Indonesian Journal of Medicine (2023), 08(04): 423-434
Masters Program in Public Health, Universitas Sebelas Maret

Meta-Analysis
Open Access

Meta-Analysis the Effect of a Potassium Nitrate Desensitizing Agent and Casein Phosphopeptide Amorphous Calcium Phosphate on Tooth Sensitivity after Office Bleaching Treatment

Diyanti Safitri[1)], Eti Poncorini Pamungkasari[2)], Bhisma Murti[1)]

[1)]Master's Program in Public Health, Universitas Sebelas Maret
[2)]Faculty of Medicine, Universitas Sebelas Maret

Received: August 10, 2023; Accepted: September 11, 2023; Available online: October 10, 2023

ABSTRACT

Background: Office bleaching is a treatment used to treat tooth discoloration, but it often results in tooth sensitivity. The desensitizing agent potassium nitrate and casein phosphopeptide amorphous calcium phosphate (CPP-ACP) can reduce tooth sensitivity because they work to inhibit nerve transmission, thereby preventing the sensation of pain. This study aimed to investigate the effect of potassium nitrate desensitization agents and CPP-ACP on tooth sensitivity after bleaching treatment.
Subjects and Method: This was a meta-analysis with the following PICO format. Population= Patients who have undergone office bleaching treatment. Intervention= desensitizing agents potassium nitrate and CPP-ACP. Comparison: without desensitizing agent. Outcome: tooth sensitivity. Keywords used "Office bleaching" AND "Tooth sensitivity" OR "Dentine hypersensitivity" AND "Potassium nitrate" AND Casein Phosphopeptide Amorphous Calcium Phosphate" OR "CPP-ACP" AND "Randomized Controlled Trial" OR "RCT". Studies published at PubMed, Springerlink, Cochrane Database, Hindawi, Elsevier, Google Scholar and Wiley Online Library databases, from 2013 to 2023. The selected articles were critically reviewed using the PRISMA checklist and analyzed using the Review Manager 5.4.1. The effect size used is the Standardized Mean Difference (SMD).
Results: A total of 13 RCTs from Brazil, Spain, India, Pakistan, Turkey, Jordan, Iran, and the United States was selected for meta-analysis. Meta-analysis of 7 articles shows that the use of potassium nitrate desensitization agents can reduce tooth sensitivity by 0.20 units lower than without the use of desensitization agents (SMD= - 0.20; 95% CI= -0.37 to -0.03; p=0.020). Meanwhile, 7 articles show that the use of CPP-ACP desensitization agents can reduce tooth sensitivity by 0.46 units lower than without the use of desensitization agents (SMD= -0.46; 95% CI= -0.67 to - 0.24; p<0.001).
Conclusion: The use of potassium nitrate desensitization agents and CPP-ACP reduces tooth sensitivity compared to without the use of potassium nitrate desensitization agents and CPP-ACP and is statistically significant.

Keywords: desensitizing agent, potassium nitrat, casein phosphopeptide amorphous calcium phosphate, tooth sensitivity, office bleaching

Correspondence:
Diyanti Safitri. Master's Program in Public Health, Universitas Sebelas Maret. Jl. Ir. Sutami 36A, Surakarta 57126, Central Java. Email: diyansafitri97@gmail.com. Mobile: 081225293094.

Cite this as:
Safitri D, Pamungkasari EP, Murti B (2023). Meta-Analysis the Effect of a Potassium Nitrate Desensitizing Agent and Casein Phosphopeptide Amorphous Calcium Phosphate on Tooth Sensitivity after Office Bleaching Treatment. Indones J Med. 08(04): 423-434. https://doi.org/10.26911/theijmed.2023.08.04.09.

BACKGROUND

The appearance of teeth is an important aspect that plays a role in human social interaction. Teeth that change color can affect a person's self-confidence and the beauty of their appearance (Lumuhu et al., 2016). Tooth discoloration can be treated by teeth whitening or bleaching. Bleaching is a process used to whiten discolored teeth until they are close to the desired tooth color (Pary et al., 2015).

Office bleaching is a teeth whitening procedure using high concentrations of hydrogen peroxide and has several advantages, such as the treatment process being very fast and carried out directly by the dentist so that the results can be seen in one visit (Apriliyani et al., 2021). The effectiveness of office bleaching has been reported in the majority of cases of tooth discoloration with good results. However, patient-reported tooth sensitivity is the most common side effect associated with office bleaching procedures, especially when high concentrations of bleaching agents are used (Rodrigues et al., 2018). Office bleaching treatments using agents with higher concentrations can cause greater tooth sensitivity than bleaching treatments carried out at home because the concentration of the agent used is lower (Martin et al., 2013).

According to Mehta and Sasaki's (2018), the large amount of tooth sensitivity experienced by patients with bleaching treatment at dentist clinics caused some patients to stop bleaching treatment so that to overcome this problem a desensitization agent was needed which could induce tooth remineralization (Mehta et al., 2018). A study conducted by Rezende et al. (2020) stated that the application of a desensitizing agent before or after bleaching treatment at the dentist's clinic (office bleaching) showed results in a significant reduction in tooth sensitivity in several clinical trials (Rezende et al., 2020).

SUBJECTS AND METHOD

1. Study Design

This was a systematic review and meta-analysis between 2013 and 2023. Search for this research article through databases, including: PubMed, Springerlink, Cochrane Database, Hindawi, Elsevier, Google Scholar and Wiley Online Library using the search keyword "Office bleaching" OR "Tooth sensitivity" OR "Dentine hypersensitivity" OR "Potassium nitrate" OR "Casein Phosphopeptide Amorphous Calcium Phosphate" OR "CPP-ACP" OR "Randomized Controlled Trial" OR –RCT".

2. Steps of Meta-Analysis

Meta-analysis was carried out in the following five steps:

a. Formulate research questions in the PICO format (Population, Intervention, Comparison, Outcome).
b. Search for primary study articles from various electronic databases including PubMed, Springerlink, Elsevier, Google Scholar and Wiley Online Library.
c. Conduct screening and critical appraisal of primary research articles.
d. Extract data and synthesize effect estimates into RevMan 5.4
e. Interpret and conclude the results.

3. Inclusion Criteria dan Exclusion Criteria

The inclusion criteria used in this study were full-text articles using a Randomized Controlled Trial (RCT) design. The analysis used was multivariate with Standardized Mean Difference (SMD). The exclusion criteria in this study were articles published before 2013 and articles that did not include a mean SD.

4. Operational Definition of Variables

The articles included in this study were adapted to PICO. The article search was

carried out by considering the eligibility criteria using the PICO model as follows: Population = Patients who have had office bleaching treatment. Intervention= desensitizing agent potassium nitrate and casein phosphopeptide amorphous calcium phosphate (CPP-ACP). Comparison= No desensitizing agent. Outcome= Tooth sensitivity.

The potassium nitrate desensitization agent is the chemical compound KNO3 which consists of potassium ions (K+) and nitrate ions (NO3-). The mechanism of action of potassium nitrate is to inhibit nerve transmission, thereby preventing the sensation of pain.

CPP-ACP desensitizing agent is an active ingredient formed by the combination of casein phosphopeptide and calcium phosphate. The mechanism of action of CPP-ACP is by blocking the flow of tubular fluid thereby closing the open dentinal tubules.

Tooth sensitivity is pain or aching in the teeth which causes the pulp to respond excessively to various stimuli.

3. Study Instrument

This research is guided by the PRISMA flow diagram and assessing the quality of research articles using the Critical Appraisal Checklist for Randomized Controlled Trial (RCT) tool). The following are the 12 questions used in the checklist (Tables 3 and 4):

1. Does this research address a clear research focus?
2. Is the Randomized Controlled Trial research method suitable for answering the research questions?
3. Were there enough subjects in the study to determine that the findings did not occur by chance?
4. Were subjects randomly allocated to experimental and control groups?
5. Are inclusion/exclusion criteria used?
6. Were the two groups comparable at the start of the study?
7. Are objective and unbiased outcome criteria used?
8. Are objective and validated measurement methods used to measure the results?
9. Is the effect size practically relevant?
10. How precise are the effect estimates? Is there a confidence interval?
11. Could there be confounding factors that have not been taken into account?
12. Can the results be applied to your research?

6. Data Analysis

The collected articles were processed using the Review Manager application (RevMan 5.4). Data processing is carried out by calculating effect sizes and heterogeneity values to determine the research combination model and form the final results of the meta analysis which are presented in the form of forest plots and funnel plots.

RESULTS

Research related to the effect of applying the desensitizing agent potassium nitrate and casein phosphopeptide amorphous calcium phosphate on tooth sensitivity after office bleaching treatment consists of 13 articles originating from the Asian continent 6 articles, the United States 5 articles, the North American continent 1 article, and the European continent 1 article can be seen in Figure 2.

The total number of primary studies included in this meta-analysis synthesis was 13 articles originating from Brazil, Spain, India, Pakistan, Turkey, Jordan, Iran, and the United States. Primary research for the use of potassium nitrate desensitization agents used 7 Randomized Controlled Trial (RCT) studies from Brazil, India, and Spain. Meanwhile, the use of the casein phosphopeptide amorphous calcium phosphate desensitization agent used 7

Randomized Controlled Trial (RCT) studies from Pakistan, Turkey, Jordan, India, the United States and Iran.

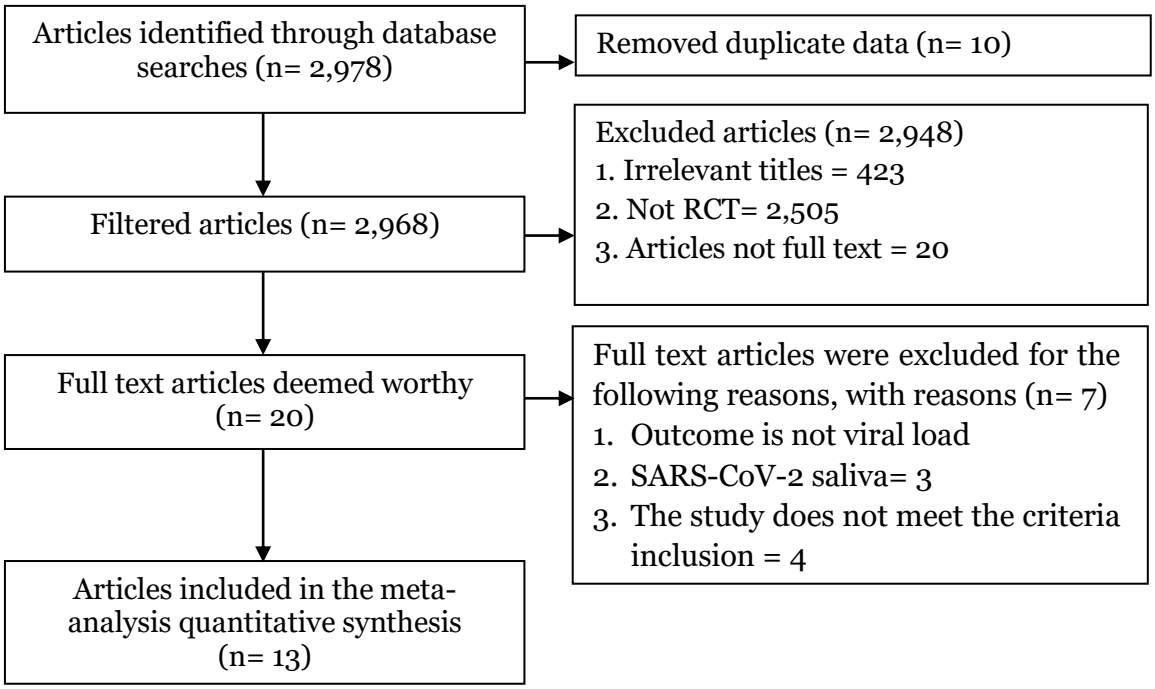

Figure 1. PRISMA flow diagram

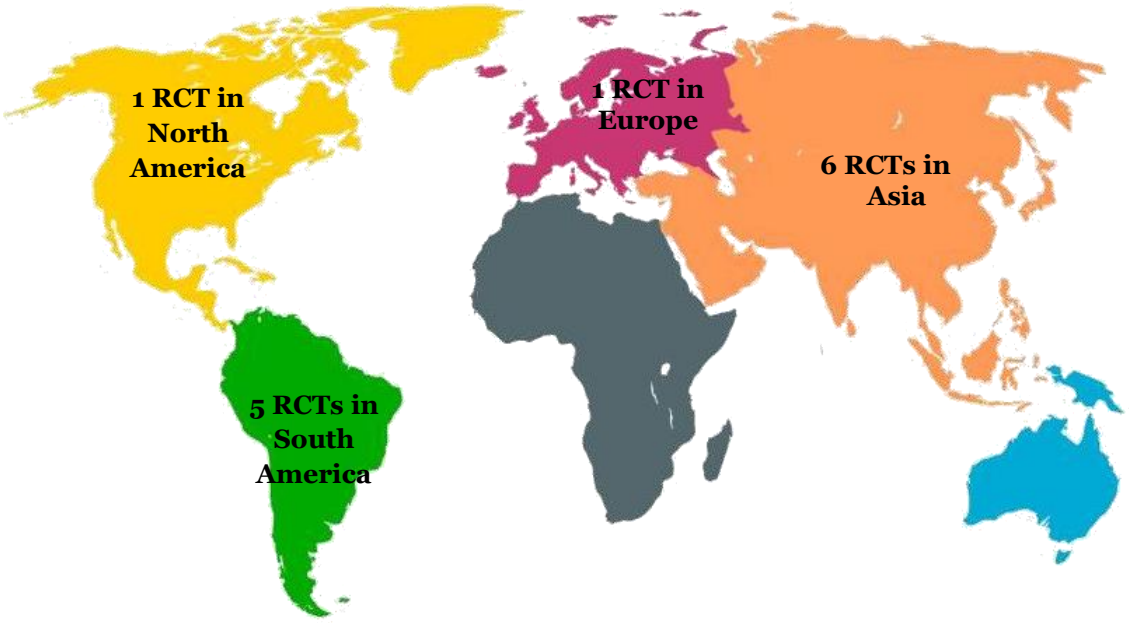

Figure 2. Map of the research area

1. Research Quality Assessment

Table 1. Quality assessment of Randomized Controlled Trial (RCT) of the effect of applying potassium nitrate desensitizing agents on tooth sensitivity after office bleaching treatment

Author(s)	Criteria												Total
	1	2	3	4	5	6	7	8	9	10	11	12	
Pale' et al., 2013	2	2	2	2	2	2	2	2	2	2	3	2	25
Nanjundasetty and Ashrafulla, 2016	2	2	2	2	2	2	2	2	2	2	3	2	25
Parreires et al., 2020	2	2	2	2	2	2	2	2	1	2	1	2	22
Martini et al., 2018	2	2	2	2	2	2	2	2	1	2	2	2	23
Rezende et al, 2020	2	2	3	2	2	2	2	2	1	1	1	2	21
Maran et al., 2020	2	2	2	2	2	2	2	2	2	2	3	2	25
Vochikovsk et al., 2021	2	2	2	2	2	2	2	2	2	1	2	2	23

Table 2. Quality assessment of Randomized Controlled Trial (RCT) of the effect of applying the desensitizing agent casein phosphopeptide-amorphous calcium phosphate on tooth sensitivity after office bleaching treatment

Author(s)	Criteria												Total
	1	2	3	4	5	6	7	8	9	10	11	12	
Maghairah et al., 2014	2	2	2	2	2	2	2	2	2	2	1	2	23
Najundasetty and Ashrafulla, 2016	2	2	2	2	2	2	2	2	2	2	3	2	25
Singh et al., 2022	2	2	2	2	2	2	2	2	2	2	3	2	25
Gumustas and Dikmen, 2021	2	2	2	2	2	2	2	2	2	2	3	2	25
Rashid and ElSalhy, 2021	2	2	2	2	2	2	2	2	1	1	1	2	20
Adil et al., 2021	2	2	2	2	2	2	2	2	2	2	3	2	25
Sadri et al., 2023	2	2	2	2	2	2	2	2	2	1	1	2	22

1 = Does this research address a clear research focus?
2 = Is the Randomized Controlled Trial research method suitable for answering the research questions?
3 = Were there enough subjects in the study to determine that the findings did not occur by chance?
4 = Are subjects randomly allocated to experimental and control groups?
5 = Are inclusion/exclusion criteria used?
6 = Were the two groups comparable at the start of the study?
7 = Are objective and unbiased outcome criteria used?
8 = Are objective and validated measurement methods used to measure the results?
9 = Is effect size practically relevant?
10 = How precise is the effect estimate? Is there a confidence interval?
11 = Could there be confounding factors that have not been taken into account?
12 = Can the results be applied to your research?

Description of the answer score:

1 = No
2 = Hesitant
3 = Yes

2. Summary of the article

a. The effect of applying potassium nitrate desensitization agent on tooth sensitivity after office bleaching treatment

Table 3. Description of Primary Studies of Potassium Nitrate Desensitizing Agents Included in the Meta-Analysis

Author (Year)	Country	Study Design	Sample	P Population	I Intervention	C Comparison	O Outcome
Martini et al., 2019	Brazil	RCT	Intervention: 90 Control : 90	Patient after office bleaching treatment	Potassium nitrate and sodium fluoride desensitizing agents	Placebo	Tooth sensitivity
Parraires et al.,2022	Brazil	RCT	Intervention: 42 Control : 42	Patient after office bleaching treatment	Desensitizing agent Potassium nitrate and glutaraldehyde	Placebo	Tooth sensitivity
Maran et al., 2022	Brazil	RCT	Intervention: 60 Control : 60	Patient after office bleaching treatment	Potassium Nitrate desensitizing agent	Experimental gel without desensitizing agent	Tooth sensitivity
Rezende et al., 2021	Brazil	RCT	Intervention: 43 Control : 43	Patient after office bleaching treatment	Potassium Nitrate desensitizing agent	Placebo	Tooth sensitivity
Nanjundasety and Ashrafullal, 2021	India	RCT	Intervention: 23 Control: 23	Patient after office bleaching treatment	Potassium nitrate desensitizing agent, CPP-ACP	Placebo	Tooth sensitivity
Vochikovsk et al., 2022	Brazil	RCT	Intervention: 50 Control : 50	Patient after office bleaching treatment	Potassium Nitrate desensitizing agent	Placebo	Tooth sensitivity
Pale' et al., 2021	Spain	RCT	Intervensi : 16 Kontrol : 16	Patient after office bleaching treatment	Potassium Nitrate desensitizing agent	Placebo	Tooth sensitivity

b. The effect of applying CPP-ACP desensitization agents on tooth sensitivity after office bleaching treatment

Table 4. Description of Primary Studies of CPP-ACP Desensitizing Agents Included in the Meta-Analysis

Author (year)	Country	Study Design	Sample	P Population	I Intervention	C Comparison	O Outcome
Adil et al., 2021	Pakistan	RCT	Intervention: 67 Control: 67	Patient after office bleaching treatment	CPP-ACP and PNSMP desensitizing agents	Placebo (without desensitizing agent)	Tooth sensitivity
Gumustas and Dikmen., 2021	Turkey	RCT	Intervention: 16 Control: 16	Patient after office bleaching treatment	Desensitizing agents CPP-ACP neutral sodium fluoride gel (NSF) and nano-hydroxyapatite solution (n-HAP)	Placebo (without desensitizing agent)	Tooth sensitivity
Maghaire et al., 2014	Jordan	RCT	Intervention: 17 Control: 17	Patient after office bleaching treatment	Desensitizing agents sodium fluoride and CPP-ACP	Placebo (without desensitizing agent)	Tooth sensitivity

Author (year)	Country	Study Design	Sample	P Population	I Intervention	C Comparison	O Outcome
Singh et al., 2017	India	RCT	Intervention: 15 Control: 15	Patient after office bleaching treatment	Desensitizing agents sodium fluoride and CPP-ACP	Experimental gel without desensitizing agent	Tooth sensitivity
Nanjunda setty and Ashrafulla, 2016	India	RCT	Intervention: 23 Control: 23	Patient after office bleaching treatment	Potassium nitrate and CPP-ACP desensitizing agents	Placebo (without desensitizing agent)	Tooth sensitivity
Rashid and El-Salhy, 2021	USA	RCT	Intervention: 23 Control: 23	Patient after office bleaching treatment	Desensitizing agent MI Paste (CPP-ACP)	Placebo (without desensitizing agent)	Tooth sensitivity
Sadri et al., 2023	Iran	RCT	Intervention: 15 Control: 15	Care after office bleaching	CPP-ACP desensitizing agent	Placebo (without desensitizing agent)	Tooth sensitivity

1. The effect of applying potassium nitrate desensitization agent on tooth sensitivity after office bleaching treatment

a. Forest plot

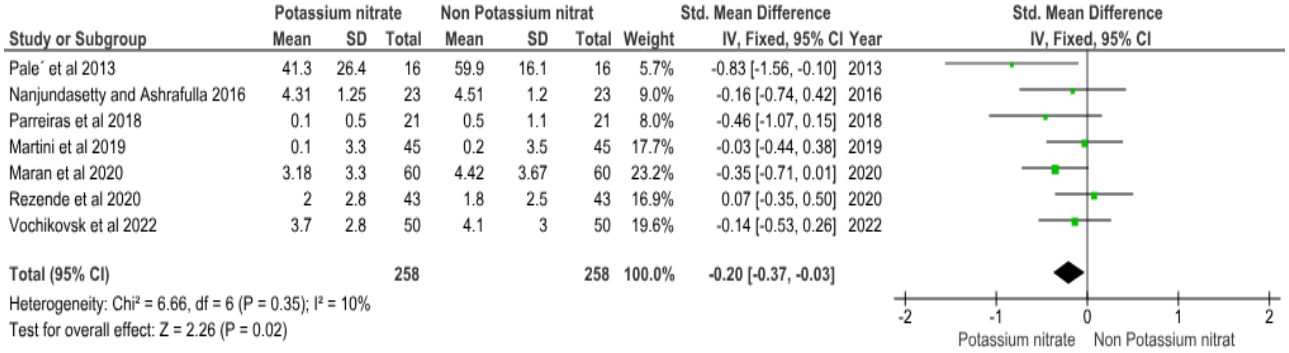

Figure 3. Forest plot The effect of applying potassium nitrate desensitization agent on tooth sensitivity after office bleaching treatment

The forest plot in Figure 3 shows that there is an effect of applying the desensitizing agent potassium nitrate on tooth sensitivity after office bleaching treatment. According to the results of the analysis, the use of potassium nitrate desensitization agents can reduce tooth sensitivity by 0.20 units lower than without the use of desensitization agents, but it is statistically significant (SMD= -0.20; 95% CI= -0.37 to -0.03; p=0.020). The forest plot shows low heterogeneity in effect estimates between studies (I^2=10%; p=0.070), therefore the calculation of the average effect estimate was carried out using a fixed effect model approach.

A forest plot is a diagram that shows at a glance information from each study examined in a meta-analysis research, as well as an estimate of the overall results. The forest plot shows the large variation (heterogeneity) between study results visually (Akobeng, 2005; Murti, 2018).

b. Funnel plot

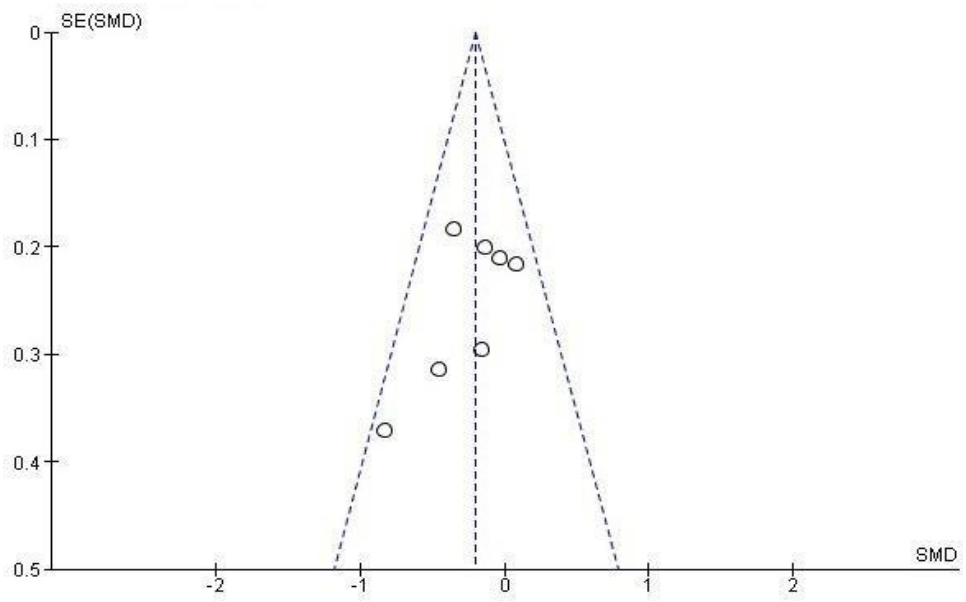

Figure 4. Funnel plot the effect of applying potassium nitrate desensitization agent on tooth sensitivity after office bleaching treatment

The funnel plot in Figure 4 shows that for studies with small samples, the distribution of effect estimates is asymmetric more to the left than to the right of the flat vertical line, thus indicating publication bias. Because the distribution of effect estimates is more to the left in the funnel plot, which is in the same direction as the diamond shape which is also to the left in the forest, publication bias tends to overestimate the true effect.

A funnel plot is a diagram of meta-analysis research that is used to demonstrate possible bias in publications. The funnel plot shows the relationship between sample size and effect size or standard error of the effect size from the various studies examined (Murti, 2018). The existence of bias in the publication of meta-analyses can be further tested statistically. There are 2 statistical tests for publication bias, namely: (1) Begg and Mazumdar's controlled correlation test; and (2) Egger et al's regression asymmetry test (D'Souza et al, 2002; Murti, 2018).

The Egger method is a method used to detect publication bias, consisting of a simple linear regression of the effect size in a study divided by the standard error, against the inverse of the standard error, then testing whether the intercept from the regression model is statistically significant ($p<0.01$) (Delgado-Rodriguez, 2001; D'Souza et al., 2002; Murti, 2018).

2. The effect of applying the desensitizing agent casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) on tooth sensitivity after office bleaching treatment

a. Forest plot

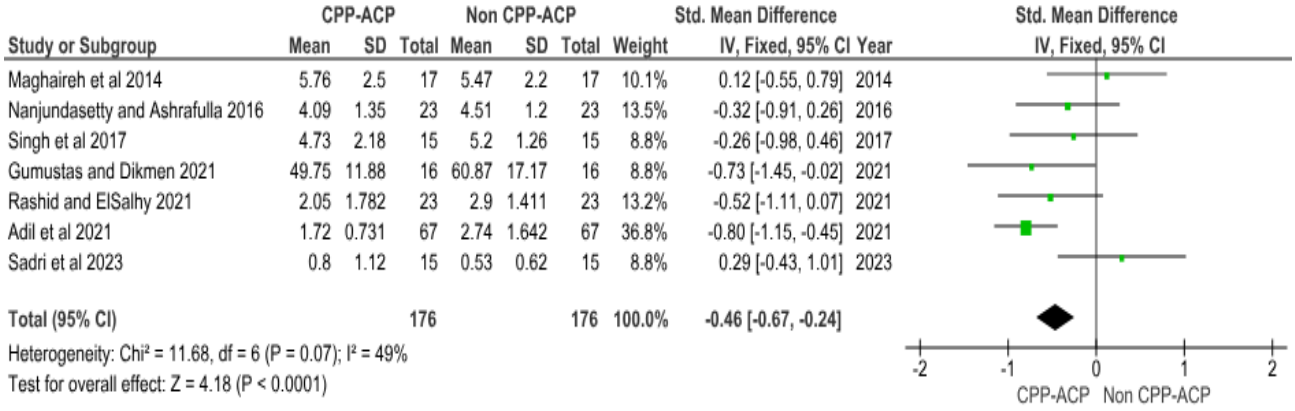

Figure 5. Forest plot of the effect of applying the desensitizing agent casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) on tooth sensitivity after office bleaching treatment

The forest plot in Figure 5 shows that there is an effect of applying the desensitizing agent casein phosphopeptide amorphous calcium phosphate (CPP-ACP) on tooth sensitivity after office bleaching. According to the results of the analysis, the use of the desensitization agent casein phosphopeptide amorphous calcium phosphate (CPP-ACP) can reduce tooth sensitivity by 0.46 units lower than without the use of the desensitization agent, but it is statistically significant (SMD= -0.46; CI 95%=-0.67 to - 0.24; p<0.001). The forest plot shows low heterogeneity in effect estimates between studies (I2=49%; p=0.070), therefore the calculation of the average effect estimate was carried out using a fixed effect model approach.

b. Funnel plot

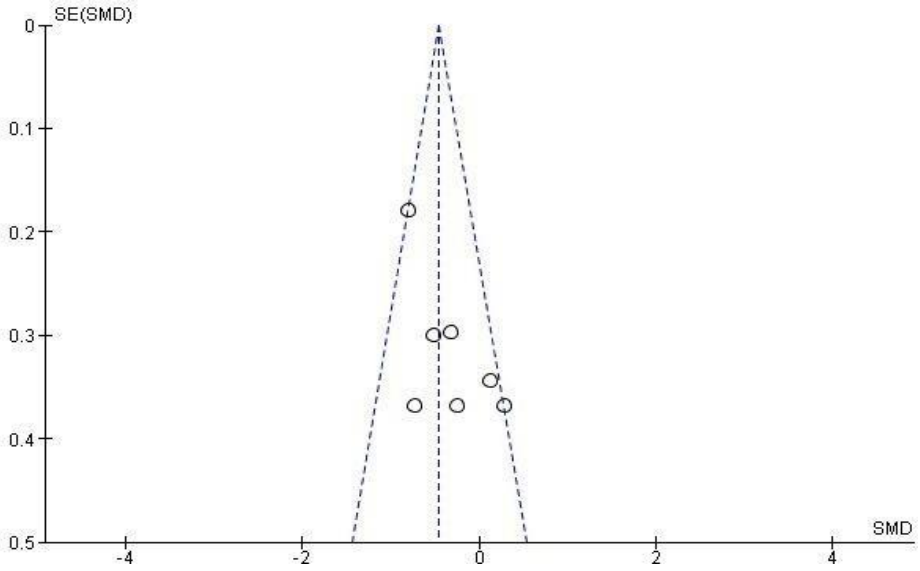

Figure 6. Funnel plot of the effect of applying CPP-ACP desensitization agent on tooth sensitivity after office bleaching treatment

The funnel plot in Figure 6 shows that for studies with small samples, the distribution of effect estimates is asymmetric more to the right than to the left of the flat vertical line, thus indicating publication bias. Because the distribution of effect estimates is more to the right in the funnel plot, which is in the opposite direction to the location of the diamond shape which is also to the left in the forest, publication bias tends to underestimate the true effect.

DISCUSSION

This systematic review and meta-analysis research discusses the effect of using chlorhexidine and povidone iodine mouthwash on the SARS-CoV-2-saliva viral load. The independent variables used in this study were the use of chlorhexidine and povidone iodine mouthwash. Meanwhile, the dependent variable used is salivary SARS-CoV-2 viral load.

1. **The effect of potassium nitrate desensitization agent on tooth sensitivity after office bleaching treatment**

Based on the analysis of 7 RCTs carried out with a systematic review and meta-analysis of the effect of applying potassium nitrate desensitization agents on tooth sensitivity after office bleaching treatment, it shows that there is homogeneity between studies (I^2 = 10%) so that the analysis using a fixed effects model. This research article shows that the application of a potassium nitrate desensitization agent can reduce tooth sensitivity by 0.20 times compared to without the application of a desensitization agent and is statistically significant (SMD= -0.20; 95% CI= -0.37 to -0.03; p=0.020).

Maran et al., 2020's study stated that the use of the desensitizing agent potassium nitrate can reduce tooth sensitivity because potassium nitrate has a calming effect on the nerves by preventing the nerves from repolarizing after experiencing depolarization in the pain cycle (Tageela et al., 2022). Research conducted by Tarique et al., 2017 showed that the application of a potassium nitrate agent for 14 days significantly reduced tooth sensitivity after bleaching treatment. Kose et al reported that the use of potassium nitrate can reduce tooth sensitivity (Tageela et al., 2022).

2. **The effect of desensitizing agent casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) on tooth sensitivity after office bleaching treatment**

Based on the analysis of 7 primary studies with a RCT carried out with a systematic review and meta-analysis of the effect of applying the casein desensitization agent phosphopeptide-amorphous calcium phosphate (CPP-ACP) on tooth sensitivity after office bleaching treatment, the results obtained from Forest The plot shows homogeneity between studies (I^2= 49%) so the analysis uses a fixed effect model. This research article shows that the application of the CPP-ACP desensitization agent can reduce tooth sensitivity 0.46 times compared to without the application of the desensitization agent and is statistically significant (SMD=-0.46; 95% CI= - 0.67 to -0.24; p<0.001).

Research by Singh et al. (2017) states that using the CPP-ACP desensitization agent for 14 days can reduce tooth sensitivity after bleaching treatment. A study conducted by Tageela et al., 2022 shows that the results of applying a desensitizing agent after office bleaching treatment carried out for 14 days can reduce tooth sensitivity. This is because the CPP-ACP desensitization agent works to close open dentin tubules by increasing

enamel density, thereby preventing the transmission of pain stimuli to nerve endings, thereby reducing tooth sensitivity (Oldoini et al., 2018).

This study shows the positive effect of applying desensitizing agents potassium nitrate and CPP-ACP on tooth sensitivity after office bleaching treatment. The results of the meta-analysis showed a significant reduction in tooth sensitivity after applying potassium nitrate desensitization agents and CPP-ACP to patients after office bleaching treatment. In this study, potassium nitrate and CPP-ACP agents have different mechanisms of action. The mechanism of action of potassium nitrate is by interfering with the neural response to painful stimuli, while the mechanism of action of CPP-ACP is by blocking the flow of tubular fluid thereby closing the dentinal tubules. The benefits of desensitization agents can be maximized by paying attention to the application time of each desensitization agent (Busman et al., 2018).

AUTHOR CONTRIBUTION

Diyanti Safitri was the main researcher who chose the topic, searched for and collected study data. Eti Poncorini Pamungkasari and Bhisma Murti played a role in analyzing the data reviewing study documents.

FUNDING AND SPONSORSHIP

This study is self-funded.

CONFLICT OF INTEREST

There is no conflict of interest in this study.

ACKNOWLEDGEMENT

We are very grateful to the database providers PubMed, Springerlink, Elsevier, Google Scholar and Wiley Online Library

REFERENCE

Apriliyani NR, Mulyawati E, Kristanti Y. (2021). The effect of various desensitizing agent application on in-*office bleaching* on the number of fibroblasts. Odonto: Jurnal Kedokteran Gigi. 8(1): 132–140. https://dx.doi.org/10.30659/odj.8.1.132-140.

Busman B, Arma U, Nofriadi N (2018). Hubungan aplikasi casein phosphopeptide amorphous calcium phosphate (cpp-acp) terhadap remineralisasi gigi (The relationship of casein phosphopeptide amorphous calcium phosphate (cpp-acp) application to tooth remineralization). B-Dent: Jurnal Kedokteran Gigi Universitas Baiturrahmah. 1(1): 18–23. https://doi.org/10.33854/jbdjbd.47

Chu CH, Lo ECM. (2014). Immediate post-application effect of professional prophylaxis with 8% arginine-calcium carbonate desensitizing paste on hypersensitive teeth. A practitioner-based clinical trial. Am J Dent. 27(1): 7–1. http://www.ncbi.nlm.nih.gov/pubmed/24902398

Irwandana PW, Kristanti Y, Daradjati S. (2016). Perbedaan perubahan warna pada bahan restorasi giomer dan kompomer pasca aplikasi bahan bleaching berbahan dasar hidrogen peroksida 40 % sebagai bahan in office bleaching (Differences in color changes in giomer and compomer restoration materials after application of 40% hydrogen peroxide based bleaching material as an in office bleaching agent). Jurnal Kedokteran Gigi. 7(2): 145–150.

Lumuhu EFS, Kaseke MM, Parengkuan WG (2016). Perbedaan efektivitas jus tomat (*Lucopersicon esculentum Mill.*) dan jus apel (*Mallus sylvestris Mill.*) sebagai bahan alami pemutih

gigi (Differences in the effectiveness of tomato juice (*Lucopersicon esculentum Mill.*) and apple juice (Mallus sylvestris Mill.) as natural teeth whitening ingredients). E-GIGI. 4(2). https://doi.org/10.35790/eg.4.2.-2016.13488

Martin J, Fernandez E, Bahamondes V, Werner A, Elphick K, Oliveira OB, Moncada G (2013). Dentin hypersensitivity after teeth bleaching with in-office systems - Randomized clinical trial. Am J Dent. 26(1): 10–14. http://www.ncbi.nlm.nih.gov/pubmed/23724543

Mehta D, Sasaki K (2018). Novel treatment of in-office tooth bleaching sensitivity: A randomized ,placebo-controlled clinical study. J Esthet Restor Dent. 30(3): 254–258. https://doi.-org/10.1111/jerd.12374

Murti B. (2018). Prinsip dan metode riset epidemiologi (Principles and methods of epidemiological research) (5th ed.). Program Studi Ilmu Kesehatan Masyarakat, Program Pascasarjana, Universitas Sebelas Maret.

Oldoini G, Bruno A, Genovesi AM, Parisi L (2018). Effects of amorphous calcium phosphate administration on dental sensitivity during in-office and at-home interventions. J Dent. 6(4): 1–8. https://doi.org/10.3390/dj60400-52

Pary FC, Kristianti Y, Hadriyanto W (2015). Pengaruh karbamid peroksida 10% dan 20% sebagai bahan home bleaching terhadap perubahan kekasaran permukaan resin komposit nanofil dan giomer (The effect of 10% and 20% carbamide peroxide as a home bleaching agent on changes in surface roughness of nanofil and giomer composite resins). Doctoral Dissertation, Universitas Gadjah Mada. 6(2): 146–152.

Rezende M, Leticia K, Silva DA, Miguel TC, Farago PV, Loguercio AD. (2020). Prior application of 10 % potassium nitrate to reduce postbleaching sensitivity : a randomized. J. Evid. Based Dent. Pract. 20(2): 401-406. https://-doi.org/10.1016/j.jebdp.2020.101406

Rodrigues JL, Rocha PS, Pardim SLS, Machado ACV, Faria-e-Silva AL, Seraidarian PI. (2018). Association between in-office and at-home tooth bleaching: A single blind randomized clinical trial. Braz. Dent. J. 29(2):13-3–139. https://doi.org/10.1590/010-3-6440201801726

Singh M, Mahajan P, Monga P, Mahajan S, Singla D, Kaur N (2017). Comparative evaluation of effectiveness of sodium fluoride and casein phosphorpeptide-amorphous calcium phosphate (CPP-ACP) in treating postoperative sensitivity associated with in office vital tooth bleaching: A clinical study. 29(1). Endod J. 29(1): 26–34. https://-//doi.org/10.4103/endo.endo

Tegeela R, Shilpa A, Yadav SS, A K, Prathibha P, Ateeq Z (2022). Efficacy of nano crystallised calcium phosphate (nccp) and casein phosphorpeptide amorphous calcium phosphate (cpp-acp) for controlling postoperative sensitivity after power bleaching-a comparative in-vivo study. Int J Med Sci Diag Res. 6(1): 10-19. https://-doi.org/10.32553/ijmsdr.v6i1.893.