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High-concentrate PRP Promotes Healing in Long-Bone Nonunions

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A study of patients with nonunited fractures of long bones found that injection of platelet-rich plasma (PRP) enhanced the rate of union, demonstrated by definitive radiographic evidence of healing.

The study, "Platelet Concentrate in Treatment of Non Union of Long Bones," was conducted by Vijay Kumar, MD; Anjan Trikha, MD; and Rajesh Malhotra, MS, who presented the results. It was conducted at the All India Institute of Medical Sciences in New Delhi, India.

Patients in the study had clinical and radiological signs of nonunion of the long bones, stable internal fixation or stable reduction with plaster immobilization, and more than 90 percent contact between the fracture fragments. Nonunion was defined as a fracture that had not shown progressive evidence of healing more than 6 months after injury or more than 4 months from last fracture site operation. Patients with gap nonunions, skin infections, or pseudarthrosis; patients unfit for autologous donation (platelet count <130 × 109/L, or age older than 60 years); and patients with thrombocytopenia or hypofibrogenemia, or patients taking medicines known to influence platelet function (like aspirin) were excluded from the study.

PRP preparation and administration
Autologous blood donations were made on the morning of surgery. The PRP was prepared in the blood bank facility within the hospital and transferred to the operating room immediately afterward for injection. PRP preparation involved a series of centrifugation and separation cycles to concentrate platelets without inducing their premature activation. Quality control of platelet concentrate in all cases confirmed a platelet count of 2,000,000/μL and leukocyte reduction.

The 60 patients had a variety of long-bone fractures: tibia (35), femur (15), humerus (5), and radius (5). Most patients (42) had undergone open reduction and internal fixation; 18 patients were treated with closed reduction and internal fixation.

The PRP injections were administered at the site of nonunion—20 mL to 30 mL, depending on the site. Fracture healing was evaluated clinically and radiologically at serial follow-ups of 2 months after injection and then every 4 weeks.

Results
Evidence of callus formation was seen in 55 patients by the end of 8 weeks. By 12 weeks, 40 of the 55 patients had bridging trabeculae; the remaining 15 patients had fracture union by 24 weeks ($P < 0.05$). Five fractures (two tibia, two femur, one radius) failed to unite at 24 weeks' follow-up. These fractures were treated with a revision of fixation and autologous cancellous iliac bone grafting; all evidenced union at 3 months postoperatively.

The average time between injury and platelet injection was 9.1 months (range: 7 to 24 months). In the patients in whom the fracture united, the platelet injection had been given within 2 to 4 months of diagnosis of nonunion. However, in the five patients in whom the fracture failed to unite, the platelet concentrate had been injected 12 months or later after the diagnosis of nonunion.

Although many PRP studies use a thrombin activator, this study used a 10 percent calcium chloride solution as an activator. According to the authors, sufficient thrombin is naturally produced in the local trauma of the needle infiltrating the fracture site. Cultural considerations also affected the choice of activator; in addition to cost and availability issues associated with thrombin, its use is unacceptable to Hindus.

Although the concentration of PRP used was quite high—nearly five times commonly used values—as was the volume given, the authors believed it was necessary.

"In nonunion, the process of healing has halted completely and the local growth factors levels are abysmally low," they report. "No previous trials have used such high doses of platelets and we believe that this could be the possible explanation for the high rates of union that could be achieved."

This was not a randomized study, however, and centrifugation was used for concentrating platelets. Because centrifugation can cause fragmentation and reduce bioactivity, the authors note that ultra-filtration may be a more effective method of preparing the PRP. Also, they note that they cannot conclude that their method would be effective in the presence of bone defects, because they selected only fractures with near-total contact between the fracture fragments.

However, "the large sample size of 60 fractures with 55 patients achieving a complete union at the end of 24 weeks is compelling evidence supporting this technique," they conclude.

Disclosure information: Dr. Trikha—*Indian Journal of Anaesthesia, Journal of Anaesthesia and Clinical Pharmacology, Journal of Obstetrical Anesthesia and Critical Care*. Mr. Malhotra and Dr. Kumar report no conflicts.

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