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Review

Topical use of platelet-rich plasma can improve the clinical outcomes after total knee arthroplasty: A systematic review and meta-analysis of 1316 patients

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HIGHLIGHTS

- We conducted a meta-analysis to compare the effectiveness and safety of PRP after TKA.
- Only high quality studies were selected.
- PRP can increase the ROM and decrease WOMAC score and pain intensity after TKA.

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ABSTRACT

Objective: Platelet-rich plasma (PRP) is extracted by centrifuging whole blood and characterized with a high concentration of platelets. The purpose of this systematic review and meta-analysis of randomized controlled trials (RCTs) and non-RCTs is to evaluate the efficacy and safety of platelet-rich plasma (PRP) versus placebo after total knee arthroplasty (TKA).

Methods: The Electronic databases of PubMed, Web of Science, Embase and Cochrane Database of Systematic Reviews were searched from inception to November 2016 and any studies involving PRP versus placebo for patients prepared for TKA were selected by two reviewers. The primary endpoint is the range of motion (ROM), which represents the function after TKA. The Western Ontario McMaster Universities Osteoarthritis Index Bellamy (WOMAC), pain at 24 h, 48 h and 7 day are also assessed the effect of PRP on the function and pain after TKA. The complications of infection is also compiled to assess the safety of PRP. Stata 12.0 was used to synthesis the final results.

Results: Eleven clinical trials with 1316 patients are included in the meta-analysis. The pooled results indicate that administration PRP significantly increase ROM on the third day (MD = 4.72, 95% CI 2.74, 6.69; P = 0.000) and 3 month postoperatively (MD = 7.55, 95% CI 5.91, 9.19; P = 0.000). There is no statistical difference between the two groups in terms of WOMAC questionnaire score in 3 months (MD = −4.88, 95% CI -12.12, 2.41; P = 0.190). There were no statistical significance between the two groups in pain intensity at 24 h, 48 h and 7 day. There is no statistically significant difference between the PRP versus placebo in terms of the occurrence of infection (RR = 0.64, 95%CI: 0.19–2.14, P = 0.464).

Conclusion: Current meta-analysis indicates that PRP is associated with increasing the ROM after TKA in short term and long term. What's more, PRP can also decrease the WOMAC score and pain intensity without increasing the occurrence of infection.

1. Introduction

Total knee arthroplasty (TKA) can effectively reduce pain and improve function and quality of life for patients with osteoarthritis or rheumatoid arthritis [1]. However, concern remains with regard to perioperative blood loss, postoperative range of motion (ROM)

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and the hospital costs [2–4]. It is reported that perioperative blood loss in unilateral TKA is 800–1500 mL and subsequent need for transfusion is 11% [5,6]. However, blood transfusion has the potential risk of incompatibility reactions, immune disorders and increases the total costs in hospital. Many strategies, such as tourniquet, tranexamic acid, autologous re-transfusion and fibrin tissue adhesive have been used to reduce the postoperative blood loss and subsequent homologous blood transfusion [7–11]. Recently, platelet-rich plasma (PRP), is extracted by centrifuging whole blood and characterized with a high concentration of platelets [12]. PRP contains at least 6 abundant platelet growth factors which have been associated with the beneficial wound healing [13]. The factors such as α-granules can be released from PRP and have been identified to accelerate wound healing after surgery [14]. The advantage of PRP not only imparts an over immune reaction, but is also expected to be effective in hemostasis, pain relief and bone healing.

Recently, many researches have focused on the effectiveness and safety of PRP in management of blood loss during TKA, however, the results are inconsistent [15,16]. In addition, whether PRP is related to pain relief or improving ROM remains controversial. Thus, we conduct a systematic review and a meta-analysis to further analyze the effects of PRP on the ROM and pain control after TKA.

2. Material and methods

2.1. Search strategy

Following databases: PubMed, Web of Science, Embase and Cochrane Database of Systematic Reviews are searched from the inception in November 2016. The search algorithm can be seen in Supplement S1. Additionally, the references of all selected full-text articles and relevant reviews about PRP after TKA are also reviewed to identify any initially omitted studies. There is no restriction made on the language and year of the publication. Two reviewers independently assess the titles and abstracts of studies identified by the retrieval. Then, the full texts of the remaining studies are reviewed according to the eligibility criteria. Disagreement is settled by referring to a third reviewer.

2.2. Inclusion criteria and study selection

Participants: Patients are prepared for primary unilateral TKA, involving adult human subjects (age>18 years) with no systemic disease. Intervention: The intervention in the experimental group is an intraoperative administration of PRP at any dose. Comparisons: The intervention in the control group is a placebo. Outcomes: ROM on third day and 3 months postoperatively, WOMAC in 3 month, pain at 24 h, 48 h and 7 day and the occurrence of infection are collected as the outcomes. Study: RCTs and non-RCTs are regarded as eligible in our study. Two independent reviewers (F-XL and Y-L) scan the title and abstracts of the identified literature after remove the duplicates of the search results. Any disagreements about the inclusion and exclusion are solved by the discussion or consultation from an expert (F-XL).

2.3. Data extraction and quality assessment

A specific extraction for is made to collect the following data from the included trials: patient general characteristic, operative approach, DVT prophylaxis, length of follow up and volume to spray the PRP. Outcomes such as ROM, pain at 24 h, 48 h and 7 day, WOMAC score in 3 months and complications are extracted and recorded in a sheet. All the data are extracted by two independent reviewers (C-WQ and J-Z) and disagreement is solved by discussion. The methodological qualities of all included RCTs are independently assessed by two reviewers. The evaluated contents are included as follows: (1) randomization generation method; (2) allocation concealment; (3) blinding of participant, personnel and assessor; (4) selective reporting and (5) other bias. The assessment is based on the “low” “unclear” “high” according to the Cochrane Handbook for Systematic Reviews of Interventions, version 5.1.0; (http://www.cochrane-handbook.org/). The quality of non-RCTs is measured by MINORS quality assessment [17].

2.4. Outcome measures and statistical analysis

Continuous outcomes (ROM on 3 day and 3 months, WOMAC for 3 months and pain score in 24 h, 48 h and 7 day) are expressed as the mean differences (MD) and respective 95% CIs. Discontinuous outcome (the occurrence of infection) is expressed as relative risk (RR) with 95% confidence (CIs). The results are calculated by the software of Stata, version 12.0 (Stata Corp., College Station, TX). Statistical heterogeneity is tested by the chi-squared test and I^2 statistic. When there is no statistical evidence of heterogeneity (I^2<50% or P>0.1), fixed effects model is adopted; otherwise, a random effect model is chosen. Publication bias is tested using funnel plots and quantitatively assessed by Begg's test. We considered there is no publication bias if the funnel plot is symmetrical and the P value is > 0.05. Statistical significance is set at $P < 0.05$ to summarize findings across the trials.

3. Results

3.1. Search results and quality assessment

Initially, 238 potentially relevant studies are identified, of which 53 are excluded because of duplicates, and 170 does not meet the eligibility criteria at the title and abstract level. Since two trials show insufficient data to the inclusion criteria, so these two trials are finally excluded [18,19]. Finally, we include 11 records (7 RCTs and 4 non-RCTs) with 1316 patients in the quantitative analysis [15,16,20–27]. The general characteristic of included studies can be seen in Table 1. The mean age in PRP group ranges from 56.43 to 77 and control group ranging from 53.79 to 78. The dosage of PRP is from 5 ml to 12 ml. Only two studies do not state the type of prosthesis and the other studies all administration cemented prosthesis (see Fig. 1).

Review Manager 5.30 is used to evaluate the risk of bias in light of the Cochrane Handbook for Systematic Reviews of Interventions. The detailed information of the risk of bias of the included articles are demonstrated in Fig. 2 and Fig. 3. All of the included articles are described as randomized. However, only three of studies are comprehensively described as the generation of a randomized sequence, and the remaining studies do not demonstrate the randomization method [15,24,26,28]. Blinding of participants, personnel and outcome assessment are performed in 3 studies [16,22,24]. Four of the included articles display a low risk of bias for the incomplete outcomes, selective outcome reporting and display a low risk of bias for other bias [20,24,26,28]. The quality of non-RCTs are shown in Table 2.

3.2. Outcomes for meta-analysis

3.2.1. ROM at 3 day and 3 months postoperatively

The data of ROM at third day and ROM at 3 month postoperatively are reported in six studies [15,16,20,26,28,29] with 655 patients. The pooled results indicated that administration PRP significantly increase ROM at third day (MD = 4.72, 95% CI 2.74, 6.69; P = 0.000, Fig. 4) and 3 month postoperatively (MD = 7.55,