REVIEW ARTICLE

Current concept for the use of PRP in arthroscopic surgery

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Summary PRP is commonly used in sports medicine and because it is supposed to increase healing capacities of damaged tissues, it is expected to be increase efficiency or god clinical outcomes when added to arthroscopic surgical procedure. The current review of literature explores the evidence-based medicine supporting the use of PRP in three arthroscopic related disorders. Regarding cartilage lesions of the knee, many studies are exploring several aspect of cartilage lesion treatment. It appears that PRP, in some protocols with specific concentration, should be more efficient than current therapies in the treatment of early stages of knee OA, but only in the field of rheumatology or sport medicine, not when used during surgery. PRP have been used in ACL reconstruction, no benefit has been reported in any study regarding clinical or radiological outcomes. In shoulder cuff disorder, to date, no clinical benefit nor increased healing rate have been clearly reported. Thus, in 2013, it is clear that there is no evidence base medicine data supporting the use of PRP in arthroscopic surgery.
Level of evidence: 2.
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Introduction

PRP can currently be used in addition to orthopaedic surgery. Focusing on arthroscopic surgery, we analyzed the literature in order to understand what is the best practice we can conclude from previous clinical studies. We thus focus on knee and shoulder disorders. After a short report of PRP principle of action, we focused on its efficiency in those joints disorders.

Rationale

The first element to understand is what PRP is. Plasma is the serum including thrombocytes (or platelets), coagulation
factors and proteins. Platelets are cells containing many elements, have no nucleus but contain almost one thousand proteins, acting as signals, located inside or outside of the membrane. They also include small granules (alpha, delta and lambda) and especially 50 to 80 alpha granules per platelet [1]. There are several types of alpha granules which composition depends of the chronology of release during the healing process. In those granules are located almost thirty types of proteins called growth factors (GF) there are are mostly involved in hemostasis and healing process [2].

Growth factors are released from platelets through a physiological activation by human thrombin after the injury and then are regularly renewed through a cascade.

Some growth factors are also released by other tissues like fat tissue or liver or can be found in the blood independently of platelet release. Most of GF have a very short half-life.

The mechanism is complex at the time of induction of tissue repair, but also during each step of tissue repair and remodeling. Thus, their action is mostly local, limited in time and location. And they have different or even opposite effects depending on other local conditions like concentration time of release, tissue in concern or other present proteins in media. Especially, the action of the same GF is different in cartilage, bone or tendon... from catabolism to healing. ...Hopefully, it is supposed that nature will find the good GF in the good condition to repair organs, and that is the rationale for PRP use.

PRP is plasma with an amount of platelets largely above serum base line (from 3 to 8). Basically, the aim is to increase the healing properties of the organ by increasing the amount of platelets thus local growth factors. PRP is obtained using spinning kits. But volume, presence of blood cells, viscosity (liquid, matrix) is very different depending of the kits on the market. Huge differences have been found between different systems of preparing in studies: some systems are reliable in quality and volume, some are not. Doctors must be aware of what they inject.

A major issue is to understand the way to use PRP. It seems very important that the local increased concentration of GF keeps intact the physiological balance of GF in order to respect interaction between GF and possibly reproduce and increase the real healing process. Once again it is supposed that the body will take whatever it needs to heal correctly.

There is a lot of experimental data suggesting that PRP should be used in clinical practice, even if the action mechanisms are not clearly explained [3,4].

We know PRP is efficient on cells (especially isolated) in vitro and in animal experimental studies. But because injected PRP is a cocktail of growth factors, it is hazardous to extrapolate those fundamental studies to clinical benefit.

The aim of the current review of literature is to better understand what is the evidence based medicine for the use of PRP in shoulder and knee disorders, independently from experimental research, in order to propose clinical recommendations.

**Cartilage lesions of the knee**

There is no evidence-based medicine regarding the use of PRP in the knee arthroscopy, but many studies are reporting data that start to be useful.

One of the first studies of Sampson [5] in 2010, was very simple: on 14 patients complaining about knee OA, the authors performed 3 injection of PRP every 4 weeks, inspired from acid hyaluronic injections. Authors noted global clinical benefit and pain decrease at 1 year FU.

The same year, Kone [6] reports an interesting prospective study focusing on rationale of PRP use. She considers that, as far as PRP increases repair and decrease catabolism of cartilage, and because PRP enhances chondrocytes anabolism and decrease synovial inflammation, there should be a clinical benefit. This study involves 80 patients, 115 knees, and three injections of 5 cc PRP every 3 weeks. Even if it is the same team, the protocol has change from previously, and the clinical outcomes are still evaluated at 1 year FU. There is a statistically significant increase of IKDC score, and a decrease of pain, but the effect is fading over one year. Some important predicting factors are identified: results are worth in elderly patients and women. Benefit is less important for advanced stages of OA or high body mass index patients. An other study from Wang-Saequisa [7] involving 261 patients with a very close protocol (three injections every 2 weeks) and clinical results at 6 months, reports statistically significant benefit without any complication. Gobbi [8] reports clinical benefit of PRP (two injections at 1 month) in 50 patients, with significant benefit at 1 and 2 years FU. It is necessary to keep in mind that the same data are found when focusing on hyaluronic acid. Thus it was naturally that comparative studies were performed.

Elisabetha Kone [9] performed a prospective comparative level 2 study including 150 patients divided in three groups: three injections of PRP in group 1, three injections of low molecular weight hyaluronic acid in group 2, and three injections of high molecular weight hyaluronic acid in group 3. Clinical assessment was performed at 2 and 6 months. PRP demonstrates superiority to other treatment in all scores used in the current study, and a significant improvement of pain. The same limitation factor was found, elderly patients did not answer to treatment.

It was also noted that if no radiographic sign of OA is seen. The clinical outcomes are better with PRP at 6 months. The more the OA is advanced, the worst the clinical benefit is shown. At the beginning radiographic stage of OA, PRP are still efficient but with lower difference compare to other treatment. For advance radiographic stage of OA, no treatment is efficient.

A double blind prospective randomized level 1 study involved 109 patients treated by PRP vs. hyaluronic acid [10]. Three injections where performed in each group. No statistically significant difference was found in any element of clinical outcomes at 6 months except for some patients who had higher local pain after PRP injection. In the current study it is interesting to point out some elements: the platelet concentration is very high, five times the natural concentration, and a high concentration of leucocytes is injected, that are subject to discussion in literature and charged to induce pain. At least, patients are older than in other study, and it has been demonstrated how it can badly affect clinical outcomes. In the current study, PRP is stored in cold before injection, element that can modulate efficiency of the platelets.

Another double blind prospective randomized level 1 study [11] involved 176 patients with a mean age of 60 years,
mostly women. Thirty-eight percent of patient treated by PRP had an increase of 50% of their WOMAC functional score compared to 24% of patient treated by hyaluronic acid with a increase of 50% of their functional score. The difference was statistically significant. No side-effect was notified in any group.

Another equivalent study demonstrated that the effect observed with PRP vs. hyaluronic acid, is still persistent at 2 years FU [12]. This tendency is always present, whatever the stage of OA is, even if efficiency is clearly better for early stages of knee OA.

**ACL reconstruction**

In a prospective randomized level one study, Nin [13] assessed the benefit of PRP during allograft ACL reconstruction in two populations of 50 patients. Clinical and MRI assessment was performed, and no statistically significant difference was seen.

In a prospective level 3 study, 25 patients had an ACL reconstruction without PRP, and 25 with PRP. Technical procedure was not always the same, and reconstruction was performed whether with bone tendon bone or hamstring ligaments graft. The only difference was noted in MRI signal of the reconstruction that seems more homogeneous in PRP group [14].

In two level one studies, it was significantly demonstrated that the use of PRP decreases pain of donor site after bone tendon bone harvesting [15,16]. PRP does not act on graft fixation at the bone tendon junction or does not influence the size modifications of tunnels [17,18].

**Shoulder cuff repair**

Chahal [19] recently performed a meta-analyze of five studies, two randomized, three not randomized, exploring the effect of PRP on cuff repair.

The first one is a prospective randomized level one study, comparing clinical outcomes when using or not PRP as a matrix. Small to moderate lesions were repaired with double row procedure, and Constant score and MRI were performed 20 months after surgery [20].

No difference was seen in any group regarding clinical result and imaging. Authors notified one failure of repair in PRP group vs. 4 in control group, but no statistically significant difference was seen, probably also related to low number of patients.

Randelli [21] did compare two groups with or without PRP injection during repair. Clinical outcomes and MRI were performed at 24 months. At 3 months all scores are better in PRP group, but with time, no difference continue. Just like in the previous study, MRI demonstrated higher failure in control group, without clinical difference.

The study of Barber [22], a level 3 study, including two groups of 20 patients, found a benefit of PRP in clinical outcome. MRI found also a higher re-tear rate in control group with a statistically significant difference.

Jo [23] study didn’t find any statistically significant difference between two groups of patient operated of a cuff repair with or without PRP injection. One more time it appears a lower re-tear occurrence in PRP group, without statistically significant difference.

Bergeson [24] analyzed the effect of PRP on challenging cuff repair, including patient exposed to rotator cuff repair failure (aged, fatty infiltration). One more time, independently of clinical outcomes, it appears that PRP statistically increases the healing rate. Authors report two cases over 16 of local infection, which is subject to caution.

In these five studies, follow up is between 19 to 31 months, 260 patients are included with a mean age of 59 years old. No statistically significant difference is seen regarding complications or clinical outcomes. There is less re-tear in the PRP group, it is significant for medium to small tears, it is just a tendency for massive tears.

One level one study including large tears reports no retear in PRP group, with statistically significant difference, but without correlation with clinical scores [25].

Last study is from Rodeo and is a prospective randomized level 2 study, using a Doppler US to assess vascularization and healing. If scores and vascularization are the same, there is a higher re-tear rate in PRP group [26].

**Conclusion**

If use of PRP is technically easy, we have to keep in mind that it is a changing cocktail of growth factors, acting just after injection, and poorly mimicking healing process.

It is reasonable to say that in knee disorders, PRP seems to be efficient to treat early stages of knee OA, this effect should be prolonged up to one year, and is superior to hyaluronic acid injection. But it is clear that exact modalities of injection are still unclear, and probably exploring this therapy is more devoted to rheumatology practice. Regarding shoulder and cuff repair, if it seems that the healing rate is increased, we have enough evidence-based medicine to say that there is no clinical benefit to use PRP in 2013. At least, it is clear that there is no evidence based medicine data supporting the use of PRP in arthroscopic surgery.

**Disclosure of interest**

The authors declare that they have no conflicts of interest concerning this article.

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