International Journal of Scientific Research in Dental and Medical Sciences

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Evaluation of the Effects of ZnONPs, Standard AgNPs, and Im-AgNPs Nanoparticles on the Microhardness of Root Canal Dentin: A Systematic Review and Meta-analysis

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ARTICLE INFO

Article history:
Received 05 September 2024
Received in revised form 26 October 2024
Accepted 20 November 2024
Available online 30 November 2024

Keywords:
Endodontics
Nanoparticles
Root Canal Irrigants

ABSTRACT

Background and aim: The present study aimed to evaluate the effect of Zinc Oxide (ZnONPs), Standard Silver(AgNPs), and Imidazolium-based Silver (Im-AgNPs) nanoparticles on the microhardness of root canal dentin.
Material and methods: The literature was screened via international databases Cochrane, Embase, and MEDLINE (PubMed and Ovid) up to October 2024 with English language restriction. Two reviewers independently performed screening and evaluation of articles. The ToxRTool® checklist information contained eighteen items to evaluate Methodological quality. The mean difference was used as an effect size indicator to analyze each included study. The fixed-effect model with the Inverse–variance method combined the effect size. All meta-analyses were performed using Stata software (version 17).
Results: A total of 219 articles were retrieved from all the databases; after applying eligibility criteria, seven studies were included. Immersion in standard AgNP irrigant significantly increased the VHN compared to the control group in the coronal (MD: 16.13 95% CI; 15.39-16.86; P<0.001). Immersion in Im-AgNPs significantly increased the VHN in the middle (MD: 6.60 95% CI; 1.90-11.31; P<0.05) and apical (MD: 10.25 95% CI; 5.78-14.72; P<0.001). ZnONPs irrigant increased the VHN, compared to the control group in the coronal (MD: 10.92 95% CI; 10.13-11.71; P<0.001).
Conclusions: Based on the present meta-analysis, root canal irrigants containing ZnONPs, Standard AgNPs, and Im-AgNPs can improve the microhardness of root canal dentin in coronal, middle, and apical regions.

1. Introduction

The important goal of root canal treatment is to remove and eradicate microorganisms.[1] No solution still meets all the requirements for the perfect endodontic irrigant. However, numerous irrigants have been proposed to improve root canal disinfection and the success of endodontic treatment.[2, 3] Sodium hypochlorite (NaOCl) is currently considered the gold standard due to its high effectiveness in dissolving organic residues and silver nanoparticles (AgNPs) against bacteria and biofilm.[4, 5] Its disadvantages include toxicity, unpleasant taste, inability to remove the smear layer completely, and adverse effects on the flexural strength of dentin.[6] Therefore, replacing other irrigation methods with higher effectiveness and fewer side effects is important.[7, 8] Research and development in science have been transformed by nanotechnology, a remarkable breakthrough in the last decade.[9] Studies have shown that AgNPs have exceptional antimicrobial properties and are effective against drug-resistant pathogens such as E. faecalis due to their nano-size, which facilitates penetration into the cell membrane of microorganisms.[10-13] Imidazolium-coated silver nanoparticles (Im-AgNPs) with antimicrobial properties and high biocompatibility have been reported as potential root canal irrigants.[14, 15] Studies reported that Im-AgNPs resulted in higher surface roughness and lower cytotoxicity.[16, 17] Other nanoparticles reported high antibacterial activity with acceptable toxicity, including zinc oxide (ZnONPs).[18-20] Studies have shown that NaOCl and ethylenediaminetetraacetic acid (EDTA) can affect the structural properties of dentin.[21] Therefore, the present study aimed to evaluate the effect of standard AgNPs, Im-AgNPs, and ZnONP nanoparticles on the microhardness of root canal dentin.

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https://doi.org/10.30485/IJSRDMS.2025.506747.1639

2. Material and methods

Strategy for searching and sources of information

Relevant keywords were searched in the international databases Cochrane, Embase, and MEDLINE (PubMed and Ovid) up to October 2024 to evaluate the influence of standard ZnONPs, Standard AgNPs, and Im-AgNPs nanoparticles on the microhardness of root canal dentin.

The search strategy used in MEDLINE (via PubMed)

((((((((("Dental Pulp Cavity"[Mesh] OR "Root Canal Preparation"[Mesh] OR "Root Canal Therapy"[Mesh] OR "Root Canal Irrigants"[Mesh] OR "Root Canal Obturation"[Mesh]) OR ("Root Canal Irrigants/classification"[Mesh] OR "Root Canal Irrigants/standards"[Mesh])) AND "Nanoparticles"[Mesh]) OR "Metal Nanoparticles"[Mesh]) OR ("Nanoparticles/adverse effects"[Mesh] OR "Nanoparticles/standards"[Mesh] OR "Nanoparticles/statistics and numerical data"[Mesh] OR "Nanoparticles/toxicity"[Mesh])) OR "Magnetite Nanoparticles"[Mesh]) AND "Sodium Hypochlorite"[Mesh]) AND "Anti-Bacterial Agents"[Mesh]) OR "Anti-Infective Agents"[Mesh].

The search strategy used by Cochrane

"Root Canal Therapy" OR "Root Canal Irrigants" AND "Nanoparticles" OR "silver nanoparticles" OR "AgNPs" OR "Imidazolium-coated silver nanoparticles" OR "Im-AgNPs" OR "zinc oxide" OR "ZnONPs" AND "microorganism "AND "microhardness."

The search strategy used in Embase

(Root Canal treatment) OR (Root Canal Therapy) OR (Root Canal Irrigants): ab, ti, kw.

Nanoparticles: ab, ti, kw.

(silver nanoparticles) OR (AgNPs) OR (Imidazolium-coated silver nanoparticles) OR (Im-AgNPs) OR (zinc oxide) OR (ZnONPs): ab, ti, kw.

Chapter' OR 'conference abstract' OR 'conference paper' OR 'conference review' OR 'editorial' OR 'erratum' OR 'letter' OR 'note' OR 'preprint' OR 'short survey'/it (Filter).

In addition to Google Scholar, the Cochrane Central Register of Controlled Trials, Web of Science, EBSCO, ISI, Elsevier, and the Scopus Wiley Online Library were consulted. The current study is based on the 27-point checklist PRISMA 2020(22).

Selection criteria

English-language publications met the inclusion requirements for this study. The answers to the questions in the current study were based on the PICO strategy (Table 1). Review studies and books; qualitative studies; animal studies; studies without comprehensive and relevant data.

Table 1. PICO strategy

PICO Strategy	
Population (P)	Human teeth needed endodontic treatment.
Intervention (I)	Nano-based irrigants (AgNPs, Im-AgNPs, and ZnONP nanoparticles)
comparison (C)	NaOCl and normal saline
Outcome (O)	Microhardness

The process of selection and data collection

Two blind researchers collected data from the selected studies, and after completion, the researcher blindly and independently reviewed all cases. The research team prepared the original form containing information such as the author's name, year of publication, study design, tooth samples, intervention group, control group, Characterization of nanoparticles, and Measurement of dentin microhardness.

Heterogeneity and publication bias

The heterogeneity across studies was examined using the Chi-square ($\chi2$) test and quantified by the I^2 statistic. According to the I^2 value, heterogeneity was classified as low (less than 50%), between 50 and 74% means moderate heterogeneity, and above 75% is considered high heterogeneity.

The chi-square test ($\chi2$) was used to analyze heterogeneity between studies and the I^2 statistic was used to quantify it. Based on the I^2 value, heterogeneity was classified as low (less than 50%), moderate (between 50% and 74%), and high (above 75%).

Methodological quality

ToxRTool® checklist information contained eighteen items(23). first determined whether the content of the article met the requirements and answered "yes" or "no." A "yes" response received a score of 1, and a "no" response received a 0. Second, the ratings were used to categorize the studies into three levels. Climatic level 1 was assigned values between 15 and 18, indicating reliable and unqualified data; Level 2 was assigned values between 11 and 14, indicating reliable and limited type data; and Level 3, which declared unreliable data, was assigned values below 11 points or that did not meet the red standard qualification.

Data analysis

The present meta-analysis used mean difference (MD) as an effect size indicator to analyze each included study. The fixed-effect model with the Inverse–variance method combined the effect size. All meta-analyses were performed using Stata software (version 17). $P < 0.05$ was considered statistically significant.

3. Results

Selection of the study

In the initial search with related keywords, 219 articles were obtained from international databases. After two independent and blind researchers reviewed the articles and removed duplicates unrelated to the study, the topic of the abstracts of 143 articles was carefully reviewed in the next step in the next step. Articles that did not meet the inclusion criteria were excluded, and the full text of 34 articles was examined. Among these articles, only seven were consistent with the purpose of the present study and were included in the study.

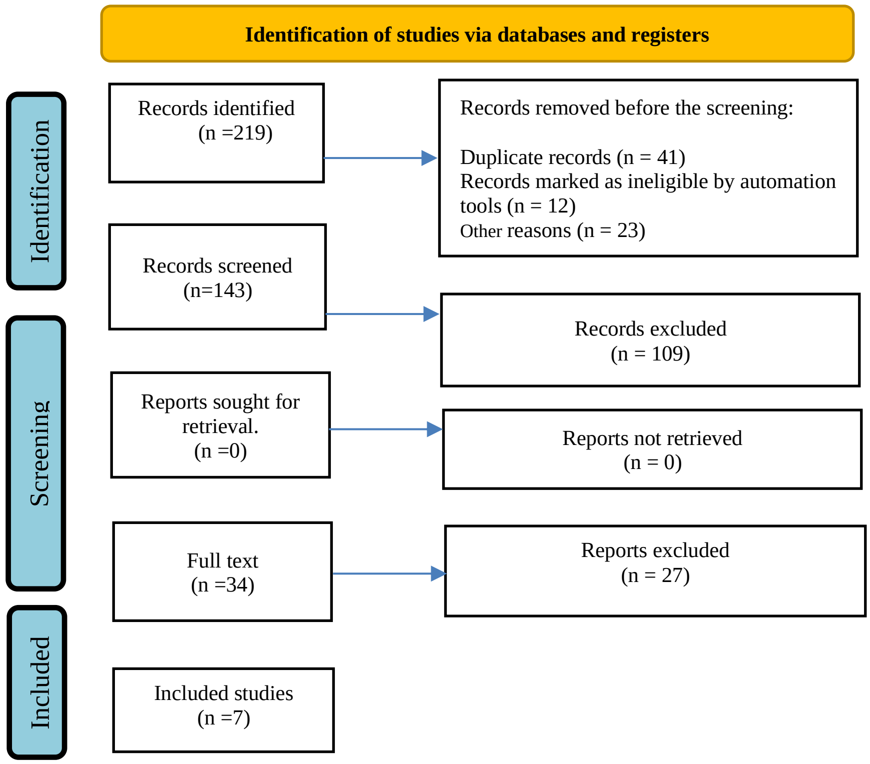

Fig. 1. PRISMA 2020 Checklist.

Study characteristics

In total, 330 extracted human teeth were utilized in the included studies. These predominantly employed single-rooted teeth like maxillary and mandibular incisors, canines, and mandibular premolars. In all studies, microhardness assessments were performed using Vickers hardness number (VHN). The characteristics of the studies were reported in Table 2.

Bias Assessments

The risk of bias in all studies was classified as moderate to low risk of bias.

Table 2. Summary of characteristics of the included studies.

Study. Years	Study Design	Tooth Samples	Teeth Type	Groups	Measurement of Dentin Microhardness
Aboudoura et al., 2024[24]	In-vitro	20	Human single canaled mandibular premolars	AgNPs (n=5) 5.25% NaOCl (n=5)	Vickers Hardness Units
Fahmy et al., 2024[25]	In-vitro	30	Human permanent single-rooted teeth	AgNPs (n=10) AgNPs+ CHX (n=10) 2% Chlorhexidine (n=10)	Vickers Hardness Units
Sahebi et al., 2023[26]	Ex-vivo	80	Human mandibular premolars	AgNPs (n=16) Im-AgNPs (n=16) 0.1% ZnONPs (n=16) 2.5% NaOCl (n=16) Normal saline (n=16)	Vickers Hardness Units
Mohamed et al., 2023[27]	In-vitro	30	Human single-rooted teeth	AgNPs (n=10) AgNPs with curcumin (n=10) Ca(OH)2 (n=10)	Vickers Hardness Units
Hassan et al., 2018[28]	In-vitro	60	Human single-rooted lower premolar teeth	AgNPs (n=20) Ca(OH)2 (n=20) Salin (n=20)	Vickers Hardness Units

Farshad et al., 2017[29]	In-vitro	50	Human permanent anterior teeth	ImSNP (n=10) Deionized water (n=10) NaOCl (n=10) CHX (n=10) EDTA (n=10)	Vickers Hardness Units
Al-Naimi et al., 2015[30]	In-vitro	60	Human mandibular premolars	AgNPs (n=10) 0.1% ZnONPs (n=10) Control (n=10)	Vickers Hardness Units

Root canal dentin microhardness

ZnONPs irrigant increased the VHN, compared to control group in the coronal (MD: 10.92 95% CI; 10.13-11.71; P<0.001 (I^2= 75.07 P<0.05)), middle (MD: 10.92 95% CI; 10.13-11.70; P<0.001 (I^2= 68.30 p=0.08)) and apical (MD: 10.86 95% CI; 10.07-11.65; P<0.001 (I^2= 88.48 P<0.001)) (Figs. 2, 3 and 4).

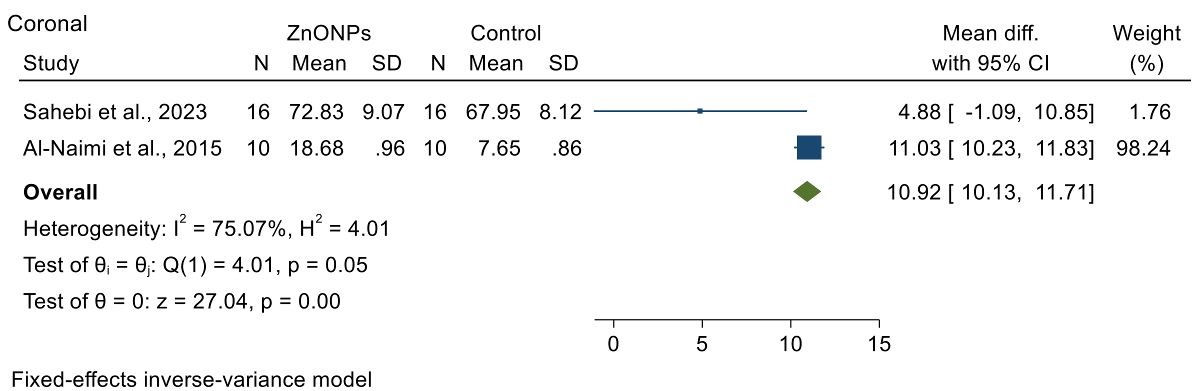

Fig. 2. The forest plot showed Mean differences in coronal microhardness following irrigation by ZnONPs.

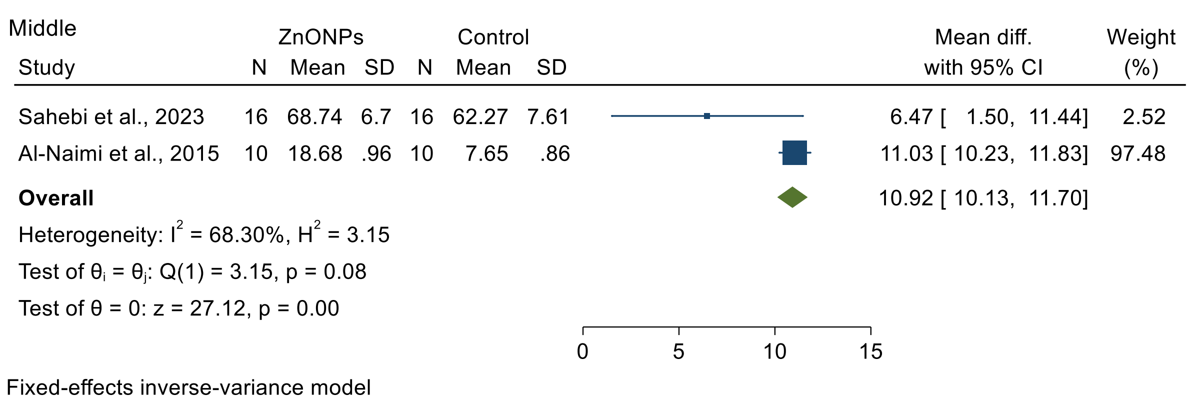

Fig. 3. The forest plot showed Mean differences of middle microhardness following irrigation by ZnONPs.

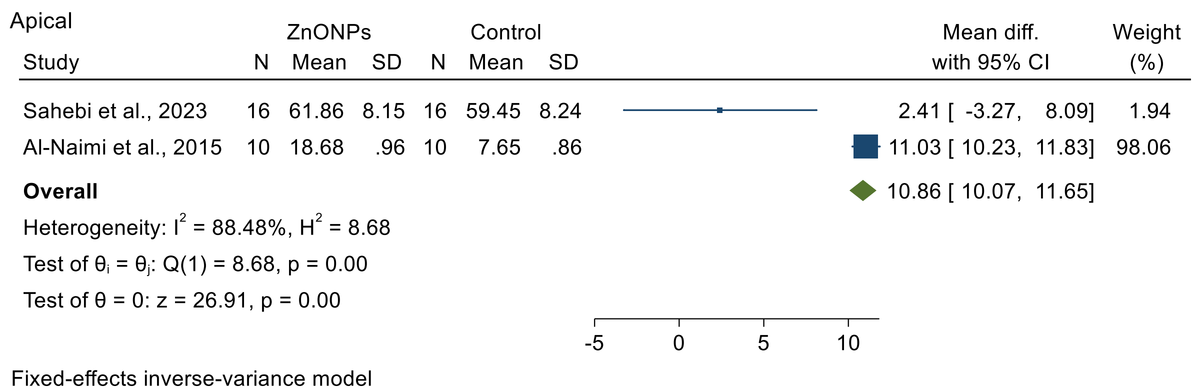

Fig. 4. The forest plot showed Mean differences of apical microhardness following irrigation by ZnONPs.

Immersion in Standard AgNPs irrigant significantly increased the VHN compared to the control group in the coronal (MD: 16.13 95% CI; 15.39-16.86; P<0.001 (I^2= 99.53 P<0.001)), middle (MD: 16.15 95% CI; 14.46-17.84; P<0.001 (I^2= 96.38 P<0.001)) and apical (MD: 14.96 95% CI; 13.09-16.85; P<0.001 (I^2= 98.14 P<0.001)) (Figs. 5, 6 and 7).

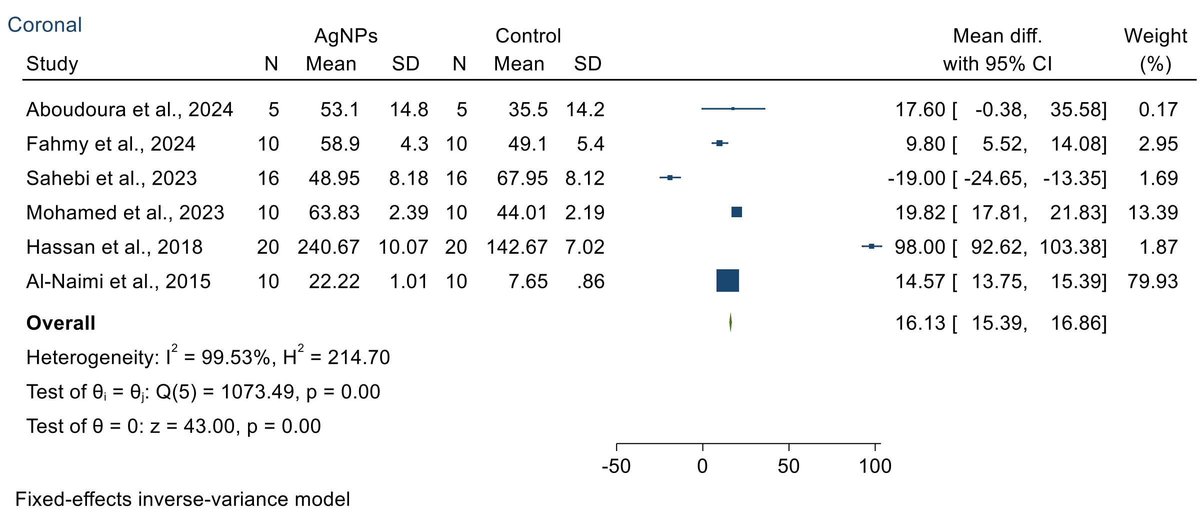

Fig. 5. The forest plot showed Mean differences in coronal microhardness following irrigation by AgNPs.

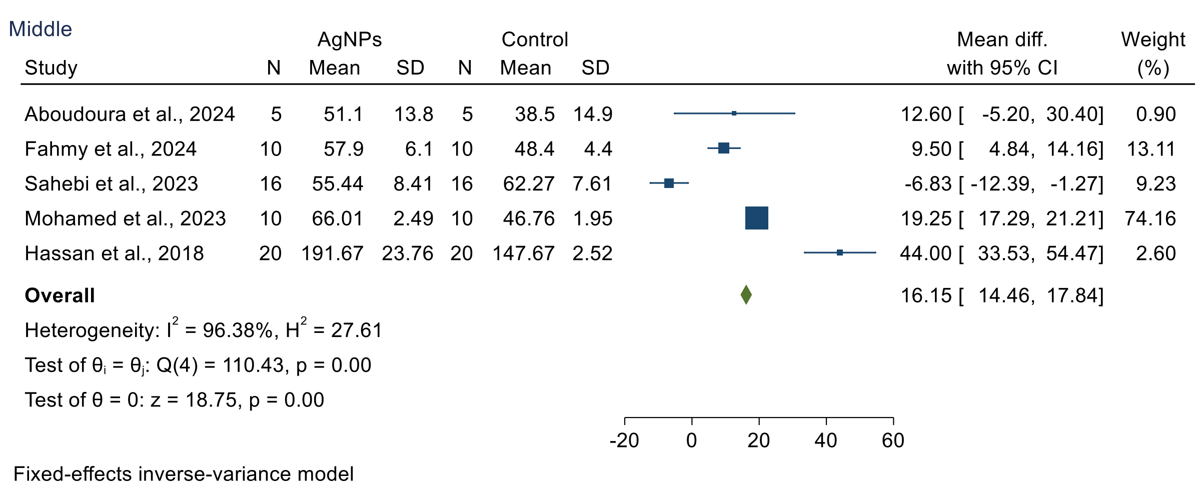

Fig. 6. The forest plot showed mean differences in middle microhardness following irrigation by AgNPs.

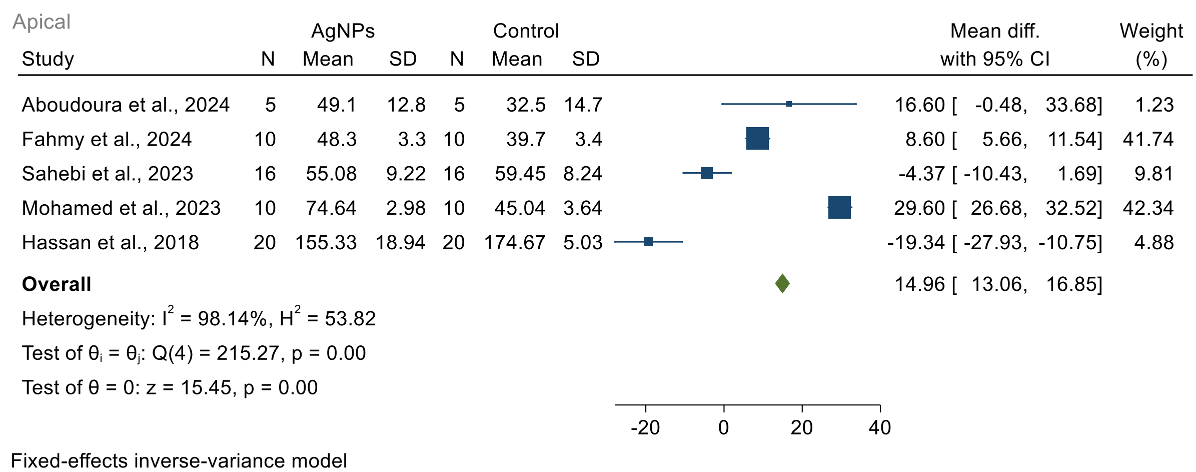

Fig. 7. The forest plot showed mean differences in apical microhardness following irrigation by AgNPs.

Immersion in Im-AgNPs decreased the VHN in the control; however, no statistical difference was observed compared to the control group (MD: -1.16 95% CI; -6.34-3.13; p=0.51 (I^2= 93.04 P<0.001)). However, immersion in Im-AgNPs significantly increased the VHN in the middle (MD: 6.60 95% CI; 1.90-11.31; P<0.05 (I^2= 91.06 P<0.001)) and apical (MD: 10.25 95% CI; 5.78-14.72; P<0.001 (I^2= 87.57 P<0.001)) (Figs. 8, 9 and 10).

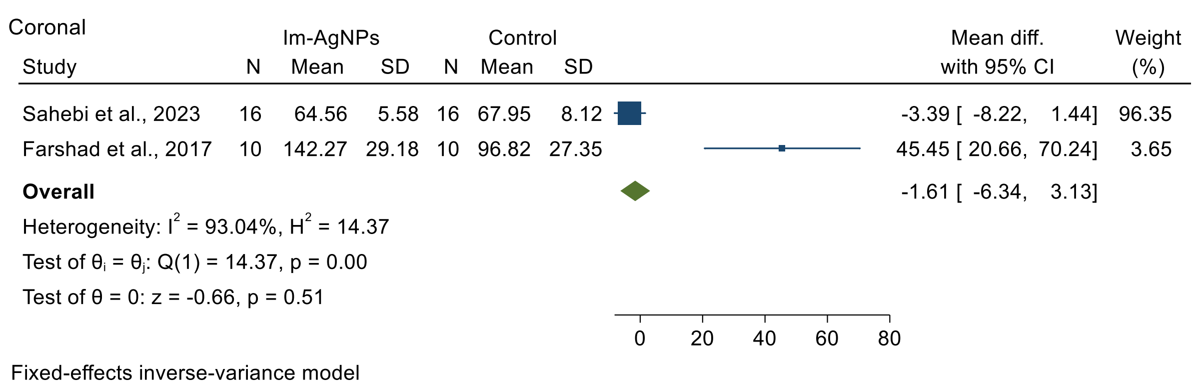

Fig. 8. The forest plot showed Mean differences in coronal microhardness following irrigation by Im-AgNPs.

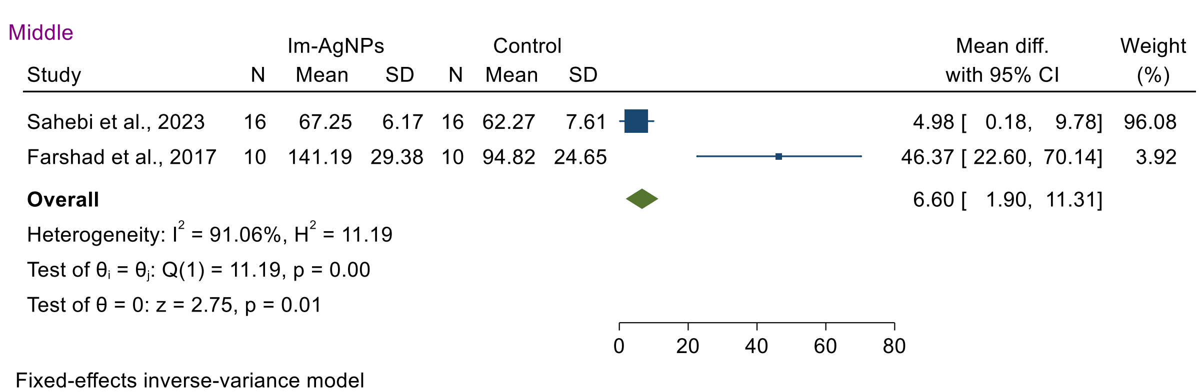

Fig. 9. The forest plot showed Mean differences in middle microhardness following irrigation by Im-AgNPs.

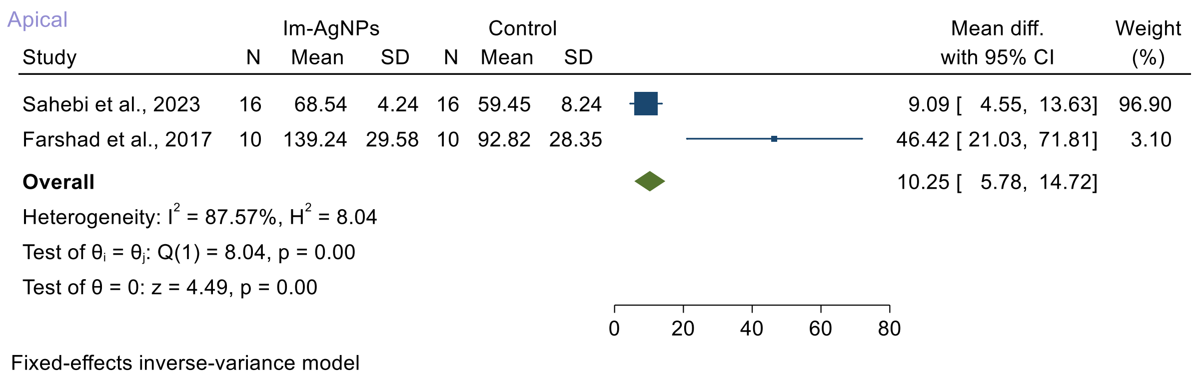

Fig. 10. The forest plot showed mean differences in apical microhardness following irrigation by Im-AgNPs.

4. Discussion

Root canal disinfection, three-dimensional obturation, and the quality and technique of chemomechanical preparation are crucial for the success of endodontic treatment.[31] Endodontic irrigants can alter the chemical composition of the material through their action on the organic and inorganic phases of dentin, reducing its microhardness and increasing the risk of tooth fractures. Therefore, it is important to carefully select irrigants to optimize effectiveness and reduce negative effects on root canal dentin.[32] Roughness, hardness, and fracture strength are some of the parameters that should be considered when assessing the physical properties of root dentin.[33] The term "hardness" describes the resistance of a solid material to destruction, plastic deformation, and elastic deformation. There are two types of tooth hardness: static and dynamic. Static indentation hardness, which includes Knoop, Vickers, and nano hardness, is the most widely used characterization technique.[34] All included studies used Vickers hardness number. The present meta-analysis showed standard AgNPs nano-based irrigant significantly increased the VHN in the coronal, middle, and apical in all studies, except Sahebi et al.[26] that reported AgNPs nano-based irrigant significantly decreased the VHN in the apical and coronal s and Hassan et al.[28] reported AgNPs nano-based irrigant significantly decreased the VHN in the apical s. According to the present meta-analysis, immersion in Im-AgNPs significantly increased the VHN in the middle and apical. Also, ZnONPs nano-based irrigant increased the VHN in the coronal, middle, and apical. Suzuki et al., 2019 found that AgNP nanoparticles had little or no influence on the mechanical properties of dentin and resin cement in different root canal thirds.[35] Hassan et al., 2018 found that applying AgNP nanoparticles as an intracanal drug increased the microhardness of root canal dentin.[28] The deposition of silver nanoparticles on the root canal wall and their deep penetration into the dentin tubules could cause these results. However, there is no documentation on the effect of intracanal drugs containing curcumin on dentin microhardness. According to Hiraishi et al., this led to an increase in dentin microhardness records.[36] Which showed that 3–8% silver diamine fluoride deposited on the surface of the root dentin and penetrated up to 40 mm deep into the dentinal tubules. The intracanal administration of AgNPs exhibited higher microhardness values by Hassan et al.[28] Jowkar et al., 2020 showed that the fracture strength of teeth that had previously received endodontic treatment increased using AgNP nanoparticles as a final irrigant.[18] In the present study, only two studies have investigated the impact of Im-AgNPs irrigant on root dentin microhardness. Chlorhexidine and NaOCl are less effective against bacteria than Im-AgNPs nanoparticles even at lower concentrations.[37] Farshad et al., found that Im-AgNPs nanoparticles improved the roughness of root dentin and changed the physicochemical properties of dentin. The main causes were either the inequality of charge distribution on the cationic part of the imidazole and dentin surface or the type of ionic liquid (imidazole).[29] Jowkar et al., ZnONP nanoparticles improved root fracture resistance in teeth subjected to endodontic treatment.[18] AgNPs had a greater positive effect on root fracture strength than ZnONPs, although with no significant differences. The results showed that sealants containing AgNPs had a greater increase in microhardness than those containing ZnONPs nanoparticles. Since metals are more complex than metal oxides, even at lower concentrations, researchers hypothesized that the higher increase in microhardness could be due to the nature of the nanoparticles.[30]

5. Conclusion

Based on the present meta-analysis, root canal irrigants containing ZnONPs, Standard AgNPs, Im-AgNPs can be used to improve the microhardness of root canal dentin in coronal, middle and apical. It is suggested to conduct further studies to determine the results with stronger evidence in examining the effect of Im-AgNPs and ZnONPs on microhardness dentin. Additionally, studies need to increase sample size and use the same cognitive methodology as other studies.

Conflict of Interest

The authors declared that there is no conflict of interest.

Acknowledgments

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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How to Cite this Article: Ahmadi S, Zamiri SS, Sedghi S, Karami Amidabadi S, Moradi M. Evaluation of the Effects of ZnONPs, Standard AgNPs, and Im-AgNPs Nanoparticles on the Microhardness of Root Canal Dentin: A Systematic Review and Meta-analysis. International Journal of Scientific Research in Dental and Medical Sciences. 2024;6(4):199-207. https://doi.org/10.30485/IJSRDMS.2025.506747.1639.