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EFFECTIVENESS OF TWO INTRACANAL IRRIGATION SOLUTIONS DELIVERED THROUGH CRYOTHERAPY ON POST-ENDODONTIC PAIN REDUCTION. A RANDOMIZED CLINICAL TRIAL

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ABSTRACT

Aim: The present randomized clinical trial was designed to investigate the effect of cryotherapy (cryo) utilizing chlorhexidine (CHX) as compared to saline (NS) on pain reduction after single visit endodontic treatment.

Methodology: Selected patients were seeking emergency treatment of painful symptomatic irreversible pulpitis with symptomatic apical periodontitis for single rooted teeth. Sixty-eight male patients, 25 to 50 years old were distributed randomly in 4 groups of 17 each according to the final irrigation protocol: control (GI): NS at room temperature, control (GII): CHX at room temperature, intervention (GIII): cryo with NS (cryo/NS), , and intervention (G IV): (cryo / CHX) before final obturation in the same visit.

Patients were trained and asked to report pain incidence and level after12, 24, 48, 72 hours and at 7 days as well as frequency of analgesic intake. Kruskal Wallis, followed by Dunn`s multiple comparisons test were used for comparison between the 4 groups, while Chi square test was used for qualitative data. The significance level was set at $p \leq 0.05$.

Results: G III: (cryo/NS) and G IV: cryo/CHX showed significantly highest pain reduction after 24, 48, and 72 hours P= 0.000 I. Significantly more prolonged pain reduction curve was found in GI: cryo/NS. Pain in both tested groups declined to no pain after 7 days. Frequency of analgesic need was insignificant for the two groups P=0.27.

Conclusions: From the results of the present study it appeared clearly that cryo helped in pain reduction whether used with CHX or NS. CHX used as a cryo material showed insignificant trend toward effective time dependent pain reduction as compared to NS. This might be because of its substantivity. Further study is needed to better clarifying this point.

KEYWORDS: Cryotherapy; chlorhexidine; single visit treatment; pain; emergency

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INTRODUCTION

Endodontic treatment of a painful symptomatic irreversible pulpitis with or without apical periodontitis is reported to be sometimes accompanied with pain that persists for few days after endodontic treatment because of central sensitization[1].

Contemporary methods for pain relief after emergency endodontic treatment are long-term anesthesia, occlusal reduction, or use of flexible analgesic strategy [2,3]

Cryo is a therapeutic procedure commonly used as an easy and available pain control adjunctive method in medicine. Specially to relieve pain associated with acute inflammations [4].It was first presented by James Arnott in 1851 who used a mixture of salt and ice to stop cancer tissue progresses[4].The cryo idea was based on the concept that, lowering the temperature of the target tissue will help in eradication or diminishing of the pain experienced by patients in many medical conditions before it was adopted to dental pain cases [5].

In endodontic literature, relatively few studies have investigated the use of intra-canal cryo[6]. Based on the histopathologic evidence that inflammation is inevitably accompanied by hotness and swelling so lowering the intra-canal apical temperature might help in pain reduction after endodontic treatment. Nonetheless, in vitro studies showed that, cold NS (2.5°C) when employed as a final irrigant for 5 minutes resulted in a reduction in temperature at the root and canal apical part that reached 10°C which act as a pain reliever and anti-inflammatory[7].

In this context, a number of studies were conducted with various study aims. Authors found that the use of intra canal cryo/NS reduced the postoperative pain after single visit root canal treatment in patients with vital pulp suffering irreversible pulpitis[5,8,9]. However, when comparing cryo effect on pulpitis with or without apical periodontitis; the letter resulted in more pain relief [10-12]. On the other hand, controversy was noted in the literature regarding the preoperative pulp and periapical condition that are mostly benefited from the cryo.

In the current literature, many trials were found that investigated the effect of changes in classic method of cryo application through NS. Al-Nahlawi(11) reported significant reduction in postoperative pain when intra-canal cryo was convoyed through negative pressure irrigation syringe.

Recently, Nandakumar tried intra-canal cold NaOCl as a cryo-pain relieving method with reported encouraging results of pain reduction [13]. On the other hand, a recent trial reported on the use of intraoral cryo-cold application as compared to intra-canal cryo with equal efficiency [14].

CHX, is a famous endodontic irrigating solution principally used for its substantivity. It was reported to reduce the postoperative pain as compared to NaOCl when used as a final irrigant [13]. In a single blind comparative study, Kumar el al tested the effect of final irrigation with MTAD or CHX on postoperative pain reduction after single visit treatment in cases diagnosed with symptomatic apical periodontitis. They found that, when used as a final rinse, after instrumentation, the two materials showed significant pain reduction to a similar extent [14].

Nevertheless, in a systematic review and meta analysis on degree of postoperative pain following use of NaOCl or CHX as a final irrigant without cryo, the authors reported no difference in pain perception. However, they recommended more studies for further confirmation [23] .

In fact, the effect of cold CHX as intra-canal cold final irrigation according to the crayo concept was not reported before.

AIM OF THE STUDY

The aim of the present clinical trial is to investigate and compare the effect of cryo utilizing intracanal final cold irrigation with NS or CHX solutions on postoperative pain relief and the frequency of analgesics needed. Control groups were irrigation with NS or CHX solutions at room temperature.

METHODOLOGY

The present clinical trial was performed on patients attending at the dental/endodontic emergency clinics in the College of Oral and Dental Surgery, 6th of October University because of dental pain during three months' period from March 2024 to May 2024. The study design was approved by the research ethical committee at 6th of October University. Approval no. RECO6U/7- March 4, 2024.

Study flow chart was made following Prirate2020 guidlines.[15] The study protocol was registered in ClinicalTrials.gov Identifier: NCT06427070.

Sample size calculation:

Sample size for a large effect size of 1.02 calculated from difference of means taken from a previously searched similar clinical trial[5,11].For an alpha error of 0.05 and power of 0.8; the sample size required was estimated to be 13 participants per group. However, taking into consideration possible 15% dropouts, suggested a total sample size of 68 with n=17 participants per group for 4 groups as an additional estimate.

Inclusion and exclusion criteria:

Inclusion criteria were: male patients diagnosed as having symptomatic irreversible pulpitis with symptomatic apical periodontitis with no or slight widening of the PDL space, patients' requiring emergency RCT in a single rooted anterior or premolar tooth, pre-operative pain score 7 on Numerical Rating (NRS) scale, no concomitant perio disease. Middle aged males (25-50 years), Medical profile ASA1[25], willing to sign the consent form, willing to answer our calls for one-week period.

Exclusion criteria were: Female patients, Medical conditions more than ASA1, Multi-rooted teeth, Patients younger than 25 or older than 50 years.

Selected patients were given all the necessary related information about the treatment before consent form signing. They were blind only to the type of irrigation solution that was used during the treatment.

Pre-treatment patient preparation

For all patients in the three study groups the following procedures were done by a trained assistant:

Demographic data revising, base line vital signs recording, preoperative pain level using a modified VAS chart - after short training for the patient.

Patient randomization:

Randomization of patients among the three test groups was done using the research randomizer web program **SEARCH SHOULDERDOC.CO.UK (figure1).**

Treatment acquisition:

All endodontic treatments were done by a single operator during the whole study period according to the following protocol:

Antiseptic mouth wash, Local anesthesia: 2% lidocaine hydrochloride with 1:80000 adrenaline. Rubber dam application and access preparation was done. Coronal pre-flaring was then made and followed by working length determination (using Root ZX apex locator (J. MORITA), confirmation radiographically and recording. For the whole study single canals preparations were done using Hyflex EDM (Colténe) rotary files system of suitable sizes

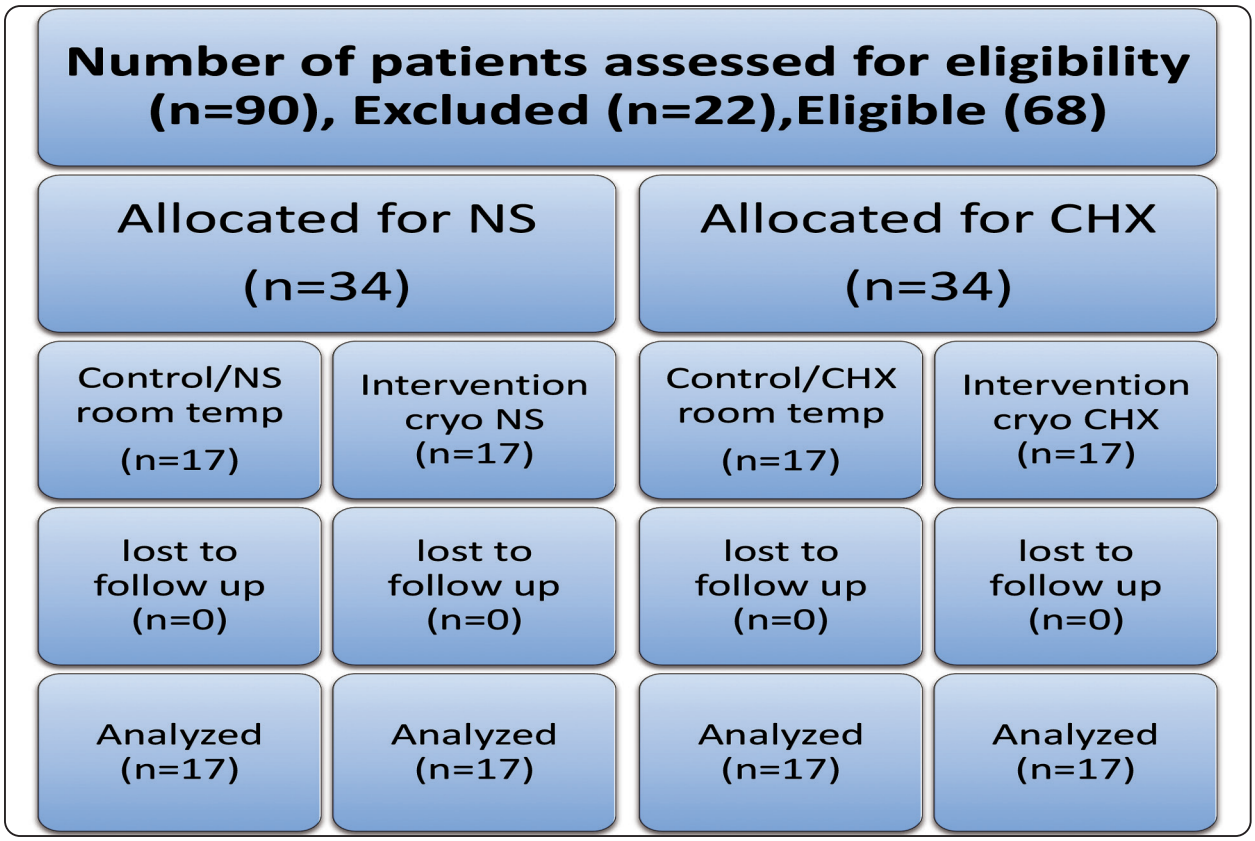

Fig. (1): Flow diagram for study methodology steps following Prirate [24]

and a VDW motor following the manufacturer recommendations.

Apical preparation width was considered done after preparation with three successive sizes after the initial file size that reached to the full working length. During the whole preparation sequence in all teeth groups; irrigation was done before and after each preparation cycle using 5. 25 %NaOCl in a side vented Endo irrigation needle (GoldenDent). Apical patency was performed using K-file #10.

Lastly, experimented teeth of the two groups had intermediate irrigation with 5ml of NS at room temperature and dried thoroughly with paper points. The trained assistant deliver to the treating dentist the assigned control or tested irrigation solution (room temp or cryo) loaded in previously marked syringes. Solution was known to the dentist but not to the patient as follows:

G I – Control: 20 ml. of NS (room temp.) was used as a final rinse over a period of 5 minutes after thorough canal dryness with paper points(Meta Biomed)

G II – Control: 20 ml. of CHX (room temp.) was used as a final rinse over a period of 5 minutes after thorough canal dryness with paper points.

G III – Intervention : 20 ml. of cryo/NS (2˚C-5˚C) was used as a final rinse over a period of 5 minutes after thorough canal dryness with paper points.

G IV – Intervention: 20ml. of cryo/CHX (2˚C-5˚C) was used as a final rinse over a period of 5 minutes after thorough canal dryness with paper points.

The loaded irrigation syringes for GIII (cryo/NS) and G IV (cryo/CHX) were kept in a refrigerator where temperature was adjusted and monitored with a digital thermometer (LCD).

Prepared canals for all study groups were dried with paper points and obturated utilizing gutta-percha (Meta Biomed) and Kerr pulp canal sealer (EWT)-Kerr in a lateral compaction technique. Post-obturation radiographs were taken. Coronal restorations were inserted and checked for any high spots.

Post treatment Patient instructions:

Patients were asked to register pain level at 12, 24, 48, and 72 hours as well as 7 days on the given VAS questionnaire. They were also allowed to take Ibuprofen 400 mg when needed because of unbearable pain and register the frequency of need during the whole week. Patients were given an appointment after one week for follow-up.

Statistical analysis:

Statistical analysis was performed with SPSS 16 ® (Statistical Package for Scientific Studies), Graph pad prism & windows excel and presented in 2 tables and 2 graphs. Exploration of the given data was performed using Shapiro-Wilk test and Kolmogorov-Smirnov test for normality which revealed that data originated from non-parametric distribution. Accordingly, comparison between 4 different groups was performed by Kruskal Wallis test, followed by Dunn`s multiple comparisons test. On the other hand, regarding qualitative data, all comparisons were performed by using the Chi square test. The significance level was set at $p \leq 0.05$.

Evaluation of pain:

Intergroup comparison (table 1):

Preoperatively, there was insignificant difference between groups regarding pain level (p=0.95). After 12 hours, there was significant difference between groups (P=0.0001), as G I (4.65 ± 0.86) showed significantly the highest pain while G II (3.47±0.62), G III (3.47 ±0.62), and G IV (3.0 ± 0.61) showed significantly lower pain with insignificant difference between them. After 24 hours, there was significant difference between groups (P=0.0001), as G I (2.94 ± 0.75) and G II (2.53 ± 0.51) showed significantly the highest pain with insignificant difference between them while G III and G IV (1.71 ± 0.47) showed significantly the least pain. After 48 hours, there was significant difference between groups (P=0.0001), as G I (2.18 ± 0.52) and G II (2.00 ± 0.50) showed significantly the highest pain with insignificant difference between them while G III (0.29± 0.47) and G IV (0.29 ± 0.47) showed significantly the least pain with insignificant difference between them . After 72 hours, there was significant difference between groups (P=0.0001), as G I (1.06 ± 0.66) and G II (1.06 ± 0.66) showed significantly the highest pain with insignificant difference between them while G III and G IV (0.18 ± 0.53) showed significantly the least pain. After 7 days, there was insignificant difference between all groups (P=0.24), as shown in table(1) and figure (2).

Intragroup comparison (table2 and figure 3):

Comparison between different intervals within each group was performed by using Friedman test which demonstrated significant difference in all group (P= 0.0001), followed by Dunn`s test for multiple comparisons which revealed that: In G I : there was a significant decrease in pain from (7.12 ± 0.33) preoperatively to (2.94 ± 0.75) 24 hours then decreased significantly to (1.06 ± 0.66) after 72 hours. In G II: there was a significant decrease in pain from (7.18 ± 0.53) preoperatively to (2.53± 0.51) 24 hours then decreased significantly to (1.06 ± 0.66) after 72 hours. In G III (NS/cryo): there was a significant decrease in pain from (7.12 ± 0.53) preoperatively to (1.71 ± 0.47) after 24 hours which then decreased significantly to (0.41± 0.53) after 48 hours to become (0.18 ± 0.53) after 72 hours. In G IV (CHX/ cryo) there was a significant decrease in pain from (7.12 ± 0.49) preoperatively to (1.71 ± 0.47) 24 hours then decreased significantly to (0.29± 0.47) and (0.18 ± 0.53) after 72 hours.

TABLE (1) Descriptive results of pain in all groups at different intervals, comparison between groups using Kruskal Wallis test followed by Dunn's multiple comparisons test:

		Minimum	Maximum	Mean	Standard Deviation	P value
Pre-op	G I	7.00	8.00	7.12 [a]	0.33	0.95
	G II	6.00	8.00	7.18 [a]	0.53	
	G III	6.00	8.00	7.18 [a]	0.53	
	G IV	6.00	8.00	7.12 [a]	0.49	
12 h.	G I	3.00	6.00	4.65 [a]	0.86	0.0001*
	G II	3.00	5.00	3.47 [b]	0.62	
	G III	2.00	5.00	3.18 [b]	0.81	
	G IV	2.00	4.00	3.00 [b]	0.61	
24 h.	G I	2.00	4.00	2.94 [a]	0.75	0.0001*
	G II	2.00	3.00	2.53 [a]	0.51	
	G III	1.00	2.00	1.71 [b]	0.47	
	G IV	1.00	2.00	1.71 [b]	0.47	
48 h.	G I	1.00	3.00	2.18 [a]	0.53	0.0001*
	G II	1.00	3.00	2.00 [a]	0.50	
	G III	0.00	1.00	0.41 [b]	0.51	
	G IV	0.00	1.00	0.29 [b]	0.47	
72 h.	G I	0.00	2.00	1.06 [a]	0.66	0.0001*
	G II	0.00	2.00	1.06 [a]	0.66	
	G III	0.00	2.00	0.18 [b]	0.53	
	G IV	0.00	2.00	0.18 [b]	0.53	
7 days	G I	0.00	1.00	0.12 [a]	0.33	0.24
	G II	0.00	1.00	0.12 [a]	0.33	
	G III	0.00	0.00	0.00 [a]	0.00	
	G IV	0.00	0.00	0.00 [a]	0.00	

Significant difference as P<0.05.** **Means with different superscript letters as P<0.05.
Means with the same superscript letters as P>0.05.
G I: NS room temp., G II: CHX room temp., G III: NS/Cryo, G IV: CHX/Cryo

TABLE (2) Mean and standard deviation of pain in all groups at different intervals, comparison between different intervals using Kruskal Wallis test followed by Dunn's multiple comparisons test:

	Group							
	GI		GII		GIII		GIV	
	Mean	Standard Deviation	Mean	Standard Deviation	Mean	Standard Deviation	Mean	Standard Deviation
Pre-op	7.12 [a]	0.33	7.18 [a]	0.53	7.12 [a]	0.53	7.12 [a]	0.49
12 h.	4.65 [ab]	0.86	3.47 [ab]	0.62	3.18 [b]	0.81	3.00 [b]	0.61
24 h.	2.94 [b]	0.75	2.53 [b]	0.51	1.71 [bc]	0.47	1.71 [b]	0.47
48 h.	2.18 [b]	0.53	2.00 [b]	0.5	0.41 [cd]	0.51	0.29 [c]	0.47
72 h.	1.06 [c]	0.66	1.06 [c]	0.66	0.18 [d]	0.53	0.18 [c]	0.53
7 days	0.12 [c]	0.33	0.12 [c]	0.33	0.00 [d]	0	0.00 [c]	0
P value	0.0001*		0.0001*		0.0001*		0.0001*	

Significant difference as P<0.05.** **Means with different superscript letters as P<0.05.
Means with the same superscript letters as P>0.05.
G I: NS room temp., G II: CHX room temp., G III: NS/Cryo, G IV: CHX/Cryo

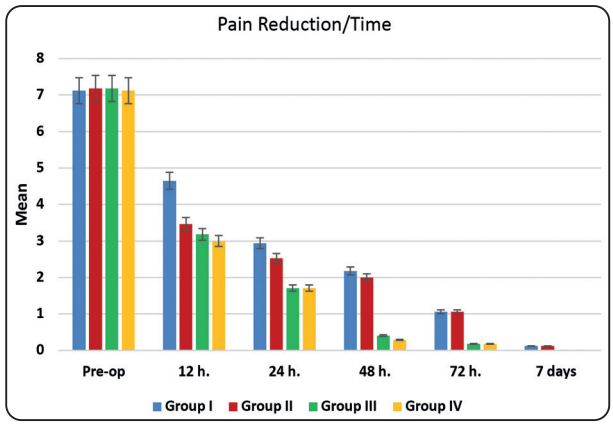

Fig. (2) Bar chart representing comparison of pain reduction in all test groups at different intervals (Intergroup comparison).

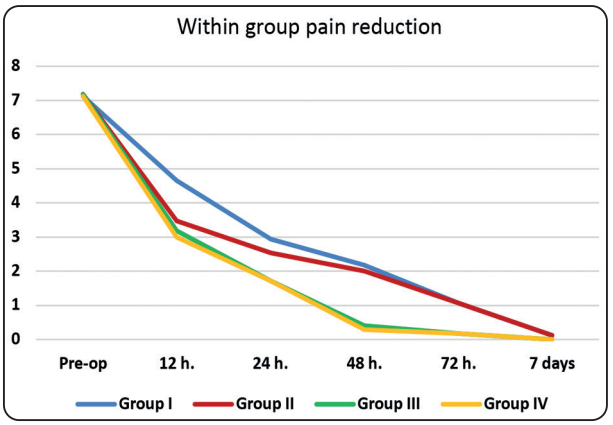

Fig. (3) Line chart representing pain reduction within each group. Group I: NS room temp., Group II: CHX room temp., Group III: NS/Cryo, Group IV: CHX/Cryo

Analgesics need (table3 and figure 4):

Frequency and percentages of analgesics need in all groups were presented in table (3) and figure (4). This was found to more frequently in G I: (NS/no cryo) reaching 41.2%. this percent diminished progressively in G II, III, and IV. The frequency of analgesic intake was similar in cryo groups as compared to the control groups. However, comparison between all groups revealed insignificant differences as P=0.46.

TABLE (3) Descriptive results of analgesics needed frequency in all groups, comparison between them using Chi square test:

	G I		G II		G III		G IV		Chi-Square Tests	
Analgesic	N	%	N	%	N	%	N	%	Chi-square	P value
No need	10	58.80%	13	76.50%	14	82.40%	14	82.4%	2565	0.46
Need	7	41.20%	4	23.50%	3	17.60%	3	17.6%		

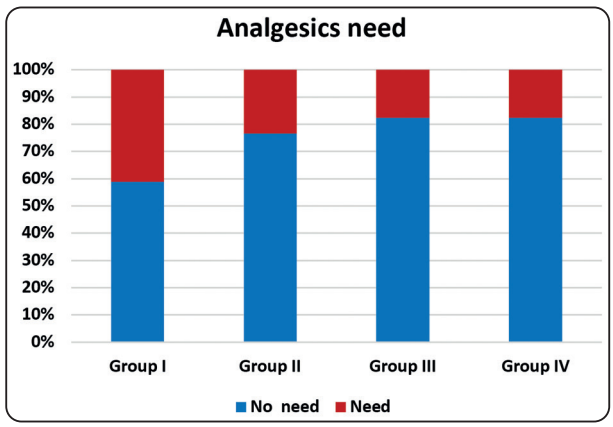

Fig. (4) Stacked bar chart representing analgesics needed in all groups.

DISCUSSION

The present randomized clinical test was done as a trial to gather the maximum and most effective pain relieve measures in as short time frame for patient presenting with vital inflamed pulp and periapex.

Single visit endodontic treatment is the recent-state of the art- treatment modality in most of the suitable clinical presentations for endodontic treatment [12,16,17]. Symptomatic irreversible pulpitis with symptomatic apical periodontitis is a special

level of pulp/periodontal disease where pain is described at maximum. Nevertheless, it was reported that, although the pulp is still viable, however, inflammatory infiltrates and osteoclastic activity starts well before actual pulpal necrosis[17]. This leads to dissemination of inflammatory mediators as well as bacterial toxins periapically [1].

Cryotherapy is a relatively new modality in endodontics that was recently tested in many clinical trials for immediate pain relief with encouraging results mostly registered [5,12,18-21]. Nevertheless, few studies reported no significant difference, while Western et al [10] specified the lack of difference between 15°C and 2°C. The classic application methodology is through cold (2-5°C) NS post-instrumentation irrigation for a reported maximum time of 5 minutes. The pain relief is due to the coldness, while the NS is the medium through which it is applied.

Additionally, few clinical trials reported on the use of cold NaOCl in a cryo mode in patients with symptomatic apical periodontitis [7]. Among them very few reported on use of crayothrapy as cold intraoral packs with comparable results to the intracanal cryotherapy [18-20].Their results showed that cold NaOCl resulted in insignificant lower pain perception.

The aim of this study was to compare the effect of cryotherapy using two different irrigation materials on pain relief after single visit endodontic treatment. Allocated teeth were diagnosed with symptomatic irreversible pulpitis and symptomatic apical periodontitis. A pulp/periapical inflammation, that was reported to be- the most painful - dental disease condition[19]. As such every effort should be done to help these patients in pain for an immediate and sustained pain relief.

In the present study, the therapeutic irrigation material-CHX- was proposed and compared for its effect on pain relief beside its substantive antibacterial effect. To our knowledge CHX was not experimented as a cryo-treatment yet. CHX was selected based on its ranking as the strongest theurapeutic irrigant, while saline the weakest [20]. Nonetheless, in cases of inflamed pulp and periapical tissues, the effective rapid pain reliever is a first choice. This was the case of patients selected for this study. In a multi-centers randomized control study, they found that the more the inflammation is –as in cases of symptomatic irreversible pulpitis with apical periodontitis, the more time it takes to subside after cryotherapy [21].

Four groups were experimented; two control at room temperature; namely: NS and CHX delivered for 5 minute using side vented needle and two experimental groups were same materials were delivered at 2-5°C for 5 min. Experimented teeth of the four groups had intermediate irrigation before the experimented and control last irrigation with 5ml of NS at room temperature and dried thoroughly with paper points. This step was made to guarantee removal of traces of NaOCl from the canals before the test materials application to prevent possible reaction between NaOCl and CHX [20].

The study was designed as a randomized double-blind clinical trial following the World Medical Association Declaration of Helsinki[22]. Patient was blind to the type of final irrigation. The treating dentist was blind to the type of irrigant in the cold needles.

The results of the present study showed a significant gradual decrease in pain after treatment in all tested groups that faded completely by the 7th day. At most of the studied periods pain reduction in GII, III, and IV was significantly higher than that in G1. For the first control group where NS/ room temperature was used; our result was in consort with most of the previous similar studies [23]. However, in a study done by Western et al [10] an intermediate temperature of 13° to 15°gave the same pain reduction as cryo at 2° -4° temperature. The intra-group analysis showed significant decrease in pain with time especially after 24hours and 72

hours (figure3). It was recognized that, although differences between G III, IV after 12 hours was insignificant, however a trend toward a lowest pain perception was found in G IV (CHX with cryo) 3.00 for CHX/cryo vs. 3.19 for NS/cryo . This trend was found again after 48 hours between cryo groups (0.29 for CHX/cryo versus 0.41 for NS/cryo) which was statistically insignificant. This appears clearly in figure 2.

Generally, the present study results showed significant pain reduction when cryo therapy was applied whether with NS or CHX with comparable results. More detailed and sensitive methods for comparison might be needed like the effect of crayotherapy on nerve conduction speed and the generation of local oxidative stresses[17]. The frequency of analgesic intake was considered low as only 23.5% versus 17.6% needed analgesics postoperatively for pain control with no significant difference between them. Our result was in consort with that of Murtezai et al [24] concerning the CHX. Comparing pain after irrigation with NaOCl and CHX in patients with irreversible pulpitis, they found that in the CHX group, pain decreased faster than NaOCl group [24]. Recently, similar rapid pain relief was also found in patients with symptomatic apical periodontitis where a final irrigation with either CHX or QMIX were tested without cryotherapy [14].

CONCLUSION

From the results of the present study it appeared clearly that cryo helped in pain reduction whether used with CHX or NS. CHX used as a cryo material showed insignificant trend toward effective time dependent pain reduction as compared to NS. This might be because of its substantivity. Further study is needed to better clarifying this point.

Conflict of Interest:

The authors declare no conflict of interest.

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