10.21608/adjc.2023.233379.1391 Advanced Dental Journal
Volume 6 | Issue 3 | Pages 417 – 430

Original Article

Effect of Nitrofurantoin Versus Calcium Hydroxide used as an Intracanal Medicament on Bacterial Load Reduction in Teeth with Necrotic Pulp: A Randomized Clinical Trial

Noha Mohammed Elsaber[1], Angie Galal Ghoniem.[1], Nadia Saeed Hosny [1]

[1]Department of Endodontics, Faculty of Dentistry, Cairo University, Egypt

Email: nohaalsaber@dentistry.cu.edu.eg

Submitted: 1-9-2023
Accepted: 10-12-2023

Abstract

Aim: The Aim of this study was to clinically evaluate the effect of using Nitrofurantoin as an intracanal medicament versus Calcium Hydroxide on bacterial load reduction in patients with necrotic single-rooted permanent mandibular premolars with single canal.

Subjects and methods: Twenty- eight patients with necrotic single canalled mandibular premolars were included. Patients were randomly assigned into two equal groups of 14 patients each. Nitrofurantoin (25 mg/mL) was used as an intracanal medicament in the teeth assigned to the intervention group; while Calcium Hydroxide was used in those assigned to the control group. Standard endodontic treatment was performed in two visits. The intracanal bacterial levels were assessed pre-instrumentation, post-instrumentation and after placement of intracanal medicament for 1 week; through microbiological sampling, transport, dispersion, dilution, culture, and counting of CFU/ml.

Results: Both Nitrofurantoin and Calcium Hydroxide revealed a significant reduction in the bacterial load following instrumentation.

Conclusion: The present study showed that both intracanal medicaments succeeded in significantly reducing bacterial levels in primary infected root canals with no statistically significant difference between the two medicaments.

Keywords: Nitrofurantoin, Calcium Hydroxide,Intracanal Medicament, Bacterial Load Reduction.

I. INTRODUCTION:

Complete eradication of bacteria, their byproducts, and pulpal tissue remains from diseased root canals, as well as the thorough sealing of the cleaned system, are fundamental goals of endodontic therapy.[1] Notably, masses of infecting bacteria and their principal substrate of necrotic pulp debris are removed by routine intracanal procedures including mechanical instrumentation and chemical disinfection. [2] Still, there is overwhelming evidence in the literature that most of the root canals contain viable microorganisms even after the completion of the chemo-mechanical preparation.[3]

The complexity of the root canal system advocates that mechanical instrumentation cannot clean difficult-to-reach locations including isthmi, lateral canals, and infected dentinal tubules.[4] A rigorous irrigation strategy and the use of intracanal medicaments are essential as they provide the optimal reinforcing step to accomplish a full disinfection of the root canal system and prolong the overall antimicrobial contact time.[5]

Calcium Hydroxide $Ca(OH)_2$ is well known to be the gold standard in endodontic therapy amongst all other intracanal medicaments. The efficiency of $Ca(OH)_2$ depends on the gradual release and diffusion of OH- ions in an aqueous medium. Its high alkaline pH (pH≈ 12.5) impacts the pH gradient across the bacterial cytoplasmic membrane. $Ca(OH)_2$ dressing may also function as a physical barrier, limiting root canal reinfection and entombing living bacteria.[6] However, its antimicrobial efficiency is heavily challenged by the buffering property of dentin.[7] $Ca(OH)_2$ does not equally and efficiently treat all endodontic infections, as some microorganisms persist the high alkalinity of $Ca(OH)_2$.[8] Other documented drawbacks of $Ca(OH)_2$ including its negative impact on the flexural strength of dentine and lack of predictable protocol to endure its complete removal, thus affecting future sealing [6], have prompted extensive endodontic research in pursuit of a new intracanal medication. Several of them are even offering more encouraging outcomes when compared to $Ca(OH)_2$.[9]

Antibiotics might be a clinically effective adjuvant in surgical and non-surgical endodontic procedures. For teeth with necrotic pulps, a systemic route of delivery appears to be of minimum aid as they are deprived of normal blood supply. Therefore, local application of antibiotics within the root canal space could be a more efficient strategy.[10]

Single and poly-antibiotic pastes are effective against an extensive range of bacteria. [11] Tetracyclines inhibits the action of clastic cells and stops the activity of collagenases, thus providing a positive outcome in regenerative procedures.[12] Antimicrobial peptides (AMPs) are promising alternatives with high antimicrobial efficacy, good biocompatibility and low bacterial resistance. Another effective antimicrobial agent is nanoparticles, including

metal, polymeric and ceramic nanoparticles that all could be incorporated into available intracanal medicaments or could be loaded with antimicrobial agents.[9]

Nitrofurantoin (Nit) is a well-acknowledged bactericidal agent, frequently prescribed as an oral antibiotic for multidrug resistant urinary tract infections (UTIs). [13] The efficiency of Nitrofurantoin against gram-positive and gram-negative bacteria along with its multiple sites of action, high local levels and low serum concentrations, are few of the advantages over other of the more recent agents.[14]

After thorough systematic online search there were no clinical studies found yet on the effect of Nitrofurantoin antibiotic used as intracanal medicament in teeth with necrotic pulps. [15] The aim of this work was to clinically evaluate the effect of Nitrofurantoin as a novel intracanal medicament on the bacterial load reduction, when compared to Calcium Hydroxide, in teeth with necrotic pulp. The null hypothesis was that there was no difference in bacterial load reduction after using Nitrofurantoin in comparison with Calcium Hydroxide as root canal medicament, following two-visit root canal treatment in necrotic single-rooted permanent mandibular premolars with a single canal.

II. SUBJECTS AND METHODS:

This study was conducted in the Endodontics department, Faculty of Dentistry, Cairo University, Cairo, Egypt between November 2021, and March 2022. The protocol was registered at the ClinicalTrials.gov Identifier: NCT05074628. Sample size was calculated using the (PS software) and was found to be 11 patients per group, making the total sample size 22 patients (2 groups), increased to 28 patients to compensate for the 25% dropout.

Inclusion and Exclusion Criteria:

The inclusion criteria were healthy patients, aged 25-45, having restorable mandibular single rooted premolars, with single root diagnosed with pulp necrosis. Patients reported positive pain on percussion denoting apical periodontitis. Radiographically, slight widening in the periodontal membrane space or periapical radiolucency not exceeding 2*2 mm.

The exclusion criteria were medically compromised, allergic patients, pregnant women and mandibular premolars that were non-restorable, vital pulp, swelling, , mobile or teeth with pocket depth greater than 5mm. Radiographically, evidence external or internal root resorption, vertical root fracture, perforation or calcification excluded the tooth.

Study Design and Settings :

The current investigation was planned as a double-blind parallel randomized controlled trial with an allocation ratio of 1:1. Recruitment and completion of the operative procedure for the study participants were done at the outpatient clinic of the Endodontic Department, Faculty of Dentistry, Cairo University, Egypt.

Randomization and blinding:

Twenty- eight numbers (1-28) were generated by computer software (http://www.random.org/) and randomly allocated to either intervention (Nitrofurantoin) or control (Ca(OH)2) group in Microsoft Excel sheet (Microsoft Corporation, Redmond, WA, USA) using block randomization of 2 blocks with 25 patients in each block and printed on a table. The randomization table was kept with and only accessed by the assistant supervisor (N.H). Eight folded numbered papers were packed in opaque envelopes by (N.H) to be dragged by the patients. The operator (N.M.) made a call to the assistant supervisor (N.H) when an outpatient met the eligibility criteria, to be assigned to one of the 2 groups according to the randomized sequence.

Numbered papers indicating the intracanal medicament to be used were packed in opaque closed envelopes prepared by (N.H). The patient picked up an envelope, after mechanical preparation. The operator (N.M.) opened the envelope and used the intracanal medicament assigned to that patient according to the number present inside the envelope, after contacting (N.H). The patient, the microbiological department's lab technician and the statistician were blinded to the intervention.

The preparation of Nitrofurantoin gel:

To overcome the inconvenience of using powders, Nitrofurantoin had to be prepared in the gel form, utilizing Methylcellulose (MC). MC is a non-toxic, biodegradable, non-allergic polymer, that acts as a binder, thickener and a stabilizing agent. Using a paste mixer (PDM-300, Daewha Tech, Republic of Korea), 80 mg of MC (Sigma-Aldrich Chemie GmbH, Schnelldorf, Germany) was first mixed with 1 ml of distilled water. The resulting solution was heated to 70oC while continuously stirred (16). The gel solution was left to cool to room temperature then combined with 25 mg of Nitrofurantoin powder (KAHIRA PHARM. &CHEM. IND.CO., Cairo,Egypt) and mixed once more to create Nitrofurantoin gel (15).

Treatment Procedure:

Informed consents were signed. Demographic data (age, gender, and tooth number) were recorded. A single operator performed all the procedures. Patients received 1.8 Ml of 2% Mepivacaine HCl with 1:100,000 epinephrine (Mepecaine-L, Alexandria Company for Pharmaceuticals and Chemical Industries, Egypt). All caries and/or coronal restorations were completely removed with a sterile bur and rubber dam was applied. The operative field was thoroughly cleaned with 30% hydrogen peroxide (LUNA Perfumes and Cosmetics, Egypt) until no further bubbling of the peroxide occurred. All surfaces were then disinfected by a sterile cotton swab with a 5.25% sodium hypochlorite solution (NaOCl) (Clorox, 10th of Ramadan, Egypt).

The access cavity was then prepared using another sterile bur (Dentsply Maillefer, Ballaigues, Switzerland). After completing the access, the operative field and the pulp chamber were cleaned and disinfected once again in the same way mentioned above. NaOCl was then

neutralized with 5% sodium thiosulfate. The sterility of tooth surfaces was checked by taking a swab sample and streaking on blood agar plates with subsequent incubation at 37 °C in both aerobic and anaerobic conditions. If any positive culture was detected, the sample was excluded.

The pre-instrumentation root canal samples (S1) were taken as follows: three sterile paper points were consecutively placed in the canal to soak up the fluid in the canal to a level approximately 1 mm short of the tooth apex based on diagnostic radiographs and estimated working length. Each paper point was left in the canal for 1 minute. Paper points were then transferred aseptically to sterile tubes containing brain heart infusion (BHI) broth.

The canal was scouted with #10 and #15 hand files (K-FILES, MANI, INC., Industrial Park, Utsunomiya, Tochigi, Japan). Working length was determined using an electronic apex locator (Root ZX, J. Morita USA, Irvine, CA) then confirmed radiographically to be 0.5 -1 mm shorter than radiographic apex.

ProTaper Next files system rotary files (Dentsply Maillefer, Ballaigues, Switzerland) with a gear reduction torque-controlled motor X-Smart (X-Smart, Dentsply, Maillefer, USA) set to the instructions provided by the manufacturer was used to prepare the canals (300 rpm, torque of 2 Ncm). The files were used sequentially till instrument X4 (40.06). The canal was irrigated and recapitulated after the use of each instrument.

EDTA gel (MD-Chelcream. META BIOMED CO., LTD, Korea) was used as a lubricant. The canal was thoroughly irrigated with 2.5% sodium hypochlorite,1 ml /min for a total of 3 mL after every instrument, using 3ml plastic disposable syringe with side vented needle with a gauge #30. The canal was then dried by using sterile paper points and then flushed with 5 ml of 5% sodium thiosulfate to inactivate NaOCl. A final flush with 5 ml saline was used. The post-instrumentation root canal samples (S2) were taken from the canals as described above. The microbiological samples were sent to the microbiology laboratory within 15 minutes.

The intervention group (Nit): Nitrofurantoin gel (25 mg/mL) was placed inside the canals using a sterile plastic syringe. The access cavity was then sealed using sterile cotton pellet and intermediate resin modified glass ionomer restoration (IMICRYL NOVA, Istanbul, Turkey).

The control group (CH) : $Ca(OH)_2$ (Metapaste. META BIOMED CO., LTD, Korea) was placed inside the canals using sterile plastic syringe. The access cavity was then sealed as mentioned above.

After seven days, rubber dam was applied, and tooth was disinfected as before. The previously sampled canal was re-entered and intracanal medicament was removed by irrigation with 10ml of sterile normal saline. A paper point was then inserted to working length to confirm the absence of exudate or foul odor. The post intracanal medication sample (S3) was taken from the canal as described above.

Master cones of 4% taper gutta-percha (Gutta Percha Points, META BIOMED CO., LTD, Korea.) was fitted to the working length corresponding to the same size of the final shaping file. A radiograph was taken to ensure proper length.

The canal was irrigated with 3 mL of 2.5% NaOCl for 1 min, activated with ED4 tip (Guilin Woodpecker Medical Instrument Co., LTD) driven by ultrasonic device (Guilin Woodpecker Medical Instrument Co., LTD) at 4/10-scale power in accordance with the manufacturer's instructions, followed by 3 mL of sterile saline. The canal was then irrigated with 3 mL of 17% EDTA for 1 min and the solution was activated as previously mentioned. A final rinse with 3 mL of sterile saline for 1 minute was used. The canal was then dried using sterile paper points.

Obturation was completed using lateral compaction technique with resin-based root canal sealer (AdSeal, META BIOMED CO., LTD, Korea). The access cavities were restored with core-build up composite resin (Ceram.x, Spercta XT, Dentsply Sirona, Ballaigues, Switzerland) and occlusal contact was checked. The details of the endodontic procedure for each patient were recorded in the patient's procedure chart.

Culturing and incubation procedure:

Microbiological analysis was determined using culture technique in the microbiological department, Cairo University. Samples in the transport medium (1 ml of BHI broth) (Brain heart infusion broth BO0366, Oxoid microbiology product, LTD, England) were dispersed with vortex in the mixer for 60 seconds by the laboratory technician.

To determine the number of common aerobes and anaerobes present in each sample, sequential 10-fold dilutions of 1/10 and 1/100 were prepared. Using a micropipette, 100 microliter (µl) of the vortexed samples were transferred into fresh, sterile tubes that held 1 millilitre (ml) of BHI broth. [17,18]

For aerobic bacterial culture, 50 µl of these diluted samples were transferred, spread out on BHI agar plates, and cultivated under aseptic conditions before being incubated at 37 °C for 24 hours. For anaerobic bacterial culture, the other 50 µl of these diluted samples were also transferred to BHI agar plates under aseptic conditions, the agar plates were placed in an anaerobic sealed jar with GasPak (Anaerogen gas pack (AN0035), Oxoid microbiology product, LTD, England) and anaerobic indicator (Anaerobic indicator BR0055B, Oxoid microbiology product, LTD, Basingstoke, Hampshire, England) followed by incubation for 48 hours at 37°C. [17,18]

Eventually, the resultant growth was visually quantified by counting the number of colony forming units per milliliter of each dilution (CFUs) on the agar medium under the microscope. Using the previously established dilution factors, the number of CFUs/ml was subsequently converted into actual counts.

Statistical Analysis:

Numerical data were explored for normality by checking the distribution of data and using tests of normality (Kolmogorov-Smirnov and Shapiro-Wilk tests). Logarithmic transformation of bacterial count data was performed due to the high range of bacterial counts. Age and percentage reduction of bacterial counts data showed normal (parametric) distribution while Log10 CFU of bacterial counts data showed non-parametric distribution. Data were presented as mean and standard deviation (SD) values.

For parametric data, Mann-Whitney U test was used to compare between mean age values in the compared groups. Wilcoxon signed rank test was used for intra group comparison. Friedman's test was used to study the changes by time within each group.

For non-parametric data, Kruskal-Wallis test was used to compare between multiple groups. Friedman's test was used to study the changes by time within each group. Dunn's test was used for pair-wise comparisons when Kruskal-Wallis or Friedman's tests are significant. Categorical data were presented as frequencies and percentages. Fisher's exact test was used for between-groups comparison. Significance level for statistical tests was set at $p < 0.05$.

III. RESULTS:

For this study, 50 patients were recruited from out-patient clinic of Endodontic department and assessed for meeting the eligibility criteria. A total of 28 patients met the inclusion criteria and were enrolled in the study. Patients were randomized into two groups of 14 patients each. All patients were included in the analysis. There were no statistically significant differences among the groups in terms of demographic data ($P > .05$) (Table 1).

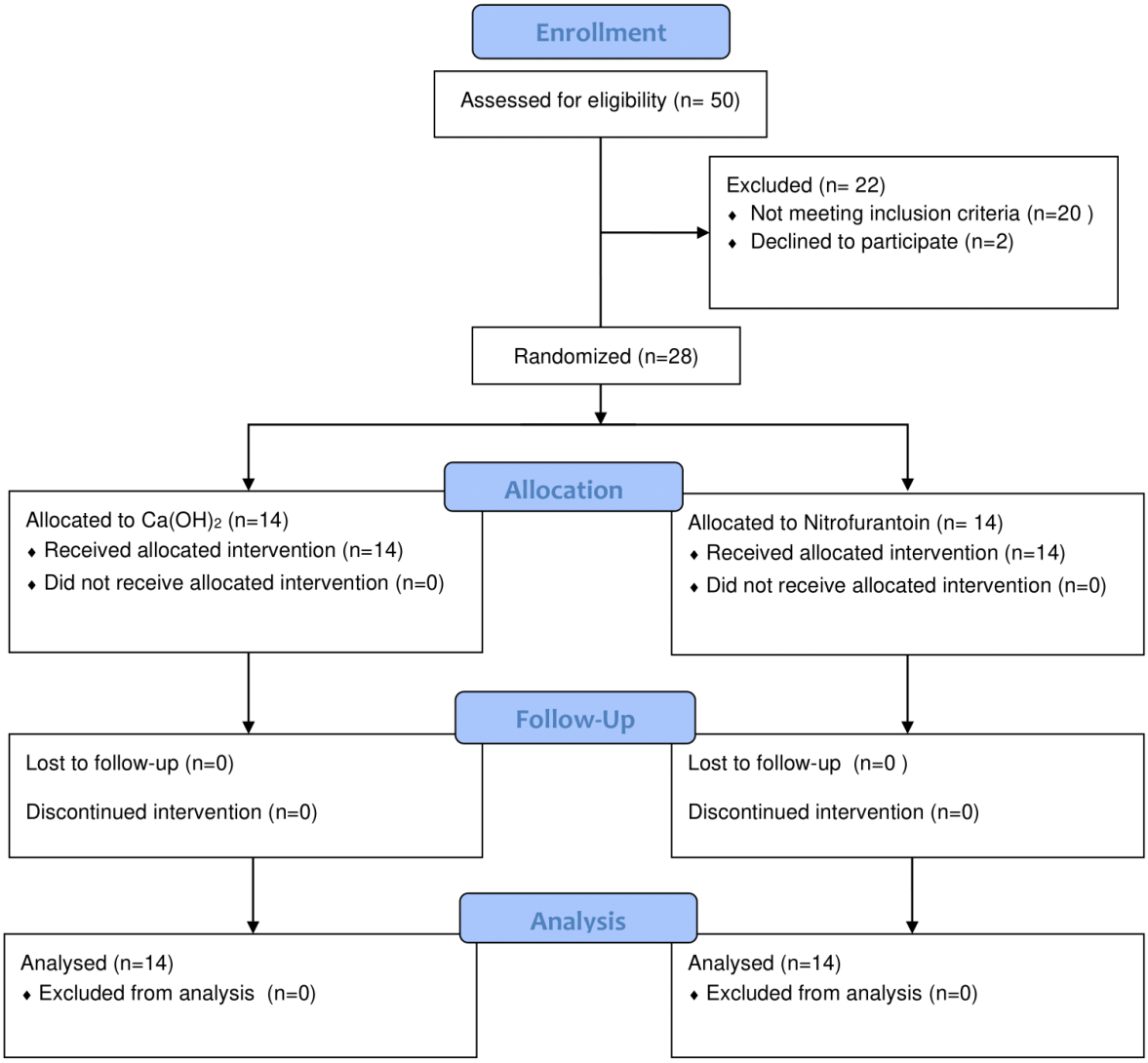

Figure 1: CONSORT flow diagram

Table 1: Summary of statistics of Demographic Data for the compared groups

Demographic data		**Ca(OH)2 paste (Control group)**		**Nitrofurantoin gel (Intervention group)**		***p*-value**
		N	**%**	**N**	**%**	
Gender (N, %)	Males	2	14.3%	6	42.9%	0.09 (ns)
	Females	12	85.7%	8	57.1 %	
Age		36.57	6.02	39	7.46	0.35 (ns)

The frequencies (n), percentages (%) and the comparison of the incidence of bacterial growth between the compared groups are presented in table (2) and figure (2). There was no

statistically significant difference in aerobic or anaerobic bacterial growth between the compared groups for all samples ($p > 0.05$).

Regarding aerobic and anaerobic bacterial percentage reduction, Nitrofurantoin rendered 79% of root canals free from cultivable aerobic bacteria, while $Ca(OH)_2$ rendered 35.7% of canals free from aerobic bacteria. Also, Nitrofurantoin rendered 93% of root canals free from cultivable anaerobic bacteria, while $Ca(OH)_2$ rendered 79% of canals free from anaerobic bacteria (Table 3). However, there was no statistically significant difference between the two intracanal medicaments. Both Nitrofurantoin and Calcium Hydroxide revealed a significant reduction in the bacterial load following instrumentation.

Table 2: frequencies (n), percentages (%) and the comparison of the incidence of bacterial growth at different time intervals between the compared groups.

Bacterial type	Incidence of bacterial growth at time intervals		Nitrofurantoin gel (Intervention group)	Ca(OH)2 paste (Control group)	*p*-value
Aerobic	**S1**	**n (%)**	14 (100%)	14 (100%)	NA
	S2	**n (%)**	11 (79%)	10 (71%)	1
	S3	**n (%)**	3 (21%)	9 (64%)	0.054
Anaerobic	**S1**	**n (%)**	14 (100%)	14 (100%)	NA
	S2	**n (%)**	8 (57%)	3 (21%)	0.12
	S3	**n (%)**	1 (7%)	3 (21%)	0.596

Figure 2: Bar chart representing the incidence of bacterial growth at different time intervals in the compared groups.

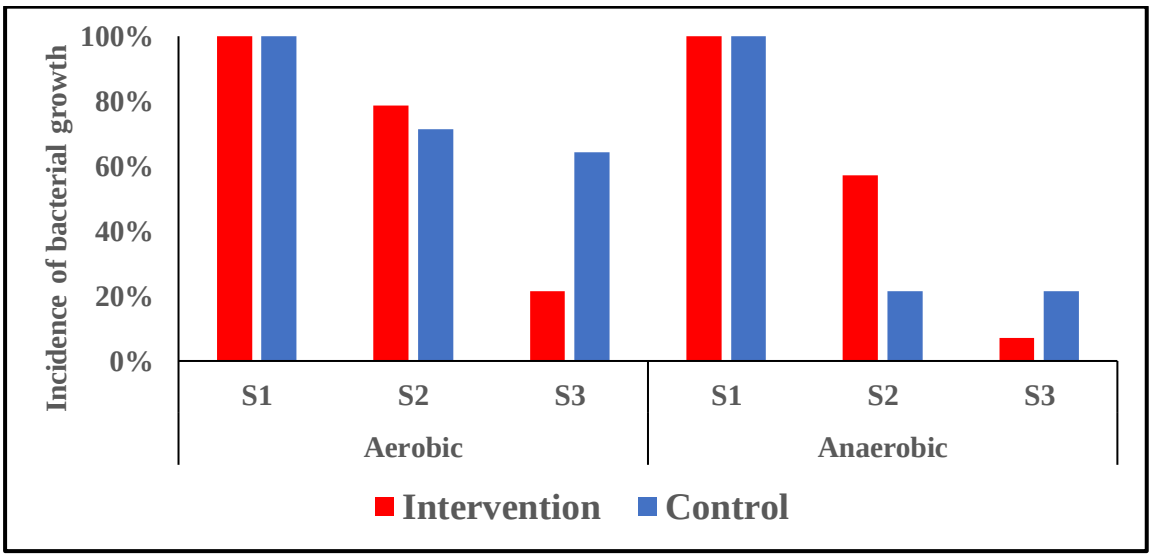

Table 3: A comparison of the bacterial percentage reduction between the compared groups.

Bacterial type	Bacterial percentage reduction		Nitrofurantoin gel (Intervention group)	Ca(OH)2 paste (Control group)	*p*-value
Aerobic	**S2**	**Mean (SD)**	78.2% (25.3%)	88.8% (15.2%)	0.144
	S3	**Mean (SD)**	94.1% (14.4%)	94.2% (8%)	0.079
Anaerobic	**S2**	**Mean (SD)**	82.8% (27.2%)	97.8% (4.8%)	**0.022***
	S3	**Mean (SD)**	98.6% (5.3%)	93.5% (18%)	0.308

Table 4: Descriptive statistics and the results of independent t test for log_{10} bacterial counts between the two groups.

	Nitrofurantoin gel (Intervention group)	Ca(OH)2 paste (Control group)	*p*-value
	Log_{10} S1 Aerobic		
Mean (SD)	1.46 (0.40)	1.58 (0.37)	0.432
Median (Range)	1.5 (0.6 - 2.10)	1.67 (1 - 2.18)	
	Log_{10} S1 Anaerobic		
Mean (SD)	1.45 (0.35)	1.47 (0.48)	0.895
Median (Range)	1.48 (1 - 2.08)	1.45 (0.7 - 2.20)	
	Log_{10} S2 Aerobic		
Mean (SD)	0.77 (0.33)	0.68 (0.51)	0.648
Median (Range)	0.54 (0 - 1.30)	0.30 (0 - 1.48)	
	Log_{10} S2 Anaerobic		
Mean (SD)	0.9 (0.17)	0.9 (0.56)	0.994
Median (Range)	0.70 (0 - 1.08)	0 (0 - 1.40)	
	Log_{10} S3 Aerobic		
Mean (SD)	0.49 (0.2)	0.36 (0.34)	0.554
Median (Range)	0 (0 - 0.70)	0 (0 - 1)	
	Log_{10} S3 Anaerobic		
Mean (SD)	0.3 ( )	0.73 (0.26)	0.296
Median (Range)	0 (0 - 0.30)	0 (0 - 1)	

IV. DISCUSSION:

The current study aimed to clinically compare the effects of using Nitrofurantoin versus Ca(OH)2 as an intracanal medication for the reduction of bacterial load, in necrotic single-rooted permanent mandibular premolars with a single canal.

Periapical inflammation is highlighted as a frequent underlying cause of postoperative pain. It occurs mainly in response to microbial persistence within the root canal system or introducing infected debris directly into the periapical tissues. Thus, the complete eradication of bacteria from infected root canals is a cardinal goal of effective endodontic therapy. 19 Several antimicrobial agents and different strategies have been proposed to ensure optimum root canal system cleanliness.

Nitrofurantoin (Nit) is a synthetic wide-spectrum antimicrobial agent of the Nitrofuran family, a first-line agent widely used for urinary tract infections (UTIs) and other multidrug resistant pathogens. [20] Uncertainty remains regarding Nitrofurantoin's exact mechanism of action; however, it acts on multiple strategic sites as it attacks several bacterial enzymes, inhibits protein synthesis and interferers with cell wall formation. [21] The Infectious Diseases Society of America (IDSA) and European Society of Clinical Microbiology and Infectious Diseases (ESCMID) recommended Nitrofurantoin as first-line agent based on evidence that it has an excellent safety profile and virtually unchanged low resistance rates since its FDA approval. After more than three decades of consistent usage, the overall experience reveals a less than 0.001% documented side-effect incidence which is extremely low.[22] Upon multiple studies conducted by different investigators arguing for the quest for the optimal intracanal medication, Nitrofurantoin seems to be a competent candidate. Few prior studies have been conducted to explore the effectiveness of Nitrofurantoin as a novel intracanal medication.[15, 23]

All confounding factors that could affect our study were eliminated as much as possible by standardizing the endodontic procedures and samples collection done in both groups. The only variable was the applied intracanal medicament.

Regarding the incidence of bacterial growth, our results showed that Nitrofurantoin rendered 79% of root canals free from cultivable aerobic bacteria, while $Ca(OH)_2$ rendered 35.7% of canals free from aerobic bacteria. Also, Nitrofurantoin rendered 93% of root canals free from cultivable anaerobic bacteria, while $Ca(OH)_2$ rendered 79% of canals free from anaerobic bacteria. Although, there was no statistically significant difference between the two intracanal medicaments. The present work revealed that Nitrofurantoin seems to be a promising root canal medicament in the clinical situation, with superior antimicrobial properties.

The post-instrumentation mean reduction in the number of CFUs/ml and % reduction of intracanal bacteria for Nitrofurantoin was more

than $Ca(OH)_2$ group but with no statistically significant difference between either two intracanal medicaments. Regarding aerobic bacteria, Nitrofurantoin showed similar efficacy to $Ca(OH)_2$ (94.1% and 94.2% respectively). For anaerobic bacteria, Nitrofurantoin showed higher level of reduction when compared to $Ca(OH)_2$, though this difference is statistically non-significant (98.6% and 93.5% respectively).

The lack of a significant difference between the two intracanal medicaments in a clinical situation could be explained by the inherent weakness in the culture method, as not all viable bacteria can be recovered or cultured, grading it of a lower sensitivity. [24, 25] However, it is still an excellent choice for providing a broad range of information regarding the endodontic microbiota and a quick method for evaluating the clinical efficacy of a novel technique or intervention.

The findings of the antibacterial activity of Nitrofurantoin are comparable with a prior in vitro investigation by Alrahman et al. [15] in which it was shown that Nitrofurantoin, even at the lowest dose, was capable of eliminating *E. faecalis* when administered as an intracanal medication. Another in vitro study by Navjot Singh et al. [23] showed that Nitrofurantoin paste exhibited negative CFUs and completely eradicated cultured *E. Faecalis* in comparison to $Ca(OH)_2$ that exhibited positive CFUs in pure culture.

The initial clinical experience and outcomes of this intracanal medicament appear promising. Further randomized clinical trials in this area are needed to confirm the findings of this study, and they should evaluate the effect of Nitrofurantoin as an antimicrobial agent in teeth with complicated anatomy such as molar teeth, and in cases of persistent infection, tracking the healing of chronic apical periodontitis radiographically over time. The relationship between changes in level of inflammatory biomarkers in the inflamed periapical tissues together with the number of endotoxins upon the application of different concentrations of Nitrofurantoin should also be explored. This study compared Nitrofurantoin against Calcium hydroxide as it's the gold standard and the most common used intracanal medicament worldwide, however further studies comparing Nitrofurantoin with other antibiotic-based intracanal medicaments are recommended.

V. CONCLUSION:

Within the limitations of the present study, it can be concluded that both intracanal medicaments succeeded in significantly reducing bacterial levels in primary infected root canals with no statistically significant difference between the two intracanal medicaments.

Conflict of Interest:

The authors declare no conflict of interest.

Funding:

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

Ethics:

This study protocol was approved by the ethical committee of the faculty of dentistry- Cairo

university on: 30/11/2021, approval number:101121.

VI. REFERENCES:

1. Siqueira, J. F., Jr., & Rôças, I. N. Clinical implications and microbiology of bacterial persistence after treatment procedures. J Endod, (2008); 34(11), 1291-1301.e1293.
2. Sjögren, U., & Sundqvist, G. Bacteriologic evaluation of ultrasonic root canal instrumentation. Oral Surg Oral Med Oral Pathol, (1987); 63(3), 366-370.
3. De Castro Kruly, P., Alenezi, H., Manogue, M., Devine, D. A., Dame-Teixeira, N., Garcia, F. C. P., & Do, T. Residual Bacteriome after Chemomechanical Preparation of Root Canals in Primary and Secondary Infections. J Endod, (2022); 48(7), 855-863.
4. Yu, D. C., Tam, A., & Schilder, H. Root canal anatomy illustrated by microcomputed tomography and clinical cases. Gen Dent, (2006); 54(5), 331-335.
5. Singh, R. D., Khatter, R., Bal, R. K., & Bal, C. S. Intracanal medications versus placebo in reducing postoperative endodontic pain--a double-blind randomized clinical trial. Braz Dent J, (2013); 24(1), 25-29.
6. Mohammadi, Z., & Dummer, P. M. Properties and applications of calcium hydroxide in endodontics and dental traumatology. Int Endod J, (2011); 44(8), 697-730.
7. Kim, D., & Kim, E. Antimicrobial effect of calcium hydroxide as an intracanal medicament in root canal treatment: a literature review - Part I. In vitro studies. Restor Dent Endod, (2014); 39(4), 241-252.
8. Kumar, A., Tamanna, S., & Iftekhar, H. Intracanal medicaments – Their use in modern endodontics: A narrative review. J Oral Res Rev, (2019); 11, 89.
9. Ordinola-Zapata, R., Noblett, W. C., Perez-Ron, A., Ye, Z., & Vera, J. Present status and future directions of intracanal medicaments. Int Endod J, (2022); 55 (3), 613–636.
10. Mohammadi, Z. Antibiotics as intracanal medicaments: a review. J Calif Dent Assoc, (2009); 37(2), 98-108.
11. Malu, K., & Khubchandani, M. Triple Antibiotic Paste: A Suitable Medicament for Intracanal Disinfection. Cureus, (2022);14(9), e29186.
12. Mohammadi Z. Local applications of tetracyclines in endodontics and dental trauma: a review. Dentistry today, (2009); 28(1), 95–101.
13. Qiao, L. D., Chen, S., Yang, Y., Zhang, K., Zheng, B., Guo, H. F., Yang, B., Niu, Y. J., Wang, Y., Shi, B. K., Yang, W. M., Zhao, X. K., Gao, X. F., Chen, M., & Tian, Y. Characteristics of urinary tract infection pathogens and their in vitro susceptibility to antimicrobial agents in China: data from a multicenter study. BMJ Open, (2013); 3(12), e004152.
14. Cunha, B. A., Schoch, P. E., & Hage, J. R. Nitrofurantoin: preferred empiric therapy for community-acquired lower urinary tract infections. Mayo Clin Proc, (2011); 86(12), 1243-1244.
15. Alrahman, M. S. A., Faraj, B. M., & Dizaye, K. F. Assessment of Nitrofurantoin as an Experimental Intracanal Medicament in Endodontics. Biomed Res Int, (2020); 2128473.
16. Hassan N, Diab A, Ahmed G. Post-operative pain and antibacterial efficacy of silver nanoparticles formulations intracanal medication: A randomized controlled clinical study. Open Access Maced. J. Med. Sci., (2021);9(D):248–56.
17. Morsy, D. A., Negm, M., Diab, A., & Ahmed, G. Postoperative pain and antibacterial effect of 980 nm diode laser versus conventional endodontic treatment in necrotic teeth with chronic periapical lesions: A randomized control trial. F1000Research, (2018); 7, 1795.
18. Elgamal SG, El-Shafei JM, Azzazy HM, Dwedar RA, El-Khodary SA. Evaluation of the antimicrobial effect of pre-synthesized novel antibiotic electrospun nanofibers as an intracanal delivery strategy for regenerative endodontics: A randomized clinical trial. Open Access Maced. J. Med. Sci, (2022); 10(D):303–10.
19. Haapasalo, M., Shen, Y., Wang, Z., & Gao, Y. Irrigation in endodontics. Br Dent J, (2014); 216(6), 299-303.
20. Yadav, N., & Pathak, S. Cost effective analysis of tab. nitrofurantoin vs. inj.

ceftriaxone as an empirical therapy in patients of urinary tract infection at a tertiary health care centre. Int J Basic Clin Pharmacol, (2018); 7, 2393.

21. Munoz-Davila, M. J. Role of Old Antibiotics in the Era of Antibiotic Resistance. Highlighted Nitrofurantoin for the Treatment of Lower Urinary Tract Infections. Antibiotics, (2014); 3(1), 39-48.
22. Das, A., Banerjee, T., & Anupurba, S. Susceptibility of Nitrofurantoin and Fosfomycin Against Outpatient Urinary Isolates of Multidrug-Resistant Enterococci over a Period of 10 Years from India. Microb Drug Resist, (2020); 26(12), 1509-1515.
23. Navjot Singh, M., Ashu, J., Kunal, S., Manu, R., & Divya, B. Nitrofurantoin: Furious Against Bacteria? an in Vitro Study to Test Nitrofurantoin as an Intracanal Medicament Against Enterococcus Faecalis. Int J Health Sci, (2022); 8510-8516.
24. Franco-Duarte, R., Černáková, L., Kadam, S., Kaushik, K. S., Salehi, B., Bevilacqua, A., Corbo, M. R., Antolak, H., Dybka-Stępień, K., Leszczewicz, M., Relison Tintino, S., Alexandrino de Souza, V. C., Sharifi-Rad, J., Coutinho, H. D. M., Martins, N., & Rodrigues, C. F. Advances in Chemical and Biological Methods to Identify Microorganisms-From Past to Present. Microorganisms, (2019);7(5).
25. Siqueira Jr., J. F., & Rôças, I. N. A critical analysis of research methods and experimental models to study the root canal microbiome. Int Endod J, (2022); 55(S1), 46-71.