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Evaluation of the effect of silver nanoparticles in root canal treatment: A systematic review and meta-analysis

Evaluación del efecto de las nanopartículas de plata en el tratamiento del conducto radicular: revisión sistemática y metanálisis

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Abstract

Objective: The present study was conducted to evaluate the effect of silver nanoparticles in root canal treatment.
Methods: All articles published in international databases such as PubMed, Scopus, Science Direct, ISI Web of knowledge, and Embase until July 2022 included. A 95% confidence interval (CI) for effect size with a fixed effect modal was calculated. Data analysis was performed using Stata/MP.V17 software.
Results: In the initial review, the abstracts of 141 studies were reviewed, two authors reviewed the full text of 30 studies, and finally, eight studies were selected. The effectiveness of silver nanoparticles compared to the control group was 86% (ES: 95% CI, 0.39 to 1.33; p<0.001).
Conclusions: Based on the findings of the present meta-analysis, AgNPs have a high antimicrobial effect in preventing the persistence of microorganisms in the root canal.

Key words: Nanoparticles, Root Canal Irrigants, Root Canal Therapy.

Resumen

Objetivos: El presente estudio se realizó para evaluar el efecto de las nanopartículas de plata en el tratamiento de conductos radiculares.
Métodos: Se incluyen todos los artículos publicados en bases de datos internacionales como PubMed, Scopus, Science Direct, ISI Web of Knowledge y Embase hasta julio de 2022. Se calculó un intervalo de confianza (IC) del 95% para el tamaño del efecto con un modal de efectos fijos. El análisis de datos se realizó utilizando el software Stata/MP.V17.
Resultados: En la revisión inicial se revisaron los resúmenes de 141 estudios, dos autores revisaron el texto completo de 30 estudios y finalmente se seleccionaron ocho estudios. La eficacia de las nanopartículas de plata en comparación con el grupo control fue del 86 % (ES: 95 % IC, 0,39 a 1,33; p<0,001).
Conclusiones: Según los hallazgos del presente metanálisis, las AgNP tienen un alto efecto antimicrobiano en la prevención de la persistencia de microorganismos en el conducto radicular.

Palabras clave: Nanopartículas, Irrigantes del conducto radicular, Terapia del conducto radicular.

Introduction

One of the reasons that can cause the root canal treatment to fail is the presence of microorganisms in the root canal, which must be done with methods such as mechanical cleaning and irrigation using antimicrobial solutions to reduce the persistence of microorganisms[1,2]. However, disinfection requires patients to visit again, or people are busy nowadays, so saving time is very important[3]. The evidence indicates that despite the disinfection of the root canal, the persistence of microorganisms in the root canal is evident[4]. Generally, an antimicrobial agent that can be effective on Gram-positive, aerobic, or Gram-negative bacteria is used for disinfection, which is an inappropriate choice and is effective only on one type of microbe[5,6]. The most common disinfectants are sodium hypochlorite and chlorhexidine. Sodium hypochlorite can dissolve tissue residues and has high antibacterial effectiveness. However, one of its advantages is that organic materials can affect its efficiency; Studies have shown that sodium hypochlorite is used in different concentrations from 0.5% to 6%. The effectiveness of chlorhexidine on antimicrobial activity is very high. However, one of its disadvantages is that it is not able to dissolve tissue residues in the canal[7,8].

As a result, there is a need for an optimal root canal cleaner to be available that has both high safety and proven effectiveness. Studies using photodynamic therapy have reported nanoparticles to have a high antimicrobial effect, which can be used to disinfect root canals[9,10]. Recent studies have suggested using nanoparticles due to their size and their effectiveness on microbes at lower levels[11-14]. One of the most popular proposed nanowires is Silver nanoparticles (AgNPs), whose action mechanism is controversial and has many challenges[11]. AgNPs can cause cell membrane perforation by affecting bacteria; Evidence has shown that cell DNA denaturation can also be affected by AgNPs[15]. There is no evidence that the size or concentration of AgNPs affects the mechanism of action. However, dentists use it because of its effective properties on antimicrobial activity. Studies have shown the positive effect of using nanoparticles on antimicrobial activity in the root canal[16-19]. Therefore, the present study was conducted to evaluate the effect of silver nanoparticles in root canal treatment.

Methods

The present study is a systematic review and meta-analysis that was conducted based on PRISMA guidelines[20]. In this study, international databases such as PubMed, Scopus, Science Direct, ISI, Web of Knowledge, and Embase were reviewed to select articles related to the purpose of this study until July 2022. Mesh keywords were used for searching in PubMed, and similar keywords were searched in other databases. In the current study, **table I** shows the response to PICO; the Google Scholar search engine was also used. MeSH terms keywords:

((((“Nanoparticles”[Mesh]) OR (“Nanoparticles/administration and dosage”[Mesh] OR “Nanoparticles/adverse effects”[Mesh] OR “Nanoparticles/classification”[Mesh] OR “Nanoparticles/standards”[Mesh] OR “Nanoparticles/statistics and numerical data”[Mesh] OR “Nanoparticles/toxicity”[Mesh])) AND “Silver”[Mesh]) AND (“Dental Pulp Cavity”[Mesh] OR “Root Canal Preparation”[Mesh] OR “Root Canal Therapy”[Mesh] OR “Root Canal Obturation”[Mesh] OR “Root Canal Irrigants”[Mesh])) OR (“Root Canal Irrigants/administration and dosage”[Mesh] OR “Root Canal Irrigants/adverse effects”[Mesh] OR “Root Canal Irrigants/classification”[Mesh] OR “Root Canal Irrigants/standards”[Mesh]).

Table I: PICO strategy.

PICO strategy	Description
P	Population: tooth roots with root canals infected with any microbial organism
I	Intervention: silver nanoparticles
C	Comparison: conventional irrigants or did not have an irrigant
O	Outcome: Effectiveness

Inclusion and exclusion criteria

In-vitro studies, articles published in English included. Studies other than In-vitro studies, conflicting data with objective, and studies without full text were excluded from the study.

Reporting and extracting study data

It used a checklist that included the author’s name, year of publication, type of study, Specimens, Bacterial Inoculation, groups, and Detection; the data of the studies were extracted and reported in **table II**.

Evaluating the quality of studies

The quality of the studies was evaluated based on the risk of bias assessment of the previous Systematic Review and Meta-analysis of In Vitro Studies[21,22]. The way of scoring the studies is such that if a study did not report one to three cases, it is of high quality (low risk of bias); Failure to report four to six cases indicates moderate quality (moderate risk of bias) and more than six cases indicates that the quality of the studies is very low (high risk of bias).

Data analysis

STATA.V17 software was used for data analysis. Effect size with 95% confidence interval (CI) with fixed effect modal and inverse-variance method were done. The level of heterogeneity was evaluated using the I^2 index test ($I^2 < 50\%$ = low levels, 50 < I2 < 75% = moderate and $I^2 > 75\%$ = high levels).

Table II: Data extracted from studies selected.

No.	Study. Years	Study design	Sample size		Bacterial Inoculation
			Experimental Group	Control group	
1	Gholami et al., 2022[23]	In-vitro	AgNP solution (1.0 mL, particle size 27.43 nm and 29.66 nm) for 20 min	Alcoholic solution of CHX (2 mg/mL)	Enterococcus faecalis
2	Farahat et al., 2022[24]	In-vitro	AgNP solution, 200ppm	SNPs Gel	Enterococcus faecalis
3	Razumova et al., 2022[25]	In-vitro	AgNP solution	CHX	Enterococcus faecalis
4	Abdelfatah et al., 2020[26]	In-vitro	AgNPs solution	CHX and sterile saline	Enterococcus faecalis
5	Kushwaha et al., 2018[27]	In-vitro	AgNP suspension (20 nm, 3 min	CHX (2 %)	Enterococcus faecalis
6	De Almeida et al., 2018[28]	In-vitro	AgNP solution (5- 20 nm, 1 min	Saline ultrasonically activated (1 min, 0.85%)	Enterococcus faecalis
7	Afkhami et al., 2017[29]	In-vitro	AgNP suspension (30 nm, 5 min	NaOCl (2.5%, 5 min)	Enterococcus faecalis
8	Wu et al., 2014[30]	In-vitro	AgNP solution (2 min)	NaOCl (2%)	Enterococcus faecalis

Table III: Data extracted from studies selected.

No.	Study. Years	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Risk of Bias
1	Gholami et al., 2022[23]	Yes	NR	Yes	Yes	Yes	Yes	Yes	NR	None	Low
2	Farahat et al., 2022[24]	Yes	NR	Yes	Yes	Yes	Yes	Yes	NR	None	Low
3	Razumova et al., 2022[25]	Yes	NR	Yes	Yes	Yes	Yes	Yes	NR	None	Low
4	Abdelfatah et al., 2020[26]	Yes	NR	Yes	Yes	Yes	Yes	Yes	NR	None	Low
5	Kushwaha et al., 2018[27]	Yes	NR	No	Yes	Yes	Yes	Yes	NR	NR	Medium
6	De Almeida et al., 2018[28]	Yes	NR	Yes	Yes	Yes	Yes	Yes	NR	None	Low
7	Afkhami et al., 2017[29]	Yes	NR	Yes	Yes	Yes	Yes	Yes	NR	None	Low
8	Wu et al., 2014[30]	Yes	NR	Yes	NM	Yes	NR	Yes	NR	None	Medium

Q1: Were Human Teeth Used as Specimens?
Q2: Was the Sample Size Statistically Calculated?
Q3: Was Bacterial Inoculation Verified?
Q4: Was Particle Size Mentioned?
Q5: Was a Control Group Present?
Q6: Were the Teeth Cleaned and Shaped before Irrigation?
Q7: Was the Irrigation Time the Same for Experimental and Control Groups?
Q8: Was the Observer/Evaluator Blind to the Groups?
Q9: Was There Any Conflict of Interest?
NR: not reported; NM: Not mentioned

Results

The search was conducted based on the mentioned keywords, and 141 studies were found in the introduced databases; After entering the studies into the EndNote. x8 software, duplicate studies were removed, and finally, the abstract of 110 studies were reviewed, and the studies that met the inclusion criteria were left out for the full-text review; at this stage, 80 studies were removed. The full text of 30 studies was carefully reviewed, and studies that had incomplete data, very low quality, or did not include the inclusion criteria and matched the exclusion criteria were excluded from the study (22 articles); finally, eight articles were selected, and their data were extracted for meta-analysis (**Figure 1**).

Characteristics

Eight in-vitro studies have been included in the present article; a summary of the data of the selected studies is reported in **table II**.

Risk assessment

According to **table III**, out of the eight selected studies, two studies were of medium quality and six studies were of high quality; the answers to 9 questions are summarized in **table III**; all studies did not report Sample Size Statistically Calculated and Observer/Evaluator Blind to the Groups.

Assessment of Antibacterial Activity

The significantly highest reduction in bacteria count was followed by silver nanoparticles groups ($p=0.00$); the effectiveness of silver nanoparticles compared to the control group was 86% (ES: 95% CI, 0.39 to 1.33; $p<0.001$). ($I2<0\%$; $P=1.00$; low heterogeneity) (**Figure 2**). Galbraith plot for heterogeneity analysis showed no inconsistency across studies (**Figure 3**).

Figure 1: PRISMA flowcharts.

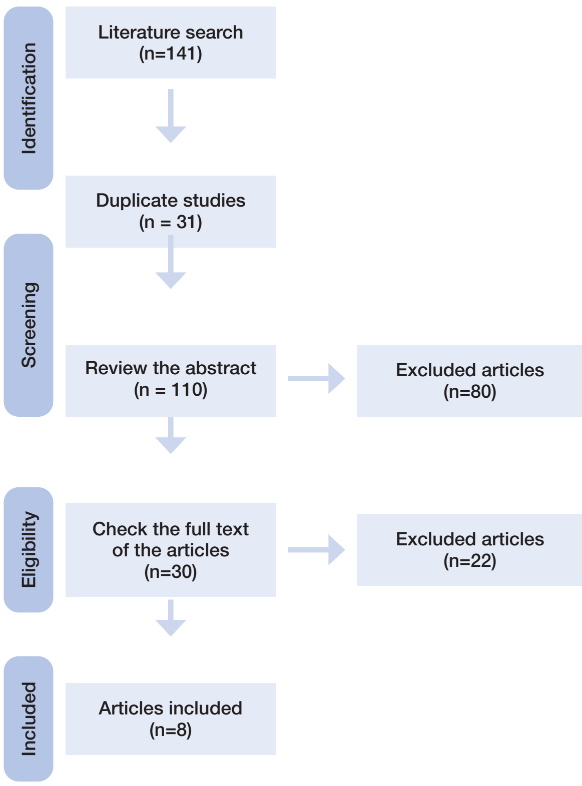


Figure 2: The Forest plot showed the effectiveness of silver nanoparticles on Antibacterial Activity.

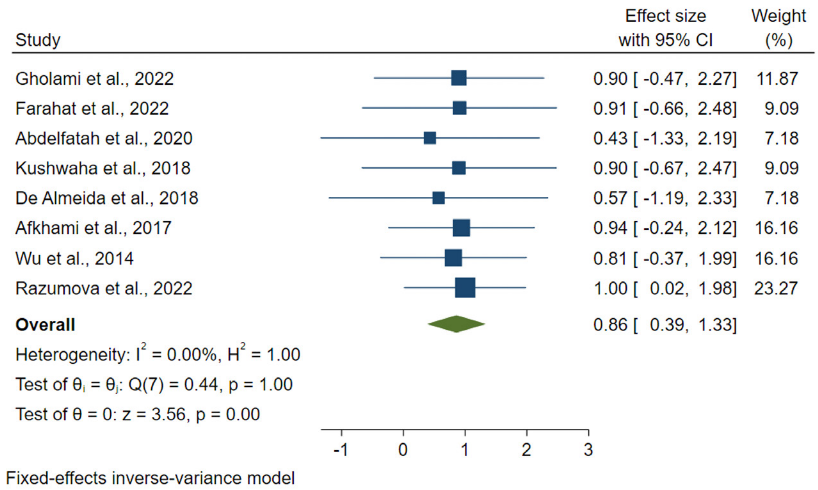
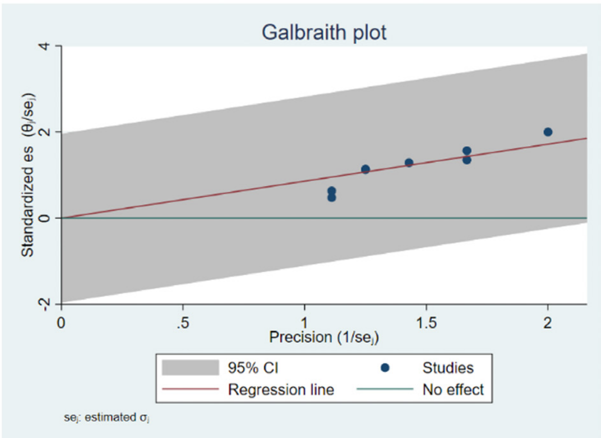


Figure 3: Galbraith plot for assessing heterogeneity.



Discussion

In recent years, the use of nanotechnology in medicine and dentistry has received much attention. In dentistry, to achieve ideal oral and dental health, nano dentistry has been proposed, which is the use of biotechnology, nanomaterials, and dental nanorobotics[31,32]. In the past years, nanotechnology has been used in orthodontic treatments, periodontal diseases, dental implants, the development of nanocomposites, drug delivery systems, and the making of disinfectant solutions[33]. Due to their small size, nanoparticles can be used in a very small volume, so they have better antimicrobial performance. As reported, several mechanisms of AgNPs make bacteria less resistant to them. As studies have shown, the main challenge in root canal treatment is treatment failure, which is caused by repeated infections and antimicrobial agents that have become resistant to the use of antibiotics[19,34-37]. Today, the effort is to introduce an ideal antiseptic so that the treatment failure can be practically reduced and root canals free from germs can be obtained for the general public. Studies have shown that Enterococcus faecalis was isolated from many examined samples[38-40]. Also, some studies have reported Fusobacteria and Pseudomonas with a high prevalence ratio[41,42]. The literature shows that nanoparticles can have antimicrobial effects[43-45]. Silver is one of the oldest nanoparticles used as antimicrobial agents[46,47]. However, the mechanism of action of AgNPs is not precisely known, and several methods have been proposed. Based on the findings of the present study, the use of AgNPs can have an antimicrobial effect; the experimental group had a significant improvement compared to the control group. Nanoparticles have increased antimicrobial activity by decreasing size due to increased surface area, which allows for greater interaction between ions and the microbial organism. The properties of nanoparticles are different from their corresponding bulk materials, resulting from a high surface-to-volume ratio[48]. It can be stated that nanoparticles perform a better antimicrobial function by increasing the surface-to-volume ratio. It affects their biocompatibility and cytotoxicity much less than conventional compounds[49-51].

One of the limitations of the present study was that most of the existing studies had used AgNPs as an additive for a detergent and were not considered due to possible confounders excluded from the study. The standard or non-standard of the tested conditions can also affect the study results, which tried to use the criteria to determine the strength of the study protocol. In the studies, the concentration of the used solution and the size of the particles were different, which can be considered a confounding factor, and the findings of the present study should be interpreted with caution. Also, one of the other limitations of the study was the time of disinfection in the studies, which was different from each other and could affect the results of the study; In the future, it is better to conduct studies with a similar method (particle size, concentration of silver nanoparticles and disinfection time) to provide better results with stronger evidence. One of the similarities of the informants was the use of syringes for AgNP; however, the needle size of the syringes was not the same. In the studies, the contact times of AgNP compared to other detergents differed from 1 to 20 minutes, which should be used with caution. More studies are needed, taking into account the size of the particles, the concentration of silver nanoparticles, the time of disinfection, similar to other studies, and taking into account the changes in the properties that affect the antimicrobial activity of silver nanoparticles to confirm the current evidence and provide more accurate and comprehensive results.

Conclusions

Based on the findings of the present study, AgNPs have a high antimicrobial effect in preventing the persistence of microorganisms in the root canal and root canal treatment failure, and AgNPs with different formulations can have an antimicrobial effect. However, the present study had limitations that should be considered when interpreting the results; Also, the size of the particles, the concentration of silver nanoparticles, and the time of disinfection can affect the antimicrobial properties of AgNPs, which requires more studies in this field.

Conflict of Interest

The authors declared that there is no conflict of interest.

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