The role of preoperative prophylactic antibiotic administration in periapical endodontic surgery: a randomized, prospective double-blind placebo-controlled study

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Abstract

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Aim To determine the value of clindamycin prophylaxis in the prevention of postoperative wound infections in patients undergoing endodontic surgery.

Methodology This study included 256 patients undergoing endodontic surgery in a prospective double-blind placebo-controlled trial comparing oral administration of an oral placebo versus a preoperative 600 mg dose of clindamycin. After randomization the study medication was administered orally 1 h before surgery in a double-blind fashion. For a period of 4 weeks the postoperative course was observed according to clinical parameters of infection. Primary endpoint was infection at the surgical site.

Results The mean age of the study population was 44.4 years (SD 11.4, range 18–82 years) with a sex distribution of 147 females (47.4%) and 109 males (42.6%). Mean age of the patients in the clindamycin group was 44.7 years (SD 12.0), and the mean age in the placebo group was 44.1 years (SD 10.8) ($P = 0.49$). In the clindamycin group, the mean duration of surgery was 32.3 min (SD 8.8) and in the placebo group the mean duration of surgery was 32.5 min (SD 8.4) ($P = 0.89$). Two infections [1.6%; 95 confidence interval (CI): 0.48–4.72] were identified in the clindamycin group and four (3.2%; 95 CI: 0.42–1.33) in the placebo group ($P = 0.448$).

Conclusions No statistically significant difference was found between clindamycin prophylaxis and placebo with regard to the prevention of postoperative infection in endodontic surgical procedures.

Keywords: antibiotic prophylaxis, periapical surgery, placebo, randomized controlled trial, surgical endodontics.

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Introduction

The preoperative and/or postoperative use of antibiotics on a routine basis in surgical endodontics has always received mixed reviews (Zuolo *et al.* 2000, Siqueira 2002). The rationale for the use of antibiotics is based on the concept that the primary cause of the periradicular lesion is bacterial and that surgical intervention may result in a superimposed bacterial infection in the surgical site. A survey on the administration of antibiotics amongst the members of the American Association of Endodontists (AAE) showed that 37% of the endodontists routinely prescribed antibiotics for endodontic surgery (Yingling *et al.* 2002). However, in a review article on the use of antibiotics in the prevention of postoperative infection, antibiotics in apical surgery in the absence of

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oro-antral communications and medical complications was not recommended (Longman & Martin 1991). In another more recent review, Longman *et al.* (2000) stated that there was no evidence that antibiotic prophylaxis given to healthy patients undergoing surgical endodontics was efficacious. These recommendations however are not based on placebo-controlled comparative studies. In the literature there are no prospective, double-blind, randomized controlled trials to support the administration of antibiotics before or after endodontic surgery.

The aim of this prospective randomized double-blind study was to evaluate the value of routine antibiotic prophylaxis for endodontic surgical procedures.

Materials and methods

Patient population

This prospective study was conducted at the Department of Oral and Maxillofacial Surgery of the Academic Medical Centre of Amsterdam. Patients who were referred for endodontic surgical procedures were recruited to participate in this double-blind placebo-controlled clinical trial. The study protocol was approved by the medical ethical committee of the Academic Medical Centre of Amsterdam and patients were given an explanation of the study purpose including benefits and associated risks. The inclusion criteria were tooth with apical periodontitis with an adequate root filling and coronal restoration. If endodontic retreatment was feasible, patients were referred back to the dental practitioner and not included in the study. Teeth with perforations of the lateral canal walls, periodontal attachment loss (pocket depth >5 mm), vertical fractures and teeth exhibiting radiographic lesions exceeding 1 cm were also not included in the study. Patients with acute symptoms of endodontic infection such as submucosal swelling and erythema were also excluded from the study as were patients who had received antibiotics prior to surgery. Other exclusion criteria were hypersensitivity for clindamycin, systemic disease or a medical condition which required prophylactic antibiotics.

Patient numbers, age, mean length of operation, treated tooth and treatment group were recorded in a database. Patients received either a single dose of 600 mg clindamycin or placebo orally 1 h before incision. Envelopes contained a study-identification number with two capsules of either placebo or clindamycin. Blind administration of study drugs was ensured through the use of labelled sets of identical looking tablets. The assisting nurse supervised drug administration procedure. Patients, oral and maxillofacial surgeons (JL, JF) and investigators (PV, HA) were blinded to random allocation throughout the study.

Surgical procedure

At the initial presentation the investigators assessed the level of oral cleanness, and if not appropriate (assessment of dental plaque or gingivitis) prior to surgery a dental hygienist improved oral hygiene in the patients included in the study. No preoperative surgical rinsing protocols with chlorhexidine 0.12% were used. Before surgery, local anaesthesia containing epinephrine was given. The surgical flap procedure was similar for all selected teeth regardless of the fact that all teeth were included ranging from anterior maxillary teeth to mandibular molars. In all cases a buccal sulcular incision was made with a mesial releasing incision. Once the incisions were made the interproximal papillae were gently elevated to make sure that they were freely mobile to avoid trauma to the flap during reflection. Full-thickness mucoperiosteal access flaps were raised and the apex of the root was located. In cases where the bone was intact, a bone crypt preparation was started at approximately the apical one-third of the root with a high-speed bone bur and copious saline irrigation. After uncovering the root apex, the apical 3 mm of the affected root was resected. The root apex was bevelled approximately 10–25° (Forbes 2000), after which ultrasonic apical preparation was performed. After having achieved haemostasis with pressure with small gauzes or haemostatic agents an intermediate restorative material (IRM; The L.D. Caulk Division, Dentsply International Inc., Milford, DE, USA) filling was placed. The flaps were replaced and sutured with 5-0 Ethilon sutures (Johnson & Johnson Medical NV, Dilbeek, Belgium). Pressure with gauze moistened in saline was applied to the wound for approximately 15 min. No periodontal dressings were placed.

Postoperative management

Verbal and written postoperative instructions were given. Systemic oral NSAIDs (ibuprofen 600 mg three times a day for 5 days) were prescribed. Patients were instructed to rinse with a 0.2% chlorhexidine solution two times a day for 1 week. Sutures were removed after 1 week.

Assessment of infectious morbidity

After inclusion in the trial, the patients were assessed 1, 2 and 4 weeks after surgery. The wound was inspected for signs of infection at each visit. Local infection was treated by drainage and a swab was taken for bacteriological culture.

Criteria for postoperative infection morbidity were defined in the study protocol in order to eliminate observer bias. Wound infection was described as:

1. Purulent drainage from an incision or drain.

2. Serosanguineous drainage and a positive wound culture for a known pathogen.

3. The wound spontaneously dehisced or was deliberately opened by the surgeon when the patient had fever or localized pain or tenderness, with a positive wound culture.

Wounds were not considered infected if dehiscence occurred without drainage of pus. Such wounds were treated with conservative saline irrigation.

Adverse drug reactions

All undesirable reactions such as skin rashes or gastrointestinal disorders occurring as a result of the antibiotic prophylaxis were noted.

Statistical analysis

Data were entered into SPSS 12.0 software (SPSS Inc., Chicago, IL, USA). Descriptive statistics including mean (±SD), median (range), and proportion were used to summarize patient characteristics. An unpaired Student's *t*-test was used to compare the differences in continuous variables, and the chi-square test (or the Fisher's exact test, for variables having expected frequencies ≤5) was used to compare the distribution of discrete variables. Risk differences between placebo and clindamycin were expressed with their 95% confidence interval (CI). Significance was set at $P < 0.05$.

Results

Over a period of 28 months, 256 patients were entered into the study and all patients returned for evaluation of wound healing. Mean age of the study population was 44.4 years (SD 11.4, range 18–82 years) with a sex distribution of 147 females (47.4%) and 109 males (42.6%). Patient characteristics for the placebo and the clindamycin group with regard to sex, mean age, mean treatment time and location of the treated teeth are summarized in Table 1. The mean age of the patients in the clindamycin group was 44.7 years (SD 12.0), and the mean age in the placebo group was 44.1 years (SD 10.8) ($P = 0.49$). In the clindamycin group the mean duration of surgery was 32.3 min (SD 8.8) and in the placebo group the mean duration of surgery was 32.5 min (SD 8.4) ($P = 0.89$).

Table 1 Patient and treatment characteristics for the placebo and the clindamycin group

	Placebo	Clindamycin	Total
Sex (M/F)	54/74	55/73	256
Mean age ± SD (years)	44.1 ± 10.8	44.7 ± 12.0	–
Mean duration of surgery ± SD (min)	32.5 ± 8.4	32.3 ± 8.8	–
Location of endodontic surgery (*n*)			
Maxillary anterior	32	21	53
Maxillary premolar	39	22	61
Maxillary molar	22	18	40
Mandibular anterior	4	8	12
Mandibular premolar	5	11	16
Mandibular molar	26	48	74

There were significantly more mandibular molars treated in the clindamycin group, whilst more maxillary premolars and anterior maxillary teeth were treated in the placebo group. Six infections were identified in 256 patients, giving an overall infection rate of 2.3%.

There were no significant differences in infection rate between the two operators ($P = 0.26$). Two infections (1.6%; 95 CI: 0.48–4.72) were identified in the clindamycin group and four (3.2%; 95 CI: 0.42–1.33) in the placebo group ($P = 0.448$) (Table 2). Infections occurred within the first postoperative week in two cases whilst, the remaining four cases were seen at the end of the second postoperative week. Patients with infections presented themselves with the clinical picture of a submucous fluctuant swelling. There was no association with the sutures or the mesial releasing incision. The infections were easily treated with removal of the sutures or a small incision at the site of the releasing incision for drainage of pus and oral

Table 2 Infection rate in the placebo and the clindamycin group ($P = 0.45$)

Infection	Placebo	Clindamycin	Total
Yes	4 (3.2%; 95 CI: 0.42–1.33)	2 (1.6%; 95 CI: 0.45–4.72)	6
No	124	126	250

amoxicillin 375 mg three times a day for 5 days. Five of the wound infections were related to the culturing of an ά-haemolytic *Streptococcus* and the sixth grew a *Peptostreptococcus* strain. The infections in the placebo group were located in the mandibular molar region in two patients, in the maxillary premolar region in one patient and in the maxillary molar region in another patient. In the clindamycin group, one infection was seen in the maxillary molar region and the other in the mandibular molar region. No adverse effects of clindamycin or the placebo were reported.

Discussion

This study is the first placebo-controlled study on antibiotic prophylaxis in endodontic surgery. A non-significant difference in wound infection between prophylactic administration of clindamycin (1.6%) and placebo (3.2%) in endodontic surgery was found. When duration of the surgical procedures was reviewed as a potential cofactor influencing the rate of infection, no statistically significant difference could be identified. The overall wound infection rate was low (2.3%) indicating that antibiotic prophylaxis did not contribute to the prevention of postoperative infection. Patients in both groups were comparable in age and operation time, but there were differences with regard to the surgical location. More maxillary anterior and premolars were treated in the placebo group versus more mandibular molars in the antibiotic group. This imperfection in randomization with regard to surgical location however had no influence on the primary outcome. With an infection rate as low as seen in this study it is safe to postulate that there is no relationship between infection rate and surgical location.

A recent national survey of the AAE showed that 37% of the respondents prescribed antibiotics routinely for endodontic surgeries (Yingling *et al.* 2002). As demonstrated in the present study the use of prophylactic antibiotics is not supported by any scientific studies and should therefore be questioned. In the AAE survey, the decision to prescribe antibiotics in some cases was influenced by patient demand, expectations of the referring dentist or medical-legal reasons.

The choice of antibiotic in oral surgical procedures has always been subject of debate (Lindeboom & van den Akker 2003). Penicillin is less expensive than most other alternatives and has been found effective against most aerobic and anaerobic organisms present in orofacial infections (Peterson 1990). In hospital settings, the availability of specific antibiotics is often decided by a committee of interested professionals, often including infectious disease physicians, clinical microbiologists, clinical pharmacists and representatives from quality assurance committees. This group will most likely base their decisions on local pathogens and their susceptibilities, an evaluation of the clinical literature and consultation with clinicians who will use the recommended antibiotics (Polk 1999). Recommendations of the hospital antibiotic committee led to the use of clindamycin as the prophylactic antibiotic in the present study. Clindamycin is a broad spectrum antimicrobial, demonstrated to be effective as perioperative prophylaxis in oral and maxillofacial procedures (Mueller *et al.* 1999). It is active against most Gram-positive cocci, and most anaerobic organisms.

Conclusion

On the basis of the findings in this study, it can be concluded that in comparison with placebo, prophylactic antibiotics do not provide additional clinical effects on postoperative infections.

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