Vascular News

The SIMCRI Consensus conference on PRP 2024

PRP in the treatment of diabetic foot ulcers

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SIMCRI (Italian Society of Multi-Specialist Regenerative Medicine and Surgery) has promoted the Consensus Conference "*Use of PRP (Platelet Rich Plasma) in the context of regenerative medicine*" according to the Italian guidelines on Consensus Conference planning. The complete text of the Consensus Conference will be published in early 2025 and will also be available on the website www.simcri.org. On the basis of an in-depth review of the literature, combined with the opinions of experts, the Committee wrote a final document focused on physiopathology, clinical use, indications, contraindications, specific clinical protocols and adverse reactions of PRP in the treatment of various diseases, whose noxa includes a deficit in repairing tissue damage. The use of autologous PRP in the treatment of diabetic foot ulcers has entered into common use and constitutes an important and essential aid.

PRP is a platelet concentrate rich in growth factors obtained from peripheral blood collected with a simple blood sample. A test tube containing an anticoagulant (usually citrate) is used, which is centrifuged with times and speeds that also depend on the geometry of the centrifuge used. This results in the separation of the erythrocytes that are placed at the bottom of the test tube, the platelet-poor plasma that occupies the most superficial part of the same while a thin whitish layer constitutes the buffy coat in which cells and platelets are concentrated. Using specific centrifugation speeds and collection methods, a product can be obtained that contains a greater or lesser number of leukocytes in addition to the platelets. The product obtained can be used as such or after platelet activation, which can be obtained in various ways. The blood used can be autologous or more rarely homologous, but in this Consensus Conference the works that involved the use of autologous blood were examined. The use of autologous blood performed extemporaneously eliminates the risk of immunological reactions and reduces the manipulation of the product.

The use of autologous PRP in the treatment of diabetic foot ulcers has entered into common use and constitutes an important and essential aid. SIMCRI (Italian Society of Multi-Specialist Regenerative Medicine and Surgery) has promoted the Consensus Conference "*Use of PRP (Platelet Rich Plasma) in the context of regenerative medicine*". Reached on the basis of an in-depth review of the literature, combined with the opinions of experts, then discussed and voted on by another group of experts who acted as a jury. A particular focus was on mechanisms, indications, contraindications, specific clinical protocols and adverse reactions of PRP, in the adjuvant treatment of many pathologies, whose noxa includes a deficit in repairing tissue damage. In this context, applications in the fields of orthopedics, andrology, urology, gynecology, reproduction, rheumatology and vulnology were examined. In the vulnology field, diabetic foot ulcers and venous ulcers were examined in particular.

The literature is rich in papers on the use of PRP in diabetic foot, most of which were carried out in developing countries, mainly India, Pakistan, Iran and Egypt, probably due to the considerable interest in these areas for low-cost, effective and self-produced dressings. In rich countries, the greater availability of advanced dressings and the strong commitment of the industry to promote them constitutes a less powerful stimulus to research in this field.

The literature includes several randomized controlled and prospective controlled studies. Despite the wealth of literature, there is a lack of double-blind randomized controlled trials. Comparing the inclusion and exclusion criteria of the different studies, it is noted that ulcers not responding to therapy were generally included, with a range between the various studies that went from 4 weeks to 6 months. Criteria such as diameter or area or anatomical location were often indicated in the studies. In most of the studies, ulcers with tendon, bone or ligament involvement or ulcers with gangrene were excluded. Patients who were undergoing anticoagulant therapy were generally excluded or the therapy was suspended, also thrombocytopenia is generally an exclusion criterion from the studies. Sometimes no inclusion criteria were indicated in the study.

In the literature, the methods used are very heterogeneous in terms of the volume of blood collected, the centrifugation method, which is often not even indicated, and the method of platelet activation. Another major limitation found in the literature is the lack of information on the final concentration of platelets and the volumes used in injectable and/or topical form. As regards the application method, the literature has studied both a perilesional injectable use and the possibility of using the platelet concentrate in gel form applied directly to the wound as a dressing. In other cases, a combination of the two methods has been used, but only one study has compared the two methods. The administrations are generally repeated, but even here there is some variability: administrations every one or two weeks are prevalent for the injectable administration, while for the topical application weekly or biweekly administrations prevail. In controlled studies, the control treatment is often saline-soaked gauze, a dressing modality also known as wet-to-dry, which is considered obsolete.

Despite these limitations, the rich literature has allowed numerous reviews[1-6] and meta-analyses[2-4,7] from which the usefulness of treatment with autologous PRP emerges. The superiority of PRP compared to controls has emerged both in terms of proportion of completely healed ulcers and healing time or speed of reduction of the wound area1-7.

All the literature agrees with the safety of PRP treatment as the proportion of adverse events has always been equal to or lower than controls, while for topical treatment, virtually no adverse effects have ever been found. The relationship with infections is also very interesting: they do not differ from controls or are even lower than them2,3. A working hypothesis is that PRP treatment may even be protective against infections, but so far there are no works specifically designed to verify this hypothesis. The protective action on infections could be due on the one hand to the fact that topical applications guarantee a physiological and self microenvironment, on the other to the presence of phagocytes in the products, both when used topically and by injection. The content of leukocytes is strictly dependent on the method of preparation of PRP, but unfortunately the literature is poor in information about the content of leukocytes in platelet concentrates.

Regarding the risk of amputation, however, treatment with topical or injectable PRP does not seem to improve it compared to control treatments (but in two meta-analysis is better2,3). This data can be explained by the fact that treatment with PRP is strictly localized and in direct relation with the wound, and a possible effect favoring neoangiogenesis that protects from amputation cold be obtained only with a regional treatment protocol.

The use of PRP in the treatment of diabetic foot ulcers is therefore a safe and effective procedure, although unfortunately the level of evidence is not particularly high due to the poor quality of the available studies. The risk of infections does not appear to be increased, but in some studies it even seems to be reduced.

It is desirable that future works are more complete in the information about the methods of preparation of the platelet concentrate, and should declare the actual platelet content in the final product and the concentration of leukocytes in it. The hypothesis that the efficacy of the treatment may be related to the total platelet load applied is growing, but the current lack of data does not allow us to use the existing literature for this line of research.

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