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Choosing Antibiotics Wisely: What Dentists Need to Know

Introduction

Antibiotic resistance, driven by antibiotic prescribing, is one of the most serious health threats facing the world today. It is estimated that dentists prescribe eight to 10 per cent of antibiotics in relation to human health (1). Reliable information on prescribing by dentists is generally not available in Canada, but data from one province indicates that during a 10-year period, antibiotic prescriptions by physicians had decreased by 18.2 per cent, while prescriptions by dentists had increased by 62.2 per cent. The reasons for this are unclear, but self-reported data from a recent survey of Canadian dentists (2) indicate that dentists require education of both the medical indications as well as the dental procedures requiring antibiotic prophylaxis (AP) for the prevention of infective endocarditis (IE); a lack of awareness of changes to antibiotic guidelines for patients with total joint replacement (TJR); variation in prescribing practices among dentists for AP for the prevention of surgical site infections; use of antibiotics for conditions where antibiotics are not necessary; and general overuse of clindamycin and underuse of penicillin V prescribing. There is a clear need for greater understanding of appropriate use of antibiotics among both dental prescribers and patients.

The purpose of this paper to present the best available evidence from a broad review of the literature, supplemented by expert opinion, to provide guidance to dentists on using antibiotics judiciously in healthy dental patients. The focus will be on prevention of surgical site or localized infections, prevention of distant site infections and dental conditions where antibiotics should not be used. The paper does not address the therapeutic use of antibiotics in periodontal therapy or in odontogenic infections with local spread or systemic involvement, nor does it address the complex topic of the use of antibiotics in immunocompromised patients.

Indications for antibiotics to prevent surgical site/local infections

When antibiotics are indicated, Peterson's five principles of AP (3) should be respected:

1. The surgical procedure should have a significant risk for infection
2. The correct antibiotic for the surgical procedure should be selected
3. The antibiotic level must be high
4. The timing of antibiotic administration must be correct
5. The shortest antibiotic exposure must be used

Surgical site infections after minor oral surgery are uncommon (less than five per cent) and rarely have severe adverse effect in healthy patients (4). When clinical judgement suggests an indication for prophylactic antibiotics, there is a significant body of evidence to support a single loading dose of pre-operative antibiotics only, with no postoperative antibiotics. Adequate tissue concentrations of the antibiotic should be present at the time of the incision and throughout the procedure for AP to be effective (5).

Extractions (excluding third molars)

There is scant literature related to AP for patients undergoing non-third molar dental extractions. One randomized control trial (RCT) compared pre-operative, post-operative and no antibiotics and found no difference in pain, swelling or other complications following simple dental extractions in healthy patients (6). Another study compared the use of peri-operative amoxicillin and placebo and reported no difference in post-operative infections, but a significant increase in adverse events (vomiting, diarrhea and stomach upset) in the antibiotic group (7).

Third molar extractions

There is a significant body of literature on AP for third molar surgery. However, many of the studies are poorly designed, underpowered and generally of low quality; compared one antibiotic to another without placebo; compared pre-op to post-op antibiotic administration; or failed to define the outcome measure of surgical site infection. This has led to conflicting results and recommendations. Importantly, most studies did not stratify according to degree of impaction and difficulty. The following studies provide the best available evidence for the use of antibiotics in third molar extractions.

In a retrospective review of 2,134 patients, Piecuch (8) considered both the site and the degree of impaction. He reported that the overall incidence of postoperative infections following third molar removal was 3.5 per cent. Infections at maxillary sites were rare, whether or not antibiotics were given. The overall infection rate for mandibular sites was 6.6 per cent. When this was further analyzed by degree of impaction, the differences in favour of antibiotics and no antibiotics were not significant for erupted and soft tissue impacted third molars, but were significant for partial bony impacted and full bony impacted third molars.

In a 2007 meta-analysis, Ren and Malmstrom (9) included only RCTs that used systemic antibiotics in the surgical extraction of impacted mandibular third molars with the primary outcome variable of postoperative inflammatory complications including alveolar osteitis (AO) and surgical site infection. The overall result using a conservative random effects model showed that, when only high quality (randomized, double blind and placebo controlled) trials were included in a subgroup analysis, patients receiving systemic antibiotics were 2.2 (CI: 1.3-3.7) times less likely to develop AO with a number needed to treat (NNT) of 13 to prevent one case of AO and 1.8 (CI: 1.1-2.9) times less likely to develop a deep wound infection, where the NNT was 25. A subgroup analysis of the timing of antibiotics supported a recommendation for a single pre-op dose of penicillin or its derivatives one hour before surgery.

A Cochrane review was carried out in 2013 (10) to determine the effect of AP on infections after dental extractions. All participants in the included studies had third molar extractions, the majority of the sites were in the mandible and the majority were impacted teeth, but there was no subgroup analysis to clarify effect by site or degree of impaction. Adverse effects were twice as likely in the antibiotic group compared to the placebo group (RR 1.98 (95% CI 1.10 to 3.59) P = 0.02), with a NNT to cause harm of 21. While the adverse effects were often mild and transient and reported in only 28 per cent of the trials, one large study (11) reported that three per cent of participants taking a five day course of clindamycin developed gastric complications requiring treatment and withdrawal from the study.

Bone grafting

Infection rates and graft failures have been shown to increase as a result of perforation of the Schneiderian membrane of the sinus floor, which may occur in greater than 40 per cent of sinus augmentations (12, 13) yielding a graft failure rate of 11.3 per cent (13).

Many of the studies analyzed for this review used antibiotics ubiquitously and there were few well-designed comparison studies. Only one prospective randomized controlled trial was found that evaluated the effectiveness of prophylactic antibiotics at preventing infection leading to graft failure (14). None of the patients who received 2 g of pheneticillin orally one hour before surgery developed infection, while 10 per cent (n=2) in the placebo group developed infections leading to graft failure (14). While this pilot study was underpowered to show a convincing effect, given the significant risk of infection from sinus floor perforations in sinus augmentation with bone grafting procedures, some recommend the use of a single pre-op dose of antibiotics (14-16).

Implants

Implant failure typically occurs in less than five per cent of cases. Given the large numbers of patients receiving this expensive, elective treatment, there is great interest in mitigating risk of failure. The rational for studying whether or not antibiotics affect this outcome is based on the hypothesis that bacteria produce a prolonged inflammatory reaction with an exaggerated macrophage response to the implant surface that interferes with the healing process and osseointegration (17). In addition, established infections of any biomaterial are extremely resistant to antibiotics as well as host defences and usually require removal of the material (17).

Studies investigating the effects on AP on the success of implant placement yield conflicting results. In attempts to sort through such results, systematic reviews and meta-analyses have been undertaken. Once again, the results of these reviews are discordant. Of the seven we analyzed from the past 10 years (18-24), four had acceptable methodological rigour and we present their findings below.

A 2008 Cochrane review (18) concluded that there is some evidence that a single pre-op loading dose of amoxicillin reduces implant failures but there were only two studies deemed rigorous enough to be included. The review was repeated in 2013 (21) with six included studies and a total of 1,162 study participants. Combination of these studies in a meta-analysis showed that a pre-op loading dose of 2 g of Amoxicillin significantly reduced implant failure rates (RR: 0.33; CI: 0.16-0.17; p = 0.002) with a NNT for benefit of 25.

Two subsequent systematic reviews agree with the 2013 Cochrane review in their main findings. Ata-Ali et al. (22) studied the number of implants that failed among a total of 2,063 implants placed in four included studies. The estimated odds ratio was 0.31 (CI: 0.16 – 0.7) in favour of antibiotics, with a NNT of 48. While both reviews show similar treatment effects — two thirds less failures with antibiotics — the Cochrane review studied the number of patients with failed implants and Ata-Ali studied the number of implants that failed. This likely explains the difference in the NNT, with the Cochrane NNT arguably reflecting a more accurate metric. Chrcanovic (23) included 14 studies with a total of 8,603 implants placed in his review. In a subgroup analysis where studies at high risk of bias were excluded from the analysis, the use of antibiotics to prevent implant failure were found to be of benefit (RR: 0.37; CI: 0.19 – 0.72).

Periodontal surgery

There is consensus in the dental literature that AP is not required for healthy patients undergoing most periodontal surgical procedures. Nevertheless, a recent review of 83 RCTs which included 2,121 patients and 2,951 surgeries related to flap surgery (25) showed that antibiotics were used in 75 per cent of the surgeries. The overall infection rate was 0.17 per cent and the NNT to prevent one infection was 203.

A retrospective analysis of 395 patients undergoing 1,053 periodontal surgeries, including soft tissue and osseous surgery, implant placement and guided tissue regenerative procedures (GTR) showed an overall infection rate of two per cent, with no benefit from systemic antibiotic therapy (26).

In a study of 45 patients with moderate to severe periodontal disease undergoing periodontal flap surgery, there were no infections in either the antibiotic or control groups (27). Similarly, Oswal et al. (28) reported no infections in 90 surgical sites, whether patients received pre-op or post-op antibiotics or placebo.

Endodontic therapy

Recent surveys of dentists and endodontists indicate that many endodontists prescribe antibiotics in clinical situations where they are not indicated (29-31), mostly because of patient expectations (29), but that endodontists are generally more prudent in the use of antibiotics than general dentists (30).

In a randomized, double-blind placebo controlled trial, Pickenpaugh (32) reported on 70 patients with asymptomatic necrotic teeth who underwent endodontic therapy. Of these, 10 per cent developed a flare-up that began about 30 hours after treatment and persisted for about 74 hours, characterized by moderate-severe postoperative pain or swelling. There was no difference between the pre-op loading dose of amoxicillin and the placebo groups, although this small subgroup analysis may have been underpowered to detect an effect.

In a high quality RCT, 256 patients were randomized to 600 mg clindamycin or placebo 1h prior to

endodontic periapical surgery and followed for four weeks, with a primary endpoint of infection at the surgical site. The overall infection rate was 2.3 per cent, characterized by a fluctuant swelling at the surgical site. There was no difference in infection rates between the two groups.

Several RCTs (33-35) administered a course of antibiotics and reported no difference between antibiotic and placebo groups in reduction of symptoms and healing of localized acute abscesses (36); post treatment flare-ups (33); or post-operative pain or swelling (35).

Indications for antibiotics to prevent distant site infections

There are very few circumstances for which prophylactic antibiotics are indicated prior to invasive dental procedures to prevent distant site infections. The rationale for prophylaxis is that invasive dental procedures cause transient bacteremia — that is, the entry of oral bacteria into the bloodstream. However, it is now known that daily activities such as chewing, flossing and tooth brushing cause bacteremia on a much more frequent basis (37-40) and that antibiotics are only partially effective at reducing the bacterial load in the blood stream (41-43). In addition most infections at distant sites — for example, non-valvular cardiac devices (44) and prosthetic joints (45) — are caused by Staphylococcus species or other organisms not usually found in the oral cavity and are usually introduced at the time of surgery (45, 46).

Patients at risk for infectious endocarditis

The 2007 guidelines from the American Heart Association (AHA) on the prevention of infective endocarditis (IE) recommend AP prior to invasive dental procedures for a small group of patients considered to be at high risk for IE (47). These include patients with (1) prosthetic cardiac valve or prosthetic material used for cardiac valve repair, (2) a history of infective endocarditis, (3) certain specific, serious congenital heart conditions and (4) heart transplant recipients that develop cardiac valvulopathyy. Similar recommendations were endorsed in Europe in 2015 (48) with the exception of the recommendation for patients with heart transplants, a recommendation for which the European Task Force felt there was no supporting evidence. In 2008 in the UK, the National Institute for Health and Care Excellence (NICE) recommended the complete cessation (for all procedures and all patients) of AP to prevent IE (49). NICE reviewed this again in 2015 and re-affirmed their 2008 Guideline (50). This has caused considerable controversy in the UK (51). A systematic review on AP for the prevention of IE published recently did not shed further light on this issue (52). It is recommended that Canadian dentists follow the AHA Guidelines, which are planned for review in 2018 (51).

Patients with nonvalvular implanted devices

In 2003, following an extensive review, the AHA released a Scientific Statement on Nonvalvular Cardiovascular Device-Related Infections(44). This states that there is no need for antibiotic prophylaxis prior to any dental procedures for patients with the following: pacemakers; implantable defibrillators; ventriculoatrial shunts; devices for patent ductus arteriosus, atrial septal defect, and ventricular septal defect occlusion; peripheral vascular stents; prosthetic vascular grafts; hemodialysis shunts; coronary artery stents; dacron parotid patches; chronic indwelling central venous catheters. They suggested, but did not provide justification, that AP be given to patients with these devices if they undergo incision and drainage of infection at other sites (e.g. abscess). However this recommendation has been removed from an update published in 2010 (46).

A systematic review found no clinical trials or documented cases where indwelling central venous catheter-related infections were associated with invasive dental procedures (53). In a 2018 study (54), 25 cancer patients with central lines who had absolute neutrophil counts (ANC) >1,000 cells/µL (average 3,860) and a minimum platelet count of 50,000//µL had periodontal scaling without antibiotics. Thirty-six per cent of patients showed bacteremia at 20 minutes that did not persist beyond 30 minutes. These patients with transient bacteremia had the highest Periodontal Screening and Recording (PSR) scores but there was no difference in the mean ANC between patients who developed bacteremia and those who did not. No patients developed catheter-related or bloodstream infections.

Patients with prosthetic joints

There has been significant controversy in the past about the role of dental bacteremia in late prosthetic joint infections and myths abound (55), but recently Canadian dentists, orthopedic surgeons and infectious disease physicians have agreed that patients with total joint replacements (TJR) do not require AP prior to any dental procedures (56). Dentists have voiced concerns about several issues, especially medical-legal liability if they do not give antibiotics and the patient develops an infection, particularly if the orthopedic surgeon has advised prophylaxis. This should be a decreasing concern as there is anecdotal evidence of increased uptake of the consensus statement in the orthopedic community with many professional groups, including the Royal College of Dental Surgeons of Ontario (RCDSO) (57), and centres of orthopedic excellence endorsing it. The evidence strongly supports no antibiotics and one could say that the tables have turned — dentists are more likely to have to defend themselves when they have caused a serious adverse event such as a *c. difficile* infection through the inappropriate use of antibiotics (55).

Conditions where antibiotics are NOT indicated

Irreversible Pulpitis

Irreversible pulpitis is an inflammatory condition that can be extremely painful, especially when it involves the periapical tissues. Although the presence of some bacteria in the periapical region has been shown (58), this is mainly an inflammatory, rather than an infectious, process. Antibiotics will not eliminate these bacteria and they do not significantly reduce the patient's perception of pain or the quantity of pain medication required (59,60). Given the intensity of pain, patients often demand and dentists are tempted to prescribe an antibiotic. However, the natural history of pulpitis is such that as pulpal necrosis progresses, pain severity lessens (61). If patients present at the height of their pain experience, a prescribed antibiotic may appear to help the pain, as its peak action will coincide with the natural decrease in pain intensity and patients and dentists may believe that the antibiotic was effective when it really had no effect at all. Optimal analgesia and not antibiotics are indicated for irreversible pulpitis, along with appropriate surgical intervention — endodontic therapy or extraction.

Localized acute apical abscess

A localized abscess should be drained and the tooth treated with root canal therapy or extraction. Antibiotics are not indicated when an abscess is localized and adequate drainage obtained (32, 34, 35, 60). In the event of systemic complications (e.g. fever, lymph node involvement or spreading infection), antibiotics may be prescribed in addition to drainage of the tooth.

Alveolar osteitis

"Dry socket" occurs when the blood clot in the extraction site fails to form or is dislodged. Its incidence is reported as three to four per cent overall, but may be as high as 25-30 per cent following removal of impacted mandibular third molars (62). The etiology is likely related to complex interactions between excessive localized trauma, bacterial invasion at surgery and subsequent fibrinolysis as well as patient behavioural and genetic factors (62). It usually peaks at three to five days but may persist for weeks if untreated. While there is some evidence suggesting that surgical antibiotic prophylaxis prior to removal of partial and bony impacted mandibular molars may reduce this complication, once established, alveolar osteitis is an inflammatory process related to poor wound healing and antibiotics are not indicated. Treatment may include removal of debris from the socket by irrigation, placement of a medicated dressing and adequate pain management.

Conclusion

Antibiotics are an increasingly scarce resource. Dentists have a responsibility to future patients and society to use antibiotics wisely in the fight against antimicrobial resistance, so that our patients, our families and ourselves can receive antibiotics when they are really needed. In everyday dental practice, there are few indications for surgical and distant site antibiotic prophylaxis for healthy patients, nor are antibiotics indicated for localized infections or inflammatory conditions. OD

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