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Incidence and factors related to flare-ups in a graduate endodontic programme

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Abstract

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Aim To investigate the incidence and factors related to endodontic flare-ups in nonsurgical root canal treatment (NSRCT) cases completed by graduate endodontic residents at University of Pennsylvania, USA.

Methodology Residents at University of Pennsylvania enter all clinical patient records into an electronic database called PennEndo database. Analysis of records of 6580 patients treated from September 2000 to July 2005 revealed a total of 26 patients with flare-ups (0.39%). Patients were categorized to have undergone flare-up when they attended for an unscheduled visit and active treatment, and when they suffered from severe pain and or swelling after initiation or continuation of NSRCT. SAS software was used to develop a logistic regression model with flare-up as a dependent variable. Independent variables included in the model were: history of previous pain, one vs. two visit NSRCT, periapical diagnosis, tooth type, rotary versus hand instrumentation, and lateral versus vertical compaction of gutta-percha.

Results The odds for developing a flare-up in teeth with a periapical radiolucency were 9.64 times greater than teeth without a periapical radiolucency ($P = 0.0090$). There was no statistically significant difference in flare-ups between one and two visits NSRCT. The odds of developing a flare-up increased 40 fold when NSRCT was completed in three or more visits. However, this result may have been confounded by addition of an unscheduled visit in patients suffering from flare-ups. Other independent variables did not have any statistically significant correlations.

Conclusions A low percentage of patients experienced flare-ups during NSRCT procedures. The presence of a periapical lesion was the single most important predictor of flare-ups during NSRCT.

Keywords: apical periodontitis, flare-up, multivariate analysis, post-treatment endodontic pain & swelling, root canal therapy/adverse effects, toothache.

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Introduction

A flare-up can be defined as an acute exacerbation of an asymptomatic pulpal and/or periradicular pathosis after the initiation or continuation of root canal treatment (Trope 1990, Walton & Fouad 1992, Seltzer & Naidorf 2004). The features responsible for flare-ups are unclear and in the absence of any gold standard, and because of the variable definitions, comparison of flare-up incidence amongst different studies is challenging.

A variety of methods have been used in defining flare-ups: self reports of patient-diagnosed uncontrollable pain or swelling (Eleazer & Eleazer 1998), prescriptions for pain medications/antibiotics for patient with flare-up symptoms, (Abbott *et al.* 1988, Morse *et al.* 1990) as well as the combination of swelling or pain and an unscheduled visit to the dentist (Imura & Zuolo 1995), combination of swelling or pain, unscheduled visit and active treatment by dentist (Walton & Fouad 1992, Walton & Chiappinelli 1993) use of a flare-up

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index (Rimmer 1991, 1993) or severe pain that disturbed normal activity with analgesics having no effect (Al-Negrish & Habahbeh 2006). Each of the above approaches may lead to the selection of different study groups with flare-ups, thereby reporting results that are widely disparate and perhaps not comparable. Therefore, it is not surprising that the flare-up rates reported in the literature range from 1.3 to 20% (Abbott *et al.* 1988, Torabinejad & Kettering 1988, Barnett & Tronstad 1989, Morse *et al.* 1990, Trope 1990, Rimmer 1991, Walton & Fouad 1992, Imura & Zuolo 1995, Eleazer & Eleazer 1998, Seltzer & Naidorf 2004). The use of a strict definition of flare-up that involved severe pain or swelling leading to an unscheduled visit as well as active treatment (Walton & Fouad 1992) may be more appropriate. This definition is more likely to select a patient population in which pain and swelling after nonsurgical root canal treatment (NSRCT) were of sufficient intensity to require an unscheduled visit. Such a definition excludes those patients that suffer from less intense post-operative pain.

The majority of previous studies have analyzed the potential association of flare-up with individual factors using only chi-squared analysis (Abbott *et al.* 1988, Torabinejad & Kettering 1988, Morse *et al.* 1990, Trope 1990, Walton & Fouad 1992, Imura & Zuolo 1995, Eleazer & Eleazer 1998, Yoldas *et al.* 2004), or ANOVA (Rimmer 1993) tests which do not allow several independent variables to be considered simultaneously. Only one study (Pickenpaugh *et al.* 2001) used a multiple regression model to conclude that a prophylactic dose of amoxicillin before endodontic treatment of asymptomatic, necrotic teeth had no effect on the flare-up.

There are numerous reasons to identify risk factors for flare-ups. An institution may wish to undertake an internal study, identify risk factors, and perhaps change protocols to improve results. If properly identified, the peri-operative predictors of flare-up combined with the clinician's experience can help to better manage patients post-operatively. A number of risk factors have been analyzed in the literature regarding prevalence of flare-ups. These factors include: age, gender, use of analgesics and antibiotics, pulpal status, preoperative pain, presence of periapical radiolucency and presence of a sinus tract (Abbott *et al.* 1988, Torabinejad & Kettering 1988, Barnett & Tronstad 1989, Morse *et al.* 1990, Trope 1990, Rimmer 1991, Walton & Fouad 1992, Imura & Zuolo 1995, Eleazer & Eleazer 1998, Pickenpaugh *et al.* 2001). However, the role of two factors in the induction of flare-ups; stainless steel hand instrumentation versus NiTi rotary instruments and lateral condensation versus warm vertical condensation have not been reported to date.

The purpose of this study was to investigate the incidence of flare-up in a large cohort of patients undergoing NSRCT within a postgraduate endodontic programme setting using a multiple regression model, and determine risk factors amongst several peroperative clinical parameters.

Materials and methods

The PennEndo database, an electronic database developed with the help of FILEMAKER software (Santa Clara, CA, USA), provided a rich patient-based dataset to identify determinants of flare-ups. The database became operational in September 2000, at which time it was opened to graduate endodontic residents at the University of Pennsylvania, USA to record clinical endodontic data of cases completed during their residency. The residents used the software to submit a common set of data regarding patients' demographics, preoperative pain history, clinical examination and test results, clinical signs and symptoms, intra-operative procedures and events, and postoperative outcomes for all patients undergoing NSRCT. The electronic data was searched to identify all patients who developed a flare-up during NSRCT procedure.

In this analysis, flare-up was used as a singular outcome variable. Patients were categorized to have undergone flare-up when they reported for an unscheduled visit and active treatment suffering from severe pain and or swelling after initiation or continuation of NSRCT.

Simply reassuring the patient without prescribing medication did not constitute a flare-up. Patients who reported severe pain or swelling but refused an unscheduled visit were not included. Patients who reported pain on normally scheduled second appointment were not categorized as flare-ups. Independent variables included in the analysis were selected based on risk factors reported in the literature and those unique to the database, and classified into three broad conceptual categories: (i) diagnostic signs and symptoms, i.e. presence or absence of periapical lesion, previous history of pain, periapical diagnosis, initial nonsurgical root canal treatment (INSRCT) versus nonsurgical root canal retreatment (NSRCR); (ii) procedural, i.e. number of visits, hand versus rotary instrumentation, warm vertical condensation versus lateral condensation of gutta-percha; and (iii) anatomical, i.e. type of tooth.

Statistical analysis

Simple descriptive statistics were used to describe the study population, followed by univariate and multivariate analyses using logistic regression to explore the association between independent variables and the outcome variable. Separate univariate and multivariate models were built using flare-up as the outcome variable. All variables significant at P-value < 0.05 were considered for inclusion in the final model. Multiple logistic regression analysis was used to simultaneously adjust for the various independent variables. Estimated crude odds ratios (ORs), and adjusted ORs with their corresponding 95% confidence intervals (CI) were calculated. Statistics were computed using SAS 8.0 (SAS Institute, Raleigh, NC, USA).

Results

Table 1 summarizes the profile and clinical data of 6580 patients at the time of NSRCT. Analysis of the records of 6580 patients treated from September 2000 to July 2005 revealed a total of 26 patients with flare-ups. Based on our definition, the incidence of flare-up for this retrospective study was 0.395%. Further breakdown of data showed that the incidence of flare-up during NSRCT was 0.387% whilst during NSRCR the incidence was 0.424% (Table 1). Inclusion of this parameter in the multiple logistic regression model did not yield statistically significant results (Table 2).

Statistically significant associations were obtained between flare-up and the presence or absence of periapical radiolucency, as well as the number of treatment visits ($P < 0.01$). The estimated crude and adjusted ORs with 95% CI for associations between independent risk factors and flare-up during the study period are presented in Table 2.

The probability of developing a flare-up in teeth with a periapical radiolucency was 9.64 times greater than teeth without a periapical radiolucency ($P = 0.0090$). There was no statistically significant difference in flare-ups between one and two visits. The odds of developing flare-up increased 40 folds when NSRCT was completed in three or more visits ($P = 0.0001$). However, this result was confounded by the definition of flare-up which required an unscheduled extra visit. In other words, the additional visits were because of the occurrence of flare-up and not vice versa.

Other independent variables, namely history of previous pain, periapical diagnosis, tooth type, instrumentation technique (rotary versus stainless steel hand) and obturation technique (lateral versus warm vertical condensation) did not show a statistically significant correlation with flare-up.

Table 1 Descriptive statistics for different predictor variables in the model

		Sample size	Flare-up	
			n	%
Fill technique	Lateral condensation	1018	4	0.39
	Warm vertical	5522	22	0.4
History of pain	No	2511	8	0.32
	Yes	3909	17	0.43
Instrumentation	NiTi	5508	22	0.40
	Stainless steel hand	1043	4	0.38
Tooth type	Anterior	1385	8	0.58
	Premolar	1404	5	0.36
	Molar	3801	13	0.34
Radiolucency	Yes	3182	21	0.66
	No	3318	3	0.09
Treatment	NSRCT	5165	20	0.39
	NSRCR	1415	6	0.42
Appointments	1	2751	7	0.25
	2	3126	6	0.19
	3	517	8	1.55
	3+	98	4	4.08

NSRCT, nonsurgical root canal treatment; NSRCR, nonsurgical root canal retreatment.

Discussion

Previously reported prevalence rates of flare-up in patients have ranged from below 1.3 to over 20% (Abbott *et al.* 1988, Torabinejad & Kettering 1988, Barnett & Tronstad 1989, Morse *et al.* 1990, Trope 1990, Rimmer 1991, Walton & Fouad 1992, Imura & Zuolo 1995, Eleazer & Eleazer 1998, Seltzer & Naidorf 2004). A flare-up incidence of 0.39%, as reported by this study, is probably one of the lowest reported in literature. This percentage closely approximates the smaller range of 1 to 3% reported by a number of studies (Abbott *et al.* 1988, Barnett & Tronstad 1989, Trope 1990, 1991, Walton & Fouad 1992, Imura & Zuolo 1995, Siqueira *et al.* 2002). It is difficult to explain the reasons for low flare-up rates reported by these studies. However, a majority of these studies diagnosed flare-up only when it was associated with an unscheduled visit. However, it is difficult to directly compare prevalence rates observed in this study with other reports due to the use of different populations and case definitions.

Other factors previously reported as predictors of flare-up, such as pre-operative pain (Torabinejad & Kettering

Table 2 Odds ratios estimates for different predictor variables

	Odds ratio estimates			
Effect	Comparison	Point estimate	95% Wald confidence limits	
Fill technique	Lateral versus warm condition	1.308	0.073	23.41
History of pain	No versus yes	0.809	0.315	2.077
Instrumentation	NiTi Rotary versus stainless steel hand	2.185	0.123	38.964
Tooth type				
Tooth type	Anterior versus premolar	1.161	0.32	4.21
Tooth type	Molar versus premolar	0.743	0.23	2.405
X-ray attachment	Radiolucency versus WNL	9.64	1.76	52.809
Retreatment	Retreatment versus initial treatment	1.017	0.377	2.74
Number of visits				
	1 vs. 3+	0.041	0.009	0.183
	2 vs. 3+	0.039	0.01	0.148
	3 vs. 3+	0.374	0.107	1.307

WNL, Within Normal Limits.

1988, Walton & Fouad 1992, Imura & Zuolo 1995, Yoldas *et al.* 2004), anatomic location (Torabinejad & Kettering 1988, Alacam & Tınaz 2002), single versus two visits (Imura & Zuolo 1995, Eleazer & Eleazer 1998, Oginni & Udoye 2004, Yoldas *et al.* 2004), antibiotics (Morse *et al.* 1987, Rimmer 1991) and analgesics (Torabinejad & Kettering 1988, Walton & Fouad 1992) did not reveal any relationship to flare-up in the study group. When all factors thought to affect flare-ups are considered simultaneously, it becomes apparent why there is little consistency between the earlier studies.

Periapical lesion

A major finding in the present study was that odds of flare-up in the presence of a periapical lesion were 9.64 times greater than for teeth without a periapical lesion. A number of studies (Barnett & Tronstad 1989, Trope 1990, 1991, Imura & Zuolo 1995) have also found a statistically significant association between presence of periapical lesion and flare-up.

Several hypotheses have been proposed to explain mechanisms involved in the induction of flare-up following NSRCT procedures. The causative factors include mechanical, chemical and/or mechanical injury to pulp and periradicular complex (Seltzer & Naidorf 2004). Examples of mechanical irritation causing periradicular inflammation include iatrogenic instrumentation whilst examples of chemical irritation include irrigants and intracanal medications.

However, inadequate debridement as well as over-instrumentation and inoculation of microorganisms into periapical tissues (Torabinejad & Cymerman 1994, Siqueira 2003) are considered likely causes of inter-appointment flare-ups. The results of this study indicate a strong correlation between flare-up and presence of apical periodontitis. Apical periodontitis is an infectious disease caused by microorganisms inside the root canal (Moller *et al.* 1981, Walton & Ardjmand 1992). The apical extrusion of infected debris into the periradicular tissues can disturb the balance between aggression and defense and may lead to development of an acute inflammatory response (Siqueira 2003). In addition, overinstrumentation may permit influx of exudates and blood into root canals, which may promote proliferation of remaining bacteria and cause exacerbation of chronic periapical lesion (Chavez de Paz Villanueva 2002). Nevertheless, the results of this study do not prove or disapprove any specific causative factor involved in the precipitation of flare-ups.

It is likely that the instrumentation technique used during NSRCT may play a role in the development of a flare-up. At the University of Pennsylvania, graduate endodontic residents complete the majority of cases with crown-down techniques, utilizing the latest generation of apex locators and NiTi rotary instruments. The apical size of canal preparation is routinely 40–50 in cases with periapical radiolucency and in retreatment cases, in mesial canals of mandibular molars and buccal canals of maxillary molars and sizes 50–100 in palatal canals, premolars and anterior teeth, depending on the first size file to bind in the apical portion and the curvature of the canal.

There are only a few studies dealing with flare-up that have described the operative technique used during NSRCT (Abbott *et al.* 1988, Barnett & Tronstad

1989, Trope 1990, Imura & Zuolo 1995, Eleazer & Eleazer 1998). Only two studies described the use of electronic apex locators (Trope 1990, 1991). At least three studies can be identified in the literature (Barnett & Tronstad 1989, Trope 1990, 1991) that used a similar instrumentation philosophy and reported a similar low percentage of flare-ups. Anatomical (Kerekes & Tronstad 1977) and microbiological evidence (Card *et al.* 2002) have indicated certain advantages of enlarging canals to larger sizes. Therefore, thorough instrumentation of root canals (Trope 1991) and proper length control (Chavez de Paz Villanueva 2002, Siqueira 2003) may be important factors in reduction of incidence of post-operative flare-ups.

At the University of Pennsylvania each graduate endodontic resident completes 30 cases with stainless steel hand instrumentation using the crown down technique. It is interesting to note that there was no difference in flare-up incidence between hand and rotary instrumentation.

Number of visits

Another independent risk factor identified in the analysis was number of visits. There was no statistically significant difference in flare-ups between one and two visits. As pointed out earlier the greater odds of flare-up obtained when NSRCT was completed in three or more visits is confounded by the definition of the flare-up used in this study. Since flare-up was defined as pain and/or swelling associated with an unscheduled visit, this lead to preferential selection of patients with multiple visits.

There is a common belief that multiple appointments with inter-appointment dressing could minimize post-treatment pain in teeth with periapical pathology and a necrotic pulp. A positive correlation between multiple appointments and flare-ups has been previously reported (Imura & Zuolo 1995). A majority of authors did not find any such relationship (Walton & Fouad 1992, Eleazer & Eleazer 1998, Al-Negrish & Habahbeh 2006). As pointed out in literature (Imura & Zuolo 1995), the lower incidence of flare-ups during single visit NSRCT may be due to the greater tendency of treating nonproblematic cases in one visit.

Pre-operative pain

The presence of pre-operative pain was not identified as a risk factor for flare-up. The cumulative flare-up rate of patients with a history of pain (0.420%) was not different than patients with no history of pain (0.32%). A number of studies (Torabinejad & Kettering 1988, Walton & Fouad 1992, Imura & Zuolo 1995, Yoldas *et al.* 2004) have identified pre-operative pain as a predictor of postoperative flare-ups. Only one study (Alacam & Tınaz 2002) did not find pre-operative pain associated with increased incidence of flare-up. In the present study, the magnitude of association of pre-operative pain with flare-up may have been diluted because of large sample size.

Medications

The relationship between flare-ups and antibiotics has been a subject of interest and conflicting findings. Thus, several studies have reported a decreased incidence of flare-up with the use of antibiotics (Abbott *et al.* 1988, Morse *et al.* 1990), but others disagree (Torabinejad & Kettering 1988, Walton & Ardjmand 1992, Walton & Fouad 1992, Alacam & Tınaz 2002). The results of this study did not show any advantage with the use of antibiotics or analgesics.

Limitation

The major limitation of this analysis is the retrospective and cross-sectional nature, which precludes establishing temporal relationships. In the absence of any objective measurements, flare-up can be misdiagnosed and the possibility of misclassification with post-operative pain cannot be ruled out. However, any such misclassification would likely be nondifferential. In the present study, all subjects with pain in the final analysis were removed but those who returned for an unscheduled visit were retained. This decision was made because both flare-up and post-operative pain are symptom-based diagnoses and a certain degree of overlap between the two conditions cannot be entirely ruled out.

One of the problems with clinical databases is the definition of the variables being entered into the database as well as the consistency of data entry. Furthermore, the data entry relies on the people that are entering the data. The PennEndo database is a robust validated database, where registrations are made by endodontic residents who have strict definitions of what goes into the database.

Conclusion

Presence of a periapical lesion is a well-established risk factor for flare-up and post-operative pain, and the current findings are consistent with this. In the present

study, flare-up during NSRCT was investigated, and the odds ratios for a number of independent variables in precipitating flare-ups was determined. The results revealed a cumulative flare-up rate of 0.66% in teeth with periapical lesions, the odds ratio for flare-up in teeth with periapical lesions was 9.64 times more than similar teeth without periapical lesions. Our findings clearly demonstrate that incidence of flare-up increases significantly in the presence of a periapical lesion. The results may point towards a microbial aetiology, but they do not prove or disprove it. Rather, they point to a more complex interrelationship amongst host, periapical lesion and endodontic procedures, the elucidation of which will almost certainly require prospective studies.

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