**Figure 1: Flow diagram summarizing the literature search, screening, and review**

Records Identified through database search (n=1217)

Number of records screened (n=1165)

Number of abstracts/full text articles assessed for eligibility (n=1165)

Number of records included in final synthesis (n=11)

**Inclusion**

**Eligibility**

**Screening**

**Identification**

Number of records excluded:

Basic science: 366

Animal studies: 381

Cadaveric: 37

Letter to editor/commentary: 45

Review articles: 113

Not diabetic foot ulcers: 88

Did not use autologous PRP: 36

Diagnostic studies: 87

Number of duplicate records removed (n=52)

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study** | **Mohamm-adi** ***et al.* 2017[6]** | **Ahmed** ***et al.* 2017[7]** | **Perez-Zabala** ***et al.* 2016[8]** | **Saad** ***et al.* 2011[9]** | **Kakagia** ***et al.* 2007[10]** | **Driver** ***et al.* 2006[11]** | **Li** ***et al.* 2015[12]** | **Saldalam-acchia *et al.* 2004[13]** | **Motolese** ***et al.* 2015[14]** | **Shan** ***et al.* 2013[15]** | **Kontopo-dis** ***et al.* 2016[16]** | **Weighted mean, SD[6]** | **P-value (PRP vs Control)** |
| Type of Study | PU | RP | CS | RP | RP | RDBP | RP | RP | PU | PU | RU | N/A | N/A |
| Level of evidence | III | II | IV | II | II | II | II | II | III | III | III | N/A | N/A |
| No. patients |
|  | PRP | 70 | 28 | 2 | 12 | 17 | 19 | 59 | 7 | 15 | 21 | 72 | 29.3 ± 25.4 | 0.104 |
|  | Control | N/A | 28 | N/A | 12 | N/A | 21 | 58 | 7 | N/A | N/A | N/A | 25.2 ± 20.0 |
| Age (mean, SD) |
|  | PRP | 53.8 ± 10.6 | 43.2 ± 18.2 | 65.5 ± 2.1 | NR | 57.0 ± 12.0 | 58.3 ± 9.7 | 61.4 ± 13.1 | 61.1 ± 9.4 | 52.3 ± 11.3 | 66.5 ± 10.8 | 65.0 | 58.4 ± 7.2 | 0.678 |
|  | Control | N/A | 49.8 ± 15.4 | N/A | NR | N/A | 55.9 ± 8.1 | 64.1 ± 9.4 | 58.1 ± 7.8 | N/A | N/A | N/A | 58.7 ± 5.9 |
| Female gender (%) |
|  | PRP | 12 (17.1) | 8 (28.6) | 0 (0.0) | NR | NR | 3 (15.8) | 22 (37.3) | 4 (57.1) | 11 (73.3) | 13 (61.9) | 14 (19.4) | 29.7% | 0.407 |
|  | Control | N/A | 10 (35.7) | N/A | NR | N/A | 5 (23.8) | 20 (34.5) | 4 (57.1) | N/A | N/A | N/A | 35.1% |
| Duration of diabetes, years (mean, SD) |
|  | PRP | 16.2 ± 7.9 | NR | 23.5 ± 13.4 | NR | NR | NR | 7.5 | 16.3 ± 7.9 | 38.2 | 6.8 ± 6.7 | NR | 14.1 ± 11.6 | 0.048 |
|  | Control | N/A | NR | N/A | NR | N/A | NR | 10 | 19.7 ± 9.9 | N/A | N/A | N/A | 11.0 ± 6.9 |
| Duration of ulcer, weeks (mean, SD) |
|  | PRP | 19.6 ± 4.7 | 12.5 ± 1.0 | 28.3 ± 9.5 | NR | 19.0 ± 8.0 | NR | 4.28 | NR | NR | 10.1 ± 12.0 | NR | 13.0 ± 8.4 | <0.001 |
|  | Control | N/A | 11.5 ± 2.8 | N/A | NR | N/A | NR | 3.3 | NR | N/A | N/A | N/A | 6.0 ± 5.8 |
| HbA1c (mean, SD) |
|  | PRP | 6.2 ± 0.7 | 7.0 ± 0.5 | 9.4 ± 3.3 | NR | 8.1 ± 2.8 | 7.8 ± 1.5 | 9.8 ± 3.1 | 9.5 ± 1.7 | NR | 9.1 ± 2.2 | NR | 7.9 ± 1.3 | <0.001 |
|  | Control | N/A | 6.9 ± 0.6 | N/A | NR | N/A | 8.1 ± 1.8 | 9.8 | 8.8 ± 1.7 | N/A | N/A | N/A | 8.7 ± 1.2 |
| Ulcer area, cm2 (mean, SD) |
|  | PRP | 6.11 ± 4.37 | 6.24 ± 0.9 | 10.25 | NR | 28.4 ± 13.6 | 3.4 ± 4.5 | 4.1 | 27.3 ± 15.6 | 13.92 | 14.0 ± 32.3 | 4.1 ± 3.9 | 7.7 ± 9.3 | <0.001 |
|  | Control | N/A | 5.72 ± 0.8 | N/A | NR | N/A | 3.6 ± 4.0 | 2.9 | 17.0 ± 8.9 | N/A | N/A | N/A | 4.6 ± 6.6 |

**Table 1** **Study Demographics**

N/A: Not applicable, PU: Prospective uncontrolled, RP: Randomized prospective, CS: Case series, RDBP: Randomized double-blind prospective, RU: Retrospective uncontrolled, NR: Not recorded, PRP: Platelet-rich plasma

**Table 2 PRP Preparation**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study** | **Mohammadi*****et al.* 2017** | **Ahmed*****et al.* 2017** | **Perez-Zabala*****et al.* 2016** | **Saad*****et al.* 2011** | **Kakagia*****et al.* 2007** | **Driver*****et al.* 2006** | **Li*****et al.* 2015** | **Saldalamac-chia *et al.* 2004** | **Motolese*****et al.* 2015** | **Shan*****et al.* 2013** | **Kontopodis*****et al.* 2016** |
| PRP spinning approach | Single | Double | Single | Double | NR | Single | Double | NR | Single | Single | Single |
| Duration of spin (min) | 10 | 5 and 5 | 7 | NR | NR | 1.5 | 4 and 6 | NR | 17 | 10 | NR |
| Company | Arya Mabna Tashkhis Co, Iran | NR | NR | NR | Biomet Biologics, Warsaw, IN, USA | Cytomedix, Rockville, MD, USA | NR | NR | Thermogenesis, Rancho Cordova, CA, USA | Haemonetics Corp, Braintree, MA, USA | RegenLab, Le Montsur-Lausanne, Switzerland |
| PRP activator | CaCl2 | Thrombin, CaCl2 | CaCl2 | Thrombin, CaCl2 | Thrombin | Thrombin | Thrombin, calcium gluconate | NR | Thrombin, CaCl2 | Thrombin, calcium gluconate | NR |
| PRP amount applied | 2 mL/cm2 | 7 mL | 3 mL | NR | NR | NR | NR | NR | 5 mL | NR | NR |
| Platelet concentration | NR | 1.0-1.2x106/μL | 1.6-1.7 x baseline | NR | NR | NR | NR | NR | NR | NR | NR |
| WBC concentration | NR | NR | Undetectable | NR | NR | NR | NR | NR | NR | NR | NR |
| PRP application method | PRP gel applied on ulcers after irrigation and debridement every week covered with non-absorbing wet dressing | PRP gel applied on ulcers after irrigation with 0.9% saline twice weekly covered with non-absorbing dressing | PRP gel applied on ulcers after irrigation twice weekly covered with foam dressings | PRP gel applied on ulcers within half an hour after preparation followed by Vaseline gauze and dressing changed every 3-4 days | PRP gel applied on ulcers covered with vapor-permeable film (Tegaderm, 3M) | PRP gel applied on ulcer with contact layer dressing covered with non-absorbent foam dressing changed every 3-4 days | PRP gel applied on ulcer after irrigation and debridement covered with Suile dressing changed every 3 days. PRP gel reapplied up to 5 times in 12 week period if wound area reduction rate <80% | Weekly topical application of PRP gel with covered with standard dressing changed weekly | 5 mL of PRP gel applied on ulcers once a week for total of 10 weeks covered with non-adherent dressing and bandage | PRP gel applied on ulces twice per week covered with occlusive dressing changed every 72 hours | PRP gel applied on ulcer twice weekly after irrigation and debridement covered with standard dressings |

NR: Not recorded, PRP: Platelet-rich plasma

**Table 3 PRP Group Individual Study Outcome Measures**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study** | **Moham-madi** ***et al.* 2017** | **Ahmed** ***et al.* 2017** | **Perez-Zabala** ***et al.* 2016** | **Saad** ***et al.* 2011** | **Kakagia** ***et al.* 2007** | **Driver** ***et al.* 2006** | **Li** ***et al.* 2015** | **Saldalama-cchia *et al.* 2004** | **Motolese** ***et al.* 2015** | **Shan** ***et al.* 2013** | **Kontopodis** ***et al.* 2016** |
| Ulcer area, cm2 (mean, SD) | Baseline | 6.11 ± 4.37 | 6.24 ± 0.9 | 10.3 | NR | 28.4 ± 13.6 | 3.4 ± 4.5 | 4.1 | 27.3 ± 15.6 | 13.9 | 14.0 ± 32.3 | 4.1 ± 3.9 |
| Final  | NR | 1.44 | NR | NR | NR | NR | NR | 8.0 ± 7.5 | NR | NR | NR |
| Ulcer healed (n,%) | 8 weeks | NR | 23 (82.1) | NR | NR | 2 (11.8) | NR | NR | NR | NR | NR | NR |
| 12 weeks | NR | 24 (85.7) | NR | NR | NR | 13 (68.4) | 50 (84.8) | NR | NR | 15 (71.4) | NR |
| Resvech 2.0 measurement | Baseline | NR | NR | 13.5 ± 0.7 | NR | NR | NR | NR | NR | NR | NR | NR |
| Final | NR | NR | 6.0 ± 1.4 | NR | NR | NR | NR | NR | NR | NR | NR |
| % wound length decrease | NR | NR | NR | NR | 14.3 ± 7.1 | NR | NR | NR | NR | NR | NR |
| % wound width decrease | NR | NR | NR | NR | 17.4 ± 8.0 | NR | NR | NR | NR | NR | NR |
| % wound depth decrease | NR | NR | NR | NR | 34.9 ± 9.9 | NR | NR | NR | NR | NR | NR |
| Time to >90% ulcer area healing, weeks (mean, SD) | 8.7 ± 3.9 | NR | 7.0 ± 2.8 | 11.5 | NR | 6.4 | 5.1 | NR | 12.7 | 7.17 ± 5.66 | 11.0 ± 4.0 |
| Healing rate per week, cm2 (mean) | 0.7 | NR | 1.46 | NR | NR | 0.53 | 0.80 | NR | 1.10 | 1.95 | 0.37 |
| Adverse effects  | 0 | 2 – wound infections | 0 | 0 | 0 | 1 – contact dermatitis | 5 – wound infections | 0 | 0 | 0 | 0 |

NR: Not recorded

**Table 4 Average Study Outcome Measures Included in Best Evidence Synthesis**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Time to >90% ulcer area healing, weeks (mean, SD)** | **Healing rate per week, cm2 (mean)** | **Adverse effects** |
| PRP | 7.8 ± 2.7 | 0.68 ± 0.56 | 8 (2.5%) |
| Control | 8.3 ± 3.7 | 0.39 ± 0.09 | 15 (10.5%) |
| P-value | 0.115 | < 0.001 | < 0.001 |

PRP: Platelet-rich plasma