



**FACULTAD DE CIENCIAS DE LA SALUD**  
**CARRERA PROFESIONAL DE ESTOMATOLOGÍA**

**"EFICACIA ANTIMICROBIANA DEL USO DEL ENJUAGUE BUCAL CON  
CLORURO DE CETILPIRIDINIO EN PROCEDIMIENTOS QUE GENERAN  
AEROSOLES. REVISIÓN SISTEMÁTICA"**

Tesis para optar el grado académico de:

**MAESTRO EN ESTOMATOLOGÍA**

Presentado por:

Jackeline Paola Arce Toribio (0000-0002-3140-9525)

Asesor:

Ana Isabel López Flores (0000-0002-1104-2439)

Lima – Perú

2023





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2023

### ACTA DE SUSTENTACIÓN DE TESIS

Lima, 28 de diciembre de 2022.

Los integrantes del Jurado de tesis:

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| Presidente: Dr. Fernando Alfonso Ortiz Culca |
| Miembro: Dr. Claudio Peña Soto               |
| Miembro: Mg Sandra Vega Seminario Peñaranda  |

Se reúnen para evaluar la tesis titulada:

EFICACIA ANTIMICROBIANA DEL USO DEL ENJUAGUE BUCAL CON CLORURO DE CETILPIRIDINIO EN PROCEDIMIENTOS QUE GENERAN AEROSOLES. REVISIÓN SISTEMÁTICA.

Presentada por la bachiller:

- Jackeline Paola Arce Toribio

Para optar el grado de MAESTRO EN ESTOMATOLOGIA

Asesorada por: Mg. Esp. Ana Isabel López Flores

Luego de haber evaluado el informe final de tesis y evaluado el desempeño del bachiller en la sustentación, se concluyen de: Manera unánime ( X )

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| Tesis: Jackeline Paola Arce Toribio |                          | Nota (en letras): Dieciséis  |                 |
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UNIVERSIDAD CIENTÍFICA DEL SUR  
POSGRADO ESTOMATOLOGÍA  
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DECLARACIÓN DE ORIGINALIDAD DE CONTENIDO DE INFORME FINAL DE TESIS<sup>13</sup>

Lima, 11 de Mayo Del 2023

Señor:

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**Presente.-**

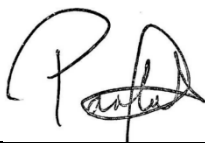
De nuestra consideración,

Yo: Jackeline Paola Arce Toribio egresado del Posgrado Estomatología de la Universidad Científica del Sur, en conjunto con la asesora de tesis Ana Isabel López Flores, declaramos que este trabajo de investigación titulado: Eficacia Antimicrobiana del uso del enjuague bucal con cloruro de Cetilpiridinio en procedimientos que generan aerosoles. Revisión Sistemática; sustentado para obtener el título de Grado Académico de Maestro en Estomatología Es original.

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## INFORME DE REVISIÓN DE ORIGINALIDAD

**Título del documento evaluado.** Eficacia antimicrobiana del uso del enjuague bucal con cloruro de cetilpiridinio en procedimientos que generan aerosoles. Revisión sistemática

**Autores.** Jackeline Paola Arce Toribio.

**Mecanismo de revisión de originalidad.** Evaluación con Turnitin (ID 2101959738).

**Resultado de la evaluación.** 6%

**Revisado por.** Magaly Kelly Guerrero Huaracallo.

**Comentarios sobre la revisión.** Filtros usados: excluir fuentes de menos de 12 palabras.

### Eficacia antimicrobiana

#### INFORME DE ORIGINALIDAD



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## DEDICATORIA

Dedico este trabajo de investigación a mi familia, quien ha estado a mi lado apoyándome en todo en cada paso que doy. Su bendición a diario a lo largo de mi vida me protege y me lleva por el camino del éxito

## AGRADECIMIENTO

Gracias a Dios por darme salud y permitirme tener y disfrutar de mi familia durante estos tiempos de pandemia que realmente han sido muy duros, gracias a mi familia por apoyarme en cada paso que doy.

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Agradezco a mi asesora de tesis, la Dra. Ana López Flores por haberme dado la oportunidad de poder trabajar nuevamente juntas y lograr que esta investigación pueda ver la luz. Gracias a sus consejos, apoyo, paciencia y creer en mi persona para lograr todo lo que me propongo. Ha sabido direccionar mis conocimientos para guiarme durante todo el proceso de la tesis en base a su experiencia y sabiduría.

Finalmente, agradezco al Dr. Heber Arbildo Vega por ser mi mano derecha durante este complicado proceso de elaboración de una investigación científica de alto impacto, como es el caso de las revisiones sistemáticas. Es cierto que no ha sido nada fácil pero finalmente los resultados son gratificantes.



**RESUMEN:**

El presente trabajo de investigación tiene como objetivo determinar la eficacia antimicrobiana de los colutorios a base de cloruro de Cetilpiridinio (CPC), previo a tratamientos dentales que generen aerosol. Se realizó una búsqueda bibliográfica hasta agosto del 2021 en cinco bases de datos: MEDLINE (vía PubMed), SCOPUS, SCIELO, Cochrane Central Register of Controlled Trials (CENTRAL) y Google Scholar. Se incluyeron ensayos clínicos aleatorizados (ECAs), basándose en la pregunta PICOS, que compare la eficacia del colutorio a base de cloruro de Cetilpiridinio (CPC) con otro colutorio, placebo o agua, previo a un tratamiento dental que genere aerosol, en los idiomas español, inglés o portugués y sin límite de tiempo. El riesgo de los estudios incluidos se evaluó con la herramienta RoB 2.0. Número de registro PROSPERO N° CRD42021275982. Se obtuvo un total de 120 artículos en la búsqueda preliminar, descartando aquellos que no cumplían con los criterios de selección, quedando sólo 3 artículos. Estos artículos informaron que el uso de CPC es efectivo para la reducción de bacterias durante el procedimiento de profilaxis con ultrasonido. El uso de los enjuagues bucales a base de CPC previo al tratamiento dental de profilaxis con ultrasonido sólo tiene eficacia antibacteriana.

**Palabras clave:** Colutorio, enjuagar, cetilpiridinio, aerosol, antisépticos, aire contaminado

## ABSTRACT

The present research aims to determine the antimicrobial efficacy of the mouthwashes based on cetylpyridinium chloride (CPC), before aerosol producing dental procedures. A data search was performed during August 2021 in five databases MEDLINE (PubMed), SCOPUS, SCIELO, Cochrane Central Register of Controlled Trials (CENTRAL) and Google Scholar. Randomized clinical trials (RCTs) were included based on the PICO question, comparing the efficacy of the mouthwashes based on cetylpyridinium chloride (CPC), versus other mouthwashes and water, before aerosol producing dental procedures, papers in English, Spanish and Portuguese were included without time limits. The risk of the included studies was evaluated with the tool RoB 2.0. Number of registration PROSPERO N° CRD42021275982. 120 papers were obtained in the preliminary search, discarding those that didn't comply with the selection criteria, leaving only 3 studies. These papers reported the use of cetylpyridinium chloride (CPC) was effective for the reduction of bacteria during the ultrasonic prophylactic procedure. The use of CPC mouthwashes previous to the dental treatment with ultrasonic prophylaxis showed only antibacterial capacity.

**Keywords:** *Mouthwash, rinse, cetylpyridinium, aerosol, antiseptics, contaminated air.*

## ANTIMICROBIAL EFFICACY OF THE USE OF MOUTHWASH WITH CETYLPYRIDINIUM CHLORIDE FOR AEROSOL PRODUCING PROCEDURES. A SYSTEMATIC REVIEW

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**Conflict of interest:** The authors declare that we have no conflict of interest.

**Ethical considerations:** The present study was approved by the Comité Institucional de Ética en Investigación de la Universidad Científica del Sur With a inscription code 222-2021-POS8, date 01 de June 2021.

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### Author contributions:

**Conceptualization and Design,** Jackeline Paola Arce-Toribio; **Literature Review,** Jackeline Paola Arce-Toribio and Ana Isabel López-Flores; **Methodology and Validation,** Ana Isabel López-Flores and Heber Isac Arbildo Vega; **Formal Analysis,** Jackeline Paola Arce-Toribio; **Investigation and Data Collection,** Ana Isabel López-Flores and Heber Isac Arbildo Flores.; **Resources,** Jackeline Paola Arce-Toribio and Ana Isabel López-Flores; **Data Analysis and Interpretation,** Heber Isac Arbildo Vega; **Writing – Original Draft Preparation,** Jackeline Paola Arce-Toribio; **Writing – Review & Editing,** Isabel López-Flores.; **Supervision,** Heber Isac Arbildo Vega; **Project Administration,** Jackeline Paola Arce-Toribio.; **Funding Acquisition,** Self financed.

## INTRODUCTION

Mouthwashes are chemical solutions that prevent diseases and reduce microorganisms in the oral cavity (1-5). They are classified into cosmetic and therapeutic mouthwashes (6-7). Cosmetics mouthwashes offer temporary relief for halitosis. The therapeutic mouthwashes contain active ingredients, such as Cetylpyridinium Chloride (CPC), fluorides, Chlorhexidine Gluconate (CHX) or essential oils such as eucalyptol, menthol, methyl salicylate and/or thymol, that reduce or control dental plaque, gingivitis, halitosis and dental cavities (8,9).

Cetylpyridinium chloride (CPC) is a monocationic quaternary ammonium compound, amphoteric surfactant (10-11), positively charged, which binds to negatively charged microorganisms, it exerts its antimicrobial activity by degradation of the lipid bilayer of the cell and the disruption of bacterial metabolism (12-14). Currently, CPC has received a label from the FDA of Generally Regarded as Safe (GRAS) (15-16), demonstrating high antibacterial potential at concentrations of 0.05% and 0.07% or 0.5 and 0.7 mg/ml (17-22). Its antiviral activity against respiratory infections, herpes virus and hepatitis B virus has also been described (23-27).

In dental procedures that use aerosol-generating equipment, such as ultrasonic scalers, high-speed handpieces or triple syringes, this equipment could cause cross-contamination in the dental office through aerosols containing microorganisms (28-32), since aerosols are particles of less than 50 micrometers in diameter that remain floating in the air for prolonged periods (33), risking the health of patients and dentists (34-37).

The condition caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has seriously affected people in a short period in recent years (38-40); Therefore, to prevent the transmission of these microorganisms with contaminated saliva, information showing mouthwashes can reduce the risk of infection of this disease was found (12,18,29,38).

For this reason, dentists and the general population both need research data that provides adequate information on the benefits of this mouthwash with CPC against these microorganisms, (41-44). The objective of this systematic review is to determine the Antimicrobial efficacy of CPC-based mouthwashes prior to aerosol-generating dental treatments.

## METHODOLOGY

### **Protocol and registration**

This systematic review was prepared following the TRANSPARENT REPORTING of SYSTEMATIC REVIEWS and META-ANALYSIS (PRISMA). It was registered in PROSPERO: A registry for systematic review protocols (N° CRD42021275982).

### **Type of study and participants**

Randomized clinical trials published until August 2021 on the antimicrobial efficacy of the use of CPC-based mouthwashes in patients who have undergone aerosol-producing dental procedures.

To prepare and structure this review, the question was formulated using the PICO format (population, intervention, comparison and results) as detailed below: a) population: patients who have received any dental treatment that generates aerosol. b) intervention: application of CPC mouthwash prior to the dental treatment. c) comparison: placebo, water, other mouthwashes or no mouthwash before dental treatment. d) results: reduction of microorganisms that are produced during dental treatments that generate aerosols.

### **PICO's Question:**

Do CPC-based mouthrinses prior to aerosol-generating dental treatment have antimicrobial efficacy?

### **Source of information and search strategy**

A bibliographic search was carried out in 5 electronic databases: Pubme/Medline, Cochrane library, Scopus, Scielo and Google Scholar until August 2021; combining the keywords and titles according to the thesaurus of each database: "anti-infective agents, local", "antiseptics", "cetylpyridinium",

"cetylpyridinium chloride", "mouthwash", "mouthrinse", "prevention mouthrinse", "mouth rinse", "rinse", "contamination", "air contamination", "aerosol". The literature search strategy is available in Supplemental material (Table 1).

### **Selection criteria**

Studies comparing CPC mouthwash with another mouthwash, placebo or water, prior to aerosol-generating dental treatment, based on the PICOS question strategy (Table 2)

### **Inclusion criteria**

The inclusion criteria of the articles were: a) randomized clinical trials; b) languages: Spanish, English or Portuguese; c) without time limit, until August 2021.

### **Exclusion criteria**

The exclusion criteria of the articles were: a) case reports; b) case series; c) preclinical studies; d) systematic reviews; e) pilot studies; f) gray literature; g) letters to the editor; h) literature reviews; i) ongoing and/or unpublished studies; j) publications in languages other than Spanish, English or Portuguese.

### **Article searchers**

Article searches of electronic databases were performed independently by two investigators (JPAT) and (AILF), who were initially blinded to report their results separately. Disagreements were resolved by discussion with a third reviewer (HIAV). After comparing them, the titles and abstracts were read, discarding articles that are not relevant and/or those that did not meet the eligibility criteria. Second, an analysis of the entire scientific article was carried out, independently extracting the necessary information. These data were compared for accuracy and to avoid any differences in the present review.

### **Data collection**

During the data collection process, a predefined table was used to collect data from each chosen study (Tablet 3) including author-year, country, total number of patients, age (range), study groups, patients by group, follow-up time, type of procedure, collection method, microbial analysis, type of microorganisms, conclusions. Data from each study was entered and analyzed into an Excel sheet for qualitative analysis. Finally, these data were recorded in a pre-established diagram, according to the PRISMA DECLARATION (Figure 1).

### **Risk of bias:**

The data search was carried out following the Cochrane Library guidelines, managing to identify the type of risk in the studies. The RoB 2.0 was used to determine the risk of bias in randomized clinical trials (Figure 2). Clinical trials were assessed across five domains, then classified as: low, some concern, or high risk of bias. Included studies were independently assessed by two calibrated authors (JPAT and AILF) using RoB 2.0. Ultimately, all disagreements were resolved by discussion with a third reviewer (HIAV).

## **RESULTS**

The results of the electronic and manual search strategy included 120 articles in total, excluding 48 duplicate articles and 67 articles eliminated by title and abstract, leaving 5 articles selected. Subsequently, 2 articles that did not meet the eligibility criteria were excluded, resulting in 3 randomized clinical trial articles that were included for qualitative synthesis (Figure 1). The reason for exclusion of the articles is shown in Table 4.

### **Characteristics of included studies**

Overall, 3 articles were included, all were parallel RCTs, and the years of publication ranged from 2010 to 2017. The countries for these articles were: Brazil and India. The total number of participants was between 40 and 60 people, with a range of years from 18 to 70 years (Table 3).

In all the articles, the experimental group was the use of CPC (in different concentrations and/or with other components) and the control group was chlorhexidine, water and the non-use of mouthwash prior to spray treatment. Follow-up time ranged from 1 to 72 hours. All articles described ultrasound prophylaxis as an aerosol-generating procedure and the microorganisms found were gram-positive and negative bacteria. All studies concluded that the use of CPC is effective in reducing bacteria during the ultrasound prophylaxis procedure; however, one of the studies mentions that CPC is better than CHX and other mentions that both are equally effective (Table 3).

In all studies, microbiological samples were collected using Blood Agar or Honokiol plates, which were placed at different locations and distances such as on the patient's chest, dentist's chest, assistant's chest, dentist's front, or on the dashboard. medium.

Regarding the microbiological analysis, the results were expressed in relation to the reduction in the number of colony-forming units (CFU) in the aerosol collection places where the agar plates were located. In all the studies, the method used was counting the total number of CFUs using Labline (32,36,37); only in two studies, a second method was used for microbiological analysis, which was through the use of the DNA-RNA checkerboard hybridization technique (36,37).

### **Analysis of risk of bias**

Three articles were considered, all at low risk of bias. (Figure 2)

### **Analysis of the results**

Data from each study was entered and analyzed in an Excel spreadsheet for qualitative analysis (Table 3).

## **DISCUSSION**

During patient care, there are various dental treatments that use aerosol-generating equipment, such as the handpiece, the triple syringe or ultrasound. These aerosols could carry microorganisms that



exist in the patient's mouth, such as viruses or bacteria (38,39), which would lead to a contaminated atmosphere or possible cross-contamination in the dental office (45). It is known that these aerosol particles can remain floating in the environment for up to 4 hours after a dental procedure (46), producing a risk for the dentist and the patient due to the possible contamination of the respiratory tract by these microorganisms, even after the end of the appointment (47).

To minimize cross-infections in the dental office, different methods have been described in the literature, such as the use of mouthwashes prior to dental treatment (10,27,36), whose purpose is to reduce the number of microorganisms in the oral cavity. These mouthwashes can present different components, as is the case of Cetylpyridinium Chloride (1,2,8,31), which has been widely mentioned in recent years in different publications [4,10], indicating that it has a great capacity antimicrobial against viruses (25-28,46) and bacteria (11,12,17,34), as reviewed in the literature.

According to the results obtained in the present investigation, all concluded that the use of CPC is effective in reducing bacteria during the dental procedure, ultrasound prophylaxis, which generate aerosol; when compared to water or no mouthwash; however, no significant difference in colony-forming unit (CFU) reduction was found when compared to CHX, indicating that CPC-based mouthrinses are equally effective as CHX-containing mouthrinses (32,36-37). This could be due to the fact that both mouthwashes are broad-spectrum antibacterial and present the same mechanism of action, degrading the bacterial membrane and producing cell lysis of the microorganism (7,11).

Joshi et al (32). They reported that the antimicrobial activity of CPC was higher when it was used at 47°C, maintaining the maximum reduction in bacterial count in all areas analyzed, compared to the use of CPC at 18°C. This may be because there would be a greater bactericidal activity of CPC at high temperatures; since as the temperature increases, the speed at which chemical reactions take place increases, known as Thermodynamic Treatment (48)

Likewise, it is observed that the antimicrobial efficacy achieved by CPC rinses is only limited to one type of bacterial microorganisms (36, 37), but no information was found on viral microorganisms. This may be due to the fact that bacteria (6, 17) are able to cultivate and grow on blood agar plates, the same culture media used in the three investigations, while viruses require a specialized medium for their growth (26); that is why it is suggested to carry out future research including these types of microorganisms.

Based on bacterial composition analysis (36,37), it showed statistically lower ratios for orange complex pathogens when CPC was compared to subjects who received no mouthwash or those who only rinsed with water. This is a beneficial effect, since certain species of the orange complex, such as fusobacteriums, can cause respiratory or ophthalmic etiologies (49, 50), which would lead to a possible reduction in cross-diseases in the dental office, as long as the CPC mouthwash is used prior to any dental procedure that generates aerosols.

Retamal-Valdes et al (37). He indicated that the use of CPC was effective in reducing bacteria found in dental aerosols, but it should be noted that, in said study, CPC was used with other additional components, such as zinc lactate and sodium fluoride. , so it could not be concluded if its antibacterial action is thanks to CPC or its other previously mentioned components.

The main limitation of the present study was that it only found results for a single dental procedure, ultrasound prophylaxis, which has been shown to have great potential for aerosol generation in the dental office (38). Therefore, it could be assumed that the CPC mouthwash, prior to dental treatments that generate aerosols, would also produce similar benefits for the dentist and the patient, if it is used with other equipment that also generates aerosols, as is the case with the piece hand or triple syringe. Finally, it is worth mentioning that this is the first study that systematically reviewed the antimicrobial efficacy of Cetylpyridinium Chloride-based mouthwash in the reduction of microorganisms prior to any treatment that generates aerosol, not finding enough information regarding this product in relation

to mouthwashes and sprays; Therefore, the results of our present investigation must be evaluated with caution. Despite demonstrating that there is a decrease in the number of microorganisms, the influence of this decrease in the infection rate towards health professionals is unknown, so there is no direct evidence indicating that cetylpyridinium chloride mouthwash can reduce the rate of clinical infection in the dental area.

## CONCLUSION

The use of CPC-based mouthwashes prior to ultrasonic prophylaxis only has antibacterial efficacy.

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**TABLES AND GRAFICS:**

Table 1. Search strategy according to database.

| Database         | Search Strategy  |
|------------------|--|
| Pubmed/Medline   | ((("anti-infective agents, local") OR "antiseptics") OR "cetylpyridinium") OR "cetylpyridinium chloride") AND (((("mouthwash") OR "mouthrinse") OR "prevention mouthrinse") OR "mouth rinse") OR "rinse") AND (((("contamination") OR "air contamination") OR "aerosol"))  |
| Scopus           | ( TITLE-ABS-KEY ( "anti-infective agents, local" ) OR TITLE-ABS-KEY ( "antiseptics" ) OR TITLE-ABS-KEY ( "cetylpyridinium" ) OR TITLE-ABS-KEY ( "cetylpyridinium chloride" ) ) AND ( TITLE-ABS-KEY ( "mouthwash" ) OR TITLE-ABS-KEY ( "mouthrinse" ) OR TITLE-ABS-KEY ( "prevention mouthrinse" ) OR TITLE-ABS-KEY ( "mouth rinse" ) OR TITLE-ABS-KEY ( "rinse" ) ) AND ( TITLE-ABS-KEY ( "contamination" ) OR TITLE-ABS-KEY ( "air contamination" ) OR TITLE-ABS-KEY ( "aerosol" ) OR TITLE-ABS-KEY ( "aerosols" ) ) AND ( TITLE-ABS-KEY ( "clinical trial" ) ) AND ( LIMIT-TO ( SRCTYPE , "j" ) ) AND ( LIMIT-TO ( DOCTYPE , "ar" ) ) AND ( LIMIT-TO ( SUBJAREA , "DENT" ) ) AND ( LIMIT-TO ( EXACTKEYWORD , "Human" ) ) |
| Scielo           | ((("anti-infective agents, local") OR "antiseptics") OR "cetylpyridinium") OR "cetylpyridinium chloride") AND (((("mouthwash") OR "mouthrinse") OR "prevention mouthrinse") OR "mouth rinse") OR "rinse") AND (((("contamination) OR "air contamination") OR aerosol) OR aerosols))  |
| Google Scholar   | cetylpyridinium + "mouthwash" + "aerosol" + "clinical trial" -"systematic review"  |
| Cochrane Library | #1 MeSH descriptor: [Anti-Infective Agents, Local] explode all trees<br>#2 MeSH descriptor: [Cetylpyridinium] explode all trees<br>#3 ("antiseptics") OR ("cetylpyridinium") OR ("cetylpyridinium chloride") AND ("anti-infective agents, local") (Word variations have been searched)<br>#4 #1 OR #2 OR #3<br>#5 MeSH descriptor: [Mouthwashes] explode all trees<br>#6 ("mouthwash") OR ("mouthrinse") OR ("prevention mouthrinse") OR ("mouth rinse") OR ("rinse") (Word variations have been searched)<br>#7 #5 OR #6<br>#8 ("contamination") OR ("air contamination") OR ("aerosol") OR ("aerosols")<br>#9 MeSH descriptor: [Aerosols] explode all trees<br>#10 #8 OR #9<br>#11 #4 AND #7 AND #10                     |

Table 2. PICO's question table.

| <b>COMPONENTE</b> | <b>DESCRIPCION</b>   |
|-------------------|--|
| P: Problem        | People who have received any dental treatment that generates aerosol.                                    |
| I: Intervention   | Application of the Cetylpyridinium Chloride (CPC)-based mouthwash prior to dental treatment.             |
| C: Comparison     | Placebo, water, other mouthwash prior to dental treatment  |
| O: Outcome        | Reduction of number of microorganisms that are produced during dental treatments that generate aerosols. |
| S: Study          | randomized clinical trials   |

Table 3. Characteristics of the Parallel RCTs included

| Author/year                | Country | Total number of patients (H/M) | Age (range)   | Study Groups                    | Patients by groups | Follow-up time | Type of procedure          | Collection method   | Microbial analysis  | Type of microorganism                              | Conclusions  |
|----------------------------|---------|--------------------------------|---------------|---------------------------------|--------------------|----------------|----------------------------|---|---|--|--|
| Retamal-Valdes et al. 2017 | Brasil  | 60 (24/36)                     | 42.32 (18-70) | No mouthwash                    | 15                 | 72 horas       | Profilaxis con ultrasonido | 5 honokiol agar plates: 3 on the support board, 1 on the participant's chest, and 1 on the clinician's forehead | 1Anaerobic culture; counting of CFU with Labline Colony Counter<br>2. Checkerboard DNA-DNA hybridization (40 species) | Anaerobic gram positive and gram negative bacteria | The results of this study showed that a mouthwash containing 0.075% CPC, 0.28% zinc lactate, and 0.05% sodium fluoride as a pre-procedure mouthwash was effective in reducing bacterial species present in oral aerosols. viable during prophylaxis with ultrasonic instruments  |
|                            |         |                                |               | water                           | 15                 |                |                            |   |   |  |  |
|                            |         |                                |               | 0.075% CPC + 0.28% Zn + 0.05% F | 15                 |                |                            |   |   |  |  |
|                            |         |                                |               | 0.12% CHX                       | 15                 |                |                            |   |   |  |  |
| Joshi et al. 2017          | India   | 40 (28/12)                     | 32.5          | 0.05% CPC 47°                   | 10                 | 1 hora         | Profilaxis con ultrasonido | 3 blood agar plates: 1 on the participant's chest, 1 on the dentist's chest, 1 on the assistant's chest         | Counting of CFU with Labline Colony Counter   | Bacteria   | The results clearly indicate that a pre-procedure mouthwash containing 0.05% CPC can be considered as a promising alternative to reduce aerosol contamination during ultrasonic scaling procedures compared to the gold standard of 0.2% chlorhexidine. %. Furthermore, the amount of viable bacteria in the aerosol is highest in the chest area of the patient followed by the operator and assistant in descending order. |
|                            |         |                                |               | 0.2% CHX 47°                    | 10                 |                |                            |   |   |  |  |
|                            |         |                                |               | 0.05% CPC 18°                   | 10                 |                |                            |   |   |  |  |
|                            |         |                                |               | 0.2% CHX 18°                    | 10                 |                |                            |   |   |  |  |
| Feres et al. 2010          | Brasil  | 60                             | (30-70)       | 0.05% CPC                       | 15                 | 1 hora         | Profilaxis con ultrasonido | 5 honokiol agar plates: 3 on the support board, 1 on the participant's chest, and 1 on the clinician's forehead | 1Anaerobic culture; counting of CFU with Labline Colony Counter<br>2. Checkerboard DNA-DNA hybridization (40 species) | Gram positive y gram negative bacteria             | Mouth rinses containing 0.05% CPC and 0.12% CHX are equally effective in reducing the levels of bacterial splash generated during ultrasonic scaling and their use could help decrease the level of microbial contamination in the dental office.  |
|                            |         |                                |               | 0.12% CHX                       | 15                 |                |                            |   |   |  |  |
|                            |         |                                |               | Agua                            | 15                 |                |                            |   |   |  |  |
|                            |         |                                |               | No mouthwash                    | 15                 |                |                            |   |   |  |  |

RCT: Randomized clinical trial, CPC: CetilpiridinioChloride, CHX: Clorhexidin, FCU: Forming Colony Units

Table 4. Reason for exclusion of scientific articles.

| Author  | Reason                     |
|---|----------------------------|
| <ul style="list-style-type: none"> <li>De Macedo Máximoa et al.</li> <li>Anderson et al.</li> </ul> | No treatment with aerosols |

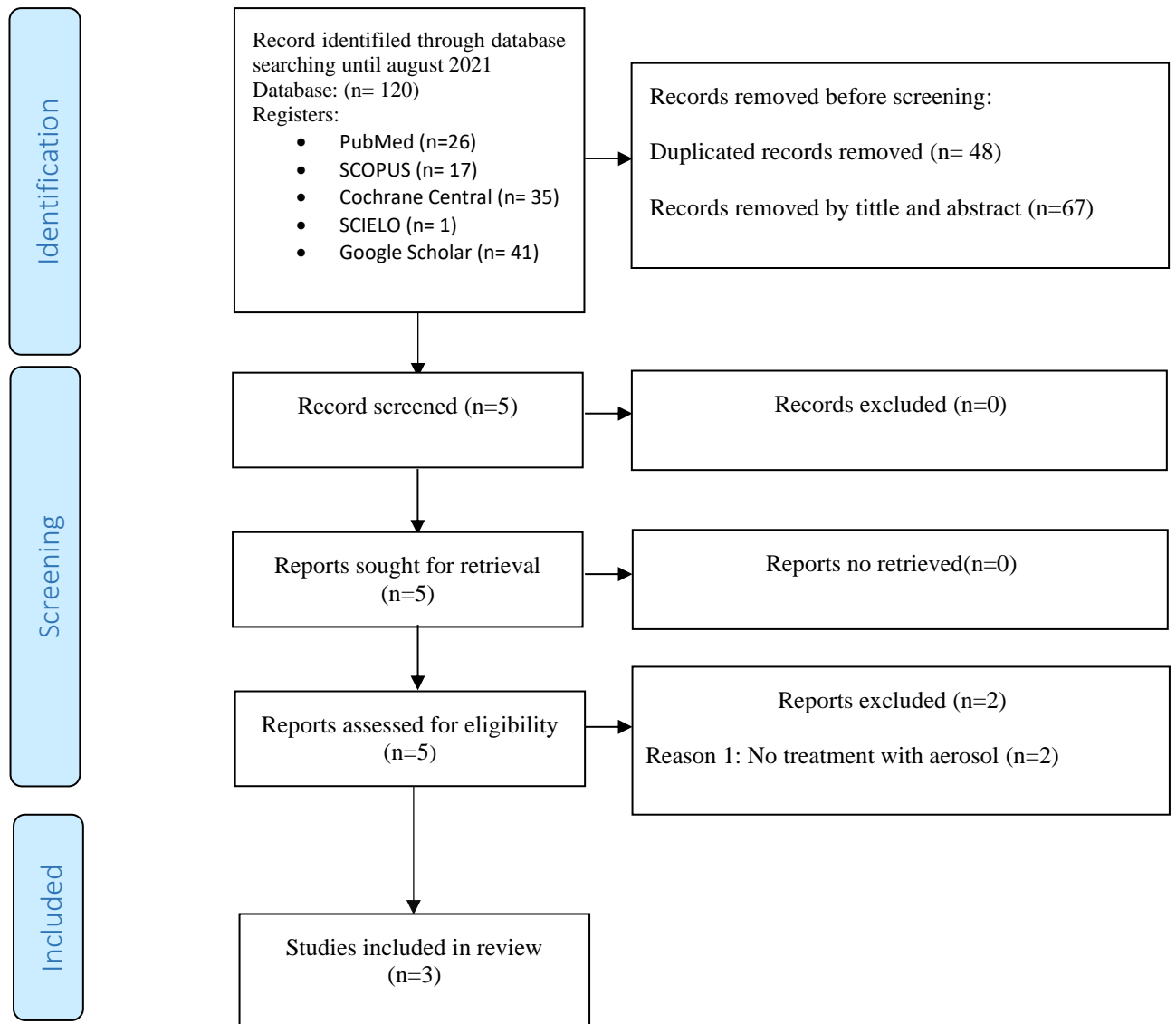


Figure 1. PRISMA diagram showing the inclusion and exclusion process of scientific articles found in the scientific search, for this Systematic Review

| Unique ID | Study ID         | Experimental | Comparator | Outcome | Weight | D1 | D2 | D3 | D4 | D5 | Overall |   |               |
|-----------|------------------|--------------|------------|---------|--------|----|----|----|----|----|---------|---|---------------|
| 1         | Retamal-Valdes e | CPC          | Placebo    | NA      | 1      | +  | +  | +  | +  | +  | +       | + | Low risk      |
| 2         | Joshi et al.     | CPC          | Placebo    | NA      | 1      | +  | +  | +  | +  | +  | +       | + | Some concerns |
| 3         | Feres et al.     | CPC          | Placebo    | NA      | 1      | +  | +  | +  | +  | +  | +       | + | High risk     |

|    |   |
|----|---|
| D1 | Randomisation process                     |
| D2 | Deviations from the intended intervention |
| D3 | Missing outcome data                      |
| D4 | Measurement of the outcome                |
| D5 | Selection of the reported result          |

Figure 2. Risk of Bias of the studies included in this research according to the Cochrane Rob 2.0 tool.

**COPIAS DE CARTAS COMO RESPUESTA A LAS OBSERVACIONES DE LOS  
REVISORES**

15 Marzo 2023, 17:28

paola arce toribio:

Gracias por enviar el manuscrito "EFICACIA ANTIMICROBIANA DEL USO DEL COLUTORIO CON CETILPIRIDINIO EN PROCEDIMIENTOS QUE GENERAN AEROSOL. REVISIÓN SISTEMÁTICA" a Odovtos International Journal of Dental Sciences. Con nuestro sistema de gestión de revistas en línea.

En caso de dudas, contacte conmigo. Gracias por elegir esta revista para publicar su trabajo.

Jessie Reyes Carmona

Dra. Jessie Reyes Carmona DDS, MSD, PhD Editor-in-chief Odovtos - International Journal of Dental Sciences

13 Marzo 2023, 9:57

Buenos días, el abstract y resumen no deben llevar subtítulos, además la contribución de los autores es como dice en la página web en inglés

Dra. Jessie Reyes Carmona DDS, MSD, PhD

Profesora Catedrática

Directora Odovtos - International Journal of Dental Sciences

Coordinadora LICIFO

Facultad de Odontología

Universidad de Costa Rica

11 Marzo 2023, 21:50

Estimada Directora Dra. Jessie Reyes Carmona, Revisor en Jefe de ODOVTOS:

A través de la presente remito el manuscrito "EFICACIA ANTIMICROBIANA DEL USO DEL COLUTORIO CON CETILPIRIDINIO EN PROCEDIMIENTOS QUE GENERAN AEROSOL. REVISIÓN SISTEMÁTICA" el cuál esperamos pueda ser publicado en la revista que usted dirige. Adjuntamos el manuscrito así como la carta de presentación de los autores.

A la vez, quisiera sugerir a dos potenciales revisoras, las cuales nombro a continuación:

1) MDs Saurav Panda.

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Sin otro particular, quedamos a la espera

Atentamente,

Jackeline Paola Arce Toribio

Especialista en Rehabilitación Oral

Estudiante de la Maestria en Estomatología de la Universidad Científica del Sur



07 Abril 2023, 20:00hrs

paola arce toribio:

We have reached a decision regarding your submission to Odovtos - International Journal of Dental Sciences, "ANTIMICROBIAL EFFICACY OF THE USE OF MOUTHWASH WITH CETYLPYRIDINIUM CHLORIDE FOR AEROSOL PRODUCING PROCEDURES. A SYSTEMATIC REVIEW":

Reviewer A:  
Recommendation: Revisions Required

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**Information contained:**

Completely original

**Title:**

Adequately informative

**Suggestions to Title:**

NA

**Structure of the manuscript Comments regarding the structure of the manuscript, abstract, keywords:**

NA

**Materials and Methods**

**Suggestions to materials and methods:**

NA

**Results:Tables and Illustrations:Suggestions to the results section, tables and illustrations :**

Considero necesario ampliar la información provista en la sección de resultados ya que no se menciona el método o los métodos utilizados para medir la eficacia antibacteriana de los enjuagues, así como la metodología utilizada para la recolección de las muestras. Al tratarse de la variable dependiente más importante es necesario ampliar sobre la variabilidad entre los estudios incluidos tanto de la recolección de las muestras como del análisis de los datos. La tabla 3 puede ser sintetizada para mejorar su presentación. Sugiero

trasladar la columna de año de publicación a la misma columna del autor. La columna de tipo de estudio se puede suprimir e indicar en el título de la tabla que todos los estudios fueron ECAs paralelos.

**Discussion and Conclusions:References:Suggestions Discussion, Conclusions and References :**

NA

**Overall scientific priority:**

Moderate

**Comments to Author:**

**Reviewer Recommendation Term:**

Article is suitable for publication prior major changes

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Dra. Jessie Reyes Carmona DDS, MSD, PhD Editor-in-chief Odovtos - International Journal of Dental Sciences

24 Abril 2023, 19:44hrs

Ya fue aceptado y enviado a arte, debes esperar el email con la copia

**Dra. Jessie Reyes Carmona DDS, MSD, PhD**

Profesora Catedrática  
 Directora Odovtos - International Journal of Dental Sciences  
 Coordinadora LICIFO  
 Facultad de Odontología  
 Universidad de Costa Rica

## INTRODUCCIÓN

Los enjuagues bucales son soluciones químicas, utilizadas para prevenir enfermedades y reducir los microorganismos en cavidad bucal (1-5). Se clasifican en enjuagues de tipo cosmético y terapéutico (6,7). Los cosméticos ofrecen un alivio temporal para la halitosis; mientras que los terapéuticos, contienen ingredientes activos, como el cloruro de Cetilpiridinio (CPC), fluoruros, Gluconato de clorhexidina (CHX) o aceites esenciales como eucaliptol, mentol, metil salicilato y/o timol, que reducen o controlan la placa dental, la gingivitis, el mal aliento y la caries dental (8,9).

El CPC es un compuesto de amonio cuaternario mono catiónico, tensioactivo anfótero (10,11), cargada positivamente, el cual se une a los microorganismos cargados negativamente, ejerciendo su actividad antimicrobiana por degradación de la bicapa lipídica de la célula y disrupción del metabolismo bacteriano; (12-14). Actualmente, el CPC ha recibido una etiqueta por la Federación Dental Americana como: Generalmente Considerado Seguro (GRAS) (15,16), demostrando tener un alto potencial antibacterial en concentraciones de 0.05% y de 0.07% o 0.5 y 0.7 mg/ml (17-22). También se ha descrito su actividad antiviral frente a infecciones respiratorias, virus del herpes y virus de la hepatitis B (23-27).

En procedimientos dentales que utilizan equipos generadores de aerosoles, como los raspadores ultrasónicos, piezas de mano de alta velocidad o jeringas triples, podrían provocar contaminaciones cruzadas en el consultorio dental por medio de aerosoles que contengan microorganismos (28-32), Ya que los aerosoles son partículas de menos de 50 micrómetros de diámetro que se mantienen flotando en el aire durante períodos prolongados de tiempo (33), arriesgando la salud de los pacientes y de los dentistas (34-37).

La afección por el Síndrome Respiratorio Agudo Severo Coronavirus 2 (SARS-CoV-2), ha afectado gravemente a las personas en un periodo de tiempo relativamente corto en los últimos años (38-40); por ello, tratando de prevenir la transmisión de estos microorganismos con saliva contaminada, se encontró información respecto al uso de enjuagues bucales capaces de reducir el riesgo de infección por esta enfermedad (12,18,29,38).

Por ese motivo, los dentistas y la población en general necesitan de investigaciones que recopilen la información adecuada sobre los beneficios de este colutorio con CPC frente a estos microorganismos, (41-44), por lo que la presente revisión sistemática tiene como objetivo determinar la eficacia antimicrobiana de los enjuagues bucales a base de CPC, previo a tratamientos dentales que generen aerosol.

## MATERIALES Y MÉTODOS

### **Protocolo y registro**

La presente revisión sistemática fue elaborada siguiendo la guía de Elementos de informes preferidos para revisiones sistemáticas y meta-análisis (PRISMA). Se registró en el área de “Dirección General de Investigación, Desarrollo e Innovación” de la Universidad Científica del Sur, obteniendo un número de registro para su desarrollo (N°222-2021-POS8). Además, se registró en el Registro Internacional Prospectivo de Revisiones Sistemáticas-PROSPERO (N° CRD42021275982)

### **Tipo de estudio y participantes**

Ensayos clínicos aleatorizados publicados hasta agosto 2021 sobre la eficacia antimicrobiana del uso de enjuagues bucales a base de cloruro de Cetilpiridinio, en pacientes que se hayan realizado algún procedimiento dental que generen aerosoles.

Para preparar y estructurar esta revisión, la pregunta focalizada fue elaborada usando el formato PICO (población, intervención, comparación y resultados) como se detalla a continuación:

- Población: Pacientes que han recibido algún tratamiento dental que genere aerosol.
- Intervención: Aplicación del colutorio a base de CPC previo al tratamiento dental
- Comparación: Placebo, agua, otros colutorios bucales o ningún colutorio previo al tratamiento dental
- Resultados: Disminución de microorganismos que se producen durante los tratamientos dentales que generan aerosoles.

### **Pregunta picos**

¿Los enjuagues bucales a base de CPC previo al tratamiento dental que genera aerosol presenta eficacia antimicrobiana?

### **Fuente de información y estrategia de búsqueda**

Se realizó una búsqueda bibliográfica en 5 bases de datos electrónicas: Pubme/Medline, Cochrane library, Scopus, Scielo y Google Scholar hasta agosto del 2021; combinando palabras clave y títulos de materias de acuerdo con el tesoro de cada base de datos: "anti-infective agents, local", "antiseptics", "cetylpyridinium", "cetylpyridinium chloride", "mouthwash", "mouthrinse", "prevention mouthrinse", "mouth rinse", "rinse", "contamination", "air contamination", "aerosol" (Tabla 1).

### **Criterios de selección**

Investigaciones que compararon el colutorio a base de cloruro de CPC con otro colutorio, placebo o agua, previo a un tratamiento dental que generó aerosol, en base a la estrategia de la pregunta PICOS (Tabla 2)

### **Criterios de inclusión**

Ensayos clínicos aleatorizados en los idiomas de español, inglés o portugués y sin límite de tiempo, hasta agosto del 2021.

### **Criterios de exclusión**

Reportes de caso, serie de casos, estudios preclínicos, revisiones sistemáticas, estudios piloto, literatura gris, cartas al editor y revisiones de la literatura, estudios en proceso de ejecución y/o que no han sido publicados. Publicaciones en idiomas distintos al español, inglés o portugués.

### **Selección de los estudios**

Las búsquedas de los artículos en las bases de datos electrónicas fueron realizadas por dos investigadoras (JPAT) y (ALF) de forma independiente, las cuales, inicialmente estaban cegados para dar sus resultados por separado. Los desacuerdos se resolvieron mediante la discusión con un tercer revisor (HIAV). Luego de la comparación de los mismos, se leyeron los títulos y resúmenes, en donde se descartaron los artículos que no son relevantes y/o aquellos que no llegaron a cumplir con los criterios de elegibilidad. Segundo, se realizó un análisis de todo el artículo científico por completo, extrayendo de forma independiente la información necesitada. Dichos datos fueron comparados para lograr una exactitud y evitar cualquier diferencia en la presente revisión.

### **Recopilación de los datos**

Durante el proceso de recolección de datos se utilizó una tabla pre definida para recolectar los datos de cada estudio elegido (Tabla 3) incluyendo: autor-año, país, numero de pacientes, edad, grupo de estudio, paciente por grupo, tiempo de seguimiento, tipo de procedimiento, método de recolección, análisis microbiológico, tipo de microorganismo, conclusiones- Los datos de cada estudio se colocaron y analizaron en una hoja de Excel para su análisis cualitativo. Finalmente, Estos datos fueron registrados en un diagrama pre establecido, de acuerdo a la DECLARACION PRISMA (Gráfico 1).

### **Riesgo de sesgo**

Se realizó siguiendo el manual de Cochrane Library, logrando identificar el tipo de riesgo en los estudios. Se utilizó la herramienta de RoB 2.0 para conocer el riesgo de sesgo existente de los ensayos clínicos aleatorizados (Imagen I). Según esta herramienta, los ensayos clínicos se evaluaron en cinco dominios, para luego ser clasificados como: bajo, algunas preocupaciones o alto riesgo de sesgo. El estudio incluido fue evaluado de forma independiente por dos autores calibrados (JPAT y ALF) utilizando como herramienta el RoB 2.0 y todos los desacuerdos se resolvieron mediante discusión con un tercer revisor (HIAV).

## **RESULTADOS**

La estrategia de búsqueda electrónica y manual arrojó un total de 120 artículos, excluyéndose 48 artículos duplicados y 67 artículos eliminados por título y resumen, quedando seleccionados 5 artículos. Posterior a ello, se excluyó 2 artículos que no cumplieron con los criterios de elegibilidad, lo que resultó en 3 artículos de ensayos

clínicos aleatorizados que se incluyeron para la síntesis cualitativa (Gráfico 1). La razón de exclusión de los artículos se muestra en la Tabla 4.

### **Características de los estudios incluidos**

En general, se incluyeron 3 estudios, de los cuales todos eran ECAs paralelos y los años de publicación oscilaron entre el 2010 y 2017. Los países en donde se realizaron los estudios fueron: Brasil e India. El total de participantes osciló entre 40 y 60 con un rango de edad de 18 a 70 años (Tabla 3).

En todos los estudios se tuvo como grupo experimental el uso de CPC (en diferentes concentraciones y/o con otros componentes) y como grupo control a la clorhexidina, el agua y el no uso de un colutorio previo al tratamiento con aerosol. El tiempo de seguimiento osciló de entre 1 a 72 horas. Todos los estudios describieron como procedimiento con aerosol a la profilaxis con ultrasonido y los microorganismos analizados fueron las bacterias tanto gram positivas como negativas. Todos los estudios concluyeron el uso de CPC es efectivo en la reducción de bacterias durante el procedimiento de profilaxis con ultrasonido, sin embargo, uno de los estudios menciona que el CPC es mejor que la CHX y en otro menciona que ambos son igualmente efectivos (Tabla 3).

En todos los estudios, las muestras microbiológicas fueron recolectadas utilizaron placas de Agar Sangre o Honokiol, los cuales fueron colocados en diferentes lugares y distancias como en el pecho del paciente, pecho del odontólogo, pecho del asistente, frente del odontólogo o en el tablero de soporte.

Con respecto al análisis microbiológico, Los resultados fueron expresados en relación a la reducción en el número de unidades formadoras de colonias (UFC) en los lugares de



recolección de aerosol donde se encontraban las placas de Agar. En todos los estudios, el método utilizado fue la contabilización del número total de UFC mediante Labline (32,36,37); sólo en dos estudios, se utilizó un segundo método para el análisis microbiológico, que fue mediante el uso de la técnica de Hibridización de tablero de ajedrez ADN-ARN (36,37).

### **Análisis del riesgo de sesgo**

Se consideró tres estudios, los cuales tenían bajo riesgo de sesgo. (Gráfico 2)

### **Análisis de los resultados**

Los datos de cada estudio se colocaron y analizaron en una hoja de Excel para su análisis cualitativo (Tabla 3).

## DISCUSIÓN

Durante la atención al paciente, existen diversos tratamientos dentales que utilizan equipos generadores de aerosol como es el caso de la pieza de mano, la jeringa triple o el ultrasonido. Estos aerosoles podrían transportar los microorganismos que existen en la boca del paciente, como virus o bacterias (38,39), los cuales conllevaría a una atmósfera contaminada o una posible contaminación cruzada en el consultorio dental (45). Es sabido que estas partículas de aerosol pueden permanecer flotando en el ambiente hasta por 4 horas después de un procedimiento dental (46), produciendo un riesgo para el odontólogo y el paciente por la posible contaminación de las vías respiratorias por estos microorganismos, incluso después de la finalización de la cita (47).

Para minimizar las infecciones cruzadas en el consultorio dental, se describieron en la literatura diferentes métodos, como el uso de enjuagues bucales previo al tratamiento

dental (10,27,36), cuya finalidad es disminuir la cantidad de microorganismos en la cavidad bucal. Estos enjuagues bucales pueden presentar diferentes componentes, como es el caso del Cloruro de Cetilpiridinio (1,2,8,31), el cual ha sido ampliamente mencionado en los últimos años en diferentes publicaciones [4,10], indicando tener una gran capacidad antimicrobiana frente a virus (25-28,46) y bacterias (11,12,17,34), según lo revisado en la literatura.

De acuerdo a los resultados obtenidos en la presente investigación, todos concluyeron que el uso de CPC es efectivo en la reducción de bacterias durante el procedimiento dental, profilaxis con ultrasonido, que generan aerosol; cuando es comparado con agua o con sin colutorio; sin embargo, no se encontró diferencia significativa en la reducción de la unidad formadora de colonias (UFC) cuando se comparó con la CHX, indicando que los enjuagues bucales a base de CPC son igualmente efectivos a los enjuagues bucales que contienen CHX (32,36-37). Esto podría deberse a que ambos son enjuagues bucales son antibacterianos de amplio espectro y presentan el mismo mecanismo de acción, degradando la membrana bacteriana y produciendo la lisis celular del microorganismo (7,11).

Joshi et al (32). Informaron que la actividad antimicrobiana del CPC fue mayor cuando se utiliza a 47°C, manteniendo la máxima reducción de recuento bacteriano en todas las áreas analizadas, en comparación al uso del CPC a 18°C. Esto puede deberse a que existiría una mayor actividad bactericida del CPC a temperaturas elevadas; ya que al aumentar la temperatura, aumenta la velocidad en que las reacciones químicas tienen lugar, conocido como Tratamiento Termodinámico (48)

Así mismo, se observa que, la eficacia antimicrobiana logrado por los enjuagues de CPC, sólo es limitado a un tipo de microorganismos de tipo bacteriano (36, 37), mas no se encontró información sobre los microorganismos de tipo viral. Esto puede deberse a que las bacterias (6, 17) son capaces de cultivarse y crecer en placas de agar sangre, los mismos medios de cultivo utilizado en las tres investigaciones, mientras que los virus requieren un medio especializado para su crecimiento (26); es por ello que se sugiere realizar futuras investigaciones incluyendo estos tipos de microorganismos.

Según el análisis de composición bacteriana (36-37), mostró proporciones estadísticamente más bajas para patógenos del complejo naranja cuando se comparó el CPC con sujetos que no recibieron colutorio o en aquellos que sólo se enjuagaron con agua. Esto es un efecto beneficioso, ya que ciertas especies del complejo naranja, como los fusobacteriums, pueden ser causantes de etiologías respiratorias u oftálmicas [49, 50], lo que conllevaría a la posible disminución de enfermedades cruzadas en el consultorio dental, siempre y cuando se utilice el colutorio de CPC previo algún procedimiento odontológico que genere aerosoles.

Retamal-Valdes *et al* (37). Indico que el uso de CPC fue efectivo para disminuir bacterias que se encuentran en los aerosoles dentales, pero cabe resaltar que, en dicho estudio, el CPC fue utilizado con otros componentes adicionales, como es el caso del lactato de zinc y el fluoruro de sodio, por lo que no se podría concluir si su acción antibacterial es gracias al CPC o a sus otros componentes anteriormente mencionados.

La principal limitación del presente estudio fue que sólo se encontró resultados para un solo procedimiento dental, profilaxis con ultrasonido, el cual ha demostrado tener un gran

potencial para la generación de aerosoles en el consultorio dental (38). Por lo tanto, se podría suponer que el colutorio con CPC, previo a tratamientos dentales que generen aerosoles, también produciría beneficios similares para el odontólogo y el paciente, si es utilizado con otros equipos que también generen aerosol, como es el caso de la pieza de mano o la jeringa triple.

Finalmente, cabe mencionar que este es el primer estudio que revisó de manera sistemática la eficacia antimicrobiana del enjuague bucal a base de Cloruro de Cetilpiridinio en la reducción de microorganismos previo a algún tratamiento que genere aerosol, no encontrándose suficiente información con respecto a este producto en relación a enjuagues bucales y aerosoles; por lo que los resultados de nuestra presente investigación deben ser evaluados con cautela. A pesar de demostrar que existe una disminución en la cantidad de microorganismos, se desconoce la influencia de esta disminución en la tasa de infección hacia los profesionales de la salud, por lo que no existe evidencia directa que indique que el enjuague bucal a base de cloruro de cetilpiridinio pueda disminuir la tasa de infección clínica en el área odontológica.

## CONCLUSIONES

El uso de los enjuagues bucales a base de CPC previo al tratamiento dental de profilaxis con ultrasonido sólo tiene eficacia antibacteriana.

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# ANEXOS

## TABLAS Y GRÁFICOS

Tabla 1. Estrategia de búsqueda según base de datos

| Base de datos    | Estrategia de búsqueda   |
|------------------|--|
| Pubmed/Medline   | ((("anti-infective agents, local") OR "antiseptics") OR "cetylpyridinium") OR "cetylpyridinium chloride") AND (((("mouthwash") OR "mouthrinse") OR "prevention mouthrinse") OR "mouth rinse") OR "rinse") AND (((("contamination") OR "air contamination") OR "aerosol")   |
| Scopus           | ( TITLE-ABS-KEY ( "anti-infective agents, local" ) OR TITLE-ABS-KEY ( "antiseptics" ) OR TITLE-ABS-KEY ( "cetylpyridinium" ) OR TITLE-ABS-KEY ( "cetylpyridinium chloride" ) ) AND ( TITLE-ABS-KEY ( "mouthwash" ) OR TITLE-ABS-KEY ( "mouthrinse" ) OR TITLE-ABS-KEY ( "prevention mouthrinse" ) OR TITLE-ABS-KEY ( "mouth rinse" ) OR TITLE-ABS-KEY ( "rinse" ) ) AND ( TITLE-ABS-KEY ( "contamination" ) OR TITLE-ABS-KEY ( "air contamination" ) OR TITLE-ABS-KEY ( "aerosol" ) OR TITLE-ABS-KEY ( "aerosols" ) ) AND ( TITLE-ABS-KEY ( "clinical trial" ) ) AND ( LIMIT-TO ( SRCTYPE , "j" ) ) AND ( LIMIT-TO ( DOCTYPE , "ar" ) ) AND ( LIMIT-TO ( SUBJAREA , "DENT" ) ) AND ( LIMIT-TO ( EXACTKEYWORD , "Human" ) ) |
| Scielo           | (((((("anti-infective agents, local") OR "antiseptics") OR "cetylpyridinium") OR "cetylpyridinium chloride")) AND (((("mouthwash") OR "mouthrinse") OR "prevention mouthrinse") OR "mouth rinse") OR "rinse") AND (((("contamination") OR "air contamination") OR aerosol) OR aerosols))   |
| Google Scholar   | cetylpyridinium + "mouthwash" + "aerosol" + "clinical trial" -"systematic review"  |
| Cochrane Library | #1 MeSH descriptor: [Anti-Infective Agents, Local] explode all trees<br>#2 MeSH descriptor: [Cetylpyridinium] explode all trees<br>#3 ("antiseptics") OR ("cetylpyridinium") OR ("cetylpyridinium chloride") AND ("anti-infective agents, local") (Word variations have been searched)<br>#4 #1 OR #2 OR #3<br>#5 MeSH descriptor: [Mouthwashes] explode all trees<br>#6 ("mouthwash") OR ("mouthrinse") OR ("prevention mouthrinse") OR ("mouth rinse") OR ("rinse") (Word variations have been searched)<br>#7 #5 OR #6<br>#8 ("contamination") OR ("air contamination") OR ("aerosol") OR ("aerosols")<br>#9 MeSH descriptor: [Aerosols] explode all trees<br>#10 #8 OR #9<br>#11 #4 AND #7 AND #10                     |

Tabla 2. pregunta PICOS

| COMPONENTE            | DESCRIPCION   |
|-----------------------|---|
| P: Paciente/ Problema | Pacientes que han recibido algún tratamiento dental que genere aerosol.                                 |
| I: Intervención       | Aplicación del colutorio a base de cloruro de Cetilpiridinio (CPC) previo al tratamiento dental.        |
| C: Comparación        | Placebo, agua, otro colutorio previo al tratamiento dental.   |
| O: Outcome            | Disminución de microorganismos que se producen durante los tratamientos dentales que generan aerosoles. |
| S: Study              | Ensayos clínicos  |

Tabla 3. Característica de los ECAs Paralelos incluidos

| Autor/<br>Año                        | País   | Total<br>paciente<br>(H/M) | Edad<br>(rango)  | Grupos                                | Pacientes<br>por grupo | Tiempo de<br>seguimiento | Tipo de<br>procedimiento      | Método de<br>recoleccion  | Análisis<br>microbiano   | Tipo de<br>microorganismo                             | Conclusiones   |
|--------------------------------------|--------|----------------------------|------------------|---------------------------------------|------------------------|--------------------------|-------------------------------|---|--|---|--|
| Retamal-<br>Valdes et<br>al.<br>2017 | Brasil | 60<br>(24/36)              | 42.32<br>(18-70) | No enjuague                           | 15                     | 72 horas                 | Profilaxis con<br>ultrasonido | Cinco (05)<br>placas de agar<br>Honokiol: 3 en<br>tablero de<br>soporte, 1 en<br>pecho de<br>participante, 1<br>en l frente del<br>odontologo | 1.UFC<br>contabilizado con<br>Labline.<br><br>2.Tecnica de<br>Hibridización<br>Checkerboard<br>ADN-ARN | Bacterias anaerobias<br>gram positivas y<br>negativas | Los resultados de este estudio mostraron<br>que un colutorio que contenía 0,075 % de<br>CPC, 0,28 % de lactato de zinc y 0,05 % de<br>fluoruro de sodio como colutorio previo al<br>procedimiento fue efectivo para reducir las<br>especies bacterianas presentes en los<br>aerosoles orales viables durante la profilaxis<br>con instrumentos ultrasónicos.   |
|                                      |        |                            |                  | Agua                                  | 15                     |                          |                               |   |  |   |  |
|                                      |        |                            |                  | 0.075% CPC +<br>0.28% Zn +<br>0.05% F | 15                     |                          |                               |   |  |   |  |
|                                      |        |                            |                  | 0.12% CHX                             | 15                     |                          |                               |   |  |   |  |
| Joshi et al.<br>2017                 | India  | 40<br>(28/12)              | 32.5             | 0.05% CPC 47°                         | 10                     | 1 hora                   | Profilaxis con<br>ultrasonido | Tres (03) placas<br>de agar sangre:<br>1 en el pecho<br>del asistente, 1<br>en el pecho del<br>odontólogo, 1<br>en el pecho del<br>paciente   | UFC analizadas<br>por un<br>contabilizador de<br>colonias (Lab<br>line Stock Center)                   | Bacterias   | Los resultados indican claramente que un<br>colutorio previo al procedimiento que<br>contiene 0,05 % de CPC se puede<br>considerar como una alternativa<br>prometedora para reducir la contaminación<br>por aerosoles durante los procedimientos de<br>detartraje ultrasónico en comparación con el<br>estándar de oro de clorhexidina al 0,2 %.<br>Además, la cantidad de bacterias viables en<br>el aerosol es máxima en la zona del tórax<br>del paciente seguido por el operador y el<br>asistente en forma descendente. |
|                                      |        |                            |                  | 0.2% CHX 47°                          | 10                     |                          |                               |   |  |   |  |
|                                      |        |                            |                  | 0.05% CPC 18°                         | 10                     |                          |                               |   |  |   |  |
|                                      |        |                            |                  | 0.2% CHX 18°                          | 10                     |                          |                               |   |  |   |  |
| Feres et<br>al.<br>2010              | Brasil | 60                         | (30-70)          | 0.05% CPC                             | 15                     | 1 hora                   | Profilaxis con<br>ultrasonido | Cinco (05)<br>placas de agar<br>Honokiol: 3 en<br>tablero de<br>soporte, 1 en<br>pecho de<br>participante, 1<br>en l frente del<br>odontologo | 1.UFC<br>contabilizado con<br>Labline.<br><br>2.Tecnica de<br>Hibridización<br>Checkerboard<br>ADN-ARN | Bacterias gram<br>positivas y negativas               | Los enjuagues bucales que contienen 0.05<br>% de CPC y 0.12 % de CHX son<br>igualmente efectivos para reducir los<br>niveles de salpicaduras de bacterias<br>generadas durante el raspado ultrasónico y<br>su uso podría ayudar a disminuir el nivel de<br>contaminación microbiana en el consultorio<br>dental.   |
|                                      |        |                            |                  | 0.12% CHX                             | 15                     |                          |                               |   |  |   |  |
|                                      |        |                            |                  | Agua                                  | 15                     |                          |                               |   |  |   |  |
|                                      |        |                            |                  | No enjuague                           | 15                     |                          |                               |   |  |   |  |

ECA: Ensayo clínico aleatorizado, CPC: Cloruro de Cetilpiridinio, CHX: Clorhexidina, UFC: Unidad formadora de colonias

Tabla 4. Razón de exclusión de los artículos científicos.

| Autores   | Razón de exclusión                          |
|---|---|
| <ul style="list-style-type: none"> <li>• De Macedo Máximoa et al.</li> <li>• Anderson et al.</li> </ul> | No se realizaron tratamientos con aerosoles |

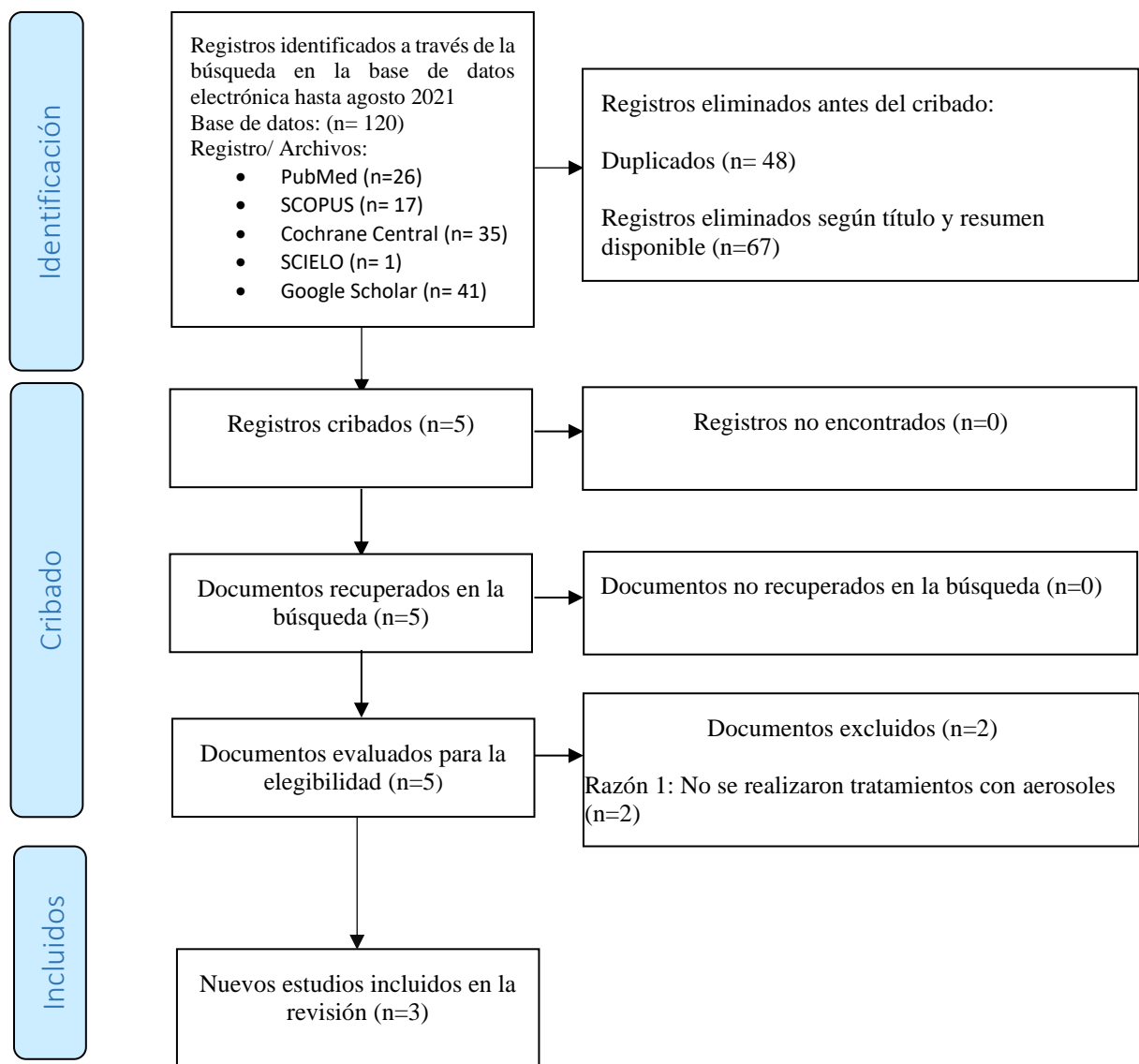


Gráfico 1. Diagrama PRISMA mostrando el proceso de inclusión y exclusión de los artículos científicos encontrados en la búsqueda científica, para la presente Revisión Sistemática.

| Unique ID | Study ID         | Experimental | Comparator | Outcome | Weight | D1 | D2 | D3 | D4 | D5 | Overall |
|-----------|------------------|--------------|------------|---------|--------|----|----|----|----|----|---------|
| 1         | Retamal-Valdes e | CPC          | Placebo    | NA      | 1      | +  | +  | +  | +  | +  | +       |
| 2         | Joshi et al.     | CPC          | Placebo    | NA      | 1      | +  | +  | +  | +  | +  | +       |
| 3         | Feres et al.     | CPC          | Placebo    | NA      | 1      | +  | +  | +  | +  | +  | +       |

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|---|---------------|
| + | Low risk      |
| ! | Some concerns |
| - | High risk     |

|    |  |
|----|--|
| D1 | Randomisation process                      |
| D2 | Deviations from the intended interventions |
| D3 | Missing outcome data                       |
| D4 | Measurement of the outcome                 |
| D5 | Selection of the reported result           |

Gráfico 2. Riesgo de Sesgo de los estudios incluidos en la presente investigación según herramienta Cochrane Rob 2.0.





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## LITERATURE REVIEW

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Antimicrobial Efficacy of the Use of Mouthwash with Cetylpyridinium Chloride for Aerosol Producing Procedures. A Systematic Review

Título en  
español

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**ABSTRACT:** The present research aims to determine the antimicrobial efficacy of the mouthwashes based on cetylpyridinium chloride (CPC), before aerosol producing dental procedures. A data search was performed during August 2021 in five databases MEDLINE (PubMed), SCOPUS, SCIELO, Cochrane Central Register of Controlled Trials (CENTRAL) and Google Scholar. Randomized clinical trials (RCTs) were included based on the PICO question, comparing the efficacy of the mouthwashes based on cetylpyridinium chloride (CPC), versus other mouthwashes and water, before aerosol producing dental procedures, papers in English, Spanish and Portuguese were included without time limits. The risk of the included studies was evaluated with the tool RoB 2.0. Number of registration PROSPERO N° CRD42021275982. 120 papers were obtained in the preliminary search, discarding those that didn't comply with the selection criteria, leaving only 3 studies. These papers reported the use of cetylpyridinium chloride (CPC) was effective for the reduction of bacteria during the ultrasonic prophylactic procedure. The use of CPC mouthwashes previous to the dental treatment with ultrasonic prophylaxis showed only antibacterial capacity.

**KEYWORDS:** Mouthwash; Rinse; Cetylpyridinium; Aerosol; Antiseptics; Contaminated air.

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**RESUMEN:** El presente trabajo de investigación tiene como objetivo determinar la eficacia antimicrobiana de los colutorios a base de cloruro de Cetilpiridinio (CPC), previo a tratamientos dentales que generen aerosol. Se realizó una búsqueda bibliográfica hasta agosto del 2021 en cinco bases de datos: MEDLINE (vía PubMed), SCOPUS, SCIELO, Cochrane Central Register of Controlled Trials (CENTRAL) y Google Scholar. Se incluyeron ensayos clínicos aleatorizados (ECAs), basándose en la pregunta PICOS, que compare la eficacia del colutorio a base de cloruro de Cetilpiridinio (CPC) con otro colutorio, placebo o agua, previo a un tratamiento dental que genere aerosol, en los idiomas español, inglés o portugués y sin límite de tiempo. El riesgo de los estudios incluidos se evaluó con la herramienta RoB 2.0. Número de registro PROSPERO N° CRD42021275982. Se obtuvo un total de 120 artículos en la búsqueda preliminar, descartando aquellos que no cumplieran con los criterios de selección, quedando sólo 3 artículos. Estos artículos informaron que el uso de CPC es efectivo para la reducción de bacterias durante el procedimiento de profilaxis con ultrasonido. El uso de los enjuagues bucales a base de CPC previo al tratamiento dental de profilaxis con ultrasonido sólo tiene eficacia antibacteriana.

**PALABRAS CLAVE:** Colutorio; Enjuagar; Cetilpiridinio; Aerosol; Antisépticos; Aire contaminado.

## INTRODUCTION

Mouthwashes are chemical solutions that prevent diseases and reduce microorganisms in the oral cavity (1-5). They are classified into cosmetic and therapeutic mouthwashes (6-7). Cosmetic mouthwashes offer temporary relief for halitosis. The therapeutic mouthwashes contain active ingredients, such as Cetylpyridinium Chloride (CPC), fluorides, Chlorhexidine Gluconate (CHX) or essential oils such as eucalyptol, menthol, methyl salicylate and/or thymol, that reduce or control dental plaque, gingivitis, halitosis and dental cavities (8,9).

Cetylpyridinium chloride (CPC) is a monocationic quaternary ammonium compound, amphoteric surfactant (10-11), positively charged, which binds to negatively charged microorganisms, it exerts its antimicrobial activity by degradation of the lipid bilayer of the cell and the disruption of bacterial metabolism (12-14). Currently, CPC has received a label from the FDA of Generally

Regarded as Safe (GRAS) (15-16), demonstrating high antibacterial potential at concentrations of 0.05% and 0.07% or 0.5 and 0.7 mg/ml (17-22). Its antiviral activity against respiratory infections, herpes virus and hepatitis B virus has also been described (23-27).

In dental procedures that use aerosol-generating equipment, such as ultrasonic scalers, high-speed handpieces or triple syringes, this equipment could cause cross-contamination in the dental office through aerosols containing microorganisms (28-32), since aerosols are particles of less than 50 micrometers in diameter that remain floating in the air for prolonged periods (33), risking the health of patients and dentists (34-37).

The condition caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has seriously affected people in a short period in recent years (38-40); Therefore, to prevent the transmission of these microorganisms with contaminated saliva, information showing mouthwashes

can reduce the risk of infection of this disease was found (12,18,29,38).

For this reason, dentists and the general population both need research data that provides adequate information on the benefits of this mouthwash with CPC against these microorganisms, (41-44). The objective of this systematic review is to determine the Antimicrobial efficacy of CPC-based mouthwashes prior to aerosol-generating dental treatments.

## METHODOLOGY

### PROTOCOL AND REGISTRATION

This systematic review was prepared following the TRANSPARENT REPORTING of SYSTEMATIC REVIEWS and META-ANALYSIS (PRISMA). It was registered in PROSPERO: A registry for systematic review protocols (N° CRD42021275982).

### TYPE OF STUDY AND PARTICIPANTS

Randomized clinical trials published until August 2021 on the antimicrobial efficacy of the use of CPC-based mouthwashes in patients who have undergone aerosol-producing dental procedures.

To prepare and structure this review, the question was formulated using the PICO format (population, intervention, comparison and results) as detailed below: a) population: patients who have received any dental treatment that generates aerosol.

b) intervention: application of CPC mouthwash prior to the dental treatment. c) comparison: placebo, water, other mouthwashes or no mouthwash before dental treatment. d) results: reduction of microorganisms that are produced during dental treatments that generate aerosols.

### PICO'S QUESTION

Do CPC-based mouthrinses prior to aerosol-generating dental treatment have antimicrobial efficacy?

### SOURCE OF INFORMATION AND SEARCH STRATEGY

A bibliographic search was carried out in 5 electronic databases: Pubme/Medline, Cochrane library, Scopus, Scielo and Google Scholar until August 2021; combining the keywords and titles according to the thesaurus of each database: "anti-infective agents, local", "antiseptics", "cetylpyridinium", "cetylpyridinium chloride", "mouthwash", "mouthrinse", "prevention mouthrinse", "mouthrinse", "rinse", "contamination", "air contamination", "aerosol". The literature search strategy is available in Supplemental material (Table 1).

### SELECTION CRITERIA

Studies comparing CPC mouthwash with another mouthwash, placebo or water, prior to aerosol-generating dental treatment, based on the PICOS question strategy (Table 2).

**Table 1.** Search strategy according to database.

| Database         | Search Strategy   |
|------------------|---|
| Pubmed/Medline   | ((("anti-infective agents, local") OR "antiseptics") OR "cetylpyridinium") OR "cetylpyridinium chloride") AND (((("mouthwash") OR "mouthrinse") OR "prevention mouthrinse") OR "mouth rinse") OR "rinse") AND (((("contamination") OR "air contamination") OR "aerosol").   |
| Scopus           | (TITLE-ABS-KEY ("anti-infective agents, local") OR TITLE-ABS-KEY ("antiseptics") OR TITLE-ABS-KEY ("cetylpyridinium") OR TITLE-ABS-KEY ("cetylpyridinium chloride")) AND (TITLE-ABS-KEY ("mouthwash") OR TITLE-ABS-KEY ("mouthrinse") OR TITLE-ABS-KEY ("prevention mouthrinse") OR TITLE-ABS-KEY ("mouth rinse") OR TITLE-ABS-KEY ("rinse")) AND (TITLE-ABS-KEY ("contamination") OR TITLE-ABS-KEY ("air contamination") OR TITLE-ABS-KEY ("aerosol") OR TITLE-ABS-KEY ("aerosols")) AND (LIMIT-TO (SRCTYPE , "r")) AND (LIMIT-TO (DOCTYPE , "ar")) AND (LIMIT-TO (SUBJAREA , "DENT")) AND (LIMIT-TO (EXACTKEYWORD , "Human")).  |
| Scielo           | ((("anti-infective agents, local") OR "antiseptics") OR "cetylpyridinium") OR "cetylpyridinium chloride") AND (((("mouthwash") OR "mouthrinse") OR "prevention mouthrinse") OR "mouth rinse") OR "rinse") AND (((("contamination") OR "air contamination") OR aerosol) OR aerosols)).   |
| Google Scholar   | cetylpyridinium + "mouthwash" + "aerosol" + "clinical trial" -"systematic review".  |
| Cochrane Library | #1 MeSH descriptor: [Anti-Infective Agents, Local] explode all trees.<br>#2 MeSH descriptor: [Cetylpyridinium] explode all trees.<br>#3 ("antiseptics") OR ("cetylpyridinium") OR ("cetylpyridinium chloride") AND ("anti-infective agents, local") (Word variations have been searched).<br>#4 #1 OR #2 OR #3.<br>#5 MeSH descriptor: [Mouthwashes] explode all trees.<br>#6 ("mouthwash") OR ("mouthrinse") OR ("prevention mouthrinse") OR ("mouth rinse") OR ("rinse") (Word variations have been searched).<br>#7 #5 OR #6.<br>#8 ("contamination") OR ("air contamination") OR ("aerosol") OR ("aerosols").<br>#9 MeSH descriptor: [Aerosols] explode all trees.<br>#10 #8 OR #9.<br>#11 #4 AND #7 AND #10. |

**Table 2.** PICO's question table.

| Component       | Description  |
|-----------------|--|
| P: Problem      | People who have received any dental treatment that generates aerosol.                                    |
| I: Intervention | Application of the Cetylpyridinium Chloride (CPC)-based mouthwash prior to dental treatment.             |
| C: Comparison   | Placebo, water, other mouthwash prior to dental treatment.   |
| O: Outcome      | Reduction of number of microorganisms that are produced during dental treatments that generate aerosols. |
| S: Study        | Randomized clinical trials.  |

#### INCLUSION CRITERIA

The inclusion criteria of the articles were: a) randomized clinical trials; b) languages: Spanish, English or Portuguese; c) without time limit, until August 2021.

#### EXCLUSION CRITERIA

The exclusion criteria of the articles were: a) case reports; b) case series; c) preclinical studies; d) systematic reviews; e) pilot studies; f) gray literature; g) letters to the editor; h) literature reviews; i) ongoing and/or unpublished studies; j) publications in languages other than Spanish, English or Portuguese.

#### ARTICLE SEARCHERS

Article searches of electronic databases were performed independently by two investigators (JPAT) and (AILF), who were initially blinded to report their results separately. Disagreements were resolved by discussion with a third reviewer (HIAV). After comparing them, the titles and abstracts were read, discarding articles that are not relevant and/or those that did not meet the eligibility criteria. Second, an analysis of the entire scientific article was carried out, independently extracting the necessary information. These

data were compared for accuracy and to avoid any differences in the present review.

#### DATA COLLECTION

During the data collection process, a predefined table was used to collect data from each chosen study (Tablet 3) including author-year, country, total number of patients, age (range), study groups, patients by group, follow-up time, type of procedure, collection method, microbial analysis, type of microorganisms, conclusions. Data from each study was entered and analyzed into an Excel sheet for qualitative analysis. Finally, these data were recorded in a pre-established diagram, according to the PRISMA DECLARATION (Figure 1).

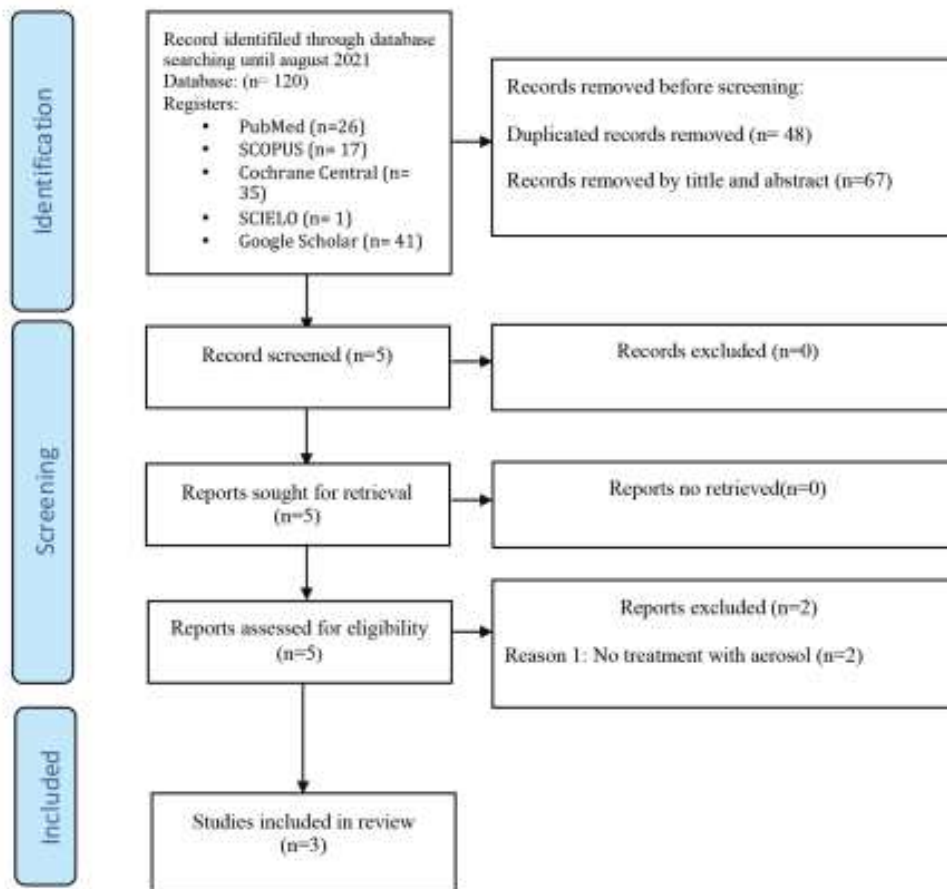
#### RISK OF BIAS

The data search was carried out following the Cochrane Library guidelines, managing to identify the type of risk in the studies. The RoB 2.0 was used to determine the risk of bias in randomized clinical trials (Figure 2). Clinical trials were assessed across five domains, then classified as: low, some concern, or high risk of bias. Included studies were independently assessed by two calibrated authors (JPAT and AILF) using RoB 2.0. Ultimately, all disagreements were resolved by discussion with a third reviewer (HIAV).

**Table 3.** Characteristics of the Parallel RCTs included.

| Author/ year               | Country | Total number of patients (N/M) | Age (range)   | Study Groups   | Patients by groups   | Follow-up time | Type of procedure       | Collection method   | Microbial analysis  | Type of microorganism                              | Conclusions   |
|----------------------------|---------|--------------------------------|---------------|--|----------------------|----------------|-------------------------|---|---|--|---|
| Retamal-Valdés et al. 2017 | Brazil  | 60 (24/36)                     | 42.32 (18-70) | No mouthwash<br>water<br>0.075% CPC<br>+ 0.28% Zn <sup>++</sup><br>0.05% F <sup>-</sup><br>0.12% CHX | 15<br>15<br>15<br>15 | 72 hours       | Proflaxis on ultrasonic | 5 inoculated agar plates: 3 on the support board, 1 on the participant's chest, and 1 on the clinician's forehead | 1. Anaerobic culture, counting of CFU with LabLine Colony Counter<br>2. Checkerboard DNA-DNA hybridization (40 species) | Anaerobic gram positive and gram negative bacteria | The results of this study showed that a mouthwash containing 0.075% CPC, 0.28% zinc lactate, and 0.05% sodium fluoride as a pre-procedure mouthwash was effective in reducing bacterial species present in oral aerosols viable during prophylaxis with ultrasonic instruments.   |
| Joshi et al. 2017          | India   | 40 (28/12)                     | 32.6          | 0.05% CPC 47"<br>0.2% CHX 47"<br>0.05% CPC 18"<br>0.2% CHX 18"                                       | 10<br>10<br>10<br>10 | 1 hour         | Proflaxis on ultrasonic | 3 blood agar plates: 1 on the participant's chest, 1 on the dentist's chest, 1 on the assistant's chest           | Counting of CFU with LabLine Colony Counter   | Bacteria   | The results clearly indicate that a pre-procedure mouthwash containing 0.05% CPC can be considered as a promising alternative to reduce aerosol contamination during ultrasonic scaling procedures compared to the gold standard of 0.2% chlorhexidine %. Furthermore, the amount of viable bacteria in the aerosol is highest in the chest area of the patient followed by the operator and assistant in descending order. |
| Ferns et al. 2010          | Brazil  | 60 (30/30)                     | (30-70)       | 0.05% CPC<br>0.12% CHX<br>Aqua<br>No mouthwash   | 15<br>15<br>15<br>15 | 1 hour         | Proflaxis on ultrasonic | 5 inoculated agar plates: 3 on the support board, 1 on the participant's chest, and 1 on the clinician's forehead | 1. Anaerobic culture, counting of CFU with LabLine Colony Counter<br>2. Checkerboard DNA-DNA hybridization (40 species) | Gram positive y gram negative bacteria             | Mouth rinses containing 0.05% CPC and 0.12% CHX are equally effective in reducing the levels of bacterial splash generated during ultrasonic scaling and their use could help decrease the level of microbial contamination in the dental office.   |

RCT: Randomized clinical trial, CPC: Cetylpyridinium Chloride, CHX: Chlorhexidin, FCU: Forming Colony units.



**Figure 1.** PRISMA diagram showing the inclusion and exclusion process of scientific articles found in the scientific search, for this Systematic Review.

| Study ID | Study ID          | Experimental | Comparator | Outcome | Weight | D1 | D2 | D3 | D4 | D5 | Overall |                 |
|----------|-------------------|--------------|------------|---------|--------|----|----|----|----|----|---------|-----------------|
| 1        | Rebatal-Maldonado | CPC          | Placebo    | NA      | 1      | ●  | ●  | ●  | ●  | ●  | ●       | ● Low risk      |
| 2        | Ishii et al.      | CPC          | Placebo    | NA      | 1      | ●  | ●  | ●  | ●  | ●  | ●       | ● Some concerns |
| 3        | Ferni et al.      | CPC          | Placebo    | NA      | 1      | ●  | ●  | ●  | ●  | ●  | ●       | ● High risk     |

|    |  |
|----|--|
| D1 | Randomisation process                      |
| D2 | Deviations from the intended interventions |
| D3 | Missing outcome data                       |
| D4 | Measurement of the outcome                 |
| D5 | Selection of the reported result           |

**Figure 2.** Risk of Bias of the studies included in this research according to the Cochrane Rob 2.0 tool.



## RESULTS

The results of the electronic and manual search strategy included 120 articles in total, excluding 48 duplicate articles and 67 articles eliminated by title and abstract, leaving 5 articles selected. Subsequently, 2 articles that did not meet the eligibility criteria were excluded, resulting in 3 randomized clinical trial articles that were included for qualitative synthesis (Figure 1). The reason for exclusion of the articles is shown in Table 4.

**Table 4.** Reason for exclusion of scientific articles.

| Author                          | Reason                     |
|---------------------------------|----------------------------|
| De Macedo Máximoa <i>et al.</i> | No treatment with aerosols |
| Anderson <i>et al.</i>          |                            |

## CHARACTERISTICS OF INCLUDED STUDIES

Overall, 3 articles were included, all were parallel RCTs, and the years of publication ranged from 2010 to 2017. The countries for these articles were: Brazil and India. The total number of participants was between 40 and 60 people, with a range of years from 18 to 70 years (Table 3).

In all the articles, the experimental group was the use of CPC (in different concentrations and/or with other components) and the control group was chlorhexidine, water and the non-use of mouthwash prior to spray treatment. Follow-up time ranged from 1 to 72 hours. All articles described ultrasound prophylaxis as an aerosol-generating procedure and the microorganisms found were gram-positive and negative bacteria. All studies concluded that the use of CPC is effective in reducing bacteria during the ultrasound prophylaxis procedure; however, one of the studies mentions that CPC is better than CHX and other mentions that both are equally effective (Table 3).

In all studies, microbiological samples were collected using Blood Agar or Honokiol plates, which were placed at different locations and distances such as on the patient's chest, dentist's chest, assistant's chest, dentist's front, or on the dashboard medium.

Regarding the microbiological analysis, the results were expressed in relation to the reduction in the number of colony-forming units (CFU) in the aerosol collection places where the agar plates were located. In all the studies, the method used was counting the total number of CFUs using Labline (32,36,37); only in two studies, a second method was used for microbiological analysis, which was through the use of the DNA-RNA checkerboard hybridization technique (36,37).

## ANALYSIS OF RISK OF BIAS

Three articles were considered, all at low risk of bias (Figure 2).

## ANALYSIS OF THE RESULTS

Data from each study was entered and analyzed in an Excel spreadsheet for qualitative analysis (Table 3).

## DISCUSSION

During patient care, there are various dental treatments that use aerosol-generating equipment, such as the handpiece, the triple syringe or ultrasound. These aerosols could carry microorganisms that exist in the patient's mouth, such as viruses or bacteria (38,39), which would lead to a contaminated atmosphere or possible cross-contamination in the dental office (45). It is known that these aerosol particles can remain floating in the environment for up to 4 hours after a dental procedure (46), producing a risk for the dentist

and the patient due to the possible contamination of the respiratory tract by these microorganisms, even after the end of the appointment (47).

To minimize cross-infections in the dental office, different methods have been described in the literature, such as the use of mouthwashes prior to dental treatment (10,27,36), whose purpose is to reduce the number of microorganisms in the oral cavity. These mouthwashes can present different components, as is the case of Cetylpyridinium Chloride (1,2,8,31), which has been widely mentioned in recent years in different publications (4,10), indicating that it has a great capacity antimicrobial against viruses (25-28,46) and bacteria (11,12,17,34), as reviewed in the literature.

According to the results obtained in the present investigation, all concluded that the use of CPC is effective in reducing bacteria during the dental procedure, ultrasound prophylaxis, which generate aerosol; when compared to water or no mouthwash; however, no significant difference in colony-forming unit (CFU) reduction was found when compared to CHX, indicating that CPC-based mouthrinses are equally effective as CHX-containing mouthrinses (32,36-37). This could be due to the fact that both mouthwashes are broad-spectrum antibacterial and present the same mechanism of action, degrading the bacterial membrane and producing cell lysis of the microorganism (7,11).

Joshi *et al.* (32). They reported that the antimicrobial activity of CPC was higher when it was used at 47°C, maintaining the maximum reduction in bacterial count in all areas analyzed, compared to the use of CPC at 18°C. This may be because there would be a greater bactericidal activity of CPC at high temperatures; since as the temperature increases, the speed at which chemical reactions take place increases, known as Thermodynamic Treatment (48).

Likewise, it is observed that the antimicrobial efficacy achieved by CPC rinses is only limited to one type of bacterial microorganisms (36,37), but no information was found on viral microorganisms. This may be due to the fact that bacteria (6,17) are able to cultivate and grow on blood agar plates, the same culture media used in the three investigations, while viruses require a specialized medium for their growth (26); that is why it is suggested to carry out future research including these types of microorganisms.

Based on bacterial composition analysis (36,37), it showed statistically lower ratios for orange complex pathogens when CPC was compared to subjects who received no mouthwash or those who only rinsed with water. This is a beneficial effect, since certain species of the orange complex, such as fusobacteriums, can cause respiratory or ophthalmic etiologies (49,50), which would lead to a possible reduction in cross-diseases in the dental office, as long as the CPC mouthwash is used prior to any dental procedure that generates aerosols.

Retamal-Valdes *et al.* (37). He indicated that the use of CPC was effective in reducing bacteria found in dental aerosols, but it should be noted that, in said study, CPC was used with other additional components, such as zinc lactate and sodium fluoride, so it could not be concluded if its antibacterial action is thanks to CPC or its other previously mentioned components.

The main limitation of the present study was that it only found results for a single dental procedure, ultrasound prophylaxis, which has been shown to have great potential for aerosol generation in the dental office (38). Therefore, it could be assumed that the CPC mouthwash, prior to dental treatments that generate aerosols, would also produce similar benefits for the dentist and the patient, if it is used with other equipment that

also generates aerosols, as is the case with the piece hand or triple syringe.

Finally, it is worth mentioning that this is the first study that systematically reviewed the antimicrobial efficacy of Cetylpyridinium Chloride-based mouthwash in the reduction of microorganisms prior to any treatment that generates aerosol, not finding enough information regarding this product in relation to mouthwashes and sprays; Therefore, the results of our present investigation must be evaluated with caution. Despite demonstrating that there is a decrease in the number of microorganisms, the influence of this decrease in the infection rate towards health professionals is unknown, so there is no direct evidence indicating that cetylpyridinium chloride mouthwash can reduce the rate of clinical infection in the dental area.

#### CONCLUSION

The use of CPC-based mouthwashes prior to ultrasonic prophylaxis only has antibacterial efficacy.

#### CONFLICT OF INTEREST

The authors declare that we have no conflict of interest.

#### ETHICAL CONSIDERATIONS

The present study was approved by the Comité Institucional de Ética en Investigación de la Universidad Científica del Sur.

With a inscription code 222-2021-POS8, date 01 de June 2021.

#### FUNDING ACQUISITION

Self financed.

#### AUTHOR CONTRIBUTION STATEMENT

Conceptualization and design: J.P.A.T.  
 Literature review: J.P.A.T. and A.I.L.F.  
 Methodology and validation: A.I.L.F. and H.I.A.V.  
 Formal analysis: J.P.A.T.  
 Investigation and data collection: A.I.L.F. and H.I.A.V.  
 Resources: J.P.A.T. and A.I.L.F.  
 Data analysis and interpretation: H.I.A.V.  
 Writing-original draft preparation: J.P.A.T.  
 Writing-review & editing: A.I.L.F.  
 Supervision: H.I.A.V.  
 Project administration: J.P.A.T.  
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COMITÉ INSTITUCIONAL DE ÉTICA EN INVESTIGACIÓN



**CONSTANCIA N° 210-CIEI-CIENTÍFICA-2021**

El presidente del Comité Institucional de Ética en Investigación de la Universidad Científica del Sur (CIEI-CIENTÍFICA) da constancia que el proyecto de investigación, cuyos datos se registran a continuación, ha sido **aprobado** por el CIEI-CIENTÍFICA.

Código de registro: **222-2021-POS8**  
 Título: **Efectos clínicos y microbiológicos en la cavidad bucal del uso de colutorios a base de cloruro de cetilpiridinio: revisión sistemática**  
 Investigador(a): **Jackeline Paola Arce Toribio**

La aprobación del proyecto de investigación implica que el documento presentado a evaluación cumple con los lineamientos de Universidad en materia de investigación y ética, los cuales se sustentan en la normativa internacional vigente. Adicionalmente, en el contexto de la pandemia de enfermedad por COVID-19, le recomendamos cumplir con las normas publicadas por el estado peruano (accesos, medidas de bioseguridad, etc.) y tener los permisos de las instituciones en las que realizará el estudio antes de ejecutarlo.

En tal sentido, esta aprobación carecerá de valor si es que el proyecto de investigación arriba indicado es modificado de cualquier forma. Toda enmienda, añadido, eliminación o eventualidad (eventos adversos, etc.) posterior a la fecha de aprobación debe ser reportado al CIEI-CIENTÍFICA.

La vigencia de la aprobación de este documento es de dieciocho (18) meses (**hasta el 31 de diciembre del 2022**), periodo en el que puede desarrollarse el proyecto. Cualquier trámite para su renovación deberá ser enviado antes del término de la vigencia de este documento, debiendo suspenderse todo desarrollo hasta que la renovación sea aprobada. La presente aprobación será ratificada en la sesión del CIEI más próxima.

Villa El Salvador, 1 de junio de 2021




Mg. Fulton Paul Rivera Albinagorta  
 Presidente  
 Comité Institucional de Ética en Investigación

**RESOLUCIÓN DIRECTORAL DE ACEPTACIÓN DEL PROYECTO DE TESIS  
Y NOMBRAMIENTO DEL ASESOR**

**RESOLUCIÓN DIRECTORAL DE LA CARRERA DE ESTOMATOLOGÍA  
N° 032-DACE-DAFCS-U. CIENTÍFICA-2021**

Lima, 05 de julio del 2021

**VISTO:**

El informe técnico del Comité Institucional de Ética en Investigación de la Universidad Científica del Sur con código N° 222-2021-POS8, se aprueba el proyecto de Tesis Titulado: **“EFECTOS CLÍNICOS Y MICROBIOLÓGICOS EN LA CAVIDAD BUCAL DEL USO DE COLUTORIOS A BASE DE CLORURO DE CETILPIRIDINIO: REVISIÓN SISTEMÁTICA”** presentado por **JACKELINE PAOLA ARCE TORIBIO**.

**CONSIDERANDO:**

Que, de acuerdo al Reglamento General de la Universidad Científica del Sur y los reglamentos de pre/posgrado para obtener el Grado Académico de **MAESTRO EN ESTOMATOLOGÍA** en la Carrera de Estomatología de la Universidad Científica del Sur, se debe desarrollar un trabajo de investigación.

Que, de acuerdo con la normativa vigente de la Universidad Científica del Sur, en uso de las atribuciones conferidas al Director Académico de Carrera.

**SE RESUELVE:**

**ART. 1º: APROBAR E INSCRIBIR** el Proyecto de Tesis titulado: **“EFECTOS CLÍNICOS Y MICROBIOLÓGICOS EN LA CAVIDAD BUCAL DEL USO DE COLUTORIOS A BASE DE CLORURO DE CETILPIRIDINIO: REVISIÓN SISTEMÁTICA”** de el/la Bach. **JACKELINE PAOLA ARCE TORIBIO**, con registro: N° 222-2021-POS8 y establecer el inicio de periodo de ejecución del mencionado proyecto, 01 de junio de 2021.

**ART. 2º: NOMBRAR** Asesor/a del trabajo de tesis señalado, a al/la **Mg. Esp. Ana Isabel López Flores**.

Regístrese, comuníquese y archívese.



**Dr. Claudio Peña Soto**  
Director Académico de la Carrera de Estomatología



cambiar **titulo** de investigacion

**JT**

Jackeline Arce Toribio

Para: Tesis Estomatología



Dom 03/04/2022 13:11

Buenos días, soy la Dra Paola Arce, egresada de la maestría de estomatología y que en la actualidad estoy realizando mi trabajo de investigación, cuyo código dado por el Comité de Ética en Investigación es el: N°222-2021-POS8, con fecha de 05JULIO2021. El motivo de mi mensaje es para pedir realizar el cambio del **titulo** inicial por el actual y/o los pasos a seguir para poder realizar el cambio:

TITULO INICIAL: "EFECTOS CLINICOS Y MICROBIOLÓGICOS EN LA CAVIDAD BUCAL DEL USO DE COLUTORIOS A BASE DE CLORURO DE CETILPIRIDINIO:REVISIÓN SISTEMÁTICA"

**TITULO ACTUAL:** " EFICACIA ANTIMICROBIANA DEL USO DEL ENJUAGUE BUCAL CON CLORURO DE CETILPIRIDINIO EN PROCEDIMIENTOS QUE GENERAN AEROSOLES: REVISIÓN SISTEMÁTICA "

Muchas gracias por su tiempo.

Atte

Paola Arce Toribio  
DNI: 46789037  
COP:31294  
RNE: 3922

**TE**

Tesis Estomatología

Para: Jackeline Arce Toribio



Vir 22/04/2022 16:50

Buen día estimada Jackeline Arce, se procede a la modificación de su título según su solicitud.

Atte.

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