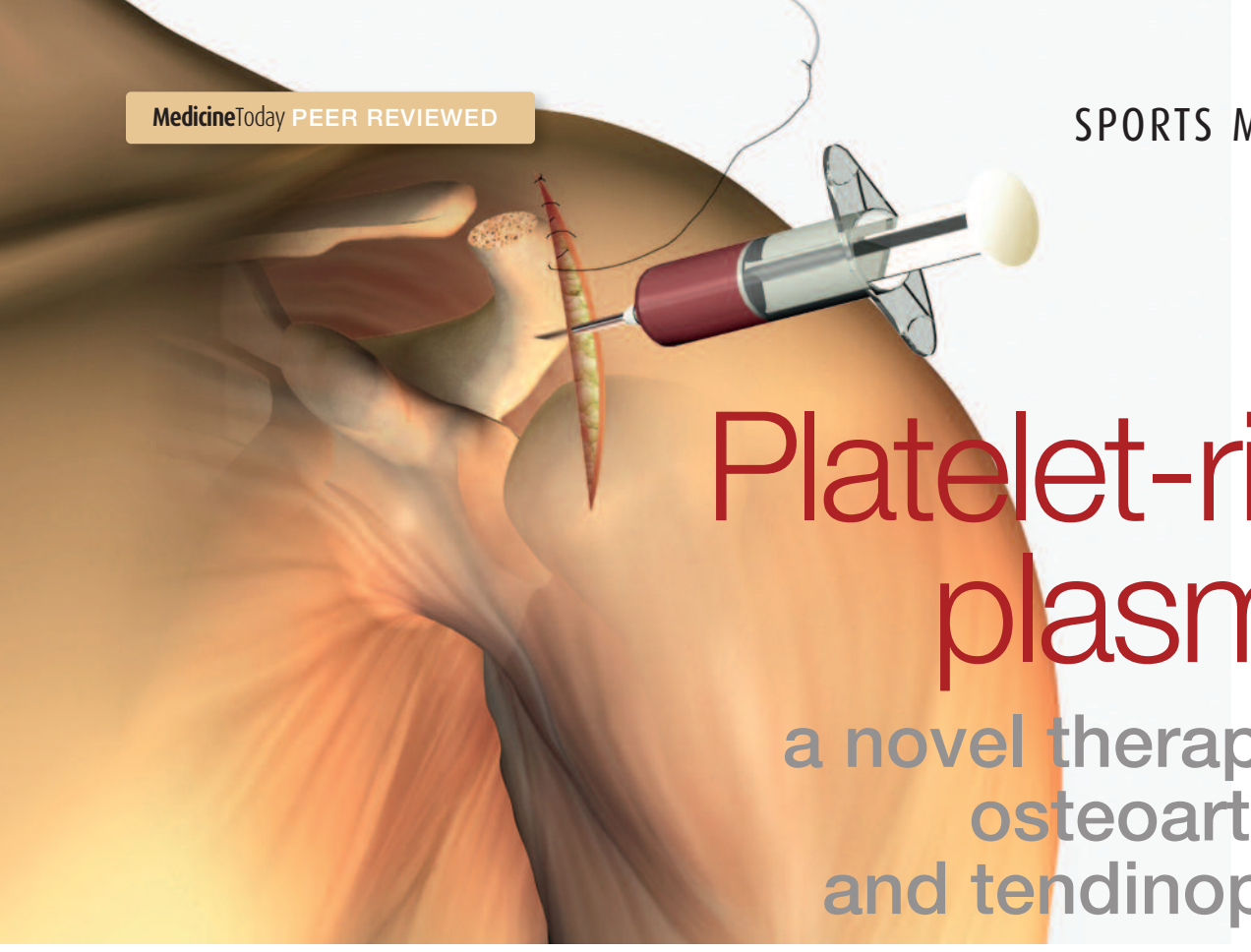

Platelet-rich plasma: a novel therapy for osteoarthritis and tendinopathy

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Platelet-rich plasma treatment involves collecting concentrated platelets from the patient's own blood and injecting them into injured areas to facilitate healing.

MedicineToday 2011; 12(11): 69-71

Platelet-rich plasma (PRP) treatment – using patients' own blood platelets to stimulate healing in injured musculoskeletal tissue – is a relatively new treatment. Although it has been in use for more than 10 years, it has only recently been employed in Australia, primarily by sports medicine physicians. It is gaining popularity because of its relative low cost, simplicity and, from the authors' experience, good clinical outcomes.

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ROLE OF THE PLATELET CELL

Blood platelet cells contain granules rich in bioactive growth factors (GFs), proteins and cytokines and these, together with other extracellular plasma proteins and cytokines, initiate and regulate tissue repair. This is a complex process involving multiple cells and cell signalling. Some of the important GFs include platelet-derived GF, vascular endothelial GF, transforming GF, fibroblast GF, epidermal GF, hepatocyte GF and insulin-like GF.

When the skin sustains a bleeding cut, platelets release clotting factors to stop the bleeding while at the same time releasing GFs to repair the injured tissues. GFs stimulate healing, whether it be making new capillaries, attracting mesenchymal stem cells to the injured area, repairing nerves or forming collagen to repair muscle, tendon, skin and chondral tissue.

WHY USE PLATELET-RICH PLASMA?

PRP treatment involves collecting concentrated platelets from the patient's own blood and usually injecting them into injured areas to facilitate healing. It uses the body's own healing mechanisms with the only unnatural aspect being the method of delivery.

In the authors' clinical experience, PRP is particularly effective for chronic tendon and joint articular cartilage injuries, probably because these anatomical areas do not have a good, direct blood supply to allow fast or effective healing. For acute injuries, the trauma from the injury often affects blood supply and transport of platelets to the injury site; therefore, direct injection of PRP into these injured areas potentially makes recovery quicker, especially for professional athletes.

HOW IS PRP THERAPY PERFORMED?

Peripheral venous blood has an average platelet concentration of 200,000/μL and platelets have a lifespan of eight to 10 days in circulation. The aim in obtaining PRP is to increase the platelet concentration in the circulating plasma by three to six times. PRP treatment is an autologous procedure: the patient is the donor and the recipient of his or her own blood product.

Plasma collection

Using conventional venipuncture methods, blood is taken from the patient. Depending on the size of the injury to be treated, between 20 and 50 mL of whole blood is required as each 10 mL of whole blood yields approximately 2 to 3 mL of PRP.

To prevent clotting, the collection tubes require sodium citrate as anticoagulant (in the form of acid–citrate–dextrose solution). Heparinised tubes or those containing EDTA should not be used as heparin and EDTA can harm the platelet cell membrane and cause platelet degranulation *in vitro* rather than at the site of injury after injection.

Plasma preparation

The collection tubes are centrifuged once in a bench-top machine for approximately 10 to 15 minutes at a rate of 1500 to 2000 rpm. The time and spin rates required to obtain the PRP concentration that is most effective (three to six times normal) vary according to the radius of the centrifuge machine used and the collection tube size.

The centrifuge process separates the blood into three distinct layers based on the particle size of the various blood components. The largest cells are the red blood cells that immediately collect in the lower 40% of the tube. Above this layer lies a thin (1 mm) intermediary 'buffy coat' of mainly white blood cells. The upper 60% of the tube contains yellow plasma. The platelets are concentrated in the lower half (1 to 2 mL) of this plasma whereas the upper portion of the plasma is nearly acellular or platelet cell poor.

PRP administration

PRP is aspirated using a 5 cm needle to reach the lower portion of the plasma fluid and then injected into the injured area. Local anaesthetic can be given to minimise the pain from the injection; however, it will dilute the concentrated platelets so it is best given in small quantities.

After injection, platelet activation occurs naturally when the platelets come into contact with fibrin or collagen at the area of injury. Fibrin forms the scaffold upon which platelets are activated to release GFs. This activation occurs within 10 minutes.

The platelets release most (95%) of the GFs in one hour but continue to synthesise and secrete more during their lifespan. GFs do not enter other cells but bind to receptors on cell membranes at the injury site, signalling the cells to play their role in the healing response. GFs do not cause tissue repair but they are the catalysts. Hence, after PRP treatment there can be an immediate anti-inflammatory effect but the complete tissue repair may not be seen for two to three months.

SAFETY OF PRP THERAPY

Immune response

Because PRP therapy uses autologous blood products, the immune system does not consider the injected platelet cells and plasma to be foreign and there is no allergic reaction. As the platelet cells are very small, flare-up from the injection is usually mild but is more common when injecting denser tissues such as tendons rather than the more spacious joints.

Some institutions take the upper 1 to 2 mm of the red cell layer together with the lower area of plasma as this can increase platelet cell numbers; however, it increases the risk of flare-up from injecting the larger and more irritating red blood cells. Debate continues as to the ideal concentration of platelets in the PRP: if it is too high, it can affect the balance required between the GFs within the platelets and those free in the plasma.[2,3]

Infection

Infection is always a risk and sterile technique needs to be strictly adhered to, especially for intra-articular injections. Additionally, the risk of infection with PRP is reduced by the antibacterial effect of PRP.[1]

Contraindications

Contraindications to the use of PRP treatment include infectious and immunodepressive diseases.

There is no tumour risk with PRP treatment as the platelets are autologous and the GFs released do not enter the cell nucleus but rather act on the cell membrane outside the cell.

The 2011 World Anti-Doping Agency code for illegal drug use in sport has declared that, because there is no evidence that PRP treatment is performance enhancing, it is no longer prohibited. It is therefore safe to use in professional athletes.

EVIDENCE FOR PRP EFFICACY

Tendinopathy

Use of PRP for treatment of tendinopathy has had mixed results in scientific studies. There has been good evidence suggesting a positive effect of PRP on gene expression and matrix synthesis in tendon and tendon cells *in vitro* and in animal models. However, there is a lack of good quality human studies.[2-7]

One study of 12 athletes found an increase in the speed of recovery and tendon quality on MRI in six athletes who were augmented with a single deposit of PRP at surgery compared with six athletes who just had surgical repair and no PRP.[8] Another study evaluated prospectively a cohort of 20 patients who failed nonsurgical treatment of lateral or medial epicondylitis. This study concluded that there was a significant improvement in pain and function in the PRP treatment group at eight weeks and six months' follow up compared with controls.[9]

A prospective study followed a cohort

of 20 athletes with chronic patellar tendinosis who each received three PRP injections at 15-day intervals, with all demonstrating some improvement at six months' follow up, good rates of satisfaction and 70% showing complete or functional recovery.[10] However, a recent study assessing chronic Achilles tendinopathy treatment using an eccentric exercise program showed neither benefit nor adverse effect with the addition of PRP treatment.[11]

Osteoarthritis

Conversely, studies assessing osteoarthritis and the use of PRP as a treatment option are very encouraging. Current theory suggests that synovitis in osteoarthritis is a major factor in causing an imbalance in the proinflammatory cytokines that cause proteolytic enzyme activation and consequent cartilage destruction. PRP appears to help correct this imbalance and potentially even lead to articular cartilage regeneration.[12]

Clinical, animal and *in vitro* studies have shown the benefits of PRP in osteoarthritis. Three separate studies showed the regenerative effects of PRP on chondral lesions in animals[13-15] and an *in vitro* study showed positive effects of PRP on the metabolism of human articular chondrocytes.[16]

According to another *in vitro* study, PRP can increase synovial cell hyaluronic acid production.[17] Human clinical studies have shown that PRP had greater benefit in symptoms and function compared with hyaluronic acid injections.[18,19]

Recent prospective studies assessed the effect of three PRP injections several weeks apart, with 12 months' follow up. All showed beneficial effects on pain and functional capacity, with two of these studies assessing more than 100 patients with osteoarthritis of the knee.[20-22] All had positive results compared with baseline at six months' follow up; the effects were not as good at 12 months but still better than baseline levels.

CONCLUSION

The authors have treated hundreds of patients with degenerative joint and tendon lesions using PRP. In their experience, autologous PRP treatment is effective in treating chronic tendinopathy and osteoarthritis. However, despite the authors' positive clinical experiences, further high-quality human studies are needed to prove its effectiveness. MT

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COMPETING INTERESTS: None.