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Platelets to the Rescue? A Literature Review of the Safety and Efficacy of Platelet-Rich Plasma for Symptomatic Osteoarthritis of the Knee

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Background
Osteoarthritis of the knee is one of the most common joint disorders in the United States with rising prevalence due to obesity and an aging population. Regarding non-surgical approaches to management, there has been growing interest in the use of intra-articular injections with Platelet Rich Plasma (PRP).

Statement of the Problem
The use of Intra-articular PRP injections for symptomatic osteoarthritis of the knee is in its infancy there have been many problems with evaluating platelet-rich plasma in the literature including: poor and inconsistent study designs, differences in platelet separation techniques, use of variety of measurement scales and indexes, lacking objective quantity and quality of PRP that was utilized. In reflection, current clinical guideline recommendations put forth by the American Academy of Orthopedic Surgeons (2013) does not recommend nor disapprove the use of IAI of PRP for the treatment of symptomatic OA of the knee.

Literature Review
A comprehensive review of eighteen clinical control trials studies was performed. The primary scope of this review focuses on outcomes related to safety (adverse events) and efficacy based on Western Ontario and McMaster University Osteoarthritis Index (WOMAC).

Research Question

Primary Research questions
In patients with symptomatic osteoarthritis of the knee,
- is platelet rich plasma safe?
- does platelet rich plasma improve pain, stiffness, and physical function?
- does one injection versus more than one injection improve outcomes?
- are there trends in the type of PRP that is most effective?

PRP by Study: Preparation, Activation, and Anticoagulation

Adverse Effects by Study

<table>
<thead>
<tr>
<th>Study</th>
<th>Injections</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>1</td>
<td>Mild pain</td>
</tr>
<tr>
<td>B</td>
<td>2</td>
<td>Severe pain</td>
</tr>
</tbody>
</table>

Injections by Study: Number and Cycles

<table>
<thead>
<tr>
<th>Study</th>
<th>Cycle 1</th>
<th>Cycle 2</th>
<th>Cycle 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>1000 rpm</td>
<td>1500 rpm</td>
<td>2000 rpm</td>
</tr>
<tr>
<td>B</td>
<td>1500 rpm</td>
<td>2000 rpm</td>
<td>2500 rpm</td>
</tr>
</tbody>
</table>

Symptom Relief

<table>
<thead>
<tr>
<th>Time</th>
<th>Global WOMAC (Percent Change from Baseline)</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 wk</td>
<td>+20</td>
</tr>
<tr>
<td>24 wk</td>
<td>+15</td>
</tr>
</tbody>
</table>

Discussion

Safety
- No severe long-term complications observed in any study
- Common transient injection reactions: localized pressure, pain, swelling, tenderness
- CaCl2 may contribute to adverse effects
- Higher concentrations of platelets and/or leukocytes may attribute to adverse effects

Efficacy
- There is evidence to suggest PRP improves pain stiffness and physical function for short-term (<6 months) management
- Multiple studies suggested that higher concentrations of PRP did not correlate with clinical outcomes.
- Multiple doses and/or cyclical injections as well as PRP preparations with concentrated growth factors may be advantageous for more substantial and longer term benefits.

Trends in Efficacy
- The influence of patient age on PRP effectiveness is controversial with conflicting studies
- More favorable outcomes have been observed in those with mild-moderate osteoarthritis.
- Multiple doses and/or cyclical injections may not provide additional benefit for those with moderate to severe OA.
- Cole, Kazar, Hussey, Pilz, & Fortier (2017) suggested that PRP may be more effective in those who are of healthy weight (BMI 18.5-24).
- Beselga García-Escudero & Miguel Hernández Trillos (2015) suggested that cyclical doses of PRP in addition to therapeutic exercise may provide sustained improvement of pain and physical function for up to 2 years.

Applicability to Clinical Practice

Utility & Application
- Outpatient setting/ <1hr
- Safety comparable to other intra-articular injections
- In those that fail traditional therapeutic management, the addition of PRP to other non-invasive modalities may be a great option for those wanting to delay or avoid joint replacement surgery
- Patients that are treated with antiplatelet medications should not receive PRP injections because these medications may inhibit or interfere with the platelet function and decrease efficacy

Cost
- The cost of PRP can range from $400-1500 with discounted rates for multiple or bilateral injections.
- There is currently no insurance coverage for PRP injections except for special circumstances involving worker’s compensation or motor vehicle insurance

The Future of PRP
- In the mist of overwhelming bias and inconsistencies in study designs and wide variability in PRP preparation, current literature may not provide strong evidence to influence changes to future national guideline recommendations
- As the application of PRP is still in its infancy, clinicians implementing PRP injections for OA of the knee should be expected to make changes in the method of preparation and administration in years to come as more clinical trials aim to improve safety and efficacy of PRP and define optimal preparation methods and clinical practice guidelines.

References

- Please see project for complete list of references...

Acknowledgements

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