

The Presence of Concentrated White Blood Cells within Platelet-Rich Plasma may be Counterproductive

Arthrex Research and Development

Objective

White blood cells (WBCs) are present within the natural healing process; their main function is the removal of bacteria from the body¹. However, increasing their concentration in platelet-rich plasma (PRP) may not prove to be beneficial, and can possibly be seen as deleterious.

Most PRP systems contain an increased concentration of WBCs and platelets. However, Autologous Conditioned Plasma (ACP) was designed to concentrate platelets while excluding the majority of WBCs¹. Companies that concentrate WBCs in their PRP argue that WBCs could 1) potentiate an antibacterial response, or 2) theoretically have the ability to debride chronic tissue and jump-start healing. By reviewing the published literature, this paper will describe how WBCs can actually be detrimental toward the healing progression.

WBCs and Neutrophils

Neutrophils make up the majority of WBCs in the bloodstream. Neutrophils provide an antibiotic effect through the release of toxic, nonspecific, reactive oxygen species and proteolytic enzymes as they become activated at the site of injury outside the blood system^{2,3,4}. Enzymes released from neutrophils include those from the matrix metalloproteinase (MMP) family such as MMPs-3, 8, 9, and 13, as well as those from the serine protease family such as cathepsin G, proteinase 3, and urokinase-type plasminogen activator⁴. Overabundant neutrophil infiltration has been described as being responsible for the chronic inflammation found in a nonhealing wound. The restoration of the wound will not occur until the infiltration of neutrophils is reduced². Phagocytosis of debris present within the wound bed is often desired and accomplished by macrophages. However, macrophages must also clear particulate debris that was left behind by neutrophils after they are activated and release proteolytic enzymes⁶.

Due to these issues, one could question the use of PRP that contains excess neutrophils. They trigger increased tissue matrix degradation and lack the ability to ignite the healing cascade. Macrophages may be desired for phagocytosis, but it is important to note that platelets release chemokines that activate and attract macrophages to the site of injury⁴. It is also becoming well-established that platelets have an antibiotic effect as well, due to the antimicrobial proteins they contain⁵.

WBCs in Wound Healing

There is a plethora of literature looking at the inflammatory response for wound healing, and some of these studies conclude that neutrophils are not critical in the healing process. In fact, they could possibly be detrimental to the healing process.

Epidermal healing proceeds faster in neutropenic mice compared to control; also, wound closure is accelerated by 50% for neutropenic, diabetic mice compared to diabetic control mice⁷. Wounds in the mouth tend to heal fast without scarring due to a reduced influx of neutrophils and macrophages, leading to lower levels of inflammatory cytokines at that particular wound site^{3,13}. PU.1 null mice, which are genetically incapable of producing neutrophils and macrophages, nonetheless repair skin wounds in a similar timeline to regular, wild-type mice. However, these PU.1 null mice repair their wounds in a scar-free manner, similar to embryonic healing, unlike the scar tissue that is formed within the regular, wild-type mice⁶. A classic article from 1972 shows that wound debridement and formation of granulation tissue are not dependent on the presence of neutrophils⁸. From these studies, it can be concluded that inflammation in wound healing could lead to slower repair and excessive fibrosis.

WBCs in Bone Healing

There is additional literature supporting the notion that WBCs might suppress bone formation and bone healing. Mice with fractured femurs that are induced with temporary neutropenia postsurgical stabilization have a higher bending moment in the fracture callus compared to mice with fractured, stabilized femurs that do not have induced neutropenia⁹. Also, immunosuppressed rats heterotopically implanted with demineralized bone matrix (DBM) displayed increased DBM resorption and enhanced new bone formation¹⁰.

Inflammation and Muscle Damage

Lastly, there is literature that describes how the inflammatory response can lead to muscle damage. Neutrophils can possibly cause damage to healing muscle and/or delay its regenerative capabilities¹¹. Also, neutrophils in injured skeletal muscle can lead to secondary destruction of the muscle through a cytotoxic effect¹².

Conclusion

Even though WBCs are present within the natural healing progression, their existence within PRP does not appear to serve a useful purpose, potentially causing detrimental effects. Having a PRP such as ACP that does not deliver additional WBCs to the site of injury could help modulate a more effective healing environment.

References

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The Double Syringe (ACP) System is used to facilitate the safe and rapid preparation of autologous platelet-rich-plasma (PRP) from a small sample of blood at the patient's point of care. The PRP can be mixed with autograft and allograft bone prior to application to an orthopaedic surgical site as deemed necessary by the clinical use requirements.