

## Effect of GuttaClear on Postoperative Pain After Root Canal Retreatment: A Randomized Clinical Trial

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### ABSTRACT

**Objective:** The aim of this study was to evaluate postoperative pain after non-surgical root canal retreatment with or without GuttaClear.

**Methods:** Sixty participants were randomly distributed in this non-inferiority trial into two parallel single-blinded experimental groups (Group1: non-solvent, Group2: solvent). After root canal retreatment, the participants completed questionnaires using direct (numerical rating scales) and indirect (number of analgesics taken) measurements of postoperative pain at immediate, 6, 12, 24, 48, and 72 h post-retreatment. The predisposing postoperative pain factors were recorded and analysed using Generalized Estimating Equations to identify correlated factors ( $\alpha=0.05$ ).

**Results:** The pain incidence was not significantly different between the groups at any time point. The highest incidence of postoperative pain occurred immediately after retreatment (35%) and then decreased to 15% at 24 h ( $P<0.05$ ). The number of participants requiring analgesics was 6.67% in the non-solvent group and 9.99% in the solvent group which were similar between the groups. Patients with a history of previous postoperative pain were 21.6-fold more likely to have postoperative pain than those without ( $P<0.05$ ).

**Conclusion:** There was no difference in postoperative pain or analgesics required after root canal retreatment with or without using GuttaClear. This study is registered in ClinicalTrials.gov (NCT04326998).

**Keywords:** Gutta-percha, GuttaClear, postoperative pain, randomized controlled trial, root canal retreatment, solvent

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### HIGHLIGHTS

- The use of a natural gutta-percha solvent, GuttaClear, in root canal retreatment did not increase the incidence of postoperative pain.
- Although the incidence of immediate pain was 35%, it significantly decreased within 24 h.
- The amount of analgesic required due to postoperative pain was similar between the solvent and non-solvent groups.

### INTRODUCTION

Non-surgical root canal retreatment is the treatment of choice to manage root canal treatment failure. The complete removal of the existing gutta-percha is an important factor in successful root canal retreatment (1). A

number of techniques have been suggested, including heat, ultrasonic, rotary instruments, hand instruments, and solvents (2). The use of solvent has been demonstrated to enhance canal cleaning (3), decrease treatment time (4) and reduce procedural errors (5), especially in

curved canals and complex root canal anatomies, compared with not using solvent.

Although chloroform has been used as the most efficient gutta-percha solvent, it is classified as a carcinogen (6) and has toxicity concerns (7). Natural gutta-percha solvents, e.g., eucalyptus oil and orange oil, are an alternative for removing gutta-percha from the root canal due to being safe, non-carcinogenic, and less toxic (8). Moreover, a new formula of natural gutta-percha solvent (GuttaClear), which is a citrus fruit oil-based solvent containing d-limonene has been introduced (9). The efficiency of d-limonene is equivalent to chloroform in dissolving gutta-percha (10). It was suggested to use solvent far away from the apex to prevent postoperative pain (11), however there is no evidence of the exact distance required.

In endodontic treatment, most patients are more concerned about postoperative pain than the quality of the treatment (12). Moreover, postoperative pain reduces a patient's confidence in the treatment outcome (13). Postoperative pain after root canal retreatment is typically due to inflammation of the periapical tissue from mechanical, chemical, and/or microbial injury (14). The extruded debris, instruments used, and chemical irrigants used in the root canal filling removal procedure can cause postoperative pain. However, using solvent during this process aids in dissolving the root canal filling materials, thus reducing the amount of apically extruded debris and lowering the likelihood of postoperative pain (15). Furthermore, psychological factors also influence the occurrence of pain due to pain perception. Patients' individual characteristics (age and sex), history of postoperative pain, anxiety, fear and pain expectation can result in postoperative pain by triggering pain perception and lowering pain thresholds (16-19).

Previous studies have compared postoperative pain after retreatment based on the types of instruments (20-22), types of medication, and the number of appointments required (23). Yoldas et al. (24) reported that retreatment performed over multiple appointments eliminated postoperative pain and decreased flare-ups compared with a single visit. In contrast, only one study using a eucalyptol-based solvent investigated the effects of gutta-percha solvent on postoperative pain (15). However, there is no clinical report on postoperative pain after using a new natural gutta-percha solvent, GuttaClear, in non-surgical root canal retreatment. Therefore, the aim of the present study was to evaluate the postoperative pain after multiple visit non-surgical endodontic retreatment cases using solvent compared with no solvent.

## MATERIALS AND METHODS

This non-inferiority trial received ethical approval from the Faculty of Dentistry and the Faculty of Pharmacy, Mahidol University, Institutional Review Board (MU-DT/PY-IRB 2019/DT100). The participants were enrolled from September 2019-June 2021. Before participating, the patients read and signed informed consent forms describing the treatment procedures they would receive. The study was conducted in accordance with the Declaration of Helsinki. ClinicalTrials.gov registered (NCT04326998).

## Case Selection

Participants over 18 years-old in good health (class I or II ASA classification) were enrolled. The participants did not have contra-indications to taking the medication used in this study (ibuprofen), i.e., drug allergy or related systemic conditions. The participants had a previously endodontic-treated single-root canal tooth in which the apical extension of the old root canal filling materials was 1-3 mm short of the radiographic apex. Patients with a tooth with an open apex, root resorption, or root perforation were excluded. In addition, patients who presented with pre-operative pain, sinus tract and/or swelling at the appointment visit, took analgesics or antibiotics less than one week before the appointment visit, or experienced problems in completing the pain questionnaires were excluded. Moreover, during treatment, teeth with a root canal filling other than gutta-percha, had a missed canal or canal patency could not be achieved at the appointment visit were excluded.

## Sample Size Calculation

The sample size in the present study was calculated based on a previous study (15). The effect size of 0.67 was obtained from the mean (1.69) and standard deviation (2.49) at 24, 48, and 72 h. The sample size was calculated using statistical software (Sealed Envelope, London, UK) available at [www.sealedenvelope.com/power/binary-noninferior](http://www.sealedenvelope.com/power/binary-noninferior) for a non-inferiority trial. The calculation using the level of significance at 5% and power of 80% indicated that the sample size needed to be at least 27 teeth per group. The sample size was increased by 10% to compensate for dropouts. Therefore, the sample size was 30 teeth per group.

## Randomization Method

Based on the stratified randomization method, the participants were randomized by one researcher (DS). Prior studies have demonstrated that the most relevant factors in postoperative pain after endodontic treatment are sex and the presence of an apical radiolucency (13, 16, 19, 22, 23). Of the sixty participants, males and females with or without apical radiolucency were allocated using a simple random allocation sequence (random-order table) to evenly distribute the participants in two parallel experimental groups (Group 1: non-solvent, Group 2: solvent) as seen in Figure 1.

The participants' pre-operative data, clinical, and radiographic features that might affect pain due to inflammation and pain perception were collected (14, 18).

## Retreatment Protocols

Patients from the Endodontics Clinic were invited to participate in this project. The participants were single-blinded to solvent use. The endodontic retreatment was performed by 2<sup>nd</sup> or 3<sup>rd</sup> year postgraduate students in the Endodontic Training Programs using a standardized protocol. None of the participants in either group received local anesthesia, and all received multiple visit treatment. The retreatment procedures were performed using a dental microscope (Zeiss Opmi; Carl Zeiss, Jena, Germany). The operators had at least 1-year experience in using the dental operating microscope for en-

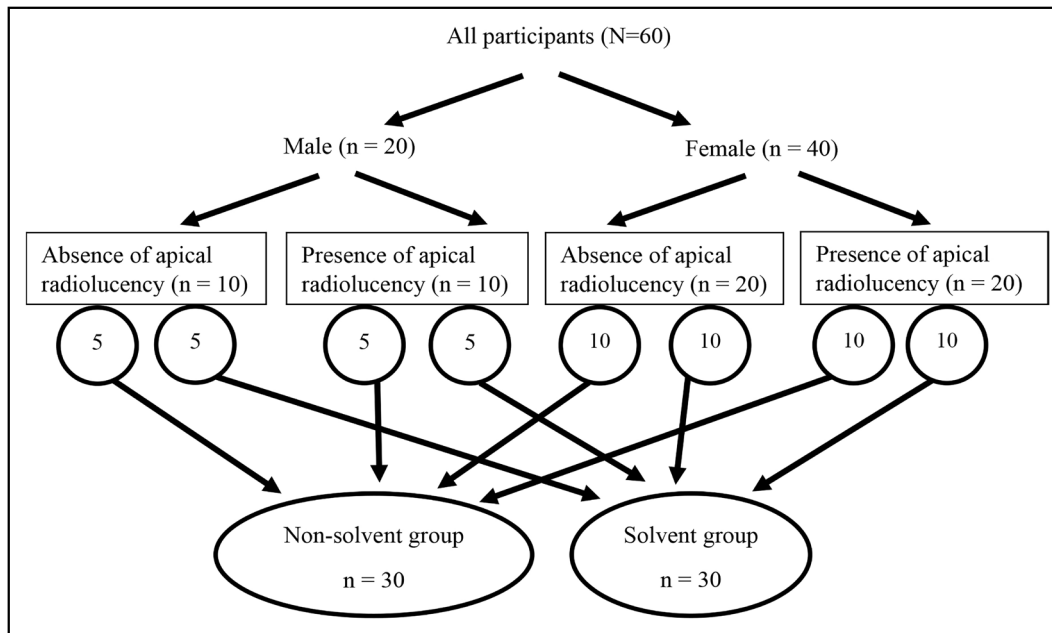


Figure 1. Four categories based on sex and the presence of an apical radiolucency

dodontic treatment. The rubber dam was placed, and any dental caries and faulty restorations were removed before access was opened until the coronal root canal filling was reached. The #1 and #2 ProTaper Universal Retreatment files (Dentsply Maillefer, Ballaigus, Switzerland), ultrasonic retreatment tip (ET-20, Acteon Satelec, Bordeaux, France), and/or #3 Gates Glidden drill (Dentsply Maillefer, Ballaigus, Switzerland) were used to remove the root canal filling materials in the coronal two-thirds of the root canal. Hedström files (Dentsply Maillefer, Ballaigus, Switzerland) were subsequently used until there was 3 mm of gutta-percha remaining in the root canal.

#### Non-solvent Group

The remaining 3 mm of gutta-percha was removed with Hedström files. The working length was reached and estimated with #15 K-files (Dentsply Maillefer, Ballaigus, Switzerland) and an electronic apex locator (Root ZX; J Morita, Tokyo, Japan).

#### Solvent Group

The GuttaClear solvent (MDent, Bangkok, Thailand) (0.5 ml) was dropped on the residual root canal filling for 2 min before the removal process was performed as in the non-solvent group (5).

During gutta-percha removal, the root canal was irrigated with 2.5% sodium hypochlorite (NaOCl, MDent, Bangkok, Thailand) using plastic syringe and a 30-gauge side-vented syringe (Max-i-Probe; Dentsply Rinn, Elgin, IL, USA) with the irrigation needle placed into the canal 1 mm short of the working length. The procedures were repeated until the gutta-percha was completely removed and confirmed by periapical radiographs. The root canals were then irrigated using 5 ml 2.5% NaOCl and/or 3 ml 17% EDTA (MDent, Bangkok, Thailand) and the root canals were dried with paper points. The canals were filled with non-setting calcium hydroxide paste (UltraCal XS, South Jordan, UT, USA), where the tip was placed 2 mm short of the working length. The access cavity was filled with Cavit

(Caviton, G.C. Corp., Tokyo, Japan) and intermediate restorative material (IRM, Dentsply, DE, USA). The participants received the postoperative pain questionnaires that were explained to them by one investigator.

At the second appointment, the participants returned the questionnaires to the operators. After enlargement with a finishing file, the root canal received a final irrigation using 5 ml 2.5% NaOCl and 3 ml 17% EDTA. The root canals were dried with paper points before filling with a gutta-percha master cone and AH-plus sealer (Dentsply Maillefer, Ballaigus, Switzerland). Finally, the access cavity was filled with Cavit and IRM.

#### Postoperative Pain Measurement

The numerical rating scale (NRS) on a defined 0-10 scale was used to collect the pain scores, where 0 was no pain and 10 was the worst pain imaginable. The participants selected the number that best represented their pain at six time points: (i) immediately after the procedure, (ii) 6 h post-treatment, (iii) 12 h post-treatment, (iv) 24 h post-treatment, (v) 48 h post-treatment, and (vi) 72 h post-treatment. Based on the NRS score, the participants were classified into 2 groups; pain, participants who had NRS>0 or no pain, participants who had NRS=0. In addition, the number of participants taking 400mg ibuprofen (Nurofen; Reckitt Benckiser, Bangkok, Thailand) was collected and analysed at the same six time points. The number of participants having pain and taking analgesics after treatment was analysed.

#### Statistical Analysis

The data were statistically analysed using SPSS software, Version 18 (IBM Corp, Armonk, New York). The pre-operative data, clinical, and radiographic features before treatment were compared using the chi-square test and Fisher's exact test to identify differences between the two groups.

The number of participants who had pain and took medication after treatment was compared between groups separately at

each time point using the chi-square test and Fisher's exact test. Furthermore, the decrease in pain compared with the immediate time point was analysed by the McNemar test. The relationships between the covariate factors and postoperative pain were also analysed by the chi-square test and Fisher's exact test, in which a  $P < 0.20$  was chosen to select factors that tended to associate with postoperative pain. Finally, the Generalized Estimating Equations (GEE) models were used to identify the significance and odds ratio of the selected factors. A  $P < 0.05$  was considered statistically significant.

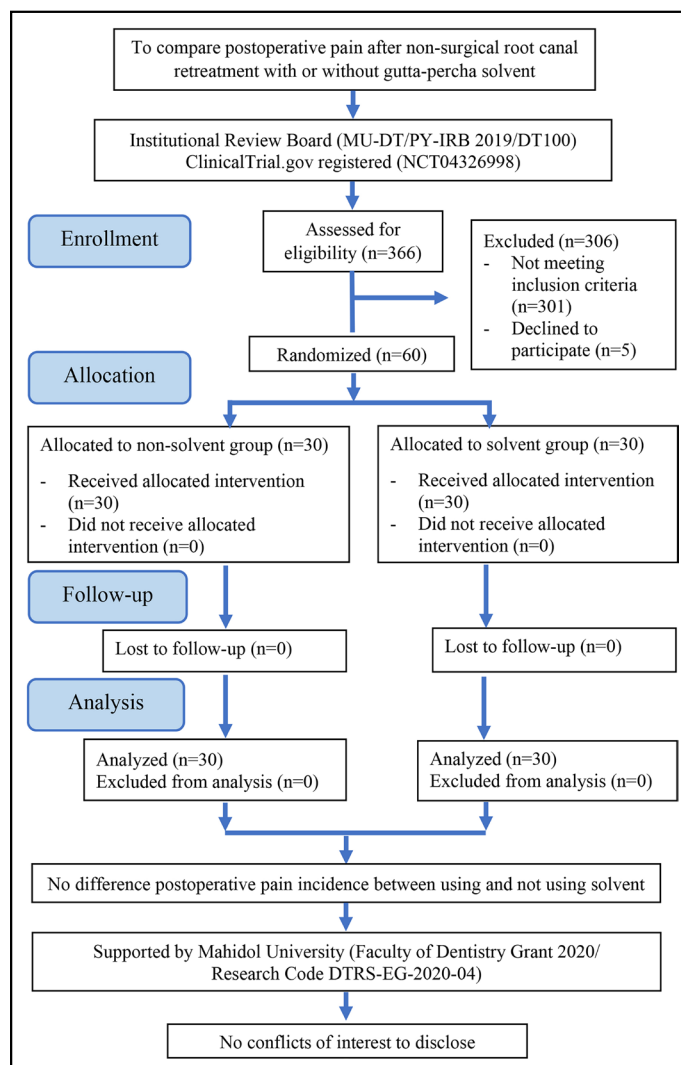
## RESULTS

None of the participants were excluded or lost to follow-up. In addition, no adverse effects occurred during the procedures. Thus, the data from 60 participants were analysed (Fig. 2). The demographic data, and the clinical and radiographic features before retreatment were not significantly different between the non-solvent and solvent groups ( $P > 0.05$ ) (Table 1).

The overall incidence of immediate postoperative pain was 35% (43.33% in the non-solvent group and 26.67% in the solvent group). The median pain scores in both groups were 2.0, which indicated mild pain at the immediate time point (Appendix 1). In addition, there were no significant differences in the incidence of postoperative pain between the groups at each time point ( $P > 0.05$ ) (Table 2). The immediate time point demonstrated the highest pain incidence that decreased time-dependently in both groups (Fig. 3). Moreover, the pain incidence significantly decreased from the immediate time point until the 24 h time point ( $P < 0.05$ ) (Table 3).

Corresponding with the pain incidence results, the number of participants taking ibuprofen was low (3.33%) in both groups at the immediate time point and 6 h post-treatment. At 12 h post-treatment, 1 participant (3.33%) in the solvent group took ibuprofen. The difference between the groups at these 3 time points was also not significant ( $P > 0.05$ ). From 24-72 h post-treatment, none of the participants took ibuprofen (Table 2).

All of the predisposing factors were initially analysed and revealed that marital status, education level, size of the lesion, pain when palpated, history of postoperative pain, and expectation of pain were the factors potentially associated with postoperative pain ( $P < 0.20$ ) (25). In contrast, other predisposing factors, including the extension of old gutta-percha (1 mm and above) were not associated with the incidence of postoperative pain (Table 4). The potentially predisposing factors were then included in the GEE models. The model demonstrated no significant differences among the groups, marital status, education level, lesion size, pain when palpated, or expectation of pain ( $P > 0.05$ ). However, the pain incidence at the immediate time point, 6-, 12-, 24- and 48 h were significantly different compared with the 72 h post-treatment time point. Therefore, the participants were 14.68-fold more likely to experience pain at the immediate time point. The participants were 11.07-, 7.30-, 3.84- and 2.75-fold more likely to experience pain at 6-, 12-, 24- and 48 h, respectively, post-treatment compared with 72 h post-treatment ( $P < 0.05$ ). However, the history of postoperative pain was a confounding factor for which the



**Figure 2.** Flow diagram according to the CONSORT (2010) and PRIRATE (2020) guidelines for the clinical trial of endodontic retreatment when using and not using GuttaClear solvent

participants with a history of postoperative pain were 21.61-fold more likely to have postoperative pain than those with no history of postoperative pain ( $P < 0.05$ ) (Table 5).

## DISCUSSION

This study employed a randomized controlled trial design, which is the best method to use to determine clinical outcomes. In addition, the Consolidated Standards of Reporting Trials (CONSORT) checklist and Preferred Reporting Items for RAnimized Trials in Endodontics (PRIRATE) checklist were used in the current study to facilitate the clarity, completeness, and transparency of the study (26, 27)

When considering the factors associated with postoperative pain, the cases with preoperative pain were excluded due to the consensus that preoperative pain influences postoperative pain as reported in related studies (20-23). Sex and the presence of an apical radiolucency were equally controlled using the randomization method to reduce bias by distributing the participants equally in the experimental groups (21-23). Moreover, the baseline characteristics, including age, tooth

**TABLE 1.** Baseline demographic and clinical features of the participants in the two groups

Demographic and clinical features	Non-solvent		Solvent		P
	n	%	n	%	
Age					
≤35 years	5	16.67	3	10	0.706
>35 years	25	83.33	27	90	
Career					
No	8	26.67	13	43.33	0.176
Yes	22	73.33	17	56.67	
Marital status					
Married	16	53.33	15	50	0.796
Unmarried	14	46.67	15	50	
Education					
Less than bachelor	12	40	13	43.33	0.793
At least bachelor	18	60	17	56.67	
Tooth localization					
Maxilla	16	53.33	14	46.67	0.606
Mandible	14	46.67	16	53.33	
Tooth type					
Anterior	13	43.33	13	43.33	1.000
Posterior	17	56.67	17	56.67	
Size of apical radiolucency					
≤5 mm.	28	93.33	26	86.67	0.671*
>5 mm.	2	6.67	4	13.33	
Quality of old root canal filling					
Poorly condensed	12	40	12	40	1.000
Well condensed	18	60	18	60	
Length of old gutta-percha from apex					
1 mm.	12	40	13	43.33	0.793
>1 mm.	18	60	17	56.67	
Pain when percussed					
Negative	19	63.33	22	73.33	0.405
Positive	11	36.67	8	26.67	
Pain when palpated					
Negative	27	90	28	93.33	1.000*
Positive	3	10	2	6.67	
Mobility					
Normal	28	93.33	29	96.67	1.000*
1 <sup>st</sup> degree	2	6.67	1	3.33	
Coronal leakage					
No	18	60	14	46.67	0.301
Yes	12	40	16	53.33	
Periapical diagnosis					
Normal apical tissue	12	40	12	40	1.000
Apical periodontitis	18	60	18	60	
History of postoperative pain					
No	3	10	6	20	0.472*
Yes	27	90	24	80	
Expectation of pain after treatment					
No pain	5	16.67	11	36.67	0.080
Have pain	25	83.33	19	63.33	

\*: Fisher's exact test

type, and tooth location did not significantly differ between the groups indicating that the appropriate randomization method was used.

The Visual Analogue Scale (VAS) and NRS are the most commonly used measures to identify pain intensity (15, 20-23, 28). Many studies have used the VAS because it is easy for

the participants to use and has high sensitivity, validity, and reliability (29). However, this scale has some disadvantages in that difficulty in responding to the VAS was found in some patients, especially children and the elderly (28, 29). The present study used the NRS, similar to a previous study, due to its convenience and simplicity and used both verbal and written forms (15).



**TABLE 2.** Number of participants experiencing pain and taking analgesics in the non-solvent and solvent groups.

	Immediate		At 6 h		At 12 h		At 24 h		At 48 h		At 72 h	
	n	%	n	%	n	%	n	%	n	%	n	%
Number of participants reporting pain												
Non-solvent (n=30)	13	43.33	12	40	9	30	5	16.67	5	16.67	2	6.67
Solvent (n=30)	8	26.67	6	20	5	16.67	4	13.33	2	6.67	1	3.33
P	0.176		0.091		0.222		1.000*		0.424*		1.000*	
Number of medication intakes												
Non-solvent (n=30)	1	3.33	1	3.33	0	0	0	0	0	0	0	0
Solvent (n=30)	1	3.33	1	3.33	1	3.33	0	0	0	0	0	0
P	1.000*		1.000*		1.000*		-		-		-	

\*Fisher's exact test

A study (20) reported that 35% of the patients had postoperative pain at 24 h after non-surgical retreatment procedures, while another study (23) found 44-65% of the patients experienced postoperative pain. In the present study, the incidence of immediate pain was 35%; however, at 24 h, the incidence decreased to 15%. Because no pre-operative pain patients or multi-rooted teeth were enrolled in our study, the pain incidence at 24 h was lower compared with these studies (19, 20, 23).

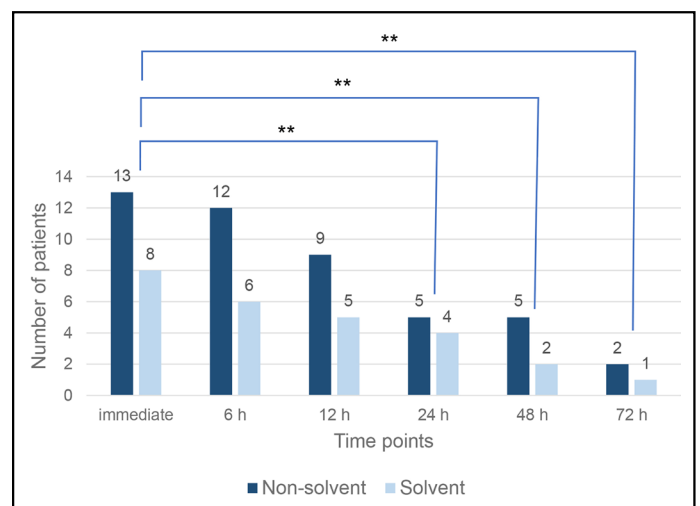
Because postoperative pain is associated with acute inflammation occurring during a short-term process, 6 time points over 3 d were evaluated in this study. Previous studies have shown that pain between 72 h (3 d) and more than 3 d were not significantly different (21, 23). In addition, Topcuoglu and colleagues (21) revealed that the highest pain at all time points occurred 6 h post-treatment, which contrasts with the present study that found the highest pain was at the immediate postoperative time point. However, these authors used local anesthesia, while the present study performed the treatment without local anesthesia, thus collecting data immediately post-treatment was possible. The present study is the first to report on pain at the immediate time point and found more pain than at 6 h. The pain incidence significantly decreased from the immediate time point by 24 h. The pain at the immediate time point was the highest because of acute inflammation; moreover, discomfort after extended chair time and the use of a rubber dam clamp can also influence pain incidence (30).

Fewer patients in the solvent group had postoperative pain compared with the non-solvent group, corresponding to Genc Sen et al. (15). These results of less pain in the solvent group may be because using a solvent when removing the root canal filling materials decreases the amount of apically extruded debris as demonstrated in *in vitro* studies (31, 32). Moreover, retreatment in the solvent group may take less time than that of the non-solvent group resulting in less discomfort compared with extended treatment time (30). However, the difference in postoperative pain between the solvent and non-solvent groups was not significant.

When considering post-treatment analgesic use, this study had fewer participants who took ibuprofen compared with

**TABLE 3.** Decrease in pain compared with the immediate time point

	Immediate pain		Total	P
	No pain	Pain		
Pain at 6h				
No pain	33	9	42	0.607
Pain	6	12	18	
Pain at 12h				
No pain	34	12	46	0.143
Pain	5	9	14	
Pain at 24h				
No pain	37	14	51	0.004 <sup>a</sup>
Pain	2	7	9	
Pain at 48h				
No pain	38	15	53	0.001 <sup>a</sup>
Pain	1	6	7	
Pain at 72h				
No pain	38	19	57	<0.001 <sup>a</sup>
Pain	1	2	3	
Total	39	21	60	

<sup>a</sup>: P<0.05**Figure 3.** Number of participants experiencing pain compared between non-solvent and solvent groups at each time point

\*\*: P&lt;0.01

**TABLE 4.** Relationships between covariate factors and number of participants experiencing postoperative pain at each time point

Covariate factors	P					
	Immediate pain	Pain at 6h	Pain at 12h	Pain at 24h	Pain at 48h	Pain at 72h
Group	0.176 <sup>b</sup>	0.091 <sup>b</sup>	0.222	1*	0.424*	1.000*
Non-solvent						
Solvent						
Time						
Immediate pain	-	0.001 <sup>b</sup>	0.012 <sup>*b</sup>	0.006 <sup>*b</sup>	0.006 <sup>*b</sup>	0.278*
Pain at 6h	0.001 <sup>b</sup>	-	0.000 <sup>*b</sup>	0.000 <sup>*b</sup>	0.000 <sup>*b</sup>	0.024 <sup>*b</sup>
Pain at 12h	0.012 <sup>*b</sup>	0.000 <sup>*b</sup>	-	0.000 <sup>*b</sup>	0.000 <sup>*b</sup>	0.011 <sup>*b</sup>
Pain at 24h	0.006 <sup>*b</sup>	0.000 <sup>*b</sup>	0.000 <sup>*b</sup>	-	0.000 <sup>*b</sup>	0.002 <sup>*b</sup>
Pain at 48h	0.006 <sup>*b</sup>	0.000 <sup>*b</sup>	0.000 <sup>*b</sup>	0.000 <sup>*b</sup>	-	0.001 <sup>*b</sup>
Pain at 72h	0.278*	0.024 <sup>*b</sup>	0.011 <sup>*b</sup>	0.002 <sup>*b</sup>	0.001 <sup>*b</sup>	-
Age	1.000*	1.000*	1.000*	1.000*	0.578*	1.000*
≤35 years						
>35 years						
Career						
No	0.712	0.679	0.532*	1.000*	1.000*	1.000*
Yes						
Marital status						
Married	0.025 <sup>b</sup>	0.866	0.887	0.474*	0.426*	1.000*
Unmarried						
Education						
Less than bachelor	0.682	0.045 <sup>b</sup>	0.079 <sup>b</sup>	0.722*	0.688*	0.258*
At least bachelor						
Tooth localization						
Maxilla	0.417	0.260	0.542	1.000*	1.000*	1.000*
Mandible						
Tooth type						
Anterior	0.299	0.909	0.234	0.482*	0.454*	0.574*
Posterior						
Size of apical radiolucency						
≤5 mm	0.171 <sup>*b</sup>	0.352*	0.617*	0.218*	0.541*	0.275*
>5 mm						
Quality of old root canal filling						
Poorly condensed	0.825	0.908	0.709	0.729*	1.000*	1.000*
Well condensed						
Length of old gutta-percha from apex						
1 mm	0.755*	0.308*	0.713*	0.668*	1.000*	1.000*
>1 mm						
Pain when percussed						
Negative	0.891	0.391	0.918	1.000*	1.000*	1.000*
Positive						
Pain when palpated						
Negative	1.000*	0.631*	0.582*	0.158 <sup>*b</sup>	0.099 <sup>*b</sup>	1.000*
Positive						
Mobility						
Normal	0.278*	0.212*	0.556*	0.391*	0.315*	1.000*
1 <sup>st</sup> degree						
Coronal leakage						
No	0.664	0.821	0.744	0.482*	0.432*	1.000*
Yes						
Periapical diagnosis						
Normal apical tissue	0.740	0.490	0.803	1.000*	1.000*	1.000*
Apical periodontitis						
History of postoperative pain						
No	0.142 <sup>*b</sup>	0.047 <sup>*b</sup>	0.100 <sup>*b</sup>	0.330*	0.580*	1.000*
Yes						
Expectation of pain after treatment						
No pain	0.028 <sup>*b</sup>	0.112 <sup>*b</sup>	0.314*	0.096 <sup>*b</sup>	0.173 <sup>*b</sup>	0.558*
Have pain						

\*: Fisher's exact test. <sup>b</sup>: P<0.2

**TABLE 5.** GEE models comparing possible confounding factors

	<b>b</b>	<b>OR (95% CI)</b>	<b>P</b>
Group non-solvent: Pain	0.654	1.92 (0.65, 5.70)	0.238
Time: Immediate	2.687	14.68 (3.76, 57.33)	<0.001 <sup>a</sup>
Time: 6 h	2.404	11.07 (3.25, 37.68)	<0.001 <sup>a</sup>
Time: 12 h	1.988	7.30 (2.23, 23.88)	0.001 <sup>a</sup>
Time: 24 h	1.345	3.84 (1.31, 11.27)	0.014 <sup>a</sup>
Time: 48 h	1.013	2.75 (1.02, 7.45)	0.046 <sup>a</sup>
Time: 72 h	0	1	-
Marital status: Married	0.118	1.13 (0.34, 3.68)	0.845
Education: More than bachelor	0.875	2.40 (0.75, 7.70)	0.141
Periapical lesion size: >5 mm	1.316	3.73 (0.83, 16.82)	0.087
Palpation: Positive	1.551	4.72 (0.35, 63.72)	0.243
History of postoperative pain: Yes	3.073	21.61 (1.16, 404.22)	0.040 <sup>a</sup>
Expectation of pain: Pain	0.554	1.74 (0.48, 6.31)	0.399

<sup>a</sup>: P<0.05. OR: Odds ratio, CI: Confidence interval

Genc Sen et al. (15). This is likely because these researchers performed root canal retreatment in one visit, which can cause more flare-ups and postoperative pain than the multiple visit treatment used in the present study. The intracanal medication applied during multiple visit treatment eliminates postoperative pain due to persistent intracanal microorganisms (24). In addition, the composition of the new natural gutta-percha solvent (GuttaClear) i.e., essential oils and d-limonene, used in the present study dissolves the filling material better compared with the eucalyptol-based solvent (9, 33, 34). This increase might result in less extruded debris and cause less postoperative pain.

It is recommended that solvent not be used near the apex to prevent the risk of softened gutta-percha extruding into periapical tissue. However, the appropriate distance for using a solvent remains unclear (11). In the present clinical study, the results demonstrated that the incidence of postoperative pain when using solvent in cases with gutta-percha 1 mm short of the apex did not differ from cases with gutta-percha farther from the apex. Therefore, natural gutta-percha solvent could be used in cases where original gutta-percha was located 1 mm from the apex.

Pain is a multidimensional perception that is composed of various dimensions, including physiological and psychological dimensions. Among the psychological factors, a history of postoperative pain was demonstrated to influence pain perception and postoperative pain (17, 18). In the present study, a history of postoperative pain was the only factor associated with postoperative pain, corresponding to a previous study (30). This may be because participants with a history of postoperative pain pay more attention to the signs of pain or anticipate having pain, resulting in more postoperative pain. A history of postoperative pain was also reported to lower the pain threshold and pain tolerance, causing more current postoperative pain (35). Moreover, a negative dental experience that results in dental fear and anxiety can cause more postoperative pain (36).

In summary, the use of natural solvent did not influence the incidence of postoperative pain after treatment. However,

pain is subjective and is multidimensionally affected by tooth characteristics and patient factors (22, 30, 36). Each tooth has unique characteristics, and some procedures may affect the amount of apically extruded debris, thus affecting postoperative pain. Furthermore, depending on their pain perception and pain threshold, patients may experience different postoperative pain levels with the same stimuli.

There were some limitations in this clinical trial. Due to the small sample size, there was insufficient information to analyse the predisposing factors. Future studies should evaluate the effect of different lengths of gutta-percha remaining from the radiographic apex (1, 2 and 3 mm). Moreover, other solvents should be evaluated.

## CONCLUSION

The present study found a comparable postoperative pain incidence and analgesic required between using and not using a natural gutta-percha solvent, GuttaClear, during retreatment procedures.

## Disclosures

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**Conflict of interest:** The authors deny any conflict of interest.

**Ethics Committee Approval:** This study was approved by The Ethical Review Committee for Human Research, Faculty of Dentistry and Faculty of Pharmacy, Mahidol University, Bangkok, Thailand (Date: 26/08/2019, Number: MU-DT/PY-IRB 2019/054.2608).

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**APPENDIX 1.** Number of participants and median pain scores (NRS) at each time point

NRS	Number of participants (N=60)					
	Immediate	At 6 h	At 12 h	At 24 h	At 48 h	At 72 h
0	39	42	46	51	53	57
1	6	5	4	3	3	1
2	7	3	4	2	1	0
3	1	5	1	0	1	1
4	4	2	2	1	1	1
5	0	1	1	1	0	0
6	1	0	0	0	0	0
7	1	1	1	1	1	0
8	1	1	1	1	0	0
9	0	0	0	0	0	0
10	0	0	0	0	0	0
Median pain scores (NRS)	2	3	2	2	2	3