The role of biological augmentation in meniscal repair

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A review of evidence from 2014-15

Basic Science

Cellular effect on meniscal healing
Mauck and Burdick performed a review of the basic science of meniscal healing, and factors that affect it. They point out that over the age of 40, patients have far fewer meniscal fibrochondrocytes at the tear interface and are therefore less able to up-regulate production of matrix proteins and enzymes in a healing response. They discuss studies that suggest this cellular factor is more important than vascularity. In-vitro studies comparing healing responses in completely vascularized foetal menisci are comparable to poorly vascularized juvenile menisci, and far superior to similarly vascularized but poorly populated adult menisci[3].

The theory of potential healing in the inner aspect of the meniscus is continued by Muhammad et al, who isolated meniscus progenitor cells (MPC’s) from the avascular portion or elderly patients with osteoarthritis. They discovered that the MPC’s are actually more active in patients with more advanced degeneration, and suggest that supplementing the existing growth factors is not what is required, but instead a further understanding of the pathways governing their proliferation and differentiation [8].

Matsukara performed an interesting study looking at the colony forming MSC concentration in synovial fluid and found it to be 250 times higher than normal in patients with a recent meniscal tear and increased in the period following injury. They concluded that the synovial fluid is the medium in which MSC are delivered to a meniscal tear in order to allow healing to occur [9].

Growth factors and meniscal healing
de Girlamo studied the systemic and local growth factors released during an ACL reconstruction and compared them to a meniscal repair, in order to establish which may be responsible for the improved meniscal healing rates when performed in conjunction with a meniscal repair over isolate repair. There was no difference in systemic concentration in any of the studied growth factors. There was no difference in the intraarticular concentration of TGF-b or bFGF, but PDGF concentrations were far higher following ACL reconstruction. They concluded that intraarticular injections of PDGF may cause an increased healing response in isolated meniscal repairs [6].

Iban et al studied the local release of growth factors in a rabbit model following injury to either the vascular or avascular zone of the meniscus. They discovered that both cause a large and similar release of VEGF-a, IGF-1, TGF-b, PDGF-b and IL-b which has returned to normal by 4 months. This suggests that it is not the vascularity that defines potential for healing [7].
Forriol performed one of the few studies looking at the effects of BMP-7 on meniscal tears in a sheep model. They found that it was associated with a far higher production of collagen as well as inhibition of MMP’s, with an increased production of fibrous scar tissue at 3 months [10].

**Basic science of stem cell therapy**

Hogan provides a useful review of tissue engineering in Sports Medicine. He outlines the principles of tissue engineering: the production of stem cell progenitor and precursor cells; conduction matrices or scaffolds to promote cell attachment and cell growth; induction using signaling proteins, cytokines and growth factors to stimulate cellular differentiation and biomechanical force stimulation to acclimate the engineered tissue. Outlined are several studies which support the use of intraarticular injections of mesenchymal stem cells in the healing of meniscal tears (and chondral damage) in an animal model (Hatsushika et al) and human model (Kwak et al and Vangsness et al) and briefly mentions delivery options [4].

**Clinical evidence**

Moran et al performed a level IV systematic review of level I-IV studies performed between 2009 and 2014 revealing 3 clinical trials, 18 preclinical studies and 68 tissue engineering in-vitro studies. 2 of the clinical trials were case series demonstrated higher than expected healing rates of meniscal repairs when augmented with autologous fibrin clot. The third was a double-blind, randomized control study investigating the safety of intra-articular injection of human mensenchymal stem cells, their ability to cause meniscal regeneration after partial meniscectomy, and the outcome on osteoarthritic changes in the knee. At two years 24% of patients had increased meniscal size by greater than 15% in the study group, compared with 0% in the control group. Those with osteoarthritic changes had clinically significant decrease in their pain with the MSC injection[2].

Pujol et al demonstrated slightly improved clinical outcomes in a case-control study comparing the outcomes following open repair of horizontal meniscal tears in patients younger than 40 years with respect to pain and sports function in the KOOS score. MRI at 12 months showed improved appearance of the meniscal tears, but this did not correlate with clinical findings[1].

Griffin looked at the use of PRP augmentation at the time of meniscal repairs in 35 patients and found no statistical difference in clinical outcome or reoperation rate [5]. They did appreciate that the study was underpowered and unlikely to show any differences with the small numbers involved.

**Conclusion**

In conclusion most studies performed have been in vitro and support the science for biological augmentation. The current situation seems to be that we don’t have a reliable delivery technique with adequate clinical evidence to support its use. There is expectation that there will be a pharmacological or surgical delivery
system of biological augmentation available in the future that will enhance the normal biological processes and encourage healing in meniscal tears that are currently failing to heal.
References: