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SYSTEMATIC REVIEW

Effect of Non-Surgical Periodontal Therapy on Chronic Kidney Disease Patients: A Systematic Review

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ABSTRACT

Objective: To evaluate the effectiveness of "non-surgical periodontal therapy (NSPT)" on periodontal and renal parameters in periodontitis patients diagnosed with chronic kidney disease. **Material and Methods:** The review protocol has been registered in Prospero (CRD42020150938). Up to November 2019, we searched the PUBMED database without language constraints. We included randomized controlled (parallel-group or cross-over) trials with CKD and chronic periodontitis in adults aged 18 years and above. Three review authors independently assessed the studies. Three review writers gathered data and simultaneously assessed the risk of bias for individual trials using traditional Cochrane procedures. **Results:** Studies showed high variability. Three randomized clinical trials (RCT) were excluded because of high heterogeneity; meta-analysis could not be performed. **Conclusion:** Non-surgical periodontal therapy effectively improves periodontal and renal parameters. However, a meta-analysis could not be performed because of the high heterogeneity among the studies.

Keywords: Kidney Diseases; Periodontitis; Therapeutics.

Introduction

Chronic Renal Disease (CRD) is a debilitating disease with deleterious effects on multisystem functioning, which may lead to kidney failure, cardiovascular disorders, and premature death. It also has a close association with psoriasis [1]. CRD is defined as the "reduction in the glomerular filtration rate (GFR) or kidney damage, reflected as abnormal urine sediments or leading to abnormalities in the renal anatomy" [2]. In the past decade, CRD has attained mounting attention as one of the leading public health problems globally [3]. As of now, patients with CRD undergo hemodialysis, but patients with "end-stage renal disease (ESRD)" often require renal transplantation. The rising cost of treatment places a significant financial strain on the healthcare system, particularly in emerging countries like India.

Periodontal diseases are multifactorial and commonly associated with bacterial plaque-induced inflammatory conditions that lead to gingival bleeding, pocket formation, and clinical attachment loss. If not intervened in the early stages, it may lead to the formation of deep periodontal pockets, which may require additional surgical procedures utilizing the open flap approach [4]. Periodontitis destroys the periodontium considerably and invariably induces local and systemic inflammatory responses. The incidence of CRD is increasing, and patients receiving dialysis will constitute a vast segment of the patients with dental problems. Severe periodontal conditions have been observed in patients undergoing hemodialysis [5]. Hemodialysis can affect the periodontal tissues with the manifestation of gingival enlargement, which is a common finding observed in association with immune-compromised renal transplantation patients. Significant increases in plaque and calculus levels commensurate with gingival inflammation have also been reported in such patients. Higher prevalence and severity of periodontal tissue destruction with compromised oral health have also been observed in CRD patients receiving hemodialysis as maintenance therapy.

The most recommended technique for controlling periodontal infections is non-surgical periodontal therapy (NSPT), the initial stage of periodontal therapy. It's sometimes referred to as “cause-related therapy” [6]. It can be defined as "plaque removal, plaque control, supragingival and subgingival scaling root planing (SRP), and adjunctive use of chemical agents." NSPT has been used with numerous adjuncts in conjunction with it, but it is still the gold standard against which other modalities are compared [7]. "Manual, sonic or ultrasonic instruments (scalers)" are used with light overlapping strokes for thorough supra or subgingival debridement that aims at the removal of bacterial biofilms comprising of various toxins and endotoxins that may sometimes induce the removal of necrosed cementum intentionally. NSPT's goal is to attain a root surface that is biologically acceptable for a healthy periodontal attachment. Reduced microbial load improves the clinical periodontal parameters like gain in the clinical attachment, reduction in pocket depth, and inflammation. The therapy renders clean, hard, and smooth root surfaces. NSPT alone is enough for periodontal maintenance, but in distinct clinical scenarios, adjuncts are used along with it. "Local drug delivery agents, host modification therapy, and systemic antimicrobials are examples of adjuncts." Maintaining the affected area after thorough debridement is critical, which is why NSPT is always followed by maintenance therapy. "Brushing technique, oral hygiene instructions (OHI), and anti-infective NSPT" are the key components of maintenance therapy. It aids in maintaining gingival sulci, making cleaning more accessible and effective.

The number of people with CRD seeking dental treatment is on the rise. Periodontal disorders and CRD are linked. However, the link between the two has yet to be well investigated. Thus, the primary goal of this review is to investigate the effectiveness of non-surgical periodontal therapy in improving renal parameters in patients with chronic kidney disease and chronic periodontitis observed in 18-year-olds with chronic kidney disease. This review examines the impact of periodontal disease in people with CRD, emphasizing the role of

periodontal interventions (NSPT) in generating evidence of improved periodontal and renal parameters in these patients.

Material and Methods

Protocol Development

The review protocol has been registered in Prospero (CRD42020150938). The protocol used to assess the methodologic quality of this systematic review was PRISMA STATEMENT, which can be accessed at www.prisma-statement.org/ (a tool to evaluate systematic reviews) [8]. It is an evolution of the original QUOROM guideline for systematic review, enabling the judgment of systematic reviews of randomized and non-randomized control trials.

Focused Question

The question that this systematic review is attempting to answer is: Based on the body of evidence gathered from existing literature of both randomised and non-randomized clinical trials, how effective is non-surgical periodontal therapy in improving renal parameters assessed in patients with chronic kidney disease who are diagnosed with chronic periodontitis observed in adults 18 years of age?

Search Methodology

A record of this study was submitted to PROSPERO on the same day, indicating that a systematic review was in progress after checking the "International Prospective Register of Systematic Reviews (PROSPERO)" to ensure that no systematic review tackled the same topic that was being undertaken as of April 8, 2019 [8]. A systematic review was done from April 4, 2019, to February 14, 2020. The analysis comprised articles published before April 16, 2019, that met the inclusion criteria. Without any language constraints, we searched the "PubMed database." "Medical topic headings (MeSH)" or equivalent terms. The text word terms were also employed. We looked through the "meta Register of Controlled Trials (mRCT) (www.controlled-trials.com/mrct)," as well as the "National Clinical Trials.gov database (www.clinicaltrials.gov)." We also searched through review "reference lists," retrieved articles for new investigations, and conducted citation searches on critical articles (Figure 1).

Criteria for Considering Studies for this Review

Types of Studies

"Randomised controlled trials (RCTs) and non-randomised trials with open or blinded outcomes assessment" were included. "RCT protocols accepted manuscripts and case reports" were also incorporated in the review.

Participant Details

The study comprised patients with a clinical diagnosis of CRD showing clinical signs of moderate to severe chronic periodontitis. Both inpatients and outpatients were eligible, regardless of the kind or stage of CRD (except end-stage renal disease) they had or their gender. Patients in the comparison group were those who were clinically diagnosed with moderate to severe periodontitis, were 18 years or older, and had no history of CKD. Flow chart 1 shows screening articles for inclusion (Prisma flow diagram).

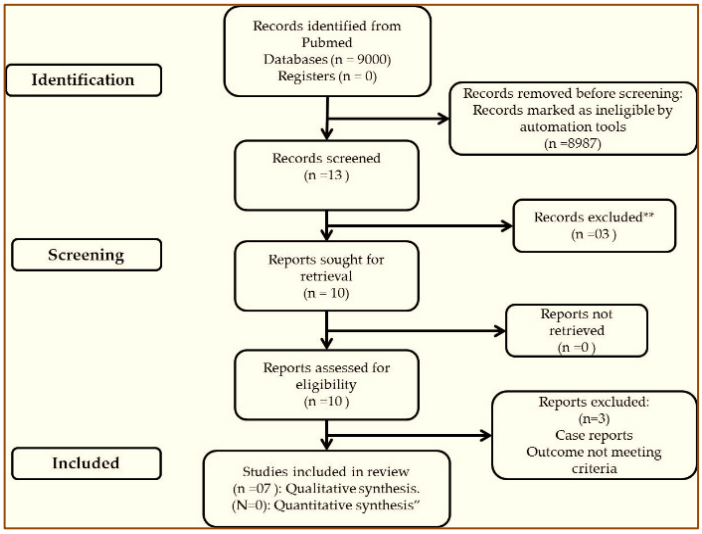

Figure 1. Consort chart for the process of screening the reports.

Types of Outcome Measures

Primary Outcome

1. Change in the indices [Plaque index (PI) [9] and Calculus index (CI)] as the difference between baseline and post-treatment.
2. Change in the clinical parameters [Bleeding on probing (BOP), periodontal pocket depth (PPD), clinical attachment loss (CAL), and gingival recession (GR)] as the difference between baseline and post-treatment.
3. Changes in the microbial environment as the difference between baseline and post-treatment.
4. Changes in carotid intermedia thickness as difference between baseline and post-treatment.

Secondary Outcome

1. Changes in kidney functions as measured by glomerular filtration rate (GFR) at baseline and post-treatment.
2. Changes in serum creatinine at baseline and post-treatment.
3. Changes in inflammatory markers measured by C-reactive protein at baseline and post-treatment.

Data Analysis

Study Selection

Using the Rayyan online screening tool [10], four writers (RO, VS, PB, and PD) independently screened the search results and retrieve15d articles. Each study's eligibility was established by reviewing the abstracts found through the search. After a review by the author, studies that did not meet the inclusion criteria were deleted (PD). All of the remaining studies were retrieved in their entirety. Primary reviewers separately screened all the texts of these articles to choose relevant studies (RO, VS, PB). If the research contained missing data or information that altered the study selection criteria, the respected authors were contacted by phone or e-mail to clarify the information. When there was a disagreement or a conflict, a third author was invited to make a decision (MNK). The studies were not anonymized before they were assessed. Any language restrictions in the study selection process were not deemed a stumbling block in completing this review. In the comprehensive evaluation, a "PRISMA flow chart" was added to indicate the detailed status of all recognised studies as recommended in "Part 2, Section 11.2.1 of the Cochrane Handbook for Systematic Reviews of Interventions" [11]. Studies were included in this review, irrespective of the reporting of outcome data.

Data Extraction

Three authors (RO, VS, PB) agreed that data from "included studies" was extracted using data extraction form, which was predefined and given in the "Characteristics of Studies Table" [12] (Table 1). Data was extracted regarding the type of study, participant details, intervention details, and reported outcomes. The third reviewer settled the dispute between the primary reviewers. Table 2 shows data from several investigations.

Measures of Treatment Effect

Unit of analysis issues: Individual participants were deemed the "unit of analysis" in parallel-group RCTs. The "cross-over" designed studies are integrated into "meta-analysis" using the approach proposed by Elbourne et al. [13]. Measurements from "experimental intervention periods" and "control intervention periods" were compared in a "parallel group study" of intervention *vs.* control.

Missing Data

Based on the amount of studies available, we conducted an intention-to-treat analysis. More information from the authors or manufacturers was requested if the published data was found to be partial, missing, or inconsistent with RCT protocols. If the included studies did not report on the outcome measures of interest, description of randomization, or intention-to-treat analysis, or if the research result had missing data, authors were contacted by e-mail or phone.

Assessment of Heterogeneity

The I2 statistic was employed to measure heterogeneity in the outcome parameters of the included studies, and the chi2 test (p-value determined as 0.10 for statistical significance) was utilised to examine clinical heterogeneity [14]. Heterogeneity was classified as large if the I2 was greater than 75%, substantial if the I2 was between 50% and 90%, moderate if the I2 was between 30% and 60%, and mild if the I2 was less than 40%. Relevant factors were investigated using predefined subgroup analysis, and if statistical heterogeneity with I2 greater than or equal to 50% was detected, a random-effects model was used and reported.

Results

Data Synthesis

A meta-analysis was only planned if the included studies' participants, interventions, comparisons, and outcomes were deemed sufficiently similar to offer a clinically significant and relevant response. For the meta-analysis, we planned to use "RevMan 2014", a statistical tool provided by the Cochrane Collaboration [15]. Data was extracted from three RCTs, but meta-analysis could not be performed because of high heterogeneity. Data entry is tabulated in Table 2. Studies showed high variability.

Subgroup Analysis and Investigation of Heterogeneity

We divided the participants into subgroups based on the type and duration of the intervention.

Included Studies

Based on the inclusion and exclusion criteria, seven studies were found. Table 1 summarizes the findings of the research. Only English-language articles were considered.

Table 1. Characteristics of studies included.

Variables	Categories	Artese et al. [17]	Fang et al. [16]	Graziani et al. [20]	Artese et al. [2]	Jamieson et al. [19]	Grubbs et al. [18]
Demographics	Country	Brazil	China	Switzerland	Colombo	Adelide, Australia	USA
	Type of Study	RCT	RCT	Exploratory trial	RCT	RCT protocol	RCT
	Number of Groups	G1: 21 predialysis patients G2: 19 with chronic periodontitis with no history of CKD	Intervention=48 Control=49	Intervention =20 NA	Intervention=16 CKD Patients Control=14 systemically healthy	Intervention=300 Control=300	Intervention=34 Control=17
Participation Details	Age	36-76 years	55-60 years	35-75 years	35-76 years	18+	34-73 years
	Gender (M/F)	NR	NR	Exploratory trial	9 females in IG and 10 in CG	NR	
	Type of periodontal disease	Chronic periodontitis	Chronic periodontitis	Generalized Chronic periodontitis	Chronic periodontitis	Periodontal disease	Chronic periodontitis
	Grade of chronic kidney disease	Grade 1 GFR-89-15ml/min	ESRD	Systemically healthy	Grade 1 GFR between 89-15 ml/l	Grade 3-5	Grade 1
Intervention	Type	SCRP + oral hygiene instructions	SCRP + oral hygiene instructions	SCRP	SCRP + oral hygiene instructions	SCRP + oral hygiene instructions	SCRP
	Duration	3 months	36 months	6 months	11 months	24 months	12 months
	Frequency	Baseline, 3 months	Baseline, 6 weeks,3 months,6 months	BL, 1 day, 7 days, 30 days, 90 days, 180 days	Baseline, 3 months	Baseline, 3 months, 6 months	BL, 4 months, 8 months, 12 months
Outcomes	Parameters	Primary - PI, CI, CAL, BOP, SUP	Primary: PI, PPD, BOP, GR, CAL. Secondary: tnfalfa.IL-6, CRP, ferritin, Alb, BUN, Cr, ALC	Positive with respect to periodontal parameters.	Primary: microbiological assessment, secondary: PPD, CAL, VP, BOP, SUP	Primary: change in carotid intima-media thickness secondary: progression of CKD	Accepted manuscript
	Technique/Definition	CAL>4mm and BOP, secondary - GFR, serum creatinine.	>1mm CAL as per AAP, 16 teeth, third molars excluded	Statistically significant improvement in periodontal parameters only	15 teeth,>4sites,3 different teeth CAL>4mm	Dialysis; egfr levels of <60 ml/min/1.73 m2 (CKD	
	Time of reporting	3 months Both groups responded well, contrary to the original hypothesis.	6 months - (IG- 6 weeks- 48, 3 months - 48 , 6 months - 46) (CG- 6weeks - 48, 3months - 48, 6 months - 46)	6 months - (1 day, 7 day, 30 days, 90 days, 120 days - 19)	3 months -(IG- 9, CG-10)	Stages 3 to 5); iii. ACR ≥30 mg/mmol irrespective of Egfr (CKD Stages 1 and 2); iv. Diabetes plus albuminuria	

NR: Not Reported; NA: Not Applicable; IG: Intervention Group; CG: Control Group; CKD: Chronic Kidney Disease; AAP: American Academy of Periodontology; PI: Plaque Index; CI: Calculus Index; BOP: Bleeding on Probing; Sup-Suppuration; GFR: Glomerular Filtration Rate; SCRP: Scaling and Root Planing; PPD: Probing Pocket Depth; GR: Gingival Recession; CAL: Clinical Attachment Loss; ESRD: End Stage Renal Disease; CRP: C Reactive Protein; CR: Creatinine; ALC: Absolute Lymphocyte Counts.

Table 2. Characteristic data of the assessed parameters in the included studies.

Outcomes	Artese et al. [17]		Fang et al. [16]		Artese et al. [2]	
Parameters	Mean of Intervention + SD	Mean of Control + SD	Change from Baseline in IG	Change from Baseline in CG	Mean of Intervention + SD	Mean of Control + SD
PPD	Pre SCRP: 29.9+12.6 Post SCRP: 1.3+2.8	Pre SCRP: 23.3+15.8 Post SCRP: -0.6+1.3	1.53+0.13	0.08+0.11	BI: 4.5+0.2 3 months: 1.8+0.2	BI: 4.5+0.4 3 months: 1.7+0.2
BOP	Pre SCRP: 60.4+16.4 Post SCRP: 46.2+15.4	Pre SCRP: 58.3+14.9 Post SCRP: 38.5+11.6	27.31+5.94	10.80+3.89	BI l: 77.8+5.2 3 months: 58.3+6.6	BI: 67.4+6.3 3 months: 53.5+4.9
CAL	Pre SCRP: 33.2+14.4 Post SCRP: 4.2+9.1	Pre SCRP: 25.4+17.0 Post SCRP: 1.6+2.9	0.35	0.01	BI: 5.3+0.4 3 months:4.3+0.4	BI: 5.3+0.4 3 months: 4.1+0.3”

IG: Intervention Group; CG: Control Group; BOP: Bleeding on Probing; SCRP: Scaling and Root Planing; PPD: Probing Pocket Depth; CAL: Clinical Attachment Loss.

Discussion

The details of the participant recruitment are given in Table 1. All the studies were considered, including participants with chronic periodontitis and CKD at different stages, such as pre and post-dialysis. Changes in clinical periodontal parameters were examined before and after scaling and root planing in the studies considered (SRP) [2,16,17]. In addition, the GFR and serum creatinine levels were assessed [17]. On the other hand, the effect of SRP on the composition of subgingival microbiota from subgingival samples was investigated by Artese et al. [2] in 2012 and analyzed by using genomic DNA probes and the "checkerboard DNA-DNA hybridization method".

Interventional studies by “Artese et al. [17] and Grubbs et al. [18]” included grade 1 chronic kidney disease patients in the interventional arm and systemically healthy individuals with chronic periodontitis in the control arm. Artese et al. [2] evaluated changes in the subgingival microbiota in CKD predialysis patients. Jamieson et al. included Aboriginal Australians with CKD having moderate to severe periodontitis [19].

Regarding primary outcome, all the included trials reported data on "plaque index (PI), calculus index (CI), periodontal pocket depth (PPD), clinical attachment loss (CAL), bleeding on probing (BOP), and gingival recession (GR)." However, Artese et al. [2] additionally reported data on microbiological assessment. In the RCT protocol by Jamieson et al. [19], the thickness of carotid intermedia was reported in addition to the abovementioned parameters. Artese et al. [17] reported findings on suppuration (SUP).

Regarding secondary outcome, Artese et al. [17] reported data on GFR, serum creatinine at baseline (immediately before SCRP), and three months post-therapy. Fang et al. [16] reported data on C-reactive protein at 3 and 6 months. Artese et al. [2] reported data on pocket depth (PD), clinical attachment loss (CAL), and visible plaque (VP).

Three studies were excluded: Graziani et al. [20], Fisher et al. [21], and Khalighinejad et al. [22]. Graziani et al. [20] was an exploratory trial, and the participants involved were systemically healthy. Periodontal disease was reviewed as a risk sign in chronic renal disease and coronary heart disease by Fisher et al. [21] colleagues; hence, it was excluded. End-stage renal illness was linked to radiographically and clinically diagnosed apical periodontitis, but there was no indication of generalised chronic periodontitis. Therefore, Khalighinejad et al. [22] was ruled out.

Conclusion

The chronic renal disease patients on dialysis with periodontitis present with medical complexity and pose several challenges to the dental practitioner and the periodontist in the management of their periodontal condition. Enhancing patient-centered outcomes necessitates consultation with the patient's nephrologist. Non-surgical periodontal therapy is the first line of treatment, followed by maintenance therapy. On the other hand, Extensive pocket formation accompanied by significant osseous abnormalities or exposure of anatomical landmarks such as root furcations may make effective oral hygiene or local root debridement difficult. The quality of evidence for all of our primary outcomes was deemed moderate based on the technique utilised and the reporting of adequate data. These conclusions should be considered cautiously as the smaller sample size in all included studies and the shorter follow-ups limited us to draw a reasonable conclusion. Based on the "Summary of findings table," it can be concluded that non-surgical periodontal therapy effectively improves periodontal parameters along with renal parameters. However, a meta-analysis could not be performed because of the high heterogeneity among the studies. Hence, we recommend more clinical trials be carried out on this particular topic as there is a lack of substantial evidence to prove the relationship between chronic kidney disease and periodontal diseases.

Authors' Contributions

RO	https://orcid.org/0000-0003-2112-7070	Conceptualization, Validation, Data Curation and Writing - Original Draft.
VS	https://orcid.org/0000-0002-0579-4036	Methodology, Formal Analysis, Writing - Original Draft and Supervision.
MNK	https://orcid.org/0000-0001-5875-8277	Methodology, Software and Supervision.
PD	https://orcid.org/0000-0002-3127-3816	Conceptualization, Formal Analysis and Writing - Review and Editing.
PB	https://orcid.org/0000-0001-9246-4811	Conceptualization, Methodology, Writing - Original Draft and Project Administration.
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RI	https://orcid.org/0000-0002-0046-3529	Methodology, Investigation, Writing - Original Draft and Writing Review and Editing.
MGS	https://orcid.org/0000-0002-4659-3425	Conceptualization, Investigation, Visualization and Funding Acquisition.
MAA	https://orcid.org/0000-0002-1961-0840	Methodology, Writing - Original Draft, Writing - Review and Editing and Visualization.

All authors declare that they contributed to a critical review of intellectual content and approval of the final version to be published.

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None.

Conflict of Interest

The authors declare no conflicts of interest.

Data Availability

The data used to support the findings of this study can be made available upon request to the corresponding author.

References

[1] Balwani MR, Pasari A, Tolani P. Widening spectrum of renal involvement in psoriasis: First reported case of C3 glomerulonephritis in a psoriatic patient. Saudi J Kidney Dis Transplant 2019; 30(1):258-260. https://doi.org/10.4103/1319-2442.252922

[2] Artese HPC, de Sousa CO, Torres MCM de B, Silva-Boghossian CM, Colombo PV. Effect of non-surgical periodontal treatment on the subgingival microbiota of patients with chronic kidney disease. Braz Oral Res 2012; 26(4):366-372. https://doi.org/10.1590/S1806-83242012005000008

[3] Zhang J, Jiang H, Sun M, Chen J. Association between periodontal disease and mortality in people with CKD: A meta-analysis of cohort studies. BMC Nephrol 2017; 18(1):1-11. https://doi.org/10.1186/s12882-017-0680-9

[4] Chavan RS, Bhongade ML, Tiwari IR, Jaiswal P. Open flap debridement in combination with acellular dermal matrix allograft for the prevention of postsurgical gingival recession: A case series. Int J Periodontics Restor Dent 2013; 33(2):217-221. https://doi.org/10.11607/prd.0416

[5] Altamimi A, AlBakr S, Alanazi T, Alshahrani F, Chalisserry E, Anil S. Prevalence of periodontitis in patients undergoing hemodialysis: A case control study. Mater Socio Medica 2018; 30(1):58-61. https://doi.org/10.5455/msm.2018.30.58-61

[6] Willmann DE, Gehrig JS, Matloff RB. Non-surgical periodontal therapy. In: Gehrig JS, Willmann DE. Foundations of Periodontics for the Dental Hygienist. 4th. ed. Philadelphia: Wolters Kluwer; 2015.

[7] Wachter RF, Briggs GP, Pedersen CE. Precipitation of phase I antigen of Coxiella burnetii by sodium sulfite. Acta Virol 1975; 19(6):500.

[8] Jain S, Sharma N. Guideline for systematic reviews. Int Dent Med J Adv Res 2016; 2(1):1-10. https://doi.org/10.15713/ins.idmjar.48

[9] Löe H. The gingival index, the plaque index and the retention index systems. J Periodontol 1967; 38(6):610-616. https://doi.org/10.1902/jop.1967.38.6.610

[10] Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan-a web and mobile app for systematic reviews. Syst Rev 2016; 5(1):1-10. https://doi.org/10.1186/s13643-016-0384-4

[11] Chaimani A, Caldwell DM, Li T, Higgins JPT, Salanti G. Undertaking network meta-analyses. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, et al. Cochrane Handbook for Systematic Reviews of Interventions. 2nd. ed. Chichester (UK): John Wiley & Sons; 2019.

[12] McKenzie JE, Brennan SE, Ryan RE, Thomson HJ, Johnston RV. Chapter 9: Summarizing study characteristics and preparing for synthesis. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, et al. Cochrane Handbook for Systematic Reviews of Interventions. 2nd. ed. Chichester (UK): John Wiley & Sons; 2019.

[13] Elbourne DR, Altman DG, Higgins JP, Curtin F, Worthington HV, Vail A. Meta-analyses involving cross-over trials: methodological issues. Int J Epidemiol 2002; 31(1):140-149. https://doi.org/10.1093/ije/31.1.140

[14] Zhao JG. Identifying and measuring heterogeneity across the studies in meta-analysis. J Hand Surg Am 2013; 38(7):1449-1450. https://doi.org/10.1016/j.jhsa.2013.05.020

[15] Basevi V, Lavender T. Routine perineal shaving on admission in labour. Cochrane Database Syst Rev 2014; 2014(11):CD001236. https://doi.org/10.1002/14651858.CD001236.pub2

[16] Fang S, Wang Y, Sui D, Liu H, Ross MI, Gershenwald JE, et al. C-reactive protein as a marker of melanoma progression. J Clin Oncol 2015; 33(12):1389-1396. https://doi.org/10.1200/JCO.2014.58.0209

[17] Artese HPC, de Sousa CO, Luiz RR, Sansone C, Torres MCM de B. Effect of non-surgical periodontal treatment on chronic kidney disease patients. Braz Oral Res 2010; 24(4):449-454. https://doi.org/10.1590/S1806-83242010000400013

[18] Grubbs V, Garcia F, Jue BL, Vittinghoff E, Ryder M, Lovett D, et al. The Kidney and Periodontal Disease (KAPD) study: A pilot randomized controlled trial testing the effect of non-surgical periodontal therapy on chronic kidney disease. Contemp Clin Trials 2017; 53:143-150. https://doi.org/10.1016/j.cct.2016.12.017

[19] Jamieson L, Skilton M, Maple-Brown L, Kapellas K, Askie L, Hughes J, et al. Periodontal disease and chronic kidney disease among Aboriginal adults; An RCT. BMC Nephrol 2015; 16(1):1-8. https://doi.org/10.1186/s12882-015-0169-3

[20] Graziani F, Cei S, La Ferla F, Vano M, Gabriele M, Tonetti M. Effects of non-surgical periodontal therapy on the glomerular filtration rate of the kidney: An exploratory trial. J Clin Periodontol 2010; 37(7):638-643. https://doi.org/10.1111/j.1600-051X.2010.01578.x

[21] Fisher MA, Borgnakke WS, Taylor GW. Periodontal disease is a risk marker in coronary heart disease and chronic kidney disease. Curr Opin Nephrol Hypertens 2010; 19(6):519-526. https://doi.org/10.1097/MNH.0b013e32833eda38

[22] Khalighinejad N, Aminoshariae A, Kulild JC, Williams KA, Wang J, Mickel A. The effect of the dental operating microscope on the outcome of non-surgical root canal treatment: A retrospective case-control study. J Endod 2017; 43(5):728-732. https://doi.org/10.1016/j.joen.2017.01.015