Influence of ProTaper/ProTaper Next, compared to other rotatory/reciprocating systems, on the risk and intensity of postoperative pain after endodontic instrumentation in adult patients: a systematic review and meta-analysis

Juliana Larocca **DE-GEUS**[1]
Letícia Maíra **WAMBIER**[2]
Alessandro Dourado **LOGUERCIO**[3]
Alessandra **REIS**[3]

DOI: https://doi.org/10.14436/2358-2545.10.2.048-059.oar

ABSTRACT

Introduction: The success of endodontic therapy depends not merely on their efficacy and proper completion but also on minimal patient discomfort. The purpose of this systematic review and meta-analysis is to evaluate the risk and intensity of post instrumentation endodontic pain in adult patients. **Methods:** A comprehensive search was performed in the MEDLINE via PubMed, Scopus, Web of Science, LILACS, BBO and Cochrane Library and SIGLE without restrictions. The annual conference of the IADR abstracts (1990-2016), and unpublished and ongoing trials registry were also searched. Dissertations and theses were searched using the ProQuest Dissertations and the Periodicos Capes Theses Databases. Only randomized clinical trials that compared the risk or intensity of pain resulting from endodontic treatment in adult patients were included. **Results:** After the removal of duplicates, 827 articles were identified. After title and abstract screening, 26 studies remained. Thirteen studies were further excluded while 10 studies remained for qualitative analyses and 7 for the meta-analysis. No significant difference in the risk/intensity of pain after endodontic treatment was observed in this study. The risk of pain ratio was 1.09, with a 95% confidence interval of 0.87 to 1.38 (p = 0.45). The Hedges g standardized difference in means of pain intensity at 24 h was -0.05, with a confidence interval varying from -0.21 to 0.11 (p = 0.53). **Conclusions:** No differences in risk and intensity of pain after endodontic treatment with ProTaper and other rotatory or reciprocating systems were found in this meta-analysis.

Keywords: Root Canal Therapy. Pain, Postoperative. Dental Instruments.

How to cite: de-Geus JL, Wambier LM, Loguercio AD, Reis A. Influence of ProTaper/ProTaper Next, compared to other rotatory/reciprocating systems, on the risk and intensity of postoperative pain after endodontic instrumentation in adult patients: a systematic review and meta-analysis. Dental Press Endod. 2020 May-Aug;10(2):48-59. DOI: https://doi.org/10.14436/2358-2545.10.2.048-059.oar

[1] Faculdade Paulo Picanço (Fortaleza/CE, Brazil). Universidade Estadual de Ponta Grossa (Ponta Grossa/PR, Brazil).

[2] Universidade Positivo (Curitiba/PR, Brazil).

[3] Universidade Estadual de Ponta Grossa (Ponta Grossa/PR, Brazil).

» The authors report no commercial, proprietary or financial interest in the products or companies described in this article.

» Patients displayed in this article previously approved the use of their facial and intraoral photographs.

Submitted: October 31, 2018. Revised and accepted: February 11, 2019.

Contact address: Juliana Larocca de Geus
Departamento de Odontologia, Faculdade Paulo Picanço, Joaquim Sá
Dionísio Torres, 900, Fortaleza/CE, 60135-218, Brasil
E-mail: juliana.degeus@facpp.edu.br

Introduction

During cleaning and shaping or root canals, irrigants, dentin chips, pulp tissue, and microorganisms may get extruded into the periradicular tissues, producing an acute inflammatory reaction and causing postoperative pain.[1] This extrusion is known as flare-up, which is likely the cause of the periapical inflammation and postoperative pain,[2] may also cause tumefaction or both, starting within a few hours or days after the instrumentation of the root canal.[3] According to the literature, the incidence of flare-ups during endodontic treatment ranges from 1.4% to 16%.[4-7]

Several factors are involved in the volume of extrusion of debris such as type and frequency of the irrigation solution,[8] final apical size.[9]

All instrumentation techniques result in the apical extrusion of debris; however, compared to rotary instrumentation, reciprocating motion may increase the amount of debris extruded beyond the apex and consequently the risk of postoperative pain.[2,12,13]

The ProTaper Universal system (Dentsply/Maillefer, Ballaigues, Switzerland) is a conventional multi-file rotary system, with a unique design and varying edges along the long axes of the instruments. The system has six preparation files: three for formatting, which have elbows that increase coronal preparation, and three for finishing, which have the reverse pattern. It has been claimed that such a design is more effective in cutting dentin.[14] The ProTaper system (Dentsply Maillefer, Ballaigues, Switzerland) is the most used rotary system.[15] This system is mainly used with the crown-down single-length technique, which was reported to produce less debris extrusion when compared with other instrumentation techniques,[16] which may be clinically translated by reduced rates of postoperative sensitivity.

However, studies on this field show controversial findings. Some authors reported that multi-file rotary instrumentation technique with ProTaper Universal extrudes significantly more debris than reciprocating single-file instrumentation technique with Wave-One files (Dentsply/Maillefer).[17] Other authors showed similar findings when the ProTaper instruments were compared with Race rotatory NiTi files.[18,19] Yilmaz and Ozyurek[20] (2017) found that the Reciproc, a reciprocant file system, led to higher levels of apical extrusion than the ProTaper Next file system. Besides that, Nekoofar et al.[21] (2015) showed that postoperative pain was significantly lower in patients undergoing canal instrumentation with ProTaper Universal rotary instruments compared with the Wave-One reciprocating single-file technique.

In face of these controversial results, the aim of this study was to answer the following PICO question (P - population; I - intervention; C - comparator; O - outcome): Does the ProTaper or ProTaper Next systems produce lower postoperative pain than other rotatory or reciprocating systems in adult patients submitted to endodontic therapy?

Materials and Methods

Protocol and registration

This study protocol was registered at the PROSPERO (CRD 42016036546) and followed the recommendations of the PRISMA statement for report.[22]

Eligibility criteria

We included only randomized clinical trials (RCTs) that compared the post-operative pain in adult participants who underwent endodontic treatment with ProTaper or ProTaper Next vs. other rotatory/reciprocating systems in adult patients. RCT studies were excluded if studies 1) compared ProTaper or ProTaper Next vs hand-files; 2) did not evaluate postoperative pain; 3) evaluated post-operative pain in periods lower than 4 hours (as participants could be still under anaesthetic effect).

Information sources and search strategy

Initially, the search strategy was defined for the MEDLINE database, via PubMed, based on controlled vocabulary (MeSH terms) and free keywords for the concepts of population, intervention and comparator. Other electronic databases (Latin American and Caribbean Health Sciences Literature database (LILACS), Brazilian Library in Dentistry (BBO) and Cochrane Library) and citation databases (Scopus and Web of Science) were included after translation of the search strategy for each database (Table 1). The reference lists of all primary studies were hand-searched for additional relevant publications. Additionally, we also hand-searched the first page of related articles link of each primary study in the PubMed database. No restrictions to publication date or languages were imposed on the search strategy.

Table 1. Electronic database and search strategy.

Pubmed (September/23/2016)		
#1 (endodontics[MeSH Terms]) OR pulpectomy[MeSH Terms]) OR root canal preparation[MeSH Terms]) OR root canal therapy[MeSH Terms]) OR "endodontic treatment"[Title/Abstract]) OR endodontics[Title/Abstract]) OR "endodontically treated teeth"[Title/Abstract]) OR pulpectomy[Title/Abstract]) OR "root canal preparation"[Title/Abstract]) OR "root canal therapy"[Title/Abstract]) OR "root canal treatment"[Title/Abstract])	#2 (dental instruments[MeSH Terms]) OR "dental instruments"[Title/Abstract]) OR rotatory[Title/Abstract]) OR reciprocating[Title/Abstract]) OR reciprocation[Title/Abstract]) OR automated[Title/Abstract]) OR protaper[Title/Abstract]) OR "wave- one"[Title/Abstract]) OR "instrumentation techniques"[Title/Abstract]) OR "NiTi instruments"[Title/Abstract]) OR "nickel-titanium instruments"[Title/Abstract]) OR reciproc[Title/Abstract]) OR unicone[Title/Abstract]) OR mtwo[Title/Abstract]) OR "easy prodesign logic"[Title/Abstract]) OR "glide path"[Title/Abstract]) OR pathfile[Title/Abstract]) OR proglider[Title/Abstract]	#3 (randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized controlled trials[mh] OR random allocation[mh] OR double-blind method[mh] OR single-blind method[mh] OR clinical trial[pt] OR clinical trials[mh] OR ("clinical trial"[tw]) OR ((singl*[tw] OR doubl*[tw] OR trebl*[tw] OR tripl*[tw]) AND (mask*[tw] OR blind*[tw])) OR (placebos[mh] OR placebo*[tw] OR random*[tw] OR research design[mh:noexp] OR comparative study[pt] OR evaluation studies as topic[mh] OR follow-up studies[mh] OR prospective studies[mh] OR control*[tw] OR prospective*[tw] OR volunteer*[tw]) NOT (animals[mh] NOT humans[mh])
#1 AND #2 AND #3		
Scopus (September/23/2016)		
#1 (TITLE-ABS-KEY (endodontics) OR TITLE-ABS-KEY (pulpectomy) OR TITLE-ABS-KEY ("root canal preparation") OR TITLE-ABS-KEY ("root canal therapy") OR TITLE-ABS-KEY ("endodontic treatment") OR TITLE-ABS-KEY ("endodontically treated teeth") OR TITLE-ABS-KEY ("root canal treatment")	#2 (TITLE-ABS-KEY ("dental instruments") OR TITLE-ABS-KEY (rotatory) OR TITLE-ABS-KEY (reciprocating) OR TITLE-ABS-KEY (reciprocation) OR TITLE-ABS-KEY (automated) OR TITLE-ABS-KEY (protaper) OR TITLE-ABS-KEY (reciproc) OR TITLE-ABS-KEY ("wave-one") OR TITLE-ABS-KEY ("instrumentation techniques") OR TITLE-ABS-KEY ("NiTi instruments") OR TITLE-ABS-KEY ("nickel-titanium instruments") OR TITLE-ABS-KEY (unicone) OR TITLE-ABS-KEY (mtwo) OR TITLE-ABS-KEY (proglider) OR TITLE-ABS-KEY ("easy prodesign logic") OR TITLE-ABS-KEY (pathfile) OR TITLE-ABS-KEY ("glide path")	
#1 AND #2		
Web of Science (September/23/2016)		
#1 Topic: (endodontics) OR Topic: (pulpectomy) OR Topic: ("endodontically treated teeth") OR Topic: ("root canal treatment") OR Topic: ("root canal preparation") OR Topic: ("root canal therapy") OR Topic:("endodontic treatment")	#2 Topic: ("dental instruments") OR Topic: (reciprocating) OR Topic: (reciprocation) OR Topic: (automated)OR Topic: ("instrumentation techniques") OR Topic: ("NiTi instruments") OR Topic: (rotatory) OR Topic: (protaper) OR Topic: ("wave-one") OR Topic: (pathfile) OR Topic: (proglider) OR Topic: ("nickel-titanium instruments") OR Topic: (reciproc) OR Topic: (unicone) OR Topic: (mtwo) OR Topic: ("easy prodesign logic") OR Topic: ("glide path")	
#1 AND #2		
Lilacs e BBO (September/23/2016)		
#1 (MH:endodontics OR MH:pulpectomy OR MH:"root canal preparation" OR MH:"root canal therapy" OR "endodontic treatment" OR "tratamiento endodóntico" OR "tratamento endodôntico" OR endodontics OR endodoncia OR endodontia OR "endodontically treated teeth" OR "dientes tratados endodónticamente" OR "dentes tratados endodonticamente" OR pulpectomy OR pulpectomía OR pulpectomia OR "root canal preparation" OR "preparación del conducto radicular" OR "prepare do canal radicular" OR "root canal therapy" OR "tratamiento del conducto" OR "tratamento de canal" OR "root canal treatment")	#2 (MH:dental instruments OR "dental instruments" OR "instrumentos dentales" OR "instrumentos dentários" OR rotatory OR rotatorio OR rotatório OR reciprocating OR "movimiento oscilante" OR reciprocante OR reciprocation OR reciprocidad OR "movimento alternado" OR automated OR automatizado OR protaper OR "wave-one" OR unicone OR pathfile OR proglider OR "instrumentation techniques" OR "técnicas de instrumentación" OR "técnicas de instrumentação" OR "NiTi instruments" OR "instrumentos NiTi" OR "instrumentos de NiTi" OR "nickel-titanium instruments" OR "instrumentos de níquel-titanio" OR "instrumentos de níquel-titânio" OR reciproc OR mtwo OR "easy predesign logic" OR glidepath)	
#1 AND #2		
Cochrane Library (September/23/2016)		
#1 MeSH descriptor: [Endodontics] explode all trees	#9 rotatory:ti,ab,kw or reciprocat*:ti,ab,kw or automated:ti,ab,kw or protaper:ti,ab,kw or "wave-one":ti,ab,kw (Word variations have been searched)	
#2 MeSH descriptor: [Pulpectomy] explode all trees	#10 instrumentation next techniques:ti,ab,kw or NiTi next instruments:ti,ab,kw or "nickel-titanium instruments":ti,ab,kw or reciproc:ti,ab,kw or unicone:ti,ab,kw (Word variations have been searched)	
#3 MeSH descriptor: [Root Canal Preparation] explode all trees	#11 mtwo:ti,ab,kw or "easy prodesign logic":ti,ab,kw or glide next path:ti,ab,kw or pathfile:ti,ab,kw or proglider:ti,ab,kw (Word variations have been searched)	
#4 MeSH descriptor: [Root Canal Therapy] explode all trees	#12 dental next instruments:ti,ab,kw (Word variations have been searched)	
#5 endodontic next treatment:ti,ab,kw or endodontics:ti,ab,kw or pulpectomy:ti,ab,kw or "endodontically treated teeth":ti,ab,kw or "root canal preparation":ti,ab,kw (Word variations have been searched)	#13 #8 or #9 or #10 or #11 or #12 #17 premedication:ti,ab,kw	
#6 "root canal therapy":ti,ab,kw or "root canal treatment":ti,ab,kw (Word variations have been searched)	#18 #1 or #2 or #3 or #4 or #5 or #6	
#7 #1 or #2 or #3 or #4 or #5 or #6	#19 #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17	
#8 MeSH descriptor: [Dental Instruments] explode all trees	#20 #18 and #19	

Grey literature was inspected by searching studies published as abstracts from the annual conference of the International Association for Dental Research (IADR) and their regional divisions (1990-2016). We also searched grey literature at the System for Information on Grey literature in Europe (SIGLE), ProQuest Dissertations and Theses Full text database, as well as the Periodicos Capes Theses database.

To locate unpublished and ongoing trials related to the review question, the following clinical trials registries were searched: Current Controlled Trials (www.controlled-trials.com), International Clinical trials registry platform (http://apps.who.int/trialsearch/), the ClinicalTrials.gov (www.clinicaltrials.gov), Rebec (www.rebec.gov.br), and EU Clinical Trials Register (https://www.clinicaltrialsregister.eu).

Study selection and data collection process

Initially, duplicates were removed, and the articles were selected by title and abstracts according to the previously described search strategy. Full-text articles were obtained and checked again to see if they met the eligibility criteria. Each study received and identification number (ID), combining first author and year of publication. Three authors retrieved information about the study design, participants, interventions and outcomes were extracted using customized extraction forms.

When data from two or three endodontic sessions were provided, their data were merged. When more than one alternate rotary/reciprocating system was included in the study, their values were also merged to make a single entry.

Risk of bias in individual studies

Two independent reviewers, using the Cochrane Collaboration's tool assessed the risk of bias of the included randomized clinical trials.[23] The assessment criteria contain six domains: sequence generation, allocation concealment, blinding of the outcome assessors, incomplete outcome data, selective outcome reporting, and other possible sources of bias. The key domains for the outcomes of this study (risk and intensity of postoperative pain) were examiner and participant blinding, sequence generation and allocation concealment.

Each domain was scored as low, high or unclear risk of bias (http://handbook.cochrane.org). At the study level, the study was considered at low risk of bias if all key domains were at low risk of bias. If one or more key domains were judged as having unclear risk of bias, the study were of unclear risk of bias. When at least one key domain from each study was judged at high risk, the study received the same judgment of high risk. If disagreements occurred between the reviewers during this process, they were solved through discussion, and if needed, by consulting a third reviewer.

Summary measures and synthesis of results

Only studies classified at low risk of bias in the key domains were meta-analyzed. The outcomes for the comparison ProTaper or ProTaper Next vs. other systems were summarized by calculating the standardized mean difference for intensity of postoperative pain at 6 and 24 hours and the risk ratio for the risk of postoperative pain. Additional meta-analysis for the same outcomes described above was performed comparing ProTaper or ProTaper Next vs. specific instrumentation systems, if we have at least two studies for each comparison.

The random-effects models were employed for meta-analyses. Heterogeneity was assessed using the Cochran Q test and I^2 statistics. We performed subgroup analysis based on the type of ProTaper system employed (the "conventional" ProTaper or the ProTaper next system). This was not pre-specified in the study protocol registered a priori, as we did not know there were many studies about ProTaper Next in the literature. Sensitivity analyses were also conducted to investigate the reasons for high heterogeneity whenever detected. Data were analyzed using Revman 5 (Review Manager Version 5, The Cochrane Collaboration, Copenhagen, Denmark). Data from eligible studies was either dichotomous (absolute risk of postoperative pain) or continuous (intensity of postoperative pain).

Results

Study Selection

After the database screening and removal of duplicates, 2798 studies were identified (Fig 1). After abstract screening, 11 studies remained, and this number was reduced to 10 after careful examination of the full-text articles.

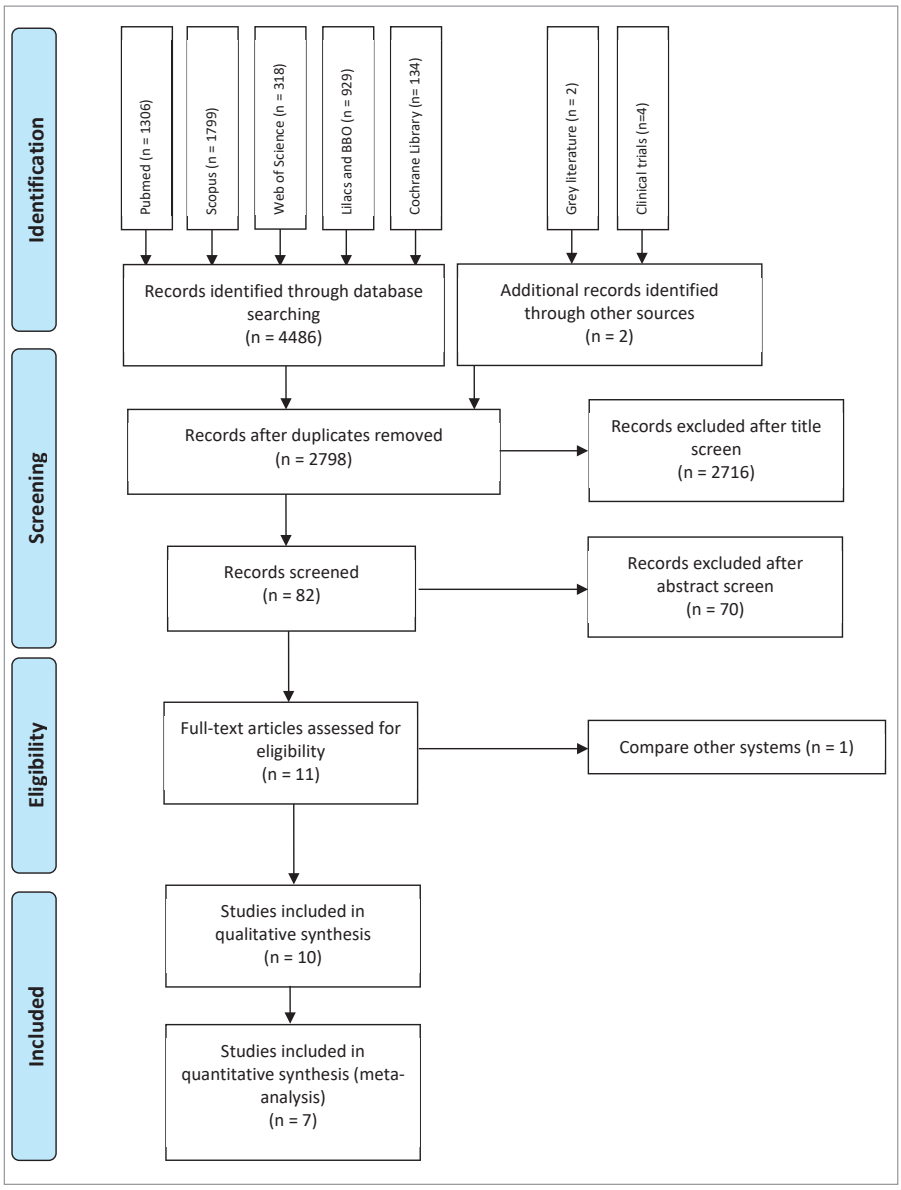


Figure 1. Flow diagram of study identification.

Characteristics of Included Articles

The characteristics of the 10 studies selected are listed in Tables 2 and 3. All studies used the parallel design.[11,15,21,24-30] The majority of studies were performed in a university setting.[11,15,21,24,25,27,29,30]

For pain evaluation, half of the studies used a 0-100 visual analog scale.[11,24,25,28,29] The others employed the 0-3 numerical rating scale,[15,26,27] the 0-4 numerical rating scale[21,24] and the Heft Parker 0-170 scale.[30]

The number of patients per group included in these studies ranged from 21 to 70. The mean age of all participants included in the clinical trials was approximately 34.3 years, ranging from 18 to 73.[15,24,26,28,30] However, five studies did not report the mean age.[11,21,25,27,29] Males prevailed in four studies,[15,21,27,30] females in three[11,24,28] and equivalent sex distribution in one.[25] The drop-outs varied from 0 to 5 participants,[11,15,24-26,28,29] and 3 studies did not report this information.[21,27,30]

Half of the studies performed the endodontic treatment in molars,[15,24,27,29,30] one in single root canal teeth[26] and one in many types of teeth.[25] Vital teeth were included in three studies,[21,28,29] and non-vital

Table 2. Summary of the studies selected for this systematic review Part 1.

Study ID	Study design [Setting]	Pain evaluation criteria	Subjects' age in mean±SD [range] (yrs)	# of subjects Male [total]	Drop-outs	Groups	Instrumentation protocol
Carvalho[24], 2016	Parallel [University]	VAS 0-100 and NRS 0-4	30,8 ± 8,4 [18 - 66]	27 [62]	4	RECIPROC[a] [31] PROTAPER NEXT[b] [31]	RECIPROC: R 25 or R40 PROTAPER NEXT: X1 - X2/X3/X4/X5
Çiçec et al.[26], 2017	Parallel [n.r.]	NRS 0-3	37,1 ± n.r. [21 - 65]	n.r. [90]	0	MANUAL[b] [30] WAVE ONE[b] [30] PROTAPER NEXT[b] [30]	HAND-FILE: modified step-back WAVE ONE: large PROTAPER NEXT: X1 - X2 - X3 - X4
Kherlakian et al.[28], 2016	Parallel [Private office]	VAS 0-100	47 ± n.r. [19 - 73]	77 [210]	0	PROTAPER NEXT[b] [70] WAVE ONE[b] [70] RECIPROC[a] [70]	PROTAPER NEXT: SX - X1 - X2 - X3 - X4 WAVE ONE: primary or large RECIPROC: R25 or R40
Krithikadatta et al.[11], 2016	Parallel [University]	VAS 0-100	n.r. ± n.r. [18 - 55]	69 [152]	3	WAVE ONE[b] [50] PROTAPER UNIVERSAL[b] [51] MTWO[c] [51]	According to manufactures' instructions
Nekoofar et al.[21], 2015	Parallel [University]	NRS 0-4	n.r. ± n.r. [15 - 55]	22 [42]	n.r.	WAVE ONE[b] [21] PROTAPER UNIVERSAL[b] [21]	PROTAPER: SX - S1 - S2 - F1/F2/F3 WAVE ONE: small or large
Pasqualini et al.[25], 2016	Parallel [University]	VAS 0-100	n.r. ± n.r. [16 - 60]	26 [52]	5	WAVE ONE[b] [26] PROTAPER UNIVERSAL[b] [26]	PROTAPER: S1 - S2 - F1 - F2 WAVE ONE: primary
Relvas et al.[15], 2016	Parallel [University]	NRS 0-3	25,8 ± 9,2 [18 - 64]	78 [78]	0	RECIPROC[a] [39] PROTAPER UNIVERSAL[b] [39]	RECIPROC: R25, R40 or R50 PROTAPER: SX - S1 - S2 - F1/F2/F3/F4
Shahi et al.[29], 2016	Parallel [University]	VAS 0-100	n.r. ± n.r. [20 - 50]	n.r. [82]	4	RACE[d] [42] PROTAPER UNIVERSAL[b] [40]	RACE: 40/0.1 - 35/0.08 - 30/.06 - 25/.04 - 30/0.04 PROTAPER: SX - S1 - S2 - F1 - F2
Shokraneh et al.[30], 2017	Parallel [University]	Heft-Parker 0-170	30,5 ± 4,6 [20 - 45]	47 [93]	n.r.	MANUAL[b] [32] WAVE ONE[b] [32] PROTAPER UNIVERSAL[b] [32]	HAND-FILE: crown-down technique WAVE ONE: primary PROTAPER: SX - S1 - S2 - F1 - F2
Wang et al.[27], 2010	Parallel [University]	NRS 0-3	n.r. ± n.r. [22 - 71]	53 [90]	n.r.	K3[c] [30] MTWO[a] [30] PROTAPER UNIVERSAL[b] [30]	K3: 25/0.10 - 25/0.08 - 25/0.06 MTWO: 10/0.04 - 15/0.05 - 20/0.06 - 25/0.06 PROTAPER: SX - S1 - S2 - F1

ID - identification; SD - standard deviation; yrs - years; # - number; n.r. - not reported; VAS (Visual Analog Scale): a 10-cm horizontal line with words ''no pain" at one end and ''worst pain" at the opposite end; NRS (Numerical Rating Scale): none, mild, moderate, considerate, severe. [a] VDW, Munich, Germany. [b] Dentsply Maillefer, Ballaigues, Switzerland. [c] SybronEndo, Mexico City, Mexico. [d] FKG dentaire SA, La Chaux-de-Fonds, Switzerland.

teeth in other three studies,[15,26,30] while the remaining performed the endodontic therapy in both vital and non-vital teeth.[11,24,25,27]

Six studies performed the endodontic treatment in one session,[15,25,26,28-30] two studies performed in 2 sessions[21,24] and two did not report the number of clinical sessions.[11,27]

In regard to the local anaesthetic, most of the studies used 2% lidocaine with 1:80.000 epinephrine[11,21,29,30] or with 1:100.000 epinephrine.[15,24,28] Three studies didn't report the type of anaesthetic agent used.[25-27]

In relation to the instrumentation protocol, most of studies used the Wave One System.[11,21,25,26,28,30] Three studies used the Reciproc System,[15,24,28] two used

Table 3. Summary of the studies selected for this systematic review. Part 2.

Study ID	Anesthesia	Dental type	Pulp condition	# of sessions	Rescue medication	Irrigation solution	Obturation technique	Endodontic cement for obturation	Assessment time of pain
Carvalho[24], 2016	2% lidocaine 1:100.000 epinephrine	Molar	Vital or nonvital	2	400 mg ibuprofen	NaOCl 2,5%	Lateral condensation	AH Plus	Every 24 h during 7 days
Çiçec et al.[26], 2017	n.r.	Single root canal	Nonvital	1	400 mg ibuprofen	NaOCl 5% + soro	Lateral condensation	AH 26	12, 24 and 48 after treatment
Kherlakian et al.[28], 2016	2% lidocaine 1:100.000 epinephrine	Maxillary or mandibular molar/premolar	Vital	1	400 mg ibuprofen	NaOCl 2,5%	Continuous wave	AH Plus	24, 48, 72 and 1 week after treatment
Krithikadatta et al.[11], 2016	2% lidocaine 1:80.000 epinephrine	Maxillary or mandibular molar/premolar	Vital or nonvital	n.r.	400 mg ibuprofen	NaOCl 5%	n.r.	n.r.	2, 4, 6, 12, 24, 36 and 48 h after treatment
Nekoofar et al.[21], 2015	2% lidocaine 1:80.000 epinephrine	Maxillary or mandibular molar/premolar	Vital	2	400 mg ibuprofen	Clorexidina 2%	Lateral condensation	AH 26	6, 12, 18, 24, 48 and 72h after treatment
Pasqualini et al.[25], 2016	n.r.	Various	Vital or nonvital	1	Unspecifiedl analgesics	NaOCl 5%	Continuous wave	Pulp canal sealer	During 7 days
Relvas et al.[15], 2016	2% lidocaine 1:100.000 epinephrine	Mandibular molar	Nonvital	1	n.r.	NaOCl 2,5% + soro	Single cone + thermomechanical compaction	AH Plus	24, 72h and 1 week after treatment
Shahi et al.[29], 2016	2% lidocaine 1:80.000 epinephrine	1st or 2nd mandibular molar	Vital	1	400 mg ibuprofen	NaOCl 2,5% + 17% EDTA gel	Lateral condensation	AH 26	4, 8, 12, 24, 48, 72h and 1 week after treatment
Shokraneh et al.[30], 2017	2% lidocaine 1:80.000 epinephrine	1st or 2nd mandibular molar	Nonvital	1	400 mg ibuprofen	NaOCl 5,25%	Lateral condensation	AH 26	6, 12, 18, 24, 48 and 72h after treatment
Wang et al.[27], 2010	n.r.	Molar	Vital or nonvital	n.r.	n.r.	NaOCl 1% + H_2O_2 3%	Lateral condensation	AH Plus	n.r.

ID - identification; # - number; n.r. - not reported

MTWO[11,27] and one used K3.[27] Three out of the 10 studies used the ProTaper Next System[24,26,28] while the others used ProTaper Universal System.[11,15,21,25,27,29,30] Two studies also included a group with the hand-file technique.[26,30]

The predominant irrigation solution was sodium hypochlorite in a concentration of 2.5% concentration[15,24,28,29] or 5 to 5.25%.[11,25,26,30] One study employed 2% chlorhexidine[21] and another one employed 1% sodium hypochlorite plus 3% hydrogen peroxide.[27]

The obturation technique used in most of studies was the lateral condensation.[21,24,26,27,29,30] The continuous wave,[25,28] single cone plus thermos-mechanical compaction[15] was also employed. Resin-based cement was the most used product,[15,21,24,26-30] however zinc oxide eugenol-based[25] was also employed.

The rescue medication used in the majority of the studies (7 out of 10) was ibuprofen 400 mg,[11,21,24,26,28-30] in another study the authors did not specify the medication, instructing patients to take analgesics whenever needed.[25]

The time of pain evaluation varied from immediate to seven days after the endodontic treatment. Only one study did not report this information.[27]

Assessment of the Risk of Bias

The risk of bias of the eligible studies is presented in Figure 2. In summary, three[21,27,29] studies had unclear risk of bias at the study and 7 were at low risk of bias.[11,15,24-26,28,30]

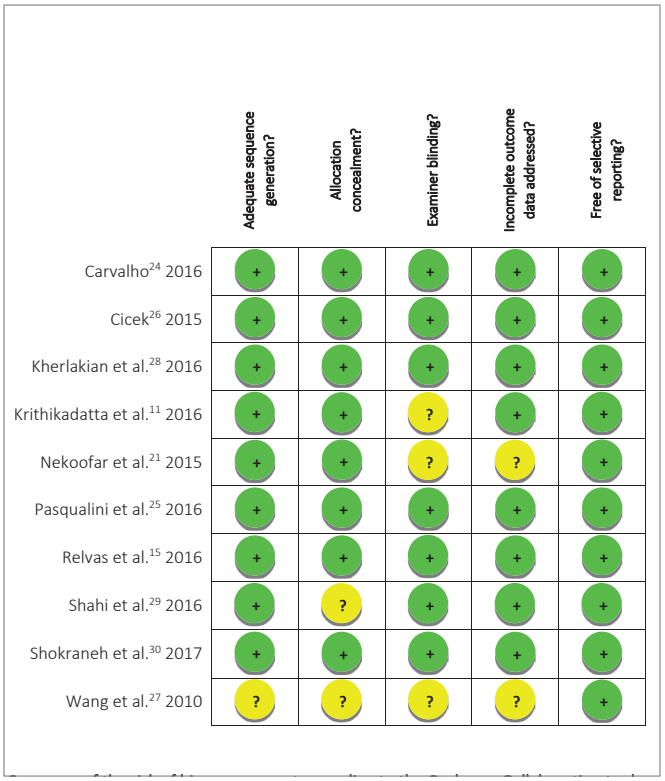


Figure 2. Summary of the risk of bias assessment according to the Cochrane Collaboration tool. Underlined authors provided extra information by e-mail.

Meta-analysis

The meta-analysis was performed only in the studies classified at low risk of bias in the key domains of the Cochrane risk of bias tool and from which the information about the outcome could be extracted. This explains why for some outcomes less than seven articles (total number of studies at low risk of bias) were included in the meta-analysis.

Risk of Pain

This analysis was based on six studies.[11,15,24,26,28,30] No significant difference between groups (p = 0.45) with the risk ratio being 1.09, with a confidence interval varying from 0.87 to 1.38. (Fig 3). Data were not heterogeneous (chi-square test, p = 0.94; I^2 = 0%; Figure 3). The subgroup analysis of ProTaper showed no significant difference between groups (p = 0.49) with the risk ratio being 1.13, with a 95% confidence interval of 0.79 to 1.62 (Fig 3). Data were not heterogeneous (chi-square test, p = 0.91; I^2 = 0%; Figure 3), which means that all studies included in the analysis share a common effect size. The subgroup analysis of ProTaper Next showed no significant difference between groups (p = 0.69) with the risk ratio being 1.07, with a confidence interval varying from 0.78 to 1.45 (Fig 3). Data were not heterogeneous (chi-square test, p = 0.61; I^2 = 0%; Figure 3).

Intensity of Pain at 24 hours

This analysis was based on seven studies.[11,15,24-26,28,30] The standardized difference in means was - 0.05, with a confidence interval varying from - 0.21 to 0.11, showing no statistically difference between groups (p = 0.53). Data were not heterogeneous (chi-square test, p = 0.87; I^2 = 0%; Figure 4).

The subgroup analysis of ProTaper showed that the standardized difference in means was 0.02, with a confidence interval varying from - 0.20 to 0.23, showing no statistically difference between groups (p = 0.88). Data were not heterogeneous (chi-square test, p = 1.00; I^2 = 0%; Figure 4). The subgroup analysis of ProTaper showed that the standardized difference in means was - 0.12, with a confidence interval varying from - 0.35 to 0.10, showing no statistically difference between groups (p = 0.28). Data were not heterogeneous (chi-square test, p = 0.45; I^2 = 0%; Figure 4).

Figure 3. Forest plot of risk of pain after endodontic treatment with ProTaper and ProTaper Next vs other systems.

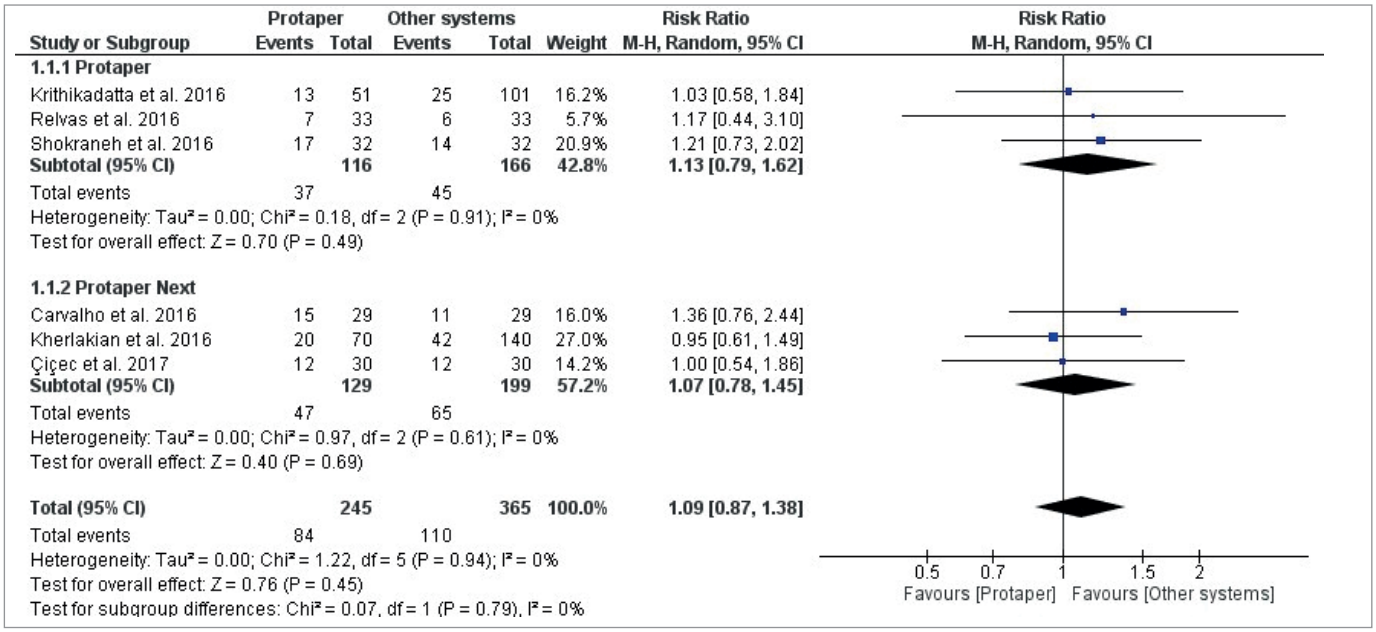
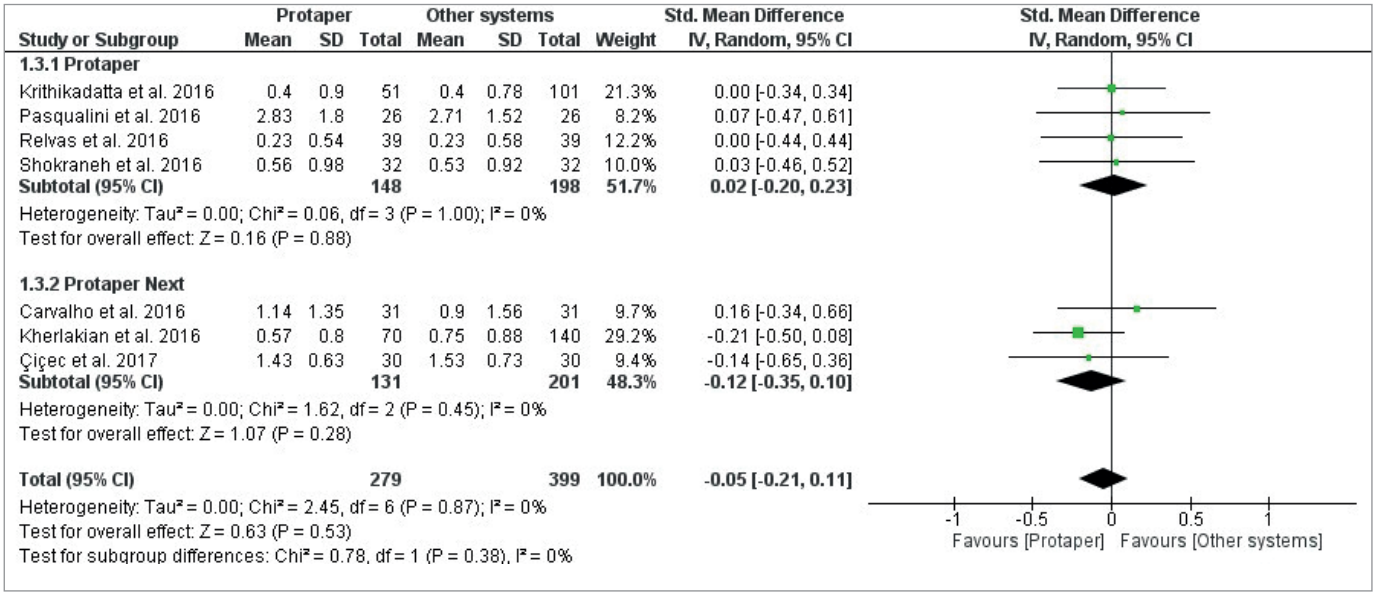


Figure 4. Forest plot of risk of pain intensity at 24 hours after endodontic treatment with ProTaper and ProTaper Next vs other systems.



Additional analysis

Additional analysis comparing ProTaper or ProTaper Next vs. other instrumentation systems were performed. No significant difference was observed between the Protaper or Protaper next vs. Wave One and Reciproc systems at 6 or 24 hours in terms of risk or intensity of pain ($p > 0.05$). In none of these outcomes and comparisons heterogeneity was detected (Table 4).

Sensitivity analysis

Although the meta-analysis herein presented only includes the data from studies at low risk of bias, the same procedure was repeated including the three studies that had unclear risk of bias. No significant difference on the results herein presented was observed (data not shown).

Table 4. Data and analyses of other outcomes.

Outcome	Studies	Participants	Statistical Method	Effect Estimate	Heterogeneity		Test for overall effect
						I^2	p-valor
Risk of pain Protaper vs Wave One	2	165	Risk Ratio (M-H, Random, 95% CI)	1.05 [0.71 – 1.57]	0.38	0%	0.79
Risk of pain Protaper Next vs Wave One	2	200	Risk Ratio (M-H, Random, 95% CI)	1.03 [0.69 – 1.54]	0.90	0%	0.89
Risk of pain Protaper Next vs Reciproc	2	198	Risk Ratio (M-H, Random, 95% CI)	1.06 [0.68 – 1.65]	0.25	25%	0.79
Intensity of pain Protaper vs Wave One (6 hours)	2	165	Std. Mean Difference (IV, Random, 95% CI)	0.05 [-0.26 – 0.35]	0.33	0%	0.76
Intensity of pain Protaper vs Wave One (24 hours)	4	259	Std. Mean Difference (IV, Random, 95% CI)	-0.10 [-0.34 – 0.15]	0.78	0%	0.44
Intensity of pain Protaper Next vs Reciproc (24 hours)	2	202	Std. Mean Difference (IV, Random, 95% CI)	-0.12 [-0.60 – 0.36]	0.11	62%	0.62

Discussion

In other to reduce the negative impact on the quality of the body of the evidence, we only included studies classified at "low" risk of bias in the key domains (randomization, allocation concealment and participant/examiner blinding) into the meta-analyses. Evidence shows that the appropriate conduction of these steps in RCTs reduces the possibility of systematic errors,[31,32] as proper randomization and allocation concealment balances both known and unknown variables that may affect the outcomes, minimizing selection bias.[23]

From the three studies classified as having unclear risk of bias, one of them[27] did not report the method used for randomization (random number tables, computer random number generator, coin tossing, shuffling cards or envelopes, throwing a dice, etc.); two studies did not mention the method of allocation concealment[27,29] and one study did not report if participant was blinded during evaluation.[21] These methodological aspects should be clearly specified in future studies to allow an analysis of the risk of bias of the studies. Although contact with authors could clarify these unclear aspects of the methodology, our previous experience with earlier systematic review and meta-analyses[33-36] has shown that authors' predisposition is to provide answers that put their studies at low risk of bias. This probably reflects their actual knowledge of the methodology of an RCT but not the knowledge they had at the time the study was performed.

Mild discomfort is usually expected after the endodontic treatment.[37] The range of the reported risk of postoperative pain among studies is high ranging from 3 to 58%.[1,38,39] In the present study, no significant difference between ProTaper and other instrumentation techniques in endodontic treatment was observed in any of the comparisons.

Although instrumentation can, per se, produce postoperative pain, there are many other factors that account for such undesirable side effect and they might have hampered the observation of the solely effect of the instrumentation system. Among the factors involved in the postoperative pain we can cite: 1) single or multiple-visit endodontic therapy. Reduced levels of pain have already been demonstrated in a single visit,[40-43] as it eliminates the potential influence of intracanal medication on postoperative pain; 2) the irrigation device. The use of a negative apical pressure irrigation device can result in a significant reduction of postoperative pain levels in comparison to conventional needle irrigation;[44] 3) the pulp condition. Teeth with vital pulp usually have a significantly higher risk and intensity of postoperative endodontic pain compared to teeth with necrotic pulp;[45] 4) the presence of pre-operative pain. A higher level of preoperative pain intensity is associated with a higher intensity of postoperative pain;[46] 5) obturation tech-

nique. For instance, Thermafil obturation technique showed higher postoperative pain level when compared to cold lateral compaction of gutta-percha and the backfill-Thermafil obturation technique,[47] probably since the Thermafil technique might cause extrusion of gutta-percha; 6) the concentration of irrigant agent. Recently it was demonstrated that 5.25% sodium hypochlorite resulted in a small reduction of postoperative pain compared with 2.5% sodium hypochlorite up to 3 days after single-visit mandibular molar endodontic treatment.[48]

Most of the factors described above varied among the primary studies of this systematic review (Tables 2 and 3). For instance, some authors have included patients with vital teeth,[21,28,29] others with non-vital teeth[15,26,30] and there are still those that include both types of pulp condition.[11,24,25,27] The number of clinical sessions for the endodontic therapy was also another source of variation. Although most studies performed the treatment in a single session, other used two clinical appointments for the procedure.

Pain perception is purely subjective depending on patient's threshold and variable experience modulated by multiple physical and psychological factors.[11] Taking this into consideration the use of a paired design to investigate sources of pain in the endodontic therapy would increase study power by reducing the within-participant variation. However, there are many limitations in the conduction of RCTs to investigate the postoperative pain after endodontic, due to large variations in the preoperative conditions of the teeth, variations in the treatment protocol, selection of pain scales for pain assessment, pain measurement, collection of the results, and data analysis of postoperative pain.[49]

Conclusion

The risk and intensity of pain after endodontic treatment with ProTaper was similar to other rotatory or reciprocating systems, probably due to the impact of the variable protocols and pulp condition during endodontic therapy among studies.

References

1. Sathorn C, Parashos P, Messer H. The prevalence of postoperative pain and flare-up in single- and multiple-visit endodontic treatment: a systematic review. Int Endod J 2008;41(2):91-9.
2. Seltzer S, Naidorf IJ. Flare-ups in endodontics: I. Etiological factors. 1985. J Endod 2004;30(7):476-81; discussion 475.
3. Tanalp J, Kaptan F, Sert S, Kayahan B, Bayirl G. Quantitative evaluation of the amount of apically extruded debris using 3 different rotary instrumentation systems. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2006;101(2):250-7.
4. Walton R, Fouad A. Endodontic interappointment flare-ups: a prospective study of incidence and related factors. J Endod. 1992;18(4):172-7.
5. Imura N, Zuolo ML. Factors associated with endodontic flare-ups: a prospective study. Int Endod J. 1995;28(5):261-5.
6. Onay EO, Ungor M, Yazici AC. The evaluation of endodontic flare-ups and their relationship to various risk factors. BMC Oral Health. 2015;15(1):142.
7. Sevekar SA, Gowda SHN. Postoperative pain and flare-ups: comparison of incidence between single and multiple visit pulpectomy in primary molars. J Clin Diagn Res. 2017;11(3):ZC09-12.
8. Brown DC, Moore BK, Brown CE Jr, Newton CW. An in vitro study of apical extrusion of sodium hypochlorite during endodontic canal preparation. J Endod. 1995;21(12):587-91.
9. Tinaz AC, Alacam T, Uzun O, Maden M, Kayaoglu G. The effect of disruption of apical constriction on periapical extrusion. J Endod. 2005;31(7):533-5.
10. Baugh D, Wallace J. The role of apical instrumentation in root canal treatment: a review of the literature. J Endod. 2005;31(5):333-40.
11. Krithikadatta J, Sekar V, Sudharsan P, Velumurugan N. Influence of three Ni-Ti cleaning and shaping files on postinstrumentation endodontic pain: a triple-blinded, randomized, controlled trial. J Conserv Dent. 2016;19(4):11-6.
12. Caviedes-Bucheli J, Castellanos F, Vasquez N, Ulate E, Munoz HR. The influence of two reciprocating single-file and two rotary-file systems on the apical extrusion of debris and its biological relationship with symptomatic apical periodontitis. A systematic review and meta-analysis. Int Endod J. 2016;9(3):255-70.
13. Bürklein S, Hinschitza K, Dammaschke T, Schäfer E. Shaping ability and cleaning effectiveness of two single-file systems in severely curved root canals of extracted teeth: Reciproc and WaveOne versus Mtwo and ProTaper. Int Endod J. 2012;45(5):449-61.
14. Bergmans L, Van Cleynenbreugel J, Beullens M, Wevers M, Van Meerbeek B, Lambrechts P. Progressive versus constant tapered shaft design using NiTi rotary instruments. Int Endod J. 2003;36(4):288-95.
15. Relvas JBF, Bastos MMB, Marques AAF, Garrido ADB, Sponchiado EC. Assessment of postoperative pain after reciprocating or rotary NiTi instrumentation of root canals: a randomized, controlled clinical trial. Clin Oral Investig. 2016;20(8):1987-93.
16. al-Omari MA, Dummer PM. Canal blockage and debris extrusion with eight preparation techniques. J Endod. 1995;21(3):154-8.
17. De-Deus G, Marins J, Silva EJNL, Souza E, Belladonna FG, Reis C, et al. Accumulated hard tissue debris produced during reciprocating and rotary nickel-titanium canal preparation. J Endod. 2015;41(5):676-81.
18. Kustarci A, Akpinar KE, Er K. Apical extrusion of intracanal debris and irrigant following use of various instrumentation techniques. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2008;105(2):257-62.

19. Garlapati R, Venigalla BS, Patil JD, Raju R, Rammohan C. Quantitative evaluation of apical extrusion of intracanal bacteria using K3, Mtwo, RaCe and Protaper rotary systems: an in vitro study. J Conserv Dent. 2013;16(4):300-3.
20. Yilmaz K, Ozyurek T. Apically extruded debris after retreatment procedure with Reciproc, ProTaper Next, and Twisted File adaptive instruments. J Endod. 2017;43(4):648-51.
21. Nekoofar MH, Sheykhrezae MS, Meraji N, Jamee A, Shirvani A, Jamee J, Dummer PM. Comparison of the effect of root canal preparation by using WaveOne and ProTaper on postoperative pain: a randomized clinical trial. J Endod. 2015;41(5):575-8.
22. Higgins JP. Cochrane handbook for systematic reviews of interventions. The Cochrane Collaboration. 2011. Available from: https://training.cochrane.org/handbook
23. Higgins JP, Altman DG, Gotzsche PC, Juni P, Moher D, Oxman AD, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ. 2011 Oct;343:d5928.
24. Carvalho CN, Sousa PO, Souza SFC, Hass V. Dor pós-operatória após o uso de diferentes cinemáticas no preparo do canal radicular: Estudo clínico randomizado [dissertação]. São Luís (MA): Universidade Ceuma; 2016.
25. Pasqualini D, Corbella S, Alovisi M, Taschieri S, Del Fabbro M, Migliaretti G, et al. Postoperative quality of life following single-visit root canal treatment performed by rotary or reciprocating instrumentation: a randomized clinical trial. Int Endod J. 2016;49(11):1030-9.
26. Cicek E, Kocak MM, Kocak S, Saglam BC, Turker AS. Postoperative pain intensity after using different instrumentation techniques: a randomized clinical study. J Appl Oral Sci. 2017;25(1):20-6.
27. Wang Y, Zhu YQ, Wang HN, Han JL, He Y, Zhu MY. Clinical effect of three kinds of rotary nickel-titanium instruments on root canal preparation of molars. Shanghai J Stomatol. 2010;19(2):118-23.
28. Kherlakian D, Cunha RS, Ehrhardt IC, Zuolo ML, Kishen A, da Silveira Bueno CE. Comparison of the incidence of postoperative pain after using 2 reciprocating systems and a continuous rotary system: a prospective randomized clinical trial. J Endod. 2016;42(2):171-6.
29. Shahi S, Asghari V, Rahimi S, Lotfi M, Samiei M, Yavari H, Shakouie S, Nezafati S. Postoperative pain after endodontic treatment of asymptomatic teeth using rotary instruments: a randomized clinical trial. Iran Endod J. 2016;11(1):38-43.
30. Shokraneh A, Ajami M, Farhadi N, Hosseini M, Rohani B. Postoperative endodontic pain of three different instrumentation techniques in asymptomatic necrotic mandibular molars with periapical lesion: a prospective, randomized, double-blind clinical trial. Clin Oral Investig. 2017; 21(1):413-8.
31. Pocock SJ. Clinical Trials: a practical approach. Chichester: John Wiley & Sons; 1983.
32. Schulz KF, Chalmers I, Grimes DA, Altman DG. Assessing the quality of randomization from reports of controlled trials published in obstetrics and gynecology journals. JAMA. 1994;272(2):125-8.
33. de Geus JL, Wambier LM, Kossatz S, Loguercio AD, Reis A. At-home vs in-office bleaching: a systematic review and meta-analysis. Oper Dent. 2016;41(4):341-56.
34. Luque-Martinez I, Reis A, Schroeder M, Munoz MA, Loguercio AD, Masterson D, Maia LC. Comparison of efficacy of tray-delivered carbamide and hydrogen peroxide for at-home bleaching: a systematic review and meta-analysis. Clinical Oral Investig. 2016;20(7):1419-33.
35. Reis A, Loguercio AD, Schroeder M, Luque-Martinez I, Masterson D, Maia LC. Does the adhesive strategy influence the post-operative sensitivity in adult patients with posterior resin composite restorations? A systematic review and meta-analysis. Dent Mater. 2015;31(9):1052-67.
36. Wambier LM, de Geus JL, Chibinski AC, Wambier DS, Rego RO, Loguercio AD, et al. Intra-pocket anaesthesia and pain during probing, scaling and root planing: a systematic review and meta-analysis. J Clin Periodontol. 2016;43(9):754-66.
37. Patil AA, Joshi SB, Bhagwat SV, Patil AS. Incidence of postoperative pain after single visit and two visit root canal therapy: a randomized controlled trial. J Clin Diagn Res. 2016;10(5):ZC09-12.
38. Gambarini G, Di Nardo D, Miccoli G, Guerra F, Di Giorgio R, Di Giorgio G, et al. The influence of a new clinical motion for endodontic instruments on the incidence of postoperative pain. Clin Ter. 2017;168(1):e23-7.
39. Gambarini G, Testarelli L, De Luca M, Milana V, Plotino G, Grande NM, et al. The influence of three different instrumentation techniques on the incidence of postoperative pain after endodontic treatment. Ann Stomatol. 2013;4(1):152-5.
40. Roane JB, Dryden JA, Grimes EW. Incidence of postoperative pain after single- and multiple-visit endodontic procedures. Oral Surg Oral Med Oral Pathol. 1983;55(1):68-72.
41. Albashaireh ZS, Alnegrish AS. Postobturation pain after single- and multiple-visit endodontic therapy. A prospective study. J Dent. 1998;26(3):227-32.
42. Su Y, Wang C, Ye L. Healing rate and post-obturation pain of single- versus multiple-visit endodontic treatment for infected root canals: a systematic review. J Endod. 2011;37(2):125-32.
43. Almeida DO, Chaves SC, Souza RA, Soares FF. Outcome of single- vs multiple-visit endodontic therapy of nonvital teeth: a meta-analysis. J Contemp Dent Pract. 2017;18(4):330-6.
44. Gondim E Jr, Setzer FC, Dos Carmo CB, Kim S. Postoperative pain after the application of two different irrigation devices in a prospective randomized clinical trial. J Endod. 2010;36(8):1295-301.
45. Gotler M, Bar-Gil B, Ashkenazi M. Postoperative pain after root canal treatment: a prospective cohort study. Int J Dent. 2012;2012;310467.
46. Alí A, Olivieri JG, Duran-Sindreu F, Abella F, Roig M, García-Font M. Influence of preoperative pain intensity on postoperative pain after root canal treatment: A prospective clinical study. J Dent. 2016;45:39-42.
47. Alonso-Ezpeleta LO, Gasco-Garcia C, Castellanos-Cosano L, Martin-Gonzalez J, Lopez-Frias FJ, Segura-Egea JJ. Postoperative pain after one-visit root-canal treatment on teeth with vital pulps: comparison of three different obturation techniques. Med Oral Patol Oral Cir Bucal. 2012;17(4):e721-7.
48. Brignardello-Petersen R. 5.25% sodium hypochlorite resulted in a small reduction of postoperative pain compared with 2.5% sodium hypochlorite up to 3 days after single-visit mandibular molar endodontic treatment. J Am Dent Assoc. 2017;148(6):e80.
49. Risso PA, Cunha AJ, Araujo MC, Luiz RR. Postobturation pain and associated factors in adolescent patients undergoing one- and two-visit root canal treatment. J Dent. 2008;36(11):928-34.