

Cost and effectiveness of Platelet Rich Plasma in the healing of varicose ulcer: Meta-analysis

Custo e efetividade do Plasma Rico em Plaquetas na cicatrização de úlcera varicosa: Metanálise

Costo y efectividad del Plasma Rico en Plaquetas en la cicatrización de úlcera varicosa: Metaanálisis

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ABSTRACT

Objectives: to analyze the evidence on the cost and effectiveness of Platelet Rich Plasma in the treatment of venous ulcers compared to other topical therapies. **Methods:** systematic review, with search in the databases: COCHRANE, EMBASE, MEDLINE via PubMed, LILACS, CINAHL, SCOPUS, without temporal cut and in the English, Portuguese and Spanish languages. **Results:** fifteen articles were included, a cost-minimization analysis showed that the cost of Platelet Rich Plasma is € 163.00 ± 65.90, slightly higher than the cost of standard dressing. Regarding effectiveness, the results of the studies associated with the meta-analysis suggest a tendency that Platelet Rich Plasma is effective in the healing of venous ulcers. **Conclusions:** it is concluded that there are few studies about the cost of Platelet Rich Plasma and this product tends to be effective in the healing of venous ulcers. However, more controlled and randomized clinical studies are necessary in order to establish a stronger recommendation.

Descriptors: Platelet-Rich Plasma; Varicose Ulcer; Costs and Cost Analysis; Wound Healing; Meta-Analysis.

RESUMO

Objetivos: analisar as evidências acerca do custo e da efetividade do Plasma Rico em Plaquetas no tratamento de úlceras venosas comparado às outras terapias tópicas. **Métodos:** revisão sistemática, com busca nas bases de dados COCHRANE, EMBASE, MEDLINE via PubMed, LILACS, CINAHL, SCOPUS, sem recorte temporal e nos idiomas inglês, português e espanhol. **Resultados:** foram incluídos 15 artigos. Uma análise de custo-minimização demonstrou que o custo do Plasma Rico em Plaquetas é de €163,00 ± 65,90, pouco superior ao custo do curativo padrão. Quanto à efetividade, os resultados dos estudos associados à metanálise sugerem uma tendência de que o Plasma Rico em Plaquetas é efetivo na cicatrização das úlceras venosas. **Conclusões:** conclui-se que há poucos estudos acerca do custo do Plasma Rico em Plaquetas e esse produto tende a ser efetivo na cicatrização de úlceras venosas. Entretanto, são necessários mais estudos clínicos controlados e randomizados para que se possa estabelecer uma recomendação mais forte.

Descritores: Plasma Rico em Plaquetas; Úlcera Varicosa; Custos e Análise de Custo; Cicatrização; Metaanálise.

RESUMEN

Objetivos: analizar las evidencias acerca del costo y de la efectividad del Plasma Rico en Plaquetas en el tratamiento de úlceras venosas comparado a las otras terapias tópicas. **Métodos:** revisión sistemática con la búsqueda en bases de datos: Cochrane Library, EMBASE, MEDLINE via PubMed, LILACS, CINAHL, SCOPUS, hay un tiempo y en inglés, portugués y español. **Resultados:** se incluyeron 15 artículos, un análisis de costo-minimización demostró que el costo del Plasma Rico en Plaquetas es de € 163,00 ± 65,90, poco superior al costo del vendaje estándar. En cuanto a la efectividad, los resultados de los estudios asociados al metaanálisis sugieren una tendencia de que el Plasma Rico en Plaquetas es efectivo en la cicatrización de las úlceras venosas. **Conclusiones:** se concluye que hay pocos estudios acerca del costo del Plasma Rico en Plaquetas y que ese tiende a ser efectivo en la cicatrización de úlceras venosas. Todavía, son necesarios más estudios clínicos controlados y aleatorizados para que se pueda establecer una recomendación más fuerte.

Descriptorios: Plasma Rico en Plaquetas; Úlcera Varicosa; Costos y Análisis de Costo; Cicatrización de Heridas; Metaanálisis.

INTRODUCTION

Venous ulcers represent 70–80% of chronic leg ulcers, and their etiology is chronic venous insufficiency and venous hypertension⁽¹⁾. Venous ulcers are considered a challenge for patients, professionals and healthcare systems, since they are recurrent, chronic and require high cost treatment. In addition, venous ulcers can have a considerable negative impact on the patient's quality of life⁽²⁾.

Compression therapy has been considered the gold standard for the treatment of venous ulcers, as it promotes the healing process and prevents recurrence⁽³⁾. However, it is necessary to use dressings that can contribute to the healing process of venous ulcers by keeping a moist environment, reducing pain, exudate and offering more comfort to the patient⁽⁴⁾.

A technology that has been considered promising in the healing process is Platelet-Rich Plasma (PRP). PRP results from the centrifugation of whole blood and it is rich in growth factors and structural proteins, which stimulate collagen and extracellular matrix production requiring minimal amounts of plasma, stimulating tissue repair, neovascularization and tissue regeneration⁽⁵⁾.

PRP acts in the different phases of healing, shortening the inflammatory phase through hemostasis, provisional fibrin matrix and reduction of biofilm, which favors the formation of granulation tissue (chemotaxis, angiogenesis and cell proliferation) and stimulates epithelial growth, proliferation, migration of keratinocytes and extracellular matrix remodeling⁽⁶⁾. PRP has been used in wounds of different etiologies and in graft integration, and its preparation technique is considered efficient, safe and low cost⁽⁷⁾.

PRP has been associated with improved quality of life of patients with diabetic ulcers and lower cost of care over a 5-year period⁽⁸⁾. Also, it has been considered a cost-effective technology that allows faster healing and that should be taken into account, especially in long-term ulcers⁽⁹⁾.

Given the need for cost-effective technologies for venous ulcer treatment, the following research questions arose: Is Platelet-Rich Plasma effective in healing venous ulcers compared to other topical therapies? Is Platelet Rich-Plasma cost-effective in treating venous ulcers compared to other topical therapies?

OBJECTIVES

To analyze the evidence on the cost-effectiveness of PRP in the treatment of venous ulcers compared to other topical therapies.

METHODS

Ethical aspects

As this is a systematic review, there is no need to obtain approval from Research Ethics Committee.

Design, period and setting

This is a systematic review, with searches conducted from July 4 to July 6, 2018. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist was used to elaborate the flowchart and for the Systematic Review and Meta-Analysis⁽¹⁰⁾.

The search was conducted in the databases COCHRANE, Evidence-Based Medicine (EMBASE), Medical Literature Analysis and Retrieval System Online (MEDLINE) via PubMed, Latin American & Caribbean Health Sciences Literature (LILACS), Cumulative Index to Nursing & Allied Health Literature (CINAHL), SCOPUS and in the references of the articles found, through the association of descriptors and free words (Boolean search) corresponding to population and intervention.

Population or sample; inclusion and exclusion criteria

The following inclusion criteria were considered: randomized and nonrandomized controlled trials; prospective studies such as cohorts and case series; quasi-experimental studies; economic studies - cost-effectiveness, cost-utility, cost-minimization, direct and/or indirect cost; studies analyzing the cost and/or effectiveness of topical application of autologous PRP in venous ulcers, regardless of age, in outpatient units or hospitals. Exclusion criteria were: studies with intradermal, subcutaneous, perilesional or wound bed PRP application; research protocols without results; PRP associated with grafts; homologous PRP; studies that included ulcers of different etiologies without subgroup analysis.

Studies using subcutaneous or intradermal PRP were excluded after reading the title, abstract or full text. The exposure of interest of this review was topical PRP. Therefore, studies with other routes of administration were excluded, as the presentation and formulation of topical PRP is different from intradermal or subcutaneous PRP, as different substances may be added to change the consistency of the PRP into a gel. In addition, the response mechanism associated with topical administration may differ from the other routes.

Study protocol

The following descriptors (Mesh terms) were used: Varicose ulcer (*Úlcera varicose*); Leg ulcer (*Úlcera da perna*); Platelet-Rich Plasma (*Plasma Rico em Plaquetas*); and related keywords *Venous ulcer*, *Venous leg ulcer*, in English, Spanish and Portuguese. Terms related to the outcomes were not used, aiming to broaden the search results, thus opting for a sensitive search. Search strategies were adapted for each database. There were no limitations to date of publication.

Database searches and selected studies were assessed for relevance to the research theme, study design, results, indications and main conclusions.

The systematic review design allows gathering evidence that can contribute for decision-making regarding the evaluation of health technologies. The steps followed were: definition of the clinical problem and searching criteria, selection of databases and descriptors, development of relevance tests, application of the Relevance Test I to the abstracts of the articles identified, application of the Relevance Test II to the full articles and elaboration of the table summarizing the articles⁽¹¹⁾. Article selection and data extraction were performed by two independent researchers, (A.P.L.R.) and (M.R.C.). After reading the title and abstract, the disagreements regarding the inclusion of articles were discussed with a third reviewer (B.G.R.B.G.). All potential studies were read in full, and then exclusion criteria were applied. Specific forms and databases were used for each step of the Systematic Review and included names of the authors, title, country

of origin, year and journal of publication, study design, population, intervention, evaluated outcomes and results.

The effectiveness of PRP in healing was evaluated considering the following outcome variables: reduction of wound area in cm², percentage of healing, number of ulcers healed (complete healing), and time to healing. The cost of PRP was evaluated considering the costs extracted from cost analyzes and economic evaluations.

Analysis of results and statistics

The level of evidence and grade for recommendation of the studies were analyzed according to the Oxford Centre for Evidence-Based Medicine, which considers the study design as the criterion for the level of evidence, which ranges from 1 to 5, and for the grades for recommendation, which range from A to D. This evaluation is made by two evaluators, with no disagreement⁽¹²⁻¹³⁾. The level of agreement between the evaluators was assessed by the Kappa coefficient, 0.873 (p-value < 0.001), with a 95% confidence interval of Kappa (1.0-0.718)

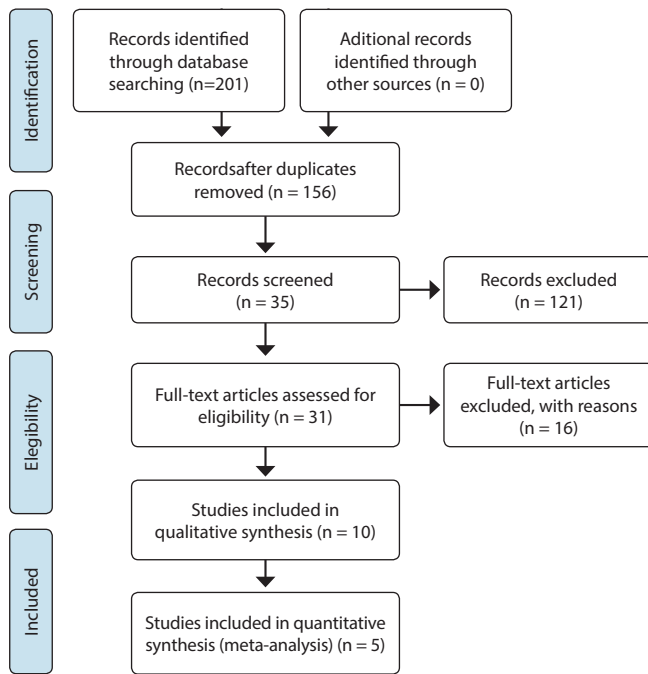


Figure 1 – Flowchart of the studies identified, 2018

A meta-analysis of controlled clinical trials was conducted. Heterogeneity was statistically evaluated using the Chi-square test, with fixed effect analysis when heterogeneity is less than 50%.

A total of 201 records were found. The flowchart of the studies is presented in Figure 1.

RESULTS

A total of 15 articles that evaluated the effectiveness of autologous Platelet-Rich Plasma were found. One of these articles presented results of a cost-minimization analysis⁽¹⁴⁾.

The cost-minimization analysis conducted by Burgos-Alonso *et al.*⁽¹⁴⁾ showed that the cost of PRP is €163.0 ± 65.9 [81.2 - 244.8] Euros when it is applied once a week in outpatient care, while the standard treatment performed 2 to 3 times a week, with a mean of 2.5 times/week, cost €147.3 ± 29.7 [110.4-184.2] (p-value=0.640), in a nine-week follow-up. The mean time of treatment of the Intervention Group was 46.6 minutes, while the Control Group presented mean time of treatment of 21.7 minutes (p < 0.001).

Table 1 presents the studies on the effectiveness of PRP in the treatment of venous ulcers.

According to Table 1, five studies (33%) are randomized controlled trials, eight (53%) are prospective studies without control group, one (7%) is a case-control and one (7%) is an observational study. Regarding location, the studies were conducted in several countries, mainly in Europe (33%) and Asia (26%), followed by the United States (20%), Egypt (7%), Australia (7%) and Chile (7%). It is observed that the term for Platelet-Rich Plasma also varied in the studies; however, the description of the method of obtaining the product showed that all had similar preparation, differing only in final form (liquid or gel). The follow-up time varied from 2.1 weeks⁽²⁴⁾ to 12 months⁽²⁰⁾.

In the studies evaluated, the mean initial wound size ranged from 5.06 ± 8.7⁽²⁰⁾ to 26.3 cm²⁽²⁵⁾. The frequency of PRP application varied from one to five times a week, with predominance of once a week, in 47% of the studies^(7,14-17,20). Only one study did not inform the frequency of application⁽²⁷⁾.

Regarding the level of evidence and grade of recommendation, 54% of the studies had level of evidence 4 and grade for recommendation C. Five studies (33%) were randomized controlled trials with evidence level 1b and grade for recommendation A. Another study had level and grade 2b/B, as it was a Cohort, and another one was a case control with level and grade 3b/B.

Table 1 –Characterization of studies on the effectiveness of Platelet-Rich Plasma in venous ulcers, 2018

Author/ Year/ Country	Study design	Interventions/ No. of participants	Level of evidence/ Grade for recommendation Oxford
Burgos-Alonso <i>et al.</i> ⁽¹⁴⁾ 2018 Spain	Pilot Randomized controlled trial with cost-minimization analysis follow-up time (FT) = 9 weeks	Platelet-Rich Plasma Gel (n = 7) versus Standard treatment (n = 5)	1b/A
Moneibet <i>al.</i> ⁽¹⁵⁾ 2018 Egypt	Case-control FT = 6 weeks	Platelet-Rich Plasma (n = 20) versus Conventional therapy with vaseline gauze and saline (n = 20)	3b/B
Cardeñosa <i>et al.</i> ⁽¹⁶⁾ 2017 Spain	Randomized controlled trial FT = 24 weeks	Platelet rich in growth factor (n = 55) versus Saline solution (n = 47)	1b/A

To be continued

Table 1 (concluded)

Author/ Year/ Country	Study design	Interventions/ No. of participants	Level of evidence/ Grade for recommendation Oxford
Somani&Rai ⁽¹⁷⁾ 2017 India	Randomized controlled trial FT = 4 weeks	Platelet-rich fibrin (n = 9) versus Saline solution (n = 6)	1b/A
Senet et al. ⁽¹⁸⁾ 2003 France	Randomized Double-blind Clinical Trial FT = 12 weeks	Frozen autologous platelets (n = 8) versus Hydrocolloid (n = 7)	1b/A
Stacey et al. ⁽¹⁹⁾ 2000 Australia	Randomized Double-blind Clinical Trial FT = 9 months	Platelet lysate (n = 42) Versus Placebo (n = 44)	
Pinto et al. ⁽²⁰⁾ 2018 Chile	Prospective Cohort FT = 1 year	Leucocyte- and platelet-rich fibrin (L-PRP) (n = 32)	2b/B
Waniczek et al. ⁽²¹⁾ 2015 Poland	Case series FT = 10 weeks	Platelet-Rich Plasma (n = 10)	4/C
Kim et al. ⁽²²⁾ 2013 Republic of Korea	Case series FT = Not informed	Autologous platelet gel or liquid (n = 3)	4/C
Park et al. ⁽²³⁾ 2013 South Korea	Pilot study FT = 6 weeks	Platelet-Rich Plasma Gel (n = 16)	4/C
Sarvajnamurphy et al. ⁽⁷⁾ 2013 India	Case series FT = 6 weeks	Platelet Gel (n = 17)	4/C
Leon et al. ⁽²⁴⁾ 2011 USA	Observational study with databases from 39 centers FT = 2.1 weeks	Platelet-Rich Plasma Gel (Autologel™) (n = 32)	4/C
Frykberget al. ⁽²⁵⁾ 2010 USA	Case series FT = 2.8 weeks	Platelet-Rich Plasma Gel (Autologel™) (n = 16)	4/C
O'Connell et al. ⁽²⁶⁾ 2008 USA	Pilot study FT = 16 weeks	Autologous platelet-rich fibrin membrane (PRFM)/ 1 to 3 applications/ (n = 17) Size. 11.2 (0.7-58)	4/C
Gürgen, M ⁽²⁷⁾ 2008 Norway	Prospective study FT = 10 months	Platelet-Rich Plasma (n = 7)	4/C

Table 2 – Main results regarding effectiveness of Platelet-Rich Plasma, 2018

Author/ Year	Area reduction in cm ² Mean (SD)		Percentage of area reduction (%) Mean (SD)		N° of ulcers completely healed/ total		Mean time to healing Mean (SD)	
	IG ¹	CG ²	IG	CG	IG	CG	IG	CG
Burgos-Alonso, 2018	3.9	3.2	82.8	40.8	4.2/7	1/5	NI ³	NI
Moneib, 2018	4.92 (11.94)	0.13 (0.27)	67.6 (36.6)	13.67 (28.06)	7/20	0/20	NI	NI
Cardeñosa, 2017	3.7	4.53	67.7 (41.54)	11.17 (24.4)	NI	NI	NI	NI
Somani & Rai, 2017	NI	NI	85.51	42.74	5/9	0/6	NI	NI
Senet, 2003	NI	NI	26.2	15.2	1/8	1/7	12 weeks ⁴	4 weeks
Stacey, 2000	NI	NI	NI	NI	33/42	34/44	75% in 3 months	75% in 3 months
Pinto, 2018	NI	NI	NI	NI	27/32	NA ⁵	9 a 15 weeks	NA
Waniczek, 2015	NI	NI	NI	NI	10/10	NA	10 weeks	NA
Kim, 2013	NI	NA	90 a 95	NA	0/3	NA	20 a 24 days	NA
Park, 2013	0.48 (0.95)	NA	NI	NA	0/16	NA	NA	NA
Sarvajnamurphy, 2013	NI	NA	94.7 (11.12)	NA	13/17	NA	5.1 (3.1) weeks	NA
Leon, 2011	NI	NA	40.2 (26.6)	NA	0/32	NA	2.1 weeks	NA
Frykberg, 2010	NI	NA	43.1 (32.4)	NA	0/16	NA	2.3 (1.4) weeks	NA

To be continued

Table 2 (concluded)

Author/ Year	Area reduction in cm ² Mean (SD)		Percentage of area reduction (%) Mean (SD)		N° of ulcers completely healed/ total		Mean time to healing Mean (SD)	
	IG ¹	CG ²	IG	CG	IG	CG	IG	CG
O'Connell, 2008	NI	NA	NI	NA	11/17	NA	7.1 weeks	NA
			02 with healing >75%					
Gürgen, 2008	NI	NA	93.2	NA	3/7	NA	35	NA
			59.7				233	
			72				238 days	

Note: IG – Intervention Group; CG – Control Group; NI – Not informed; NA – Does not apply.

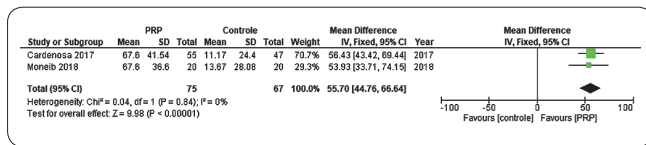


Figure 2 – Meta-analysis of the outcome complete healing of venous ulcers, 2018

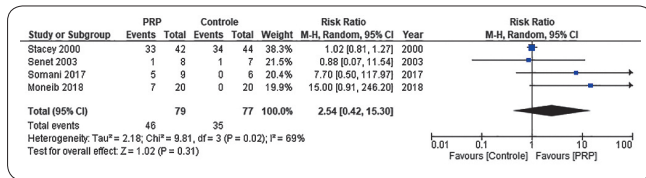


Figure 3 – Meta-analysis of the outcome reduction in wound area, 2018

Table 2 presents the outcomes regarding the effectiveness of the PRP in the studies included.

As there was only one study that presented the cost of PRP⁽¹⁴⁾, it was not possible to perform the meta-analysis of the outcome cost and/or cost-effectiveness. Figure 2 presents the meta-analysis of the outcome complete healing of venous ulcers.

Figure 2 shows that there was no significant difference regarding the effectiveness of PRP considering the outcome complete healing. Figure 3 presents the meta-analysis of the outcome reduction in wound area.

Figure 3 shows that Platelet-Rich Plasma was effective in reducing area, according to the meta-analysis of the two studies that evaluated this outcome.

DISCUSSION

The studies were analyzed according to the following categories:

Category 1: PRP Cost

In this review, it was found that in the cost-minimization analysis performed by Burgos-Alonso et al.⁽¹⁴⁾ the cost of PRP was higher than the cost of standard treatment (p-value 0.640). Even though PRP was applied once a week and standard treatment 2 to 3 times a week, the time spent with PRP was longer than with standard treatment (p < 0,001)⁽¹⁴⁾.

In the analysis⁽¹⁴⁾, to calculate the cost, the items evaluated were: time spent with treatment, cost of performing the procedure and labor cost referring to the nurse and assistant professionals, frequency of changes, dressings and costs of PRP preparation material. PRP

treatment occurred in five steps: Collection of autologous blood; Centrifugation; Separation of red blood cells and leukocytes PRP; Coagulation of PRP to form a biological cover applied to the wound bed; and secondary dressing made of foam, polyurethane or hydrofiber.

A cost-effectiveness analysis of Rich Platelet Plasma in skin ulcers, with meta-analysis of five articles addressing ulcers of various etiologies and using the Markov Model, demonstrated that the probability of healing was 56% using PRP and 31% with standard treatment, while associated direct costs were €5224 and €5133 respectively. The incremental cost to achieve additional healing is € 364 Euro, within a 48-week time of treatment⁽²⁸⁾.

In another comparative study, the cost of PRP was evaluated with 81 participants with ulcers of various etiologies, of which eight were venous ulcers in the hospital and outpatient setting. It was found that the use of PRP reduced the average length of stay (11 ± 2.5 days), and cost € 785.25, while in the control group, which used the standard treatment (povidone-iodine gel, Olasol™ spray, Actovegin™ gel and interactive dressing) the cost was € 1649.02, and the mean length of stay in the hospital was 23.1 ± 1.5 days. The direct costs assessed were related to PRP treatment for 90 days and considered days of hospitalization, blood collection and PRP preparation, dressings and outpatient care⁽²⁹⁾.

The only study⁽¹⁴⁾ found in the literature that used autologous topical PRP specifically for venous ulcers performed a cost-minimization analysis, which evaluated only the cost without considering the effectiveness of the technologies involved. The authors' suggested conducting studies with larger samples for cost-effectiveness evaluation: In another study⁽²⁸⁾, conducted a cost-effectiveness analysis; it evaluated skin ulcers of various etiologies and concluded that the use of PRP is cost-effective, since the extra cost with the use of PRP is much lower than the long-term use of standard treatment. The direct costs of PRP treatment presented in another study⁽²⁹⁾ show that it had a lower cost and was considered cost-effective; however, no actual cost-effectiveness assessment was performed and the sample was composed of ulcers of various etiologies, without specific cost analysis of the venous ulcer subgroup.

Thus, further studies applying more robust methodology and assessing the cost-effectiveness of PRP specifically in venous ulcers are required to accurately determine whether topical autologous PRP is cost-effective for treating these ulcers and then make a stronger recommendation.

Category 2: Effectiveness of the PRP

PRP has been considered a promising technology for ulcer healing because it stimulates fibroblasts, macrophages, mesenchymal

cells and growth factors that promote re-epithelization and neovascularization in chronic ulcers⁽³⁰⁾.

Considering the prospective (case series) and observational studies and the randomized controlled trials included in this meta-analysis, there is a tendency for PRP to be effective in complete healing and reduction of venous ulcers.

It was found that the relative risk (RR) of a venous ulcer to completely heal after PRP was 2.54, with a Confidence Interval (CI) of 0.42-15.30. However, the result was not statistically significant, as the CI includes the value 1. There was a discrepancy between recent^(15,17) and older studies⁽¹⁸⁻¹⁹⁾, with most promising results in studies conducted in 2017 and 2018^(15,17). However, it should be noted that the number of study participants was limited because, despite of the fact that venous ulcers presented a 7.7 times greater chance of completely healing in the study by Somani & Rai⁽¹⁷⁾ (RR: 7.70, 95%CI: 0.50-117.97) and 15 times greater chance in the study by Moneib et al.⁽¹⁵⁾ (RR: 15.0, 95%CI: 0.91-246.20), the confidence intervals in these studies are very broad and include 1, which indicates that caution is required when interpreting these findings. The evaluation of the outcome reduction in wound area showed that venous ulcers treated with PRP had a 55.7% greater reduction in area than control group ulcers (Mean: 55.70, 95%CI: 44.76-66.64), $p < 0.005$. Therefore, further studies with methodological rigor and higher number of participants should be conducted to validate this favorable tendency of PRP use.

A review that evaluated the effectiveness of various types of venous ulcer treatment demonstrated that the few randomized clinical trials that evaluated the effectiveness of PRP do not confirm the effectiveness of venous ulcer healing and, therefore, more studies should be performed⁽³¹⁾.

A recent review evaluating the effectiveness of Platelet-Rich Plasma in chronic ulcers showed that, of the 10 randomized controlled trials evaluated, four were with patients with chronic ulcers, three were with patients with venous ulcers and three with patients with diabetic ulcers. It concluded that it was unclear whether autologous PRP improved the healing of chronic ulcers overall compared to standard treatment but considered that PRP enhances the healing of diabetic ulcers. In the case of venous ulcers, the effectiveness of PRP was unclear, and more controlled clinical studies should be performed for a recommendation⁽³²⁻³³⁾.

The reviews cited evaluated the randomized controlled trials^(31,33) published prior to this review, and did not consider cost assessment. Thus, this review provides evidence of the cost-effectiveness of PRP in recent studies, and also presents the results of prospective studies that, even with level of evidence C, showed good results with the use of PRP.

Study Limitations

As limitations of this review, we highlight the small number of studies that assessed the cost of PRP specifically in venous ulcers, making it difficult to compare cost-effectiveness. Regarding the effectiveness of PRP, it is observed that the number of studies is also reduced, limiting the results for the elaboration of meta-analysis.

Contributions to the area of Nursing, Health or Public Health

The evidence found in this study contributes to the knowledge of health professionals, such as orthopedists, dentists and also nurses, regarding technology for the treatment of venous ulcers. It is considered that nurses have an important role in decision making regarding the technologies used for venous ulcer healing.

In addition, this study generated evidence that can assist the decision making of managers of public and private health. Thus, it enables a debate in Brazilian public health about an issue that is already an agenda of the National Health Surveillance Agency⁽³⁴⁾ and the Professional Councils⁽³⁵⁻³⁶⁾.

Further research on cost-effectiveness is encouraged, especially in the Brazilian healthcare context, as the Unified Health System is quite different compared to countries where evidence of the cost-effectiveness of PRP was found.

CONCLUSIONS

The PRP cost found in the cost-minimization analysis was €163.0 ± 65.9 [81.2 - 244.8] Euros, slightly more expensive than the standard treatment, €147.3 ± 29.7 [110.4 - 184.2] (p-value= 0.640). The mean duration of the PRP procedure was 46.6 minutes.

As for effectiveness, the meta-analysis of two studies suggests that Platelet-Rich Plasma was effective in reducing venous ulcer area. Regarding complete healing, the results of prospective studies included in the meta-analysis suggest a trend towards the effectiveness of Platelet-Rich Plasma.

Further studies to evaluate the cost-effectiveness of PRP should be conducted, especially in the Brazilian context, allowing a stronger recommendation regarding its use and supporting decision making of managers and other professionals, such as nurses, in clinical practice.

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