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Review

Quality evaluation of Systematic Reviews (PRISMA, AMSTAR-2) of platelet rich plasma as a method of tissue regeneration in odontology.

Evaluación de Calidad (PRISMA, AMSTAR-2) de las Revisiones Sistemáticas del plasma rico en plaquetas como método de regeneración tisular en odontología.

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Abstract: To evaluate methodologically (PRISMA) and report (AMSTAR-2) quality of systematic reviews regarding platelet rich plasma (PRP) as a method of tissue regeneration in dental procedures. Material and Methods: A search of systematic reviews (SR) of PRP was performed in the databases *PUBMED, EBSCO, The Cochrane Library, Web of Science, Lilacs, Epistemonikos,* and supplemented by manual review of the bibliography of the selected articles. Covering articles published from January 2008 to August 2018, in English or Spanish. The advanced search was performed using Boolean terms AND and OR. The quality of the SRs was evaluated with the PRISMA guidelines, and the methodological quality was evaluated with the checklist of the AMSTAR-2 tool. Result: Seventeen SRs were selected. From the selected articles, 11 were cataloged as of Very good quality, three as Good and three as Moderate. Regarding the methodological quality, two articles were classified as Critically Low, one as Low, 10 Moderate and four as High quality. Conclusion: Most SRs are of high quality regarding their report and methodology, and provide an accurate summary of the results of the primary studies available. However, there is a lower percentage of RS whose methodological and drafting deficiencies make their results and conclusions unreliable, and therefore, their clinical applicability is questionable, and offer a wrong clinical vision, which is not the best and safest therapeutic measure for patients and may compromise their well-being.

Keywords: Dentistry; platelet-rich plasma; systematic review; quality; research report; checklist.

Resumen: Evaluar la calidad metodológica (PRISMA) y del reporte (AMSTAR-2) de las revisiones sistemáticas en relación al plasma rico en plaquetas (PRP) como método de regeneración tisular en odontología. Material y Metodos: Se realizó una búsqueda de revisiones sistemáticas (RS) de PRP en las bases de datos *PUBMED, EBSCO, The Cochrane Library, Web of Science, Lilacs, Epistemonikos,* y complementada mediante revisión manual de bibliografía de los artículos seleccionados. Abarcando artículos publicados desde Enero de 2008 hasta Agosto de 2018, en idioma inglés o español. La búsqueda avanzada se realizó utilizando términos booleanos AND y OR. Las RS fueron evaluadas con pauta PRISMA la calidad del reporte, y con check-list de la herramienta AMSTAR-2 la calidad metodológica. Resultados: Fueron seleccionadas 17 RS. Los artículos seleccionados fueron catalogados con calidad del reporte Muy bueno 11 artículos, 3 como Buenos y 3 como Regulares. En relación a la calidad metodológica, 2 artículos fueron catalogados como Críticamente baja, 1 Baja, 10 Moderada y 4 alta calidad. Conclusión: La mayoría de las RS cuentan con calidad en su reporte y en su metodología, y proveen un resumen preciso de los resultados de los estudios primarios disponibles. Sin embargo, hay un porcentaje menor de RS cuyas deficiencias metodológicas y de redacción hacen no fidedignos sus resultados y conclusiones y, por tanto, su aplicabilidad clínica es cuestionable y puede formar un juicio clínico errado que no sea la mejor y más segura medida terapéutica para el paciente y comprometer su bienestar.

Palabras Clave: *Odontología; plasma rico en plaquetas; revisión sistemática; calidad; informe de investigación; lista de verificación.*

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INTRODUCTION.

Systematic reviews (SR) are qualitative or quantitative syntheses generated from the best existing evidence, and commonly obtained from randomized controlled clinical studies. In relation to health, SR are frequently consulted to support clinical decision making and, when they are well-designed,[1] are catalogued as the most valuable evidence in accordance with evidence-based medicine.

Given the great surge and development of new procedures, the available evidence is constantly evolving and some studies start to become outdated, whereas others gradually lose their value for decision making.

For this reason, it is necessary to assign an objective value to systematic reviews in order to facilitate clinical decision making, so as to base choices on the most recent information and that such information has been selected taking into account the highest quality studies. There are patterns that allow to assure the quality of evidence and the quality of the report, such as the PRISMA declaration and the AMSTAR-2 tool, respectively.

Platelet-rich plasma (PRP), defined as an autologous concentration of platelets in a small amount of plasma,[2] and considered a rich source of autologous growth factors (key elements in tissues regeneration promotion, manifested during the different stages of healing); PRP has been regularly used in medical and dental surgical procedures, particularly in oral and maxillofacial surgery[3] during sinus graft procedures, alveolar preservation techniques, and also as joint procedure to support the regeneration process in infraosseous periodontal defects and furcation defect.[4]

Since literature in PRP is substantial and results are diverse, it is quite difficult to order and read available data because of the great quantity of protocols related with preparation, terminology and material presentation techniques, and a myriad of potential applications.[5]

Aiming to provide relevant information to consolidate a clinical judgment based on the evidence to offer the best and safest therapeutic measures, the aim of this study is to evaluate the quality of systematic reviews as a method of tissue regeneration in dentistry by using the PRISMA and AMISTAR-2 guidelines.

MATERIALS AND METHODS.

Descriptive observational study based on a previously developed protocol.

Objective population was literature referring to PRP use as a tissue regeneration method in dentistry, for which a search in the databases *PubMed, EBSCO, The Cochrane Library, Web of Science, LILACS* and Epistemonikos was carried out including published studies from January 2008 to August 2018.

For the articles search, the MeSH terms "dentistry" and "platelet-rich plasma" were used; the free terms dentistry, platelet-rich plasma, guided tissue regeneration, bone regeneration, tooth socket, maxillary sinus, dental implant as described below:

1. *Medline* (via PubMed): "dentistry [MeSH Terms]" AND "platelet-rich plasma" AND ("bone regeneration" [All Fields] OR "tooth socket" [All Fields] OR "maxillary sinus regeneration" [All Fields] OR "dental implant" [All Fields] OR "soft tissue scarring" [All Fields])

2. *EBSCO*, The Cochrane Library, Web of Science, LILACS, Epistemonikos: "dentistry" AND "platelet-rich plasma".

In addition, the search was complemented by manual literature review. The decision of including an article was based on the compliance with inclusion and exclusion criteria after reading the title, abstract, or the whole article if available. Inclusion criteria were the following: mention PRP in the title or abstract; use in a dental procedure or treatment; integrative scientific articles (systematic review and meta-analysis).

Whereas exclusion criteria were: paper unavailable in English or Spanish; studies in animals or *in vitro*.

The bibliographic search was carried out by three reviewers (FB, VF, and CG) who, independently, selected the articles that met the selection criteria after reading the title, abstract and full text. In case of any disagreement that could not be solved through the full paper discussion among reviewers during selection, the opinion of an external reviewer (JD) was sought and the exclusion or inclusion of the study in question would be justified.

Once selected, articles were fully read and the report quality was evaluated by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) pattern (Meet/Does Not Meet each of the

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27 items and, according to the compliance percentage, the report quality was classified as: Very good/Good/Moderate/Poor/Insufficient, as indicated in Table 1. The methodological quality of systematic review through the A Measurement Tool to Assess Systematic Reviews-2 (AMSTAR-2) tool (Meet Yes/No, in the cases to which corresponds Yes partially/No meta-analysis, according to the available check-list on: *https://amstar.ca/Amstar_Checklist.php*), quality was catalogued as independently by the three reviewers (FB, VF, CG) as: High/Moderate/Low/Extremely low.

Furthermore, quality was registered in a worksheet designed for summarizing the main information of each study: Title, Main Author, Year and Journal, Type of Publication (systematic review/meta-analysis), Objective, PRP use, Method, Result/Conclusions, Bias, Conflicts of Interest, Report Quality, Methodological Quality and, Global Evaluation of Quality and Applicability (reliable results applicable to the clinic/questionable results, their clinical applicability is left to the reader/unreliable results, questionable clinical applicability.)

Evaluation data of report quality and methodological quality were analyzed through descriptive statistics with the SPSS25 software (IBM, Chicago, USA).

RESULTS.

The search revealed 325 results on PubMed, 155 on EBSCO, 8 on Cochrane, 75 on Web of Science, 46 on LILACS and 77 on Epistemonikos (Figure 1).

After erasing repeated articles, inclusion and exclusion criteria were applied to 596 studies obtaining 17 systematic reviews (8 also conducted a meta-analysis), whose main characteristics are registered in Table 2. Report quality was evaluated through the 27 items of the PRISMA guidelines and methodological quality, through the check-list of AMSTAR-2 tool.

Selected articles were catalogued in the report quality as: 11 articles as Very good 6-16, three as Good17, 18, 19, and three as Moderate20, 22. Regarding methodological quality, two articles were catalogued as Extremely low,[20,22] one as Low[21,10] as Moderate[8-11,13-19] and four as High quality;[6,7,12,14] two of them are Cochrane reviews[12,14] and were catalogued as having high methodological quality without applying a quality scale because of having been conducted under high quality standards described in the Cochrane's systematic reviews manual.

From sections of the PRISMA guidelines (Table 3), only one article did not include RS in the title, despite being a Cochrane review; all articles include a structured summary and a justification of the review, but only 13 present the objective using the P.I.C.O format (Presentation, Intervention, Comparison, Outcome).

Regarding Methods, all studies include eligibility criteria, complete search strategy and specify the study selection process; however, most did not indicate the existence of a review protocol. Most of studies described information sources, data collecting process; listed and defined variables for which data were collected, methods to evaluate risks, indicated summary measures and results syntheses. Main flaws were observed in the risk evaluation of bias or in the description of additional analysis methods.

In the Results section, flaws were observed in items of results presentation associated with risk of bias among additional studies and analysis.

In the Discussion, evidence was mostly appropriately summarized, included limitations and conclusions. Only eight articles (out of 17) described sources of funding.

From the sections of the AMSTAR-2 instrument (Table 4) —in its critical domains- only three articles explicitly state that the review methods were established prior to their implementation; eight studies carried out an in—depth bibliographic search and two did it only partially; most studies justify the excluded studies, three do so in part and three do not justify exclusion. The nine articles that included meta-analysis used appropriated methods. Only one article did not consider the risk of bias in the interpretation of the results. Regarding the assessment of the presence and probable impact of publication bias, 4 out of 9 studies that used meta-analysis did so appropriately and five did not.

In relation to the global evaluation of quality and applicability, four articles were classified as presenting reliable and applicable results to the clinic by having a high methodological quality and a good report quality; 10 articles were classified with questionable results and their clinical applicability will remain up to the reader's criteria by having a moderate methodological quality, but

Table 1. Characteristics of the selected studies.

Title	Author	Year - Publication	Type of study	Objective use of PRP	Method	Results - Conclusions	Biases	Conflict of interest	Report quality	Methodological quality
The effect of platelet-rich plasma on clinical outcomes of the surgical treatment of periodontal intrabony defects: A systematic review and meta-analysis.	Hou *et al.*[6]	2016 BMC Oral Health	Systematic review and meta-analysis.	To assess the efficacy of PRP in the periodontal surgical treatment of infrabone defects by comparing clinical outcomes among patients who received PRP along with periodontal treatment and those who did not. Wound Healing	Human studies, up to June 2015, randomized clinical trials.	The use of PRP in conjunction with traditional grafting procedures may have a beneficial treatment approach, particularly with hydroxyapatite. However, when combined with regeneration techniques, such as guided tissue regeneration, the beneficial effect of PRP in the treatment of intraosseous periodontal defects may be negligible. PRP has a significant positive effect in the treatment of infraosseous periodontal defects.	No manual searching of publications or use of unpublished studies. Most of the selected studies did not make a sample estimate prior to the study, which limits the assessment of the efficacy of autologous PRP. The studies used very small amples and the selected studies had different ways of comparing treatments, some using "split mouth", which decreases inter-subject variability to estimatetreatment efficacy as opposed to parallel group design.	No	Very Good	High
Effectiveness of platelet-rich plasma as an adjunctive material to bone graft: a systematic review and meta-analysis of randomized controlled clinical trials.	Pocaterra *et al.*[7]	2016 Int J Oral Maxillofac Sur	Systematic review and meta-analysis.	To assess the scientific evidence on the effectiveness of PRP as an adjuvation technique. Maxillary sinus elevation.	Human studies from 1999 to November 2014, randomized clinical trials.	PRP does not provide an additional benefit in bone formation, nor does it improve the survival rate of the implant.	Few studies were included, thus reducing the potential for statistically significant differences. In performing the risk of bias analysis, most studies had small sample sizes, flaws in randomization and allocation concealment. The studies had high heterogeneity in the outcome of bone formation, which could be due to the difference in PRP production, graft materials and choice criteria.	No	Very Good	High
Effects of platelet-rich plasma in association with bone grafts in maxillary sinus augmentation: a systematic review and meta-analysis.	Lemos *et al.*[8]	2016 Int J Oral Maxillofac Sur	Systematic review and meta-analysis.	To assess the effect on bone formation and implant survival by combining PRP with bone grafts in sinus elevation. Sinus Elevation, Implants.	Human studies, from January 2000 to January 2015, randomized clinical trials and prospective studies.	There was no statistically significant impact on the role of PRP associated with bone grafting in implant survival rate or stability. Neither was there a significant impact on bone formation in sinus elevation in response to the combination of PRP related to bone grafting, nor on decreased marginal alveolar bone loss or bone height.	One of the main difficulties in comparing the studies is that different amounts/concentrations of PRP and different centrifuge systems were employed. In addition, few studies were used, which may influence the outcome of the statistical analysis.	No	Very Good	Moderate
Platelet-rich plasma for periodontal regeneration in the treatment of intrabony defects: a meta-analysis on prospective clinical trials.	Roselló-Camps *et al.*[9]	2015 Oral Surg Oral Med Oral Pathol Oral Radiol.	Systematic review and meta-analysis.	To assess the influence of PRP on the regeneration of infraosseous periodontal defects by evaluating clinical and radiographic outcomes in prospective clinical trials in humans. Treatment of infraosseous defects.	Randomised controlled clinical trials.	Most studies showed changes in favor of PRP for clinical insertion level parameters, as well as changes in the position of the gingival margin and radiographic change of bone level.	High heterogeneity between studies and only low heterogeneity for radiographic changes and gingival margin. According to the studies, no clear answer/conclusion can be obtained from the results obtained in the bibliographic search.	No	Very Good	Moderate

Additive effect of autologous platelet concentrates in treatment of intrabony defects: a systematic review and meta-analysis.	Panda *et al.*[10]	2016 J Investig Clin Dent.	Systematic review and meta-analysis.	To systematically assess the additive effect of autologous platelet concentrates in the treatment of infraosseous defects when these are used in combination with other regenerative procedures and when used alone, clinically and radiographically. Wound Healing.	Human studies, up to June 30, 2012, randomized clinical trials.	Platelet concentrates (PRP) have a positive effect when used with other surgical regeneration procedures, except with guided tissue regeneration, as his can conceal the results due to their efficacy. PRP is effective when used with bone grafts on defects. PRP increases bone filling radiographically even if not clinically perceived, improving hard tissue regeneration. PRP is statistically significant in clinical insertion level gain, but not in probing depth.	Most studies did not mention how they determined sample size, which may lead to heterogeneity of studies, nor did they reveal reference comparison of defect characteristics (whether it was 1, 2 or 3 walls). The type of graft used in combination with the PRP could not be evaluated.	Not mentioned	Very Good	Moderate
Effects of platelet-rich plasma on sinus bone graft: meta-analysis.	Bae *et al.*[11]	2011 J Periodontol.	Meta-Analysis	To observe if there is any positive effect on the use of PRP in sinus bone grafting when used in combination with bone grafting materials in bone regeneration. Maxillary sinus elevation.	Human clinical trials in Pubmed from 2000 to January 2010, Cochrane from 2002 to 2010 and Embase from 2000 to January 2010.	There is sufficient evidence to support the use of PRP in bone formation, but there is no significant effect on bone grafts for implant survival and implant to bone contact. In bone grafts PRP reduces healing time and increases bone formation in early stages, but does not have a significant effect on implant survival in the long term.	Heterogeneity of the studies: different types of indexes analysed (implant survival, bone to implant contact and bone formation), different types of grafts used (autogenic and allogenic) and different preparation and concentration of platelet concentrates (in the absence of a protocol, this cannot be compared). Few studies, very short follow-up and limited results to assess the effects of PRP on sinus bone grafts.	No	Very Good	Moderate
Effectiveness of sinus lift procedures for dental implant rehabilitation: a Cochrane systematic review.	Esposito *et al.*[12]	2010 Eur J Oral Implantol.	Systematic Review and Meta- Analysis.	To prove null hypothesis showing that there is no difference in implant success results, function, complication rate and patient satisfaction as a result of bone augmentation in comparison with no augmentation. In addition, proving whether there is no difference between the various maxillary sinus augmentation techniques for treatment of dental implants. Maxillary sinus lift.	Randomized clinical trial in humans	PRP treatment with autogenous bone graft or bone substitutes may not improve sinus lift procedures results for implants rehabilitation.	Some conclusions were based on trials with few patients, occasionally, with a short clinical follow-up and often tried with a high risk of bias.	No	Very Good	High
Effects of Platelet Concentrates Used in Alveolar Ridge Preservation: A Systematic Review.	Niu *et al.*[13]	2018 Implant Dent.	Systematic Review.	To assess clinical efficiency of platelet concentrates used in PRP procedure (alveolar ridge preservation ARP) and compare the difference between various platelet concentrates types (PC) Ridge preservation.	In humans, randomized clinical trial	Leukocytes-rich fibrin and platelet-rich fibrin (PRF) may have possitive effects by reducing the loss of vertical and horizontal height of the alveolar ridge in ARP, however, PRP may not have relevant effects. PC can have a positive effect on pain	Heterogeneity of studies by different designs. Most of the sites in the control and test groups included in the study came from different parts of the mouth. Only one study used a split-mouth study whereas the others (4) used a parallel design. Some studies showed that the greatest	Not	Very Good	Moderate

						and post-operative discomfort after an ARP procedure. It cannot be inferred that PC can improve the percentage of new vital bone. Due to the limited number of clinical trials included in this review and heterogeneity of studies, the evidence was insufficient to come to a definitive conclusion on the effect of PC.	horizontal bone resorption was observed in the premaxila more than in other regions. Different regions may give different results.			
Interventions for re placing missing teeth: augmentation procedures of the maxillary sinus.	Esposito *et al.*[14]	2014 Cochrane Database Syst Rev.	Systematic Review.	To evaluate the effect of sinus lift on augmentation of bone volume in edentulous patients and to compare different techniques used for augmentation of bone volume in implant rehabilitation. Sinus lift.	Randomized clinical trials.	Only 2 of 18 PRP and sinus lift rela ted publications were found with 67 patients. No data statistically significant showing that the use of PRP may facilitate maxillary sinus lift procedure were found.	Found publications were clasified as unclear bias and high risk of bias (the latter had the highest number of patients (57)). Lack of standardized studies.	Not mentioned	Very Good	High
Platelet-rich plasma for the therapeutic management of temporomandibular joint disorders: a systematic review.	Bousnaki *et al.*[15]	2018 Int J Oral Maxillofac Surg	Systematic Review.	To determine To determine the efficacy of intra-articular injections of PRP in patients with TMD compared to other treatments, such as injections of hyaluronic acid or saline. ATM treatment.	Randomized Clinical trials.	Provides light evidence of the possible benefits of intra-articular injections of PRP in patients with TMJ-OA. PRP has been shown to contain a variety of growth factors; however, not all of them may contribute to the therapeutic management of TMJ-OA. Well-designed randomized clinical trials with standardized protocols for PRP preparation are required to obtain strong evidence of the role of PRP in the treatment of TMJ-OA.	Difference in diagnosis of the patients included in each study. Different protocols used in the prepa ration of the PRP and its administration No characterization of the injected PRP content. Follow-up in varied time in 3 points.	Not	Very Good	Moderated
The adjunctive use of platelet-rich plasma in the therapy of periodontal intraosseous defects: a systematic review.	Kotsovilis *et al.*[16]	2010 J Periodontal Res	Systematic Review.	To tackle the question: What is the efficacy, in terms of clinical, radiotherapeutic bioactive agents/procedures compared to the efficacy of the same agents/procedures without the use of complementary PRP in the treatment of intrabony periodontal defects in patients with chronic periodontitis and without systemic diseases that could influence the outcome of periodontal therapy?	Randomized controlled clinical trials.	Clinical use of PRP is an entirely safe procedure without adverse events or postoperative complications. Several results (positive and negative) have been reported on the efficacy of PRP combined with various bioactive therapeutic agents/procedures, suggesting the limited and heterogeneous data available and possibly showing that specific selection of agents/procedures combined with PRP might be important.	Publication bias (only some databases), specific publication types (language and time delay).	Not	Very	Moderated

				Periodontal therapy of intraosseous defects.						
Effect of platelet-rich plasma on bone regeneration in dentistry: a systematic review.	Plachokova *et al.*[17]	2008 Clin Oral Implants Res	Systematic Review.	To identify and structurally analyze the reported effects of PRP on bone regeneration in humans. Healing of wounds.	Clinical trials, until June 2006	The evidence available in dental literature for beneficial effects in sinus lift is limited. Conclusions about PRP for other applications on odontology are not possible.	Heterogeneity of included studies due to differences in the protocols used in the production of PRP. It did not exclude articles that did not describe or omit the use of coagulation promoters (use, proportion with PRP).	Not mentioned	Good	Moderate
Efficacy of platelet-rich plasma applied to post-extraction retained lower third molar alveoli. A systematic review.	Barona-Dorado *et al.*[18]	2014 Med Oral Patol Oral Cir Bucal.	Systematic review.	To evaluate the available scientific evidence related to the application of PRP in alveoli after extraction of retained third molars. Preservation of post-extraction alveolus.	Human studies, until June 30, 2013, Randomized clinical trials.	The quality of the information was poor when the GRADE guide was applied and therefore the use of PRP cannot be recommended for the post-operative extraction of third molars.	Few studies (3). Meta-analysis could not be performed. The studies analyzed did not use the same method of obtaining platelet concentrate.	Not mentioned	Good	Moderate
Efficacy and safety of the use of autologous plasma rich in platelets for tissue regeneration: a systematic review.	Martínez-Zapata *et al.*[19]	2009 Transfusion.	Systematic Review.	To assess the efficacy and reliability of PRP on tissue regeneration. Tissue regeneration.	Randomized clinical trials.	In the treatment of chronic periodontitis, there is an improvement in the reduction of gingival recession depth and level of clinical insertion in severe stages In relation to PRP in the treatment of surgical wounds, there is no significant difference when compared to the control group. More randomized clinical trials are needed to certainly determine the role of PRP for tissue regeneration.	Studies with samples, in general, small; heterogeneous studies.	Not mentioned	Good	Moderated
Does PRP enhance bone integration with grafts, graft substitutes, or implants? A systematic review.	Roffi *et al.*[20]	2013 BMC Musculoskelet Disord.	Systematic review.	To analyze clinical studies in order to investigate the role of PRP, favouring the integration of bone grafts, graft substitutes or implants, and to identify materials in which additional use of PRP may be associated with superior bone and soft tissue integration. Wound Healing, Implants, Sinus Elevation.	Human and animal studies from 2002 to 2012, randomized clinical trials and compa rative studies.	16 studies showed favorable results of the PRP, 18 did not obtain significant differences and 6 underlined the ambiguous role of the PRP. No material has been identified that appears to benefit from the use of the PRP. PRP should not be indicated in tricalcium beta phosphate implants. Controversial results were reported on augmentation with autologous bone and better augmentation potential has been observed with hydroxyapatite implants. PRP does not appear to have a negative effect.	Different procedures were used to obtain PRP, which leads to qualitative and quantitative differences, differences in PRP activation methods (non-activated, thrombin, calcium chloride) and application protocols (quantity, number of administrations and timing of administration). Also, differences in study designs, defect sizes and a low number of patients studied.	No	Moderate	Critically low

Platelet-Rich Plasma in Sinus Augmentation Procedures: A Systematic Literature Review: Part II.	Arora *et al.*[21]	2010 Implant Dent.	Systematic Review.	To revise literature to determine: a. whether PRP with bone or bone substitutes allow for clinical bone regeneration faster and more effective in a clinical, radiographic and histological way with sinus lift procedures. b. Does it exist any clinical data similar to animal experimentation providing clinical evidence during sinus lift procedures? Bone regeneration, Sinus lift.	Published and unpublished studies of controlled clinical trials or randomized controlled clinical trials.	There are few controlled clinical trials related with PRP benefits in sinus lift. Discrepancy in study designs, surgical technique and different evaluations of variants used makes it difficult to evaluate the benefits of using PRP in sinus graft. Need for controlled randomized clinical trials to evaluate PRP benefits in sinus lift. Standardized protocol is needed to extract and prepare PRP, since these factors influence its success rate. These are some factors that may have a direct impact on decisions for PRP use in treatment compared to the cost of PRP preparations.	Great diversity among studies evaluating the regenerative potential of PRP, which complicates the comparison with its results. Lack of standardized studies, inadequate number of participants in the research, lack of a consistent single outcome variant for sinus lift studies.	No	Moderate	Low
Efectividad del Plasma Rico en Plaquetas en la Cicatrización de Implantes Dentales: Una revisión Sistemática.	Bravo *et al.*[22]	2013 Int J Odontostomat.	Systematic Review and meta -analysis.	To assess the efficacy of PRP in the healing of dental implants by systematic review and meta -analysis, allowing a clinical recommendation based on evidence to be generated. Implants.	Randomized Clinical trials.	PRP shows a high concentration of growth factors and platelets, showing in this analysis that, when combined with rehabilitation through implants, sinus elevation and bone grafts, an improvement is obtained in bone quality and in the type of healing. It is evident that it increases the efficacy of the therapy itself, over other alternatives for healing and subsequent rehabilitation, improving treatment, achieving greater stability and quality of healing.	No bias mentioned. It uses a fixed-effect model, assuming that any variation found in results was due to the experimental error of each particular study, all with 95% reliability. It performs meta-analysis of heterogeneity (I2) of 82%, considered high, exceeding the 75% established as the upper limit of results variability.	Not mentioned	Moderate	Critically low

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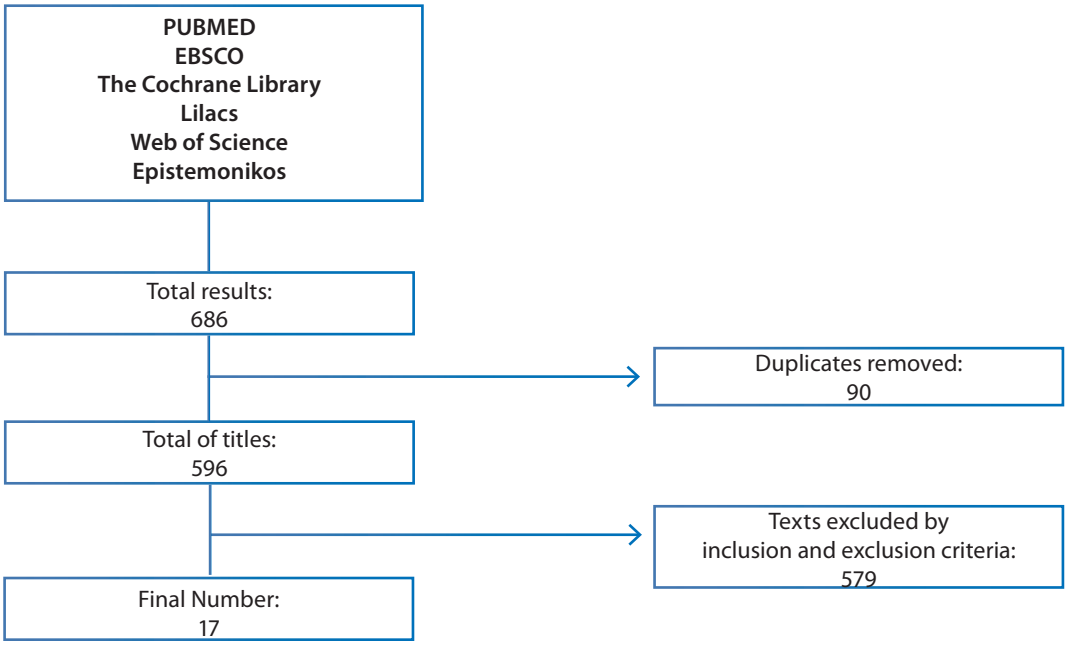
Table 2. Number of studies that meet the PRISMA guideline sections.

	Title	Summary	Introduction		Material and Methods												Results						Discussion			Funding
Section #	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**	**23**	**24**	**25**	**26**	**27**
Meet	16	17	17	13	8	17	14	17	17	15	14	13	14	11	8	9	16	16	12	16	13	10	11	17	16	17	8
Does not meet	1	0	0	4	9	0	3	0	0	2	3	4	3	6	9	8	1	1	5	1	4	7	6	0	1	0	9

Table 3. Summary of AMSTAR-2 tool sections.

	AMSTAR-2 check-list items															
Item #	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**
Yes	14	3	8	3	12	12	12	8	9	2	8	7	14	15	4	11
No	1	12	7	2	3	3	3	2	3	13	0	1	1	0	5	4
Partially	-	0	-	10	-	-	0	5	3	-	0	-	-	-	-	-
No Meta-analysis	-	-	-	-	-	-	-	-	-	-	7	7	-	-	6	-
	15	15	15	15	15	15	15	15	15	15	15	15	15	15	15	15

Figure 1. Flow-chart of the literature search process.



a good or very good report quality; three articles were classified with unreliable results by having a questionable clinical applicability due to showing a low or critically low methodological quality and a moderate report quality.

DISCUSSION.

In clinical practice, the effectiveness of the use of PRP has been described in sinus lift procedures, alveolus preservation techniques, and also as a joint procedure to support the regeneration process in periodontal intrabony defects and furcal defects.[4]

The data is difficult to sort and understand due to differences in preparation protocols, terminology and presentation of materials. For this reason, systematic reviews or meta-analyses are essential and very useful in order to improve the reading of original articles, which are being published more frequently. They allow the proposal of new hypotheses for future studies and the measurement of the magnitude of publication bias, since they synthesize and make the relevant information of many scientific articles homogeneous, articles that have different variables, perspectives and results that can be heterogeneous or

contradictory, and as such systematic reviews are considered top level evidence within the evidence levels pyramid.

Despite being very useful instruments, SRs have methodological limitations such as being retrospective, and therefore it may present biases during the search process due to the fact that many studies do not get the expected results and are less cited, they take longer to be published or are not published at all, and become more difficult to identify. Duplicate publications are also contributing to this type of bias along with the fact that no other languages rather than English are considered when doing the bibliographic search.

In addition, selection biases must be taken into account due to the quality of the original research and the heterogeneity of the studies in terms of context, problems, doses, selected population and the number of participants, among others, that affect the meta-analysis quality, analysis bias and synthesis of information by using wrong analysis techniques. Therefore, authors must take all precautions available in order to prevent or reduce every bias variable. Also, it should be taken into account that the performance of the SR or meta-analysis is limited by quantity and quality of previously conducted studies. The PRISMA Statement, including its 27 checklist items, is applicable to all types of SRs and was designed as a tool to contribute to improving clarity and transparency in the publication of systematic reviews.[1]

In assessing the quality of publication of systematic reviews, it becomes evident that the main problem (and hence the opportunities for improvement to be taken into account for analysis and for the publication of future systematic reviews) is mainly related to: the review protocol and the way it is registered, specification of any risk of bias assessment that may affect cumulative evidence and description of additional methods of analysis, appropriate presentation of the results of any risk of bias assessment between the studies and the results of additional analyses, and lastly a declaration of the sources of funding for the systematic review and other support (*e.g.* data contribution), as well as the role of funders in SR.

According to Shea *et al.,*[23] the 16-domain questionnaire with simple answer options (Yes/No/Partial Yes) AMSTAR-2 allows for a more detailed evaluation of SRs that also include non-randomized studies of health interventions. However, it does not provide an overall rating of the vulnerabilities in the seven domains considered critical, since they can significantly affect the validity of a review and its findings. It is important to highlight that AMSTAR-2 assesses the methodological quality of systematic reviews and does not assess the methodological quality of clinical studies covered by it, although it does include items related to the evaluation, documentation and adequate use in the conclusions of the scientific quality of the studies. The studies conducted by Roffi *et al.,*[20] and Bravo *et al.,*[22] present critically low methodological quality due to more than one critical deficiency, making the results of these SRs unreliable. In addition, both articles have a moderate report quality.

The study conducted by Arora *et al.,*[21] presents low methodological quality and the report quality is moderate, therefore the SR cannot provide an exact and complete summary of the available studies. Articles with high methodological quality[6,7,12,14] have very good report quality as they provide an accurate and complete summary of the results of the available studies. Whereas studies with moderate methodological quality[8-13,15-19] present mostly very good report quality, providing an accurate summary of the results of the available studies.

The biases of this research are language-related due to the fact that it was restricted to publications in English and Spanish. The risk of selection was minimized since three researchers were in charge of the study, selection and analysis of the articles and, if no agreement was reached, a fourth researcher was consulted. The risk of location bias was also minimized by using multiple databases and journals; however, no unpublished papers or research presented at conferences, nor all available search engines and journals were evaluated.

Regarding the limitations of this study, it mainly relates to the first inclusion criterion "Mention PRP in title or abstract", since articles containing relevant information about PRP within the concept of CP could have been excluded from the analysis.

The conclusion is that most of the SRs of PRP in dental procedures have adequate report quality (moderate - high), their methodology is well described and they provide an accurate summary of the results of the available primary studies. However, there is a smaller proportion of SRs

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whose methodological and writing deficiencies make their results and conclusions unreliable.

A correct evaluation of the report quality and the methodological quality of the SRs that endorse its results and conclusions is essential, regardless of its quality as an integrative scientific article of the first level of evidence, as if the research methodology is deficient, the risk of publication bias increases and consequently its results will be unreliable and its clinical applicability will be questionable, leading to an erroneous clinical judgment that is not the safest or offer the best therapeutic measure for the patients and that compromises their well-being.

Nowadays, the SRs regarding PRP as a method of tissue regeneration in dental procedures are very heterogeneous and, in certain cases, are not comparable due to differences in the preparation of the PRP, both in its activation and centrifugation, the method of usage, the design of the study, sample size or follow-up time, among others. Therefore, it is imperative to standardize the protocol for the use of PRP in order to improve the quality of future research.

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REFERENCES.

1. Huttona B, Catalá-Lópeza, Mohera D. La extensión de la declaración PRISMA para revisiones sistemáticas que incorporan metaanálisis en red: PRISMA-NMA. Med Clin. 2016.
2. Marx RE. Platelet-rich plasma: evidence to support its use. J Oral Maxillofac Surg. 2004;62(4):489-96.
3. Agrawal AA. Evolution, current status and advances in application of platelet concentrate in periodontics and implantology. World J Clin Cases. 2017;5(5):159-71.
4. Saleem M, Pisani F, Zahid FM, Georgakopoulos I, Pustina-Krasniqi T, Xhajanka E, et al. Adjunctive Platelet-Rich Plasma (PRP) in Infrabony Regenerative Treatment: A Systematic Review and RCT's Meta-Analysis. Stem Cells Int. 2018;2018:9594235.
5. Dohan Ehrenfest DM, Sammartino G, Shibli J, Wang H-L, Zou DR, Bernard JP. Guidelines for the publication of articles related to platelet concentrates (Platelet-Rich Plasma - PRP, or Platelet-Rich Fibrin - PRF): The international classification of the POSEIDO. POSEIDO. 2013;1:17-27.
6. Hou X, Yuan J, Aisaiti A, Liu Y, Zhao J. The effect of platelet-rich plasma on clinical outcomes of the surgical treatment of periodontal intrabony defects: A systematic review and meta-analysis. BMC Oral Health. 2016;16(1):71.
7. Pocaterra A, Caruso S, Bernardi S, Scagnoli L, Continenza MA, Gatto R. Effectiveness of platelet-rich plasma as an adjunctive material to bone graft: a systematic review and meta-analysis of randomized controlled clinical trials. Int J Oral Maxillofac Surg. 2016;45(8):1027-34.
8. Lemos C a. A, Mello CC, dos Santos DM, Verri FR, Goiato MC, Pellizzer EP. Effects of platelet-rich plasma in association with bone grafts in maxillary sinus augmentation: a systematic review and meta-analysis. Int J Oral Maxillofac Surg. 2016;45(4):517-25.
9. Roselló-Camps À, Monje A, Lin GH, Khoshkam V, Chávez-Gatty M, Wang HL, Gargallo-Albiol J, Hernandez-Alfaro F. Platelet-rich plasma for periodontal regeneration in the treatment of intrabony defects: a meta-analysis on prospective clinical trials. Oral Surg Oral Med Oral Pathol Oral Radiol. 2015;120(5):562-74.
10. Panda S, Doraiswamy J, Malaiappan S, Varghese SS, Del Fabbro M. Additive effect of autologous platelet concentrates in treatment of intrabony defects: a systematic review and meta-analysis. J Investig Clin Dent. 2016;7(1):13-26.
11. Bae J-H, Kim Y-K, Myung S-K. Effects of platelet-rich plasma on sinus bone graft: meta-analysis. J Periodontol. 2011;82(5):660-7.
12. Esposito M, Grusovin MG, Rees J, Karasoulos D, Felice P, Alissa R, et al. Effectiveness of sinus lift procedures for dental implant rehabilitation: a Cochrane systematic review. Eur J Oral Implantol. 2010; 3(1):7-26.
13. Niu W, Wang P, Ge S, Ji P. Effects of Platelet Concentrates Used in Alveolar Ridge Preservation: A Systematic Review. Implant Dent. 2018;27(4):498-506.
14. Esposito M, Felice P, Worthington HV. Interventions for replacing missing teeth: augmentation procedures of the maxillary sinus. Cochrane Database Syst Rev. 2014;(5):CD008397.
15. Bousnaki M, Bakopoulou A, Koidis P. Platelet-rich plasma for the therapeutic management of temporomandibular joint disorders: a systematic review. Int J Oral Maxillofac Surg. 2018;47(2):188-98.
16. Kotsovilis S, Markou N, Pepelassi E, Nikolidakis D.

The adjunctive use of platelet-rich plasma in the therapy of periodontal intraosseous defects: a systematic review. J Periodontal Res. 2010;45(3):428-43.
17. Plachokova AS, Nikolidakis D, Mulder J, Jansen JA, Creugers NHJ. Effect of platelet-rich plasma on bone regeneration in dentistry: a systematic review. Clin Oral Implants Res. 2008;19(6):539-45.
18. Barona-Dorado C, González-Regueiro I, Martín-Ares M, Arias-Irimia O, Martínez-González JM. Efficacy of platelet-rich plasma applied to post-extraction retained lower third molar alveoli. A systematic review. Med Oral Patol Oral Cir Bucal. 2014;19(2):e142-8.
19. Martínez-Zapata MJ1, Martí-Carvajal A, Solà I, Bolibar I, Angel Expósito J, Rodriguez L, García J. Efficacy and safety of the use of autologous plasma rich in platelets for tissue regeneration: a systematic review. Transfusion. 2009;49(1):44-56.
20. Roffi A, Filardo G, Kon E, Marcacci M. Does PRP enhance bone integration with grafts, graft substitutes, or implants? A systematic review. BMC Musculoskelet Disord. 2013;14:330.
21. Arora NS, Ramanayake T, Ren Y-F, Romanos GE. Platelet-rich plasma in sinus augmentation procedures: a systematic literature review: Part II. Implant Dent. 2010;19(2):145-57.
22. Bravo SE, Oliva MP. Efectividad del plasma rico en plaquetas en la cicatrización de implantes dentales: una revisión sistemática. Int J Odontostomat. 2013;7(1):87-92.
23. Shea BJ, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, Moher D, Tugwell P, Welch V, Kristjansson E, Henry DA. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. BMJ. 2017;358:j4008.

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