nonunion often occurs in fractured bones with critical-size defects, with infections, without proper mechanical stability, or could occur in patients with bone fractures who have certain diseases (such as diabetes) or risk factors (such as smoking) [14][15]. Indeed, bone regeneration is a complex process that needs numerous basic requirements as well as proper biological and mechanical conditions to accomplish, and the lack of one or more of the requirements and conditions may lead to the occurrence of delayed union or nonunion [16]. To date, despite continuous advances in the treatment strategies of bone fractures, delayed union or nonunion is still not uncommon and remains a challenge in orthopedics [4][17][18][19][20]. Please note that, although two different terms “delayed union” and “nonunion” are often used simultaneously to describe this tough clinical scenario as in the text above, it is believed that in many cases it is difficult to clearly indicate that a healing process is just delayed, or impaired with no possibility of healing [3].

The U.S. Food and Drug Administration defines a nonunion as a fracture that is at least nine months old and has not shown any signs of healing for three consecutive months, while some researchers define a nonunion as a fracture that has no possibility of healing without further intervention according to the treating physician [4][20]. The causes of nonunion are complex and multifactorial and are related to the type of fracture, the severity of fracture, as well as the physical conditions, diseases, and risk factors in the patient [3][4][9][11][21][22]. Nonunions usually involve symptoms including pain, deformity, and functional disability [3][20] and could significantly decrease the health-related quality of life of patients and cause associated socio-economic problems [10]. Hence, bone nonunion remains a major public health issue that causes problems in many aspects, and there is a crucial need to better understand the underlying mechanisms and improve the treatment strategies of nonunions in order to meet the needs of patients and reduce the associated problems.

2. Research on Using Platelet Gel to Reconstruct Bone Defects Associated with Surgery

In a study presented by Leonardi et al. [23], the researchers showed a positive treatment effect of using allogenic bone graft mixed with autologous platelet gel on reconstructing bone defects for two patients treated for hip revision with a partial pelvis replacement ring. These two patients suffered from bone loss after the previous surgery; therefore, a revision surgery was required to restore the integrity of the bone. During the revision surgery, the allogenic bone graft mixed with autologous platelet gel was molded to fill the bone defect after positioning and fixing the ring. The researchers reported that, after spraying platelet gel onto the bone graft, the platelet gel was absorbed by the bone graft in about 10 s. Thirty seconds later, the platelet gel started to retract, keeping the morselized bone graft tight but still plastic enough to be positioned under the ring. Then, after 2 to 3 min, the mixture of bone graft and platelet gel became solidified, keeping the bone graft firm. The researchers believed that platelet gel can provide enhancement and help to keep the morselized bone graft firm, making it easier to fix the bone graft at the site of the bone defect and to densely fit the bone graft into the bone defect. The mean follow-up time was 27.2 months. For the two patients, the X-ray radiographic examinations confirmed the successful healing of the bone defect while the clinical examinations showed satisfactory outcomes.

In a brief report presented by Franchini et al. [24], the researchers showed a positive treatment effect of using autologous platelet gel mixed with hydroxyapatite on reconstructing bone defects for 19 patients undergoing reconstructive bone surgeries. The indications for surgery include fibrous dysplasia, fracture, osteomyelitis, pseudoarthrosis, total hip arthroplasty with acetabular reconstruction for acetabular dysplasia, bilateral lower-extremity lengthening, bilateral hip arthroplasty with acetabular reconstruction for rheumatoid arthritis, or revision of hip prosthesis. Autologous platelet gel was mixed with hydroxyapatite and then applied during the surgery, but the researchers did not describe how they applied the mixture of platelet gel and hydroxyapatite during the surgery. The follow-up examinations using X-ray radiography after a median follow-up time of 12.9 months showed improved osteoblastic reaction and restoration of bone structure in all patients, while progressive incorporation of hydroxyapatite into the surrounding bone could be observed. The clinical outcomes of all patients were also

satisfactory without complications. The researchers concluded that the results demonstrated the osteoinductive effectiveness of autologous platelet gel to stimulate bone regeneration following reconstructive bone surgery.

In a similar study presented by Franchini et al. [25], the researchers showed a positive treatment effect of using allogenic bone graft mixed with autologous platelet gel on reconstructing bone defects for 25 patients who underwent reconstructive bone surgeries. The patients enrolled had severe bone disorders (osteomyelitis, pseudoarthrosis, or bone defects due to unreported reasons) and had undergone several previous surgeries, but all surgeries failed to solve their problems. Allogenic bone tissues from a tissue bank were fragmented using a mechanical miller, and the resulting bone chips were mixed with autologous platelet gel. The mixture of bone graft and platelet gel was applied to fill the bone defect during the surgery. The mean follow-up time was 16.9 months. The results of the post-operative follow-up showed satisfactory outcomes for all patients based on the biological, X-ray radiographic, and clinical examinations, although a patient underwent an amputation of the leg 8 months after the surgery due to the primary disease of that patient. The researchers concluded that allogenic bone graft mixed with autologous platelet gel is efficient in the regenerative treatment of complex bone disorders.

In a study presented by Savarino et al. [26], the researchers showed a positive treatment effect of using allogenic bone chips mixed with autologous platelet gel on reconstructing bone defects for patients undergoing high tibial osteotomy for treating genu varus due to osteoarthritis. Ten patients were enrolled and divided equally into a patient group and a control group. In the patient group, the mixture of lyophilized allogenic bone chips and autologous platelet gel was applied to fill the bone defect during the surgery. In the control group, lyophilized allogenic bone chips were applied to fill the bone defect alone without using platelet gel. The follow-up examinations 6 weeks after the surgery showed that there was no difference in the clinical and functional outcomes between both groups. However, the histological, histomorphometric, and microradiographic analyses showed signs of accelerated healing and regeneration (as evidenced by new bone and vessel formation) in the group with the use of platelet gel compared to the control group, although X-ray diffraction analysis showed that there was no difference in the microstructure between both groups. Based on the results, the researchers concluded that the mixture of allogenic bone chips and autologous platelet gel can promote osteogenesis and accelerate bone healing and regeneration.

In a similar study presented by Dallari et al. [27], the researchers showed a positive treatment effect of using allogenic bone chips mixed with autologous platelet gel or allogenic bone chips mixed with autologous platelet gel and bone marrow stromal cells on reconstructing bone defects for patients undergoing unilateral opening-wedge high tibial osteotomy for treating genu varum. Twenty-eight patients were enrolled and divided into three groups. In group A (9 patients), the mixture of lyophilized bone chips and platelet gel was applied to fill the bone defect during the surgery. In group B (10 patients), the mixture of lyophilized bone chips, platelet gel, and bone marrow stromal cells was applied. In the control group (9 patients), lyophilized bone chips alone were applied. The histological and histomorphometric analyses 6 weeks after the surgery showed signs of accelerated healing and regeneration (as evidenced by new bone and vessel formation) in the groups A and B compared to the control group. The X-ray radiographic examinations 1 year after the surgery showed better osteointegration in the groups A and B compared to the control group. However, there was no difference in the clinical and functional outcomes among the three

groups. The researchers concluded that adding platelet gel or platelet gel combined with bone marrow stromal cells to lyophilized bone chips can enhance the osteogenetic potential of lyophilized bone chips for treating of massive bone loss, while complete osseointegration was not achieved in some patients with the use of lyophilized bone chips alone.

In a study presented by Feiz-Erfan et al. [28], the researchers showed that there was no significant effect of using autologous platelet gel alone to enhance earlier fusion and increase fusion rate for patients undergoing anterior cervical fusion with allograft and internal fixation. Eighty-one disc levels were treated surgically in the 50 enrolled patients, in which 29 patients had degenerative cervical disc disease and 21 patients had herniated cervical disc disease. Forty-two disc levels were assigned to be treated using allograft mixed with autologous platelet gel, and thirty-nine disc levels were assigned to be treated using allograft without autologous platelet gel. The X-ray radiographic examinations 1 year after surgery showed that the overall fusion rate was 84% (68 of 81), and there was no significant difference in the fusion rate between patients with and without receiving platelet gel. For all patients, the outcomes of the pain and disability examinations showed significant improvements without significant differences. The researchers concluded that the use of autologous platelet gel alone had no significant effect in enhancing earlier fusion and increasing fusion rate for patients undergoing anterior cervical fusion with allograft and internal fixation.

In a study presented by Sabbagh et al. [29], the researchers showed a positive treatment effect of using autologous platelet gel on promoting the healing of phalangeal fractures after fixation by Kirschner wires for 20 patients. Platelet gel was used alone and was not mixed with bone graft or other materials. The X-ray radiographic and clinical examinations showed signs of healing at 12 weeks for 70% of patients, and 16 weeks for another 30% patients. The researchers concluded that autologous platelet gel was useful to promote healing and decrease recovery time in phalangeal fractures after fixation by Kirschner wires.

3. Research on Using Platelet Gel to Reconstruct Bone Defects in Patients with Bone Tumors

In a study presented by Loquercio et al. [30], the researchers showed a positive treatment effect of using β-tricalcium phosphate, commercialized bone graft material and autologous platelet gel on reconstructing bone defects for 16 patients with giant cell tumors treated with curettage surgery. These three materials were applied simultaneously to fill the bone defect during curettage surgery. For all patients, the X-ray radiographic and computerized tomographic examinations showed complete healing at an average of four months, while the functional examinations showed satisfactory outcomes. Four patients showed recurrence during the follow-up period. The researchers concluded that the use of autologous platelet gel as a supplementation can significantly reduce the time required for bone healing after curettage surgery for giant cell tumor and can achieve satisfactory functional outcomes.

In a study presented by Mostafa et al. [31], the researchers showed a positive treatment effect of using autologous platelet gel mixed with hydroxy appetite/beta tri-calcium phosphate bone substitutes on reconstructing bone

defects after extended curettage surgery for 20 patients with benign bony cystic lesions. The mean follow-up time was 18 months. The X-ray radiographic and clinical examinations showed satisfactory outcomes in all patients, although two patients showed recurrence. The researchers concluded that autologous platelet gel mixed with hydroxy appetite/beta tri-calcium phosphate bone substitutes can be useful to reconstruct bone defects.

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