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Research Paper

The Effect of Autologous Platelet-rich Plasma on Posterolateral Arthrodesis After Lumbar Spine Posterior Stabilization Surgery

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ABSTRACT

Background and Aim: Lumbar spine posterior stabilization surgery is based on the formation of bone structures around the device placement. However, if these bone structures are not formed well, the conditions for pseudoarthrodesis are provided. In recent years, the use of platelet-rich plasma (PRP) as an induction of bone formation after spinal stabilization has received attention, but its results have been different and sometimes controversial. This study was conducted to accurately evaluate the effect of this method on arthrodesis after lumbar spine posterior stabilization surgery.

Methods and Materials/Patients: Twenty patients under the age of 70 years who were candidates for posterior spinal stabilization surgery were selected, and on the day of surgery, PRP was prepared from their venous blood, and at the end of the surgery, a combination of PRP and allograft bone was used on one side of the spine, and a combination of normal saline and allograft bone was used on the other side for arthrodesis. Then, the arthrodesis in the patients was evaluated with a computerized tomography (CT) scan in the third, sixth, and twelfth months after the operation by two radiologists based on the Hounsfield index.

Results: In all 20 patients, the arthrodesis was significant during the third, sixth, and twelfth months in the intervention side and in the control side and had a decreasing trend (P<0.001). In the comparison of the arthrodesis rate in the third and twelfth months after the operation, no significant difference was observed between the intervention and control groups (P=0.120 and P=0.405, respectively). In the sixth month, the rate of arthrodesis between the intervention and control groups was borderline statistically significant (P=0.061).

Conclusion: The use of PRP in the stabilization of the lumbar spine does not affect the increasing rate of spinal arthrodesis, and it may only accelerate the rate of arthrodesis in the sixth month.

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Highlights

- Arthrodesis in spinal stabilization surgeries is reduced in the first year.
- The use of platelet-rich plasma (PRP) in spinal stabilization surgeries does not affect the increasing rate of spinal arthrodesis.
- The use of PRP in spinal stabilization surgeries may only accelerate the rate of arthrodesis in the first six months.

Plain Language Summary

Lumbar spine instrumentation surgery is one of the most common spinal stabilization procedures, which, of course, fails in the case of pseudoarthrodesis and aggravates the complications of surgery. The effect of platelet-rich plasma (PRP) in healing tissue damage has been proven today, and in this study, we will examine its role in improving bone formation.

In this study, we selected 20 patients who were candidates for lumbar spine instrumentation surgery and used PRP prepared from their blood to check the amount of arthrodesis. Then we re-evaluated the patients using computerized tomography (CT) scans in the third, sixth, and twelfth months after surgery.

After the investigation, we concluded that the rate of arthrodesis decreases during the first year after surgery, and the use of PRP does not have a significant effect on the rate of arthrodesis, but it may accelerate the rate of arthrodesis during the first six months.

1. Introduction

Lumbar spine stabilization surgery using pedicle screws and rods is known as the most common surgical technique for fusion, which is based on the formation of interosseous and interarticular structures around the device site. Posterolateral ossification is defined as the development of intervertebral bone structures throughout the lamina and transverse process [1]. To achieve this goal, various autograft and allograft bone structures have been used; however, the probability of non-union of bone is still in the range of 5%-45%, therefore, the use of techniques that increase bone repair and fusion and at the same time for safety and ease of access, has been given more attention by surgeons [2-4].

Currently, the use of autologous iliac crest bone graft is still considered the gold standard for inducing ossification after spinal stabilization, although this procedure causes complications, such as hematoma, fracture, infection, and patient pain after surgery. For this reason, the use of allograft bones by surgeons is increasing, but these bones lack bone-forming cells and proteins due to the prevention of sensitivity in the recipient [2, 5-7].

In the wound healing process, platelets secrete growth factors, such as platelet-dependent growth factor, vascular endothelial growth factor, transforming growth factor, and insulin-like growth factor by binding to the damaged tissue. This inflammatory process along with vascular proliferation provides the basis for the differentiation of mesenchymal cells. In this way, nutrients, blood vessels, and mesenchymal cells necessary for reproduction and ossification of bone are provided [8] The use of platelet-rich plasma (PRP) is completely safe because it is prepared from the patient, and it also has antimicrobial properties due to the chemotaxis of white blood cells [9]. In recent years, the use of PRP as an induction of bone formation after spinal stabilization has increased [10-12]. In some studies, the use of PRP has been beneficial to induce ossification in patients with jaw and facial injuries [13-15].

Therefore, considering the possibility of no bone fusion after stabilization of the vertebral column and the absence of cells and proteins inducing ossification, and the ease of using PRP to supply these elements, this study was designed to investigate the effect of PRP on ossification after stabilization of the vertebral column.

2. Materials and Methods

In this clinical trial, 20 patients referred to Hazrat Rasool Akram Medical Research Center who were candidates for posterior spinal stabilization surgery due to lumbar vertebrae fracture, lumbar canal stenosis, or lumbar spondylolisthesis were selected. On the day of surgery, 26 cc of whole venous blood was taken from the patient under sterile conditions and placed in 3 special tubes for the preparation of PRP (manufactured by Becton Dickinson) containing 1.5 cc of acid citrate dextrose with a volume of 8.5 cc, it is transferred to the laboratory unit of Hazrat Rasool Akram Hospital.

In the laboratory, PRP is prepared by the double spin method, in this way, first all 3 tubes are placed in a centrifuge (Pars Azma model SH.13) with a revolution of 1600 for 12 minutes and after finishing the layer work, the plasma is separated under sterile conditions and enters the test tube without anticoagulant. Then it is placed again in the centrifuge at 2700 rpm for 5 minutes. After finishing the work, the upper two-thirds of the plasma is separated from the tube and the remaining one-third is gently shaken in a pendulum after a 5-minute rest so that the concentrated platelets merge with the plasma. Then the PRP was transferred to the operating room and at the end of the operation, 2 cc per vertebra in combination with bone paste and bone allograft (manufactured by Ceno Bone Company) in the posterolateral space of one side of the vertebral column (intervention side). Then the combination of bone paste and bone graft with 2 cc of normal saline serum is placed for each vertebra in the posterolateral space of the other side of the vertebral column (control side).

Then the patient was followed up for one year with a computerized tomography (CT) scan (Aquilion Lightning model, Canon Medical) with fine parts and coronal and sagittal reconstruction in the third, sixth, and twelfth months after the operation and the amount of ossification based on the average of the Hunsfield index in the posterior region. The side of the spine was recorded numerically in separate questionnaires by two radiologists who did not know about the side of the intervention.

The sample size was determined using G*Power software, version 3.1.9.2. Based on the repeated-measures analyses of variance (ANOVAs), within-between interaction statistical test; 40 total participants (20 per group) were enrolled.

Examining the conformity of the frequency distribution of dependent variables with the theoretical normal distribution through the Kolmogorov-Smirnov statistical test.

Investigating the interaction of groups and time using repeated measure analysis of variance (ANOVA) 2x3 groups (intervention and control) and time (three months, six months, and twelve months).

Statistical tests were performed with SPSS software, version 27, and confidence limits of 95% and α=0.05.

3. Results

Out of the total of 20 patients studied, 13 cases (65%) were women and 7 cases (35%) were men. In terms of age, the minimum age of the patients was 26 years and the maximum age was 66 years, and the mean age of the patients was 51 years.

Six cases (30%) had diabetes and 7 cases (35%) were smokers. In terms of pathology, 9 cases (45%) suffered from lumbar canal stenosis, 7 cases (35%) had lumbar spondylolisthesis and 4 cases (20%) had lumbar spine fractures.

In all 20 examined patients, the amount of bone formation during the third, sixth, and twelfth months, regardless of the intervention or control side, had a significant difference and its trend was decreasing (P<0.001). In other words, regardless of whether they contain PRP or not, the allograft bones are absorbed and their density decreases during the studied times.

In the comparison between the amount of bone formation in the intervention side and the control side in the third and twelfth months after the operation, based on the mean of the Hunsfield index, the P was calculated as 0.120 and 0.405, respectively, which was not statistically significant and as a result, no difference was observed between the intervention and control groups.

In the comparison between the amount of bone formation in the sixth month between the intervention and control groups, the P was calculated as 0.061, which is statistically borderline and needs further investigation.

Having diabetes and smoking did not affect the amount of bone formation in all periods, either in the intervention or the control side. Gender also did not affect the amount of bone formation in the sixth and twelfth months, either in the control or in the intervention side, but in the male population, the bone formation rate was higher in the third month after the operation

in both the intervention and control sides compared to women (P=0.030). These results may not be reliable due to the small sample size.

4. Discussion

Following a bone fracture in humans, several chemical factors play a role in healing and re-ossification. Granules in platelets contain large amounts of these proteins, including platelet-derived growth factor, insulin-like growth factor, transforming growth factor, and vascular endothelial growth factor. These substances cause the proliferation and differentiation of mesenchymal stem cells and accelerate the bone formation process [16, 17]. Today, it is possible to produce platelets with high concentrations using various methods, the most appropriate and cost-effective of which is the use of PRP. The crucial advantage of this method is its autologous origin, which is prepared from the patient's venous blood, thus minimizing the possibility of immune responses and transmission of blood diseases.

According to the studies, to use the ossification properties of platelets, it is necessary to first concentrate them in a very high amount and then place them next to the damaged tissue to secrete the proteins that stimulate ossification over time [16].

Currently, the use of PRP has many uses in plastic surgery, dentistry, orthopedics, and maxillofacial surgery due to its many growth factors [18-22]. In the past years, its use in spinal stabilization operations as an ossification-inducing agent in combination with cancellous allograft bone has been considered, and its effectiveness has been questioned due to the different and contradictory results of recent studies [11, 23]. In a study that used PRP in combination with allograft bone for the intervertebral cage and followed up the patients with CT scan, no effect on bone formation was observed [24]. In the Acebal-Cortina prospective study, which was conducted on 107 patients, the amount of posterolateral ossification in the use of PRP was investigated and the patients were followed up with plain radiography for 2 years, the amount of ossification in the study group of 67 patients compared to the control group of 40 patients not only did not increase but also decreased [25]. Another study was conducted on 38 patients who underwent posterior spinal stabilization surgery with a posterior intervertebral cage, and the patients were followed up with CT scans in the third, sixth, twelfth, and twenty-fourth months; also, no effect was observed on the amount of bone formation in the use of PRP [26].

In several studies, the combination of PRP with allograft bone has been used in posterolateral stabilization and posterior and anterior intervertebral fusion surgeries [27, 28], which we chose due to easier access and a more detailed examination of the amount of ossification in posterolateral stabilization. Follow-up of patients in some studies is done by using simple radiography and evaluating the amount of bone formation qualitatively or based on the amount of displacement in flexion-extension imaging [29, 30]. Considering the impossibility of accurate statistical studies and the dependence of this evaluation on the opinion of radiologists, as well as the limitation of the effectiveness of flexion and extension imaging in the patient's pain condition and the impossibility of accurate calculation in the presence of pedicle screws, in this study, CT scan was used. With fine cuts and coronal and sagittal reconstruction along with calculating the Hunsfield index, the amount of posterolateral ossification in the region of interest area was calculated and evaluated by radiologists who were unaware of the intervention and control groups. Also, in our study, to eliminate the confounding effects caused by the selection of patients in the control and study groups, each sample was used simultaneously as a control and intervention. However, in our study, similar results were obtained with other studies, and the amount of bone formation in the third, sixth, and twelfth months of the patients was not significantly different compared to the control group.

Contrary to the results of the studies mentioned above as well as the results of our study, in Landi et al.'s study, which was conducted on 14 patients and evaluated the amount of posterolateral ossification with CT scan in the third and sixth months, the amount of ossification in the study group was significantly higher, which, of course, the small number of patients and the short follow-up period of the patients are limitations of this study [31].

In Tarantino et al.'s study, the amount of posterolateral ossification in 20 patients was evaluated during the third, sixth, and twelfth months after the operation, in the sixth month after the operation, the amount of fusion was higher in the study group, but in the twelfth month, no significant difference was observed between the study and control groups [32].

5. Conclusion

The use of PRP in combination with allograft bone, although theoretically it can induce bone formation and this amount is significant in the sixth month after surgery, but in the clinical examination after one year

of surgery, it does not make a difference in the amount of ossification. Also, considering the cost and time of PRP preparation and imposing the risk of infection on patients, this action is not recommended in terms of benefit and effect.

Ethical Considerations

Compliance with ethical guidelines

The Ethics Committee of the Iran University of Medical Sciences approved the protocol (Code: IR.IUMS.FMD.REC.1400.492) and it is registered in the Iranian Registry of Clinical Trials (IRCT) (No.: IRCT20171124037606N4). Written informed consent was obtained from all participants.

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Authors' contributions

Data collection: Amin Hessam and Mohamad Reza Ayoubpour; Data analysis and data interpretation: Amin Hessam and Alireza Tabibkhooei; Drafting of the manuscript: Amin Hessam; Critically revising the article: Alireza Tabibkhooei and Hamed Kheradmand; Reviewing the manuscript: Amin Hessam, Alireza Tabibkhooei, and Hamed Kheradmand; Final approval: All authors.

Conflict of interest

The authors declared no conflict of interest.

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