

Flare-ups after Endodontic Treatment: A Meta-analysis of Literature

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Abstract

The purpose of this study was to determine the frequency of flare-ups and to evaluate factors that affect it by using meta-analysis of results of previous studies. MEDLINE database was searched by using Entrez PubMed search engine and Medical Subject Headings (MeSH) search with EviDents Search Engine to identify the studies dealing with endodontic flare-up phenomenon. The search covered all articles published in dental journals in English from 1966–May 2007, and the relevancy of 119 selected articles was evaluated by reading their titles and abstracts, from which 54 were rejected as irrelevant and 65 were subjected to a suitability test. Six studies that met all the above mentioned criteria were included in the study. Average percentage of incidence of flare-ups for 982 patients was 8.4 (standard deviation ± 57). There were insufficient data to investigate the effect of the influencing factors. (*J Endod* 2008;xx:xxx)

Key Words

Flare-up, meta-analysis, postoperative pain, root canal treatment

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Flare-up is one complication of endodontic treatment, defined as acute exacerbation of asymptomatic pulp or periradicular pathosis after the initiation or continuation of root canal treatment (1). Other characteristics are occurrence of pain and/or swelling during endodontic treatment (2) or pain and/or swelling that require nonintentional treatment, including active interference from the dentist (3). Lack of an exact definition of flare-up resulted in estimated frequency differences from as low as 1.5% (4) to as high as 20% (5). In addition, there is no unified opinion as to the reasons for flare-up progression. The present accepted hypotheses describe flare-up as a polyetiologic phenomenon, whereas mechanical factors (preparation beyond apical terminus, over-instrumentation, pushing dentin chips and the remainder of the infected pulp tissue into the periapical area, overextension of root canal filling), chemical factors (irrigants, intracanal dressings, and sealers), and microbiologic factors contribute to its appearance (6).

Infection is considered as the most significant factor in flare-up pathogenesis (7). Pushing an infected organic substance into the periapical region during root canal preparation might cause exacerbation (7). Another hypothesis is selective growth of certain bacterial species inside the root canal as a result of ecologic changes during endodontic therapy (7). Consequently, acute reaction of the periapical tissues might occur. In addition, new microorganisms might penetrate into the root canal from the oral cavity as a result of nonmeticulous root canal preparation or inappropriate temporary sealing in multi-appointment therapy that could lead to flare-ups (7).

The intensity of the inflammatory reaction might be influenced by various factors such as extent of existent pathologic changes in the periapical region (8), presence of specific bacterial species in the root canal (9), tooth type, pulp diagnosis, occurrence of preoperative pain, and presence of a sinus tract (3–5, 10, 11). Demographic factors such as age, gender, and general health state (existence of allergies) also affect the frequency of flare-ups (3, 11). Endodontic therapy (initial root canal therapy as opposed to recurrent treatment, one- or multi-appointment therapy, leaving the tooth “open” between appointments) plays an important role in evolving exacerbation of inflammation in the periradicular region (3, 4, 7, 11–14). Although there is abundant information in the literature, it is a challenge to unequivocally conclude the pathogenesis and frequency of flare-ups and to indicate factors that affect them.

The purpose of this study was to determine the frequency of flare-ups and to evaluate factors that affect them by using meta-analysis of results of previous studies.

Materials and Methods

To obtain unified information, flare-up is defined as a strong pain with or without swelling that occurs after the initiation or continuation of root canal treatment. The exhaustive search was undertaken to identify studies that deal with endodontic flare-up phenomenon in the database MEDLINE by using Entrez PubMed search engine (<http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?DB=pubmed>) and Medical Subject Headings (MeSH) search by using EviDents Search Engine (<http://medinformatics.uthscsa.edu/EviDents/>). The following Key words were used: “flare-up;” “interappointment pain;” “post-obturation pain;” “post-treatment pain;” and “interappointment emergency.” Fig. 1 presents the search strategy as automatically created by EviDents Search Engine. The search covered all articles published in dental journals in English from 1966–May 2007 and resulted in 107 articles including 7 reviews. Also; all related articles for the review studies that appeared in the MEDLINE search engine link were evaluated; and reference lists of all review articles were hand-checked. An additional 12 studies were

flare-up OR inter appointment OR interappointment pain OR postobturation OR post obturation pain OR post-treatment pain OR interappointment emergency AND ("Endodontics"[MeSH] OR "Root Canal Filling Materials"[MeSH] OR "Dental Pulp Test"[MeSH] OR "Dental Pulp Diseases"[MeSH] OR "Periapical Abscesses"[MeSH] OR endodontics[Text Word] OR root canal filling materials[Text Word] OR dental pulp test[Text Word] OR dental pulp diseases[Text Word] OR periapical abscess[Text Word] OR apicoectomy[Text Word] OR pulpectomy y[Text Word] OR pulpotomy[Text Word] OR root canal therapy[Text Word] OR dental pulp devitalization[Text Word] OR root canal obturation[Text Word] OR root canal preparation[Text Word] OR retrograde obturation[Text Word] NOT (("Dental Implantation, Endosseous, Endodontic"[MeSH] OR "Dental Pulp Capping"[MeSH] OR "Tooth Replantation"[MeSH]) NOT ("Apicoectomy"[MeSH] OR "Pulpectomy"[MeSH] OR "Pulpotomy"[MeSH] OR "Root Canal Therapy"[MeSH])) NOT ("animals"[MeSH:nox] NOT humans[MESH])

Figure 1. Search strategy as automatically formulated by EviDents search engine.

identified. The relevancy of 119 selected articles was evaluated by reading their titles and abstracts; from which 54 were rejected as not relevant to the topic of the current study. The remaining 65 studies were subjected to a suitability test in accordance with the inclusion and exclusion criteria (Table 1). The full texts of the studies were obtained and independently reviewed by 2 observers (I.T. and V.F.) and in cases of disagreement were discussed together until agreement was achieved. Reference lists from these articles were searched to identify additional relevant articles.

Table 2 shows the excluded articles according to the exclusion criteria (n = 59). Only 6 prospective case series that met all the aforementioned criteria were included in the study (15–20) (Table 3).

A standard form was constructed to evaluate various factors that might have affected the appearance of flare-ups:

Gender: male/female

Health status: noncontributory/complicated

Age: <20, 20–40, 40–60, >60 years

Tooth type: maxillary–anterior; premolar; molar and mandibular anterior; premolar; molar

Pretreatment spontaneous pain: no pain; mild; moderate to severe

Pretreatment percussion pain: no pain; mild; moderate to severe

Sinus tract: absent; present

TABLE 1. Inclusion and Exclusion Criteria Used in the Meta-analysis

Inclusion criteria	
1.	Randomized control trials and prospective case series
2.	Flare-up defined as strong pain with or without swelling that occurs after initiation or continuation of root canal treatment
3.	Patients had not received any medicinal therapy either before or after endodontic treatment
4.	Presented detailed diagnosis of pulp and periapical region
5.	Pain intensity and swelling occurrence estimated within 24 or 48 hours after endodontic treatment (pain intensity in both time periods, for purpose of analysis; the strongest one between the two was selected)
6.	Severe pain estimated by using VAS by each patient separately
Exclusion criteria	
1.	Retrospective studies, case reports, review articles, expert opinions
2.	Different definition of flare-up
3.	Timing of pain level evaluation was not mentioned or was not within 24–48 hours after treatment
4.	No pain level estimation by using VAS or no differentiation between various degrees of pain
5.	Patients had received medicinal therapy either before or after endodontic treatment

TABLE 2. Studies Excluded from Systematic Review

Excluded Studies	Exclusion Criteria
Aqrabawi 2006 (25)	5
Gesi et al. 2006 (26)	3
Ghoddusi et al. 2006 (74)	5
Cheng et al. 2006 (27)	1
Contardo et al. 2005 (55)	4
Oginni and Udoye 2004 (24)	4
Yoldas et al. 2004 (28)	3
Tani-Ishii and Teranaka 2003 (29)	3
Siqueira 2003 (56)	1
Chávez de Paz Villanueva 2002 (57)	1
Siqueira et al. 2002 (10)	3
Alaçam and Tinaz 2002 (30)	2
DiRenzo et al. 2002 (31)	3
Ree 2001 (58)	1
Henry et al. 2001 (73)	5
Pickenpaugh et al. 2001 (59)	1
Kvist and Reit 2000 (32)	5
Rogers et al. 1999 (33)	5
Eleazer and Eleazer 1998 (13)	4
Sim 1997 (60)	1
Weisman 1996 (61)	1
Ehrmann 1996 (62)	1
Matusow 1995 (63)	1
Imura and Zuolo 1995 (4)	3, 4, 5
Cohn 1995 (64)	1
Figdor 1995 (65)	1
Rimmer 1993 (66)	1
Walton and Chiappinelli 1993 (34)	2
Selden 1993 (67)	1
Mor et al. 1992 (35)	1, 2
Walton and Fouad 1992 (3)	2
Rimmer 1991 (36)	2, 5
Trope 1991 (12)	2
Trope 1990 (37)	2
Morse 1990 (38)	2, 5
Morse and Esposito 1990 (75)	1
Glassman et al. 1989 (39)	4, 5
Abbott et al. 1988 (40)	2, 5
Yesilsoy et al. 1988 (41)	4
Torabinejad et al. 1988 (11)	1, 2
Morse et al. 1988 (42)	2, 5
Matusow 1988 (68)	1
Goldman et al. 1988 (69)	1
Morse et al. 1987 (43)	2, 4
Morse et al. 1987 (44)	2, 5
Genet et al. 1987 (45)	1
Glassman 1987 (70)	1
Morse et al. 1986 (5)	2
Genet et al. 1986 (46)	1
Burke 1986 (71)	1
Alaçam 1985 (47)	3
Walton 1984 (72)	1
Harrison et al. 1983 (48)	4
Harrison et al. 1983 (49)	4
Oliet 1983 (50)	4
Roane et al. 1983 (51)	3, 4
Mulhern et al. 1982 (52)	2, 5
Pekruhn 1981 (53)	4, 5
Harrison et al. 1981 (54)	4, 5

Type of endodontic treatment: initial treatment; retreatment

Pulp status: normal pulp; irreversible pulpitis; necrotic pulp

Periapical radiolucency: absent; present <3 mm; present >3 mm

Number of appointments: single; multiple

Medicaments: camphorated phenol; calcium hydroxide; formocresol

TABLE 3. Summary of the Results of the Studies Included in the Meta-analysis

Study No. & Reference	Type of Teeth	No. of Patients	Total Incidence (%)	Flare-ups (%)				Pulp Status	
				No. of Appointments		Gender		Vital	Non-vital
				1	2	M	F		
1 – Al-Negrish et al. (20)	Asymptomatic maxillary central incisors with PN	112	4.5	3.7	5.2	3.8	5.0		
2 – Al Bashaireh and Al Negrish (17)	All	291	8.9	7	10.8	3.9	5.2	2.6	11.2
3 – Fava (15)	Asymptomatic maxillary central incisors with PN	60	0						
4 – Fava (16)	Asymptomatic maxillary central incisors with PN	60	0						
5 – Koba et al. (18)	All groups with PN and chronic AP	44	4.3						
6 – Ng et al. (19)	Teeth with PN or previous RCT and chronic AP	415	12.0						

PN, pulp necrosis; AP, apical periodontitis; RCT, root canal treatment.

Operator: undergraduate student; general practitioner; postgraduate student; endodontist

Information regarding the influencing factors was used from articles in which the specific connection between strong pain (with or without swelling occurrence) and those factors was mentioned.

Statistical Methods

To determine flare-up frequency according to the 6 studies, the weighted average was calculated. Between the studies, the heterogeneity of percentage of incidence was assessed by using the standard χ^2 test of Q-statistic.

Pearson χ^2 test was performed to examine the change in a dichotomous variable, such as gender and number of appointments, across 2 studies in which these variables were available. p value was set at .05.

Results

The average percentage of incidence of flare-ups for 982 patients was 8.4 (standard deviation ± 57). Table 4 shows the incidence level, frequency of patients with a particular incidence level out of 982 patients, percentage, cumulative frequency, and cumulative percentage. The 6 studies were heterogeneous. On the basis of the χ^2 test for equal proportions, there was a significant difference in the frequency levels between the studies (with Q-statistic = 473.12, $df = 4$, $p < .0001$).

Frequency of male and female patients for studies 1 (20) and 2 (17) and frequency of patients with 1 and 2 appointments for studies 1 and 2 are presented in contingency Tables 5 and 6, respectively.

TABLE 4. Incidence Level of Flare-ups, Frequency of Patients with a Particular Incidence Level, and Cumulative Frequency on the Basis of 6 Studies (15–20) and 982 Patients

Incidence Level (%)	Frequency of Patients (%)	Cumulative Frequency and Percentage
0	120 (12.2)	120 (12.2)*
4.3	44 (4.5)	164 (16.7)
4.5	112 (11.4)	276 (28.1)
8.9	291 (29.6)	567 (57.7)
12	415 (42.3)	982 (100)

*Studies 15 and 16 were combined because of same methodology.

The Pearson χ^2 test showed no significant difference between the distribution of patients according to gender and number of appointments between studies 1 and 2 ($p > .5$).

There were insufficient data in the studies to evaluate the influence of gender, number of appointments, and/or pulp status on the incidence level (regression analysis). Gender and number of appointments were available as explanatory variables in 2 studies (17, 20) and with pulp status explanatory variable in one (17).

Discussion

Meta-analysis is a statistical procedure that integrates the results of several independent studies considered to be combinable (21). Pooled data from multiple studies usually increase the sample size and power, thus providing a more precise estimate of a treatment effect and possibly explaining heterogeneity between the results of individual studies (22). In the present study to overcome heterogeneity of information regarding incidence of endodontic flare-ups and to obtain unified information and reliable and clinically relevant results, flare-up was defined for searching process as strong pain with or without swelling occurring after the initiation or continuation of root canal treatment. Only prospective case series and clinical trials were included.

Pain perception is a highly subjective and variable experience modulated by multiple physical and psychological factors, and pain reporting is influenced by factors other than the experimental procedure (23). In addition, pain measurement is fraught with hazards and opportunities for errors (20). Different scales and methods have been used to assess pain after endodontic therapy (20). In the current study visual analog scale (VAS) was used as a result of its valid and reliable ratio scale to measure pain (20).

TABLE 5. Frequency of Male and Female Patients with Incidence Level of Flare-ups of 4.5% and 8.9% for Studies (20) and (17), Respectively

Study	Gender		Total
	Male (%)	Female (%)	
Al-Negrish and Hababbeh (20)	4 (3.8)	6 (5.0)	10
Al Bashaireh and Al Negrish (17)	11 (3.9)	15 (5.2)	26
Total	15	21	36

TABLE 6. Frequency of Patients with 1 and 2 Appointments with an Incidence Level of Flare-ups of 4.5% and 8.9% for Studies (20) and (17), Respectively

Study	Appointment No.		Total
	1 (%)	2 (%)	
Al-Negrish and Habahbeh (20)	4 (3.7)	6 (5.2)	10
Al Bashaireh and Al Negrish (17)	20 (7.0)	31 (10.8)	51
Total	24	37	61

Six studies published between 1989 and 2006 dealing with post-operative pain in endodontics were identified according to the selected inclusion criteria presented in the current study. There was a significant difference in frequency levels of flare-up between the studies, which could be due to various populations receiving treatment, different treatment techniques, and various numbers and experience of operators. Meta-analysis of pooled data from these studies showed an 8.4% frequency of flare-ups, which agrees with the 8% shown by Eleazer and Eleazer (13) and 8.1% by Oginni and Udoye (24) for multiple-appointment groups and 3% and 18.3%, respectively, for single-appointment groups. The present study did not evaluate the influence of the number of appointments on the incidence of flare-ups because of insufficient data in the 6 reviewed studies.

An incidence rate of 3.2% has been reported by Walton and Fouad (3) and 1.6% by Imura and Zoulo (4). These values are significantly lower than those in the current study as a result of different inclusion criteria. In the former studies flare-up was defined as severe pain and/or swelling after endodontic treatment, requiring an unscheduled appointment and active treatment. Therefore, patients who experienced pain after endodontic treatment and did not require active treatment were excluded from the previous studies.

Trope (12) also used a similar definition and reported flare-ups in 1.8% of 226 cases with different preoperative diagnoses treated in single appointments. Interestingly, in this study, an 8-fold higher (13.6%) incidence of flare-ups was found in retreatment cases involving teeth with apical periodontitis. The frequency of flare-ups in the current study (8.4%) was between the aforementioned figures. Neither the preoperative diagnoses nor the number of appointments were considered.

An incidence rate of 1.9% has been reported by Siqueira et al. (10) after endodontic treatment in 627 teeth. Flare-up was defined as severe pain and/or swelling after intracanal procedures. Despite the similarity of the definitions of flare-up, the incidence in the present study was almost 5 times higher than that in the former study (10). In that study, the timing of evaluating the pain level was not mentioned. This means that many cases might be excluded if pain level was evaluated after more than 48 hours after treatment. In the present study postoperative pain and/or swelling were registered within 48 hours after the procedure.

Recently in a systematic review regarding the prevalence of post-operative pain and flare-up after endodontic treatment, the difference in the frequency of flare-ups and postoperative pain was evaluated between single- and multiple-appointment root canal treatments (14). Contrary to the present study, randomized clinical trials, prospective case series, and retrospective studies were analyzed. Flare-up was defined as severe pain and/or swelling after endodontic treatment requiring an unscheduled appointment and active treatment. Postoperative pain of any degree was considered, and timing of the postoperative pain measurement was not mentioned. Nevertheless, this approach allowed collection of more data in which to compare treatment strategies with a different number of appointments than was possible in the present study. However, meta-analysis could not be conducted to yield meaningful results as a result of the heterogeneity among the included studies.

Conclusions

Flare-up frequency was 8.4% on the basis of 982 patients from 6 studies that defined flare-up as strong pain with or without swelling that occurred after the initiation or continuation of root canal treatment and estimated within 48 hours after the procedure. The relatively high frequency of flare-ups should be considered in planning root canal therapy.

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