Apical extrusion of debris using hypochlorite and chlorhexidine gel as auxiliary substances in endodontic instrumentation

Extrusão apical de debris utilizando o hipoclorito de sódio e a clorexidina gel como substância auxiliar na instrumentação endodôntica

Extrusión apical de detritos utilizando hipoclorito de sodio y gel de clorhexidina como sustancia auxiliar en instrumentación endodôntica

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Abstract
*Aim***:** This study evaluated the amount of extruded debris after canal preparation using three root canal irrigating substances. *Methodology***:** Thirty human extracted single-rooted lower premolars were randomly assigned into 3 groups (n = 10) according to the chemical substance used for irrigation. G1: 2.5% sodium hypochlorite; G2: 2% chlorhexidine gel; and G3: 0.9% saline solution. The canals were instrumented using Reciproc Blue file (VDW, Munich, Germany). Apically extruded debris was collected into a pre-weighed Eppendorf tube filled with agar gel. Extruded debris were calculated by subtracting the tooth-free apparatus weight from the post preparation weight value. The data were analyzed using the ANOVA test at a 5% significance level. *Results***:** No statistically significant differences were noted between the groups. However, G3 had the largest extrusion weight, and G2 produced less debris when compared to the other groups ($p > .05$). *Conclusion***:** Within the limitations of this in vitro study, our data suggest that all chemical substances tested caused debris extrusion, although no statistically significant differences were found between the three substances.
Keywords: Root canal therapy; Dental leakage; Root canal irrigants.

Resumo
Objetivo: Este estudo avaliou a quantidade de resíduos extruídos após o preparo do canal usando três substâncias irrigantes do canal radicular. *Metodologia:* Trinta pré-molares unirradiculares inferiores humanos extraídos foram divididos aleatoriamente em 3 grupos (n = 10) de acordo com a substância química usada para irrigação. G: hipoclorito de sódio 2,5%; G2: gel de clorexidina 2%; e G3: solução salina a 0,9%. Os canais foram instrumentados com lima Reciproc Blue (VDW, Munique, Alemanha). Os detritos estruídos apicalmente foram coletados em um tubo eppendorf pré-pesado preenchido com gel de ágar. A quantidade de resíduos e irrigantes estruídos foi calculada subtraindo o valor do peso antes e após o preparo do canal radicular. Os dados foram analisados pelo teste ANOVA com nível de significância de 5%. Resultados: Não foram observadas diferenças estatisticamente significativas entre os grupos. Porém, o G3 apresentou o maior peso, e o G2 produziu menor quantidade de resíduo quando comparado aos demais grupos (p> 0,05). *Conclusão:* Dentro das limitações deste estudo *in vitro*, nossos dados sugerem que todas as substâncias químicas testadas causaram extrusão de detritos, embora não tenham sido encontradas diferenças estatisticamente significativas entre as três substâncias.
Palavras-chave: Terapia do canal radicular; Extrusão dentinária; Irrigantes dos canais radiculares.

Resumen
Objetivo: Este estudio evaluó la cantidad de detritos extruidos después de la preparación del conducto utilizando tres sustancias de irrigación del conducto radicular. *Metodología:* Treinta premolares radiculares inferiores humanos extraídos se dividieron aleatoriamente en 3 grupos (n = 10) según el químico utilizado para la irrigación. G1- hipoclorito de sodio al 2,5%; G2 - gel de clorhexidina al 2%; y G3- solución salina al 0,9%. Los canales se equiparon con un archivo Reciproc Blue (VDW, Munich, Alemania). Los desechos extruidos apicalmente se recogieron en un tubo eppendorf pesado previamente lleno de gel de agar. La cantidad de residuos e irrigantes extruidos se calculó restando el valor del peso del aparato sin la presencia del diente, del valor del peso posterior a la preparación. Los datos se analizaron mediante la prueba ANOVA con un nivel de significancia del 5%. *Resultados:* No hubo diferencias estadísticamente significativas entre los grupos. Sin embargo, G3 tuvo el mayor peso de extrusión y G2 produjo la menor cantidad de desechos en comparación con los otros grupos (p> 0.05). *Conclusión:* dentro de las limitaciones de este estudio in vitro, nuestros datos sugieren que todos los productos químicos probados causaron la extrusión de escombros, aunque no se encontraron diferencias estadísticamente significativas entre las tres sustancias.
Palabras clave: Terapia de conducto radicular; Extrusión de dentina; Irrigadores de conductos radiculares.

1. Introduction

The endodontic therapy's main goal is to eliminate microorganisms from the root canal systems, remove pulp tissue, and prevent debris' extrusion through the apical foramen (Young et al., 2007). These goals aim to eliminate pain and inflammation and create an environment that is most favorable for periapical area healing (Siqueira & Roças, 2008).

Endodontic treatment requires chemomechanical preparation of the root canal system. This preparation is performed with endodontic files and irrigating substances, that mechanically and chemically act, respectively, in the root canals' decontamination (Young et al., 2007).

Root canal instrumentation generates dentin debris. Unintentional leakage of debris and irrigants into the periapical tissue may happen during chemomechanical preparation (Tanalp & Güngör, 2014). Even when the necessary precautions are taken, debris extrusion is still a risk (Lambrianidis et al., 2001). Extruded infected debris and irrigants may predispose to acute periradicular abscesses, possibly one of the main causes of postoperative pain (Siqueira, 2003). This may occur due to changes in periapical tissue pressure, microbial factors, effects of chemical mediators, immunological response (Seltzer & Naidorf, 1985), and some irrigating substances' cytotoxicity (Haapasalo et al., 2014).

Instrumentation associated with irrigating substance was the leading factor for debris extrusion (Vande & Brilliant, 1975). Concerning the instrumentation techniques, studies revealed that the use of the crown-down technique and rotary files extruded less debris in comparison with the step-back technique and hand files (Kuştarci et al., 2008; Ruiz-Hubard et al., 1987). Besides that, reciprocating motion with a single file seemed to exert better control over the apically extruded material (De-Deus et al., 2015).

The literature is scarce on the association of irrigating substances with debris extrusion (Barbosa-Ribeiro et al., 2018). However, it is suggested that different irrigants produce different amounts of extruded debris (Tanalp & Güngör, 2014).

Irrigation plays a central role in endodontic treatment during and after instrumentation, facilitating the removal of debris and microorganisms (Haapasalo et al., 2014).

Sodium hypochlorite (NaOCl) has a broad antimicrobial spectrum and the capacity to dissolve vital and necrotic tissues. However, NaOCl produces toxic effects if it leaks beyond the apical foramen and may result in undesirable outcomes, such as pain and inflammation (Lambrianidis et al., 2001; Haapasalo et al., 2014). Chlorhexidine (CHX) has high substantivity to dentin, low toxicity, and bactericidal effect (Gomes et al., 2013). As a gel, CHX can suspend debris (Gomes et al., 2013), and it may decrease the risk of debris extrusion during endodontic treatment. Both (NaOCl and CHX) are effective in reducing biofilm (Arias-Moliz et al., 2009).

This study evaluated the amount of extruded debris after canal preparation using, 2.5% NaOCl, 2% gel-based CHX, and 0.9% saline solution (NaCl), in extracted single-rooted lower premolars during instrumentation with Reciproc Blue file (VDW, Munich, Germany). The null hypothesis was that saline, hypochlorite and chlorhexidine gel would produce the same amount of extruded debris.

2. Methodology

Thirty human single-rooted lower premolars were used in the present study. The teeth were extracted for orthodontic or periodontal recommendations. All patients signed a free informed consent form approved by the local Research Ethics Committee. The sample size calculation was estimated based on previous results of Lu et al. (2013). The calculation was carried out under an infinite population and a quantitative variable. Based in an error margin of 0.00136, with a 95% confidence level, a total of 30 samples were needed for the research.

The teeth were disinfected in 5% NaOCl for 1 hour, the external surfaces were cleaned with periodontal curettes, and they were stored in 0.9% NaOCl at room temperature until use (Miot et al., 2011). The teeth were radiographed using a digital sensor on the mesiobuccal and buccolingual planes to check the degree of curvature. Inclusion criteria: teeth with a curvature of at most 5° according to Schneider's classification (Schneider, 1971), single-rooted teeth with a single canal according to the Vertucci's classification (Vertucci et al., 1984), teeth with fully formed apices, and a foramina diameter of at most 0.15 mm (Toyoglu & Altunbas, 2017). Teeth with endodontic treatment, internal or external reabsorptions, root caries, cracks, and/or calcifications were excluded from the research.

Coronal access was achieved with high-speed 1014HL burs (KG Sorensen Ind. e Com. Ltda., São Paulo, SP, Brazil), undercooling. The working length (WL) was assessed by the insertion of a hand K file #10 (Mani, Inc, Tochigi, Japan) into the root canal until its tip could be seen in the apical foramen using an operating microscope (DF Vasconcelos, Valença, RJ, Brazil) at a 20x magnification. The file tip observation in the apical foramen determined the root canal full length, which corresponded to the WL used in the present study.

The maximum apical size of 0.15 mm diameter dimension for specimen's inclusion was confirmed by observing a #15 Flexofile fitting at the apical foramen observed with a dental operating microscope (40X).

All teeth' lengths were standardized in 17 mm from the apex by sectioning the crown using a low-speed bur with a diamond disc (Isomet 5000 saw; Buehler, Ltd. Lake Bluff, New York, USA) under continuous water irrigation. A size 10 k-file (Dentsply Sirona, Ballaigues, Switzerland) was used to confirm the root length of 17 mm and confirm apical patency when the instrument exceeded 1.0 mm from the apical foramen.

Test Apparatus

In the present study, debris extrusion was assessed using the modified method developed by Lu et al. (2013) and shown in Figure 1. The roots were covered with a Teflon band, except the last 1 mm of the apical third (Uslu et al., 2018), and inserted into an orifice made in the Eppendorf tube cap. Later, the interface between the tube cap and the tooth (apparatus) was hermetically sealed with cyanoacrylate and covered with a top dam (FGM, Joinville, SC, Brazil) to prevent leakage fluids into the tube during the root canal preparation. The apparatus was numbered and weighed three times on a high-precision 10-4 electronic balance (NOVAK, São José do Rio Preto, SP, Brazil), and the mean value was calculated (weight 1). Then, two milliliters of 1.5% agar gel (Kasvi, São José dos Pinhais, PR, Brazil) were injected into the Eppendorf tubes, the apparatus was inserted in the tubes (filled with agar), and this set was placed upside down, so the roots were completely embedded in the agar. After agar gelation, the tubes' weights, including the agar and the apparatus, were recorded three times to calculate the mean value (weight 2). Finally, each tube's weight with the agar (weight 3) was calculated by subtracting weight 1 from weight 2 (Keskin et al., 2017). The measurements were performed this way, so the Eppendorf tubes were opened only after instrumentation. This procedure would prevent agar displacement that would influence the final weight. The Eppendorf tubes were then placed in a glass bottle using a rubber dam to hold them in place. The rubber dam did not allow the operator to see the dental root during the endodontic preparation, thus avoiding bias.

Chemomechanical preparation

The same operator carried out chemomechanical preparation of all samples. The instrumentation was made with a Reciproc Blue 25.08 activated by a Reciproc Silver VDW motor (VDW, Munich, Germany) in reciprocating mode according to the manufacturer's instructions. Three pecking motions inside the canal with a range of 3 mm per motion were done. After that, the file was removed from the root canal cleaned with sterile gauze soaked in 70% alcohol, and the pecking motion was repeated until the file reach WL (Toyoğlu & Altunbaş, 2017). A c-pilot #10 file (VDW) was used for root canal patency over 1 mm of the apical foramen.

The teeth were randomly divided into three experimental groups (n = 10) using a computer algorithm (http://www.ramdom.org) according to the auxiliary chemical substance used for chemomechanical preparation. The groups were: Group 1: 2.5% sodium hypochlorite (Asfer, São Caetano do Sul, SP, Brazil); Group 2: 2% chlorhexidine gel (Maquira, Maringá, PR, Brazil); and Group 3: 0.9% saline solution (Asfer, São Caetano do Sul, SP, Brazil). The irrigation was performed by a peristaltic pump, model LPD 101-3 (MS Tecnopon, Piracicaba, SP, Brazil), and a 25-mm, 27 G Endo-Eze irrigation needle (Ultradent, Indaiatuba, SP, Brazil), at a flow rate of 5 mL/minute.

In the 2.5% NaOCl group, initial irrigation was performed by injecting 1 mL of 2.5% NaOCl into the canal until the needle reached the length of 9 mm. Patency was confirmed and another 1 mL of 2.5% NaOCl was injected into the canal until the needle reached the length of 9 mm. Instrumentation of the cervical third was initiated until the file reached the length of 9 mm. After that, 1 mL of 2.5% NaOCl was injected into the canal up to the length of 9 mm. Patency was confirmed. Furthermore, another 1 mL of 2.5% NaOCl was injected into the canal up to the length of 9 mm. For instrumentation of the middle third, the file reached the length of 13 mm. Then 1 mL of 2.5% NaOCl was injected into the canal up to the length of 13 mm. Patency was confirmed. Another 1 mL of 2.5% NaOCl was injected into the canal up to the length of 13 mm. Instrumentation of the apical third was performed until the file reached the length of 17 mm (WL). 1 mL of 2.5% NaOCl was injected into the canal up to the length of 15 mm (2 mm short of the WL). Patency was confirmed. Final irrigation was carried out by injecting 1 mL of 2.5% NaOCl into the canal up to the length of 15 mm. A total of 8 mL irrigating substance was used.

In the 2% gel-based CHX group, the root canal preparation was done the same as the first group; however, the irrigating substances used were 5 mL of 0.9% NaCl and 3 mL of 2% gel-based CHX. Before each instrumentation with the Reciproc Blue R25 file, 1 mL of 2% gel-based CHX was injected. In the 0.9% NaCl group, the chemomechanical preparation was the same as the NaOCl group but with 8 mL of 0.9% NaCl. The irrigating substance's aspiration was standardized for all groups, using capillary tips of 0.36 mm (Ultradent Products INC, South Jordan, UT, USA).

Data collection and analysis

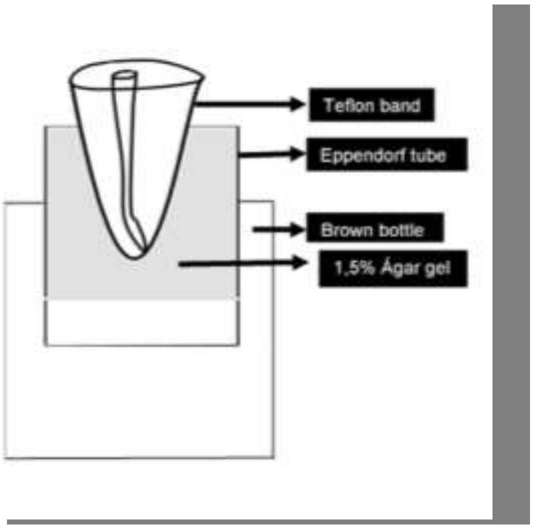
After the end of chemomechanical preparation, Eppendorf tubes were removed from glass vials, and the apparatus was removed. The tubes containing only agar and the extruded debris and irrigants were consecutively weighed three times (weight 4). The amount of extruded debris (Table 1) was calculated by subtracting weight 4 from weight 3.

The mean and standard deviation of quantitative variables were estimated. The Kolmogorov-Smirnov test was used to assess the normality of the data. The different chemical substances were assessed by Bonferroni post-hoc analysis of variance (ANOVA). P values < 0.05 were considered to be significant. The statistical analysis was made using Statistical Package for the Social Sciences version 20 (SPSS, Chicago, IL, USA).

3. Results

The amount of extruded debris was recorded for all groups (Table 1). No statistically significant differences were noted between the groups (p = 0.330). However, the 0.9% NaCl group had the most considerable extrusion weight, and the 2% gel based CHX group produced less debris when compared to the other groups.

Figure 1. A schematic presentation of the agar gel model. A tooth is positioned in an Eppendorf tube and immersed in 1.5% agar gel. The apparatus was placed and fixed in an opaque glass bottle.



Source: Authors.

Table 1. The minimum, maximum, mean, and standard deviations (SD) of apically extruded debris by the Reciproc Blue file instrumentation according to each group (n=10) in Grams.

Groups	Minimum	Maximum	Mean	SD
2.5% sodium hypochlorite	0.0001	0.0192	0.0068a	0.0067
2% chlorhexidine gel	0.0007	0.0134	0.0048a	0.0043
0.9% saline solution	0.0001	0.0226	0.0092a	0.0070

Equal letters indicate that there was no statistically significant difference (p> 0.05) between the groups. Source: Authors.

4. Discussion

Debris extrusion can lead to an immune response and postoperative pain (Lambrianidis et al., 2001, Tanalp et al., 2014). This study aimed to evaluate the amount of apically extruded debris using three different irrigants during endodontic instrumentation. The null hypothesis was accepted, which held those different irrigants, such as, 2.5% NaOCl, 2% gel-based CHX, and 0.9% NaOCl would produce the same amount of extruded debris.

No statistically significant differences in the extrusion of debris were observed between the groups. However, the 2% gel-based CHX showed less extrusion of debris. This result is in agreement with a previous report (Barbosa-Ribeiro et al., 2018). Nevertheless, they compared the 2% gel-based CHX with a 6% NaOCl concentration and used the Reciproc instrumentation system. In the present study, we used the Reciproc Blue file with an innovative heating process, used to modify its molecular structure for improving flexibility and resistance to cyclic fatigue (Aksoy et al., 2019).

Chlorhexidine gel 2% is used clinically as a root canal irrigant because its antimicrobial effects similar to 5.25% sodium hypochlorite (Vianna et al.,2004; Ferraz et al.,2007) with no cytotoxicity to periapical tissues (Gomes et al., 2013).

Gel-based CHX may have produced less debris because the gel reduces smear layer formation as a result of its rheological action. This action maintains the debris suspended due to its viscosity, with dentinal tubules' patency (Vianna et al.,2004). Besides, chlorhexidine gel lubricates the root canal walls, reducing the attrition between the file and the dentin (Gomes et al., 2013). This property facilitates the instrumentation and allows better mechanical cleaning of the root canal. Gel-based CHX also seems to eliminate organic tissues, which compensates for its incapacity to dissolve them (Ferraz et al., 2001).

NaOCl is the most frequently used irrigant in the field of endodontics. NaOCl, in association with reciprocating instruments, can significantly reduce the bacterial count within the root canal (Dal Bello et al., 2019). Nevertheless, the possible crystallization of this substance during the root canal irrigation may have influenced the higher values of extruded debris when compared to the 2% gel-based CHX group (Koçak et al., 2013). Uzunoglu et al. (2014) observed that after NaOCl evaporation, it formed crystals that, combined with the volume used may have led to the more significant extrusion of debris.

A crown-down instrumentation technique was used in the present study. This instrumentation technique produces a significantly smaller amount of extruded debris than the step-back technique (Ruiz-Hubard et al., 1987). The file chosen for instrumentation in this study was the Reciproc Blue R25. This file has a high fracture resistance and produces a small amount of debris (De-Deus et al., 2019; Keskin & Sarıyılmaz, 2018).

Regarding the WL, apex size, curvature, and canal length, we have standardized them to prevent possible biases towards the outcomes (Tanalp & Güngör,2014). Previous studies have shown that curvature (Leonardi et al., 2007), canal length, and apex size have not influenced debris extrusion (Hinrichs et al., 1998). Another study demonstrated that instrumentation at the apex or 1 mm shorter of the apical foramen did not significantly alter the amount of extruded debris (Mendonça de Moura et al., 2019).

Lu et al. (2013) described the method used to collect apically extruded debris, as we tried to mimic the periapical barrier. The agar gel can provide resistance to the debris extrusion, bearing a close resemblance to what occurs in the clinical conditions (Lu et al., 2013). Previous studies have suggested the use of 1.5% agar gel in models of debris' extrusion to replicate the periodontal tissue, as the density of this substance is compatible with that of the periodontal tissue (agar: 1045 kg/m3 vs. human tissue: 1000-1100 kg/m3) (Lu et al., 2013; Keskin & Sarıyılmaz, 2018; Robert et al., 2005).

Based on this study's results, regardless of the auxiliary chemical substance used, all groups extruded debris. Further studies reproducing clinical conditions and comparing NaOCl with CHX should be performed to evaluate these auxiliary chemicals substances' action during endodontic preparation concerning debris extrusion. Since the less extruded debris, the minor damage to periapical tissues and, consequently, more post-treatment comfort.

5. Conclusion

Within the limitations of this *in vitro* study, our data suggest that all chemical substances tested caused debris extrusion, although no statistically significant differences were found between the three substances.

References

Aksoy, Ç., Keriş, E. Y., Yaman, S. D., Ocak, M., Geneci, F., & Çelik, H. H. (2019). Evaluation of XP-endo Shaper, Reciproc Blue, and ProTaper Universal NiTi Systems on dentinal microcrack formation using micro–computed tomography. *Journal of endodontics*, 45(3), 338-342.

Arias-Moliz, M. T., Ferrer-Luque, C. M., Espigares-García, M., & Baca, P. (2009). Enterococcus faecalis biofilms eradication by root canal irrigants. *Journal of Endodontics*, 35(5), 711-714.

Barbosa-Ribeiro, M., Arruda-Vasconcelos, R., Fabretti, F. L., Silva, E. J. N. L., De-Deus, G., Gomes, B. P. F. A. (2018). Evaluation of apically extruded debris using positive and negative pressure irrigation systems in association with different irrigants. *Braz Dent J*, 29(2), 184-188.

Berutti, E., Chiandussi, G., Paolino, D. S., Scotti, N., Cantatore, G., Castellucci, A., & Pasqualini, D. (2011). Effect of canal length and curvature on working length alteration with WaveOne reciprocating files. *Journal of endodontics*, 37(12), 1687-1690.

Dal Bello, Y., Mezzalira, G. I., Jaguszewski, L. A., Hoffmann, I. P., Menchik, V. H. S., Cecchin, D., & Souza, M. A. (2019). Effectiveness of calcium and sodium hypochlorite in association with reciprocating instrumentation on decontamination of root canals infected with Enterococcus faecalis. *Australian Endodontic Journal*, 45(1), 92-97.

De-Deus, G., Neves, A., Silva, E. J., Mendonça, T. A., Lourenço, C., Calixto, C., & Lima, E. J. M. (2015). Apically extruded dentin debris by reciprocating single-file and multi-file rotary system. *Clinical oral investigations*, 19(2), 357-361.

De-Deus, G., Cardoso, M. L., Belladonna, F. G., Cavalcante, D. M., Simões-Carvalho, M., Souza, E. M., ... & Silva, E. J. N. L. (2019). Performance of reciproc blue R25 instruments in shaping the canal space without glide path. *Journal of endodontics*, 45(2), 194-198.

Ferraz, C. C., Gomes, B. P., Zaia, A. A., Teixeira, F. B., & Souza-Filho, F. J. (2007). Comparative study of the antimicrobial efficacy of chlorhexidine gel, chlorhexidine solution and sodium hypochlorite as endodontic irrigants. *Brazilian dental journal*, 18(4), 294-298.

Ferraz, C. C. R., de Almeida Gomes, B. P. F., Zaia, A. A., Teixeira, F. B., & de Souza-Filho, F. J. (2001). In vitro assessment of the antimicrobial action and the mechanical ability of chlorhexidine gel as an endodontic irrigant. *Journal of Endodontics*, 27(7), 452-455.

Gomes, B. P., Vianna, M. E., Zaia, A. A., Almeida, J. F. A., Souza-Filho, F. J., & Ferraz, C. C. (2013). Chlorhexidine in endodontics. *Brazilian dental journal*, 24(2), 89-102.

Haapasalo, M., Shen, Y., Wang, Z., & Gao, Y. (2014). Irrigation in endodontics. *British dental journal*, 216(6), 299-303.

Hinrichs, R. E., Walker III, W. A., & Schindler, W. G. (1998). A comparison of amounts of apically extruded debris using handpiece-driven nickel-titanium instrument systems. *Journal of endodontics*, 24(2), 102-106.

Keskin, C., Sariyilmaz, E., & Sariyilmaz, O. (2017). Effect of solvents on apically extruded debris and irrigant during root canal retreatment using reciprocating instruments. *International endodontic journal*, 50(11), 1084-1088.

Keskin, C., & Sarıyılmaz, E. (2018). Apically extruded debris and irrigants during root canal filling material removal using Reciproc Blue, WaveOne Gold, R-Endo and ProTaper Next systems. *Journal of dental research, dental clinics, dental prospects,* 12(4), 272.

Koçak, S., Koçak, M. M., Sağlam, B. C., Türker, S. A., Sağsen, B., & Er, Ö. (2013). Apical extrusion of debris using self-adjusting file, reciprocating single-file, and 2 rotary instrumentation systems. *Journal of endodontics*, 39(10), 1278-1280.

Kuştarcı, A., Akpınar, K. E., Suemer, Z. E. Y. N. E. P., Er, K., & Bek, B. (2008). Apical extrusion of intracanal bacteria following use of various instrumentation techniques. *International endodontic journal*, 41(12), 1066-1071.

Lambrianidis, T., Tosounidou, E., & Tzoanopoulou, M. (2001). The effect of maintaining apical patency on periapical extrusion. *Journal of Endodontics*, 27(11), 696-698.

Leonardi, L. E., Atlas, D. M., & Raiden, G. (2007). Apical extrusion of debris by manual and mechanical instrumentation. *Brazilian dental journal*, 18(1), 16-19.

Lu, Y., Wang, R., Zhang, L., Li, H. L., Zheng, Q. H., Zhou, X. D., & Huang, D. M. (2013). Apically extruded debris and irrigant with two N i-T i systems and hand files when removing root fillings: a laboratory study. *International endodontic journal*, 46(12), 1125-1130.

Mendonça de Moura, J. D., da Silveira Bueno, C. E., Fontana, C. E., & Pelegrine, R. A. (2019). Extrusion of debris from curved root canals instrumented up to different working lengths using different reciprocating systems. *Journal of endodontics*, 45(7), 930-934.

Miot, H. A. (2011). Sample size in clinical and experimental trials. *J Vasc Bras*, 10(4), 275-278.

Robert, G. H., Liewehr, F. R., Buxton, T. B., & McPherson III, J. C. (2005). Apical diffusion of calcium hydroxide in an in vitro model. *Journal of endodontics*, 31(1), 57-60.

Ruiz-Hubard, E. E., Gutmann, J. L., & Wagner, M. J. (1987). A quantitative assessment of canal debris forced periapically during root canal instrumentation using two different techniques. *Journal of Endodontics*, 13(12), 554-558.

Schneider, S. W. (1971). A comparison of canal preparations in straight and curved root canals. *Oral surgery, Oral medicine, Oral pathology*, 32(2), 271-275

Siqueira Jr, J. F., & Rôças, I. N. (2008). Clinical implications and microbiology of bacterial persistence after treatment procedures. *Journal of endodontics*, 34(11), 1291-1301.

Seltzer, S., & Naidorf, I. J. (1985). Flare-ups in endodontics: I. Etiological factors. *Journal of Endodontics*, 11(11), 472-478.

Siqueira Jr, J. F. (2003). Microbial causes of endodontic flare-ups. *International Endodontic Journal*, 36(7), 453-463.

Tanalp, J., & Güngör, T. (2014). Apical extrusion of debris: a literature review of an inherent occurrence during root canal treatment. *International endodontic journal*, 47(3), 211-221.

Toyoğlu, M., & Altunbaş, D. (2017). Influence of different kinematics on apical extrusion of irrigant and debris during canal preparation using K3XF instruments. *Journal of endodontics*, 43(9), 1565-1568.

Uslu, G., Özyürek, T., Yılmaz, K., Gündoğar, M., & Plotino, G. (2018). Apically extruded debris during root canal instrumentation with Reciproc blue, HyFlex EDM, and XP-endo shaper nickel-titanium files. *Journal of endodontics*, 44(5), 856-859.

Uzunoglu, E., & Görduysus, M. (2014). Apical extrusion of debris and irrigant using novel preparation systems. *J Contemp Dent Pract*,15(4),423-427.

VandeVisse, J. E., & Brilliant, J. D. (1975). Effect of irrigation on the production of extruded material at the root apex during instrumentation. *Journal of Endodontics*, 1(7), 243-246.

Vertucci, F. J. (1984). Root canal anatomy of the human permanent teeth. Oral surgery, oral medicine, oral pathology, 58(5), 589-599.

Young, G. R., Parashos, P., & Messer, H. H. (2007). The principles of techniques for cleaning root canals. *Australian Dental Journal*, 52, S52-S63.

Vianna, M. E., Gomes, B. P., Berber, V. B., Zaia, A. A., Ferraz, C. C. R., & de Souza-Filho, F. J. (2004). In vitro evaluation of the antimicrobial activity of chlorhexidine and sodium hypochlorite. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology*, 97(1), 79-84.