Fundamental research of Platelet Rich Plasma (PRP) in standardized tendon lesions in the horse and humans

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Tendinopathy is common in both human and equine orthopaedic practice; also in the horse, tendon lesions can limit sports participation and even prevent return to prior sporting level, being one of the major reasons for retirement from athletic activity. Therefore, equine tendons have been a heavily researched structure and this long-standing effort together with a better availability of material and easier experimental work has offered the equine researchers some advantage in fundamental and applied tendon research in comparison with human medicine. Moreover, the larger digital flexor tendons in horses are comparable to the Achilles tendon in man, with respect to ultrastructure, biomechanical function (serving as an elastic energy saving spring) and pathophysiology of the tendon tissue. The pathogenesis of tendinopathy is not very well defined; sometimes there is a single traumatic event but there is growing evidence that in the majority of cases repetitive overload is the primary aetiological factor, leading to multiple micro-trauma and/or molecular inflammation and finally to degeneration of the tendon tissue. At the other end of the spectrum, stress-deprivation might play an important role too. Whatever the pathway that leads to disintegration of the collagenous matrix, with its relatively low cellularity and sparse vascularization, tendons are notorious for their slow and functionally inferior healing capacity, leading to a high re-injury rate.
The field of Regenerative Medicine aims at achieving regeneration of cells and matrices. Isolated growth factors have been used for this purpose, but there is growing insight that it is the concerted action of many members of the panel of naturally occurring growth factors and anti-inflammatory mediators that is most effective. In this line, increasing attention is given to autologous sources of growth factors, such as Platelet Rich Plasma (PRP). The application of PRP has been reported to be clinically effective by stimulating the repair process of tendinopathy, but there is little conclusive evidence for its fundamental working mechanisms. Therefore, a placebo controlled experimental trial was performed to test the hypothesis that a single intra-tendinous PRP treatment would enhance the quality of tendon repair.
In 6 horses, standardized, well-defined, tendon lesions were created surgically in the Superficial Digital Flexor Tendons (SDFT) of both front limbs, one of which was treated with PRP (GPS II by Biomet, enrichment of platelets with factor 3.8, of leucocytes with factor 6.0)) and the other with saline at 1 week post-surgery. Subsequently, repair processes were monitored regularly by means of a novel method for computerized ultrasonographic tissue characterization (UTC) and by Doppler flowmetry. At end-stage after 24 weeks the tendons were harvested for biochemical, biomechanical and histological evaluations.
Most significant observations in this in vivo study were:
on UTC monitoring, PRP appeared to affect all phases of repair e.g. **less inflammation (first 2 weeks post-treatment), better early fibrillogenesis (starting from 1 till 7 weeks), advanced organization and remodeling (starting from 11 weeks)**
on Doppler flowmetry, PRP **increased neovascularization during all phases**
at end-stage, collagen, glycosaminoglycan and DNA (cellularity) contents were higher in PRP treated tendons
at end-stage, the material properties of repair tissue in the PRP group showed a higher strength at failure and an increase in elastic modulus
Histologically, PRP treated tendons featured increased metabolic activity of fibroblasts, **advanced organization of the collagenous matrix into uni-axially arranged fiber bundles** (fasciculi), and increased vascularization with neovessels properly arranged in interfascicular, endotenon septa

It is concluded that a **single intra-tendinous PRP treatment, administered early in the proliferative phase of tendon healing, indeed has a significant positive effect on biochemical, biomechanical and histological properties of the repair tissue** in surgically induced tendon lesions in horses. Importantly, the repair tissue was **much stronger**, although still clearly subnormal, being able to withstand a significantly higher load and featuring a significantly **higher elastic modulus**. Lesions in this study were induced by a burr, creating trauma without removing damaged tendon tissue. After demarcation of these remnants during the early inflammatory stage, a central "compartment" developed that facilitated the intra-tendinous application of 3 ml PRP. Other advantages of this model are the fact that these lesions showed striking similarities with clinical cases and can be standardized. However, the pathogenesis of these lesions is clearly different from the degenerative pathway usually leading to tendinosis. Whether PRP will also be beneficial for these cases remains to be elucidated.

Comments:

This is extremely impressive and well-performed scientific research demonstrating the benefits of PRP for tendon healing. In summary the authors have shown the following effects of PRP with an array of tests:

on quantitative ultrasonography:

1. less inflammation
2. early fibrillogenesis
3. earlier bundle formation and alignment
4. improved remodelling

on Doppler:

1. Increased vascularization

on Histology:

1. improved vascularization with vessels more regularly arranged and clearer lumens
2. increased cellularity
3. increased matrix formation
4. earlier restoration collagen organisaton into aligned bundles
5. increased cell metabolism

on mechanical testing:

1. 35% improved tendon strength
2. 66% better elasticity

References

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