ABSTRACT

Antibiotic prophylaxis can prevent the development of either systemic or local infectious complications

The indications for the use of antimicrobials in dentistry are (i) treatment of acute infection and (ii) prophylaxis against infection (single-dose prophylaxis and perioperative prophylaxis). Antibiotic prophylaxis refers to the administration of antimicrobials in situations where there is no actual infection, but where the risk of infection is substantial, for example, in the case of invasive procedures at contaminated sites. The aim of antibiotic prophylaxis is to prevent the development of either systemic or local infection complications. Severe underlying diseases including immunosuppressive illnesses and their treatment have been shown to predispose the patient to systemic odontogenic infections. Manipulation of infected oral tissues, such as measurement of periodontal pockets, calculus removal and tooth extraction, in particular, is known to cause bacteraemia. Therefore, antibiotic prophylaxis is used in connection with invasive procedures in infected areas in patients at elevated risk for endocarditis or other systemic infection complications. In addition, preoperative single-dose prophylaxis is also appropriate in generally healthy patients when treating infection foci surgically and if antimicrobial treatment is needed. Amoxicillin is the first-line drug of choice, due to its appropriate antimicrobial spectrum and especially its excellent absorption.

Prophylactic use of antibiotics in dentistry

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The indications for antimicrobials in dentistry are treatment of acute infection and infection prophylaxis (single-dose prophylaxis and perioperative prophylaxis). Prophylaxis means protection, primary prevention, and preemptive measures. Antibiotic prophylaxis refers to the administration of antimicrobials in situations where there is no actual infection, but where the risk of infection is substantial, for example, in connection with invasive procedures at contaminated sites. The aim of antibiotic prophylaxis is to prevent either systemic (endocarditis prophylaxis, endoprosthesis prophylaxis, sepsis prophylaxis) or local (wound infection) infection complications. In dentistry, the following forms of antibiotic prophylaxis are known: preoperative single-dose prophylaxis, preoperative prophylactic antimicrobial course, postoperative prophylactic antimicrobial course and preoperative single-dose prophylaxis combined with postoperative antimicrobial course. Evidence in favour of their use is only available for the effect of preoperative single-dose prophylaxis and a preoperative dose in combination with a 3-5 day postoperative course (perioperative prophylaxis) (1-4).

Who is at risk of infection complications of oral origin?

Manipulation of infected oral tissues, such as measurement of periodontal pockets, calculus removal, over-instrumentation during root canal treatment and especially tooth extraction are known to cause bacteraemia (5). Infection in a tooth or its surrounding tissues may also lead to spontaneous bacteraemia, if the infection spreads to adjacent blood

KEY WORDS

Antibiotic prophylaxis; dentistry; sepsis; endocarditis

Risk factors
1. Previously healthy patients - Patients whose dental infection has repeatedly been treated with antibiotics alone without care to the infection focus
2. Patients at increased risk of infection - Uncomplicated diabetes (B-GHb-A1C < 8 %, < 64 mmol/mol) - Patients with autoimmune disease with no medication or on mild immunosuppressive therapy (prednisolon in adults < 10 mg/day, no more than one immunosuppressant) - Rheumatic disease in remission and no infection complications after previous operations - Patients who have undergone solid organ transplantation and are on mild immunosuppression (> 6 months from the transplantation) - Previous endocarditis or rheumatic fever (> 12 months from illness onset) - Patients with joint or vascular prosthesis after postoperative healing time (> 6 months), if they have several or problematic prostheses - Clinically asymptomatic liver cirrhosis or exhibiting minimal symptoms - Drug-induced or other mild leukopoenia (< 2,5 x109/l) or mild neutropoenia (> 1 x109/l) - Patients treated repeatedly for oral infection with antimicrobial agents without dental procedures in the focus of infection
3. Patients at moderate risk of infection - Unstable or complicated diabetes (B-GHb-A1C 8-9 %, 64-75 mmol/mol, clear organ complications such as nephropathy, retinopathy, neuropathy) - Patients with advanced kidney disease, predialysis and dialysis patients (P-Crea > 300 µmol/l) - Compensated liver cirrhosis associated with a decrease in coagulation factors - Patients who have undergone stem cell transplantation and have continuous need for immunosuppression - Patients with autoimmune diseases or rheumatoid arthritis who are on several immunosuppressive drugs or biologics - Joint or vascular prosthesis patients over a period of 6 months post-operatively - A metastatic infection within the past year likely to be of oral origin, such as sepsis, endocarditis or a remote abscess caused by oral bacteria
4. Patients at high risk of infection - Acute blood malignancies (leukaemias, lymphomas) and their treatment (chemotherapy, patients scheduled for stem cell transplantation) - Medication-induced or other deep neutropenia (< 1 x109/l) - Liver failure with clinical manifestations: jaundice, s-bilirubin more than 2-3 times elevated, or liver enzymes highly elevated - Patients awaiting organ transplants or patients who have recently undergone organ transplantation (less than 6 months ago) - A mechanical heart valve or other vascular prosthesis (also cardiac biovalve or vascular stent) within less than 12 months - Heart failure with poor treatment balance - Acute generalised or metastatic infection that is likely to be of oral origin

Table 1. *Patient-dependent risk factors for infection (6-8,13,14).*

vessels. Severe underlying diseases including immunosuppressive illnesses and treatments have been shown to predispose the patient to systemic odontogenic infection complications (Table 1) (6,7). Mortality due to odontogenic infections is also known to be highest in these patient groups. Improving the level of oral hygiene and management of general oral infection status prior to dental procedures decreases procedure-related bacteraemia significantly and is at least as important as a single-dose of antibiotics (8).

When should antibiotic prophylaxis be considered?

Antibiotic prophylaxis is used in connection with invasive procedures such as tooth extraction, calculus removal, abscess incision or other surgical procedures in an infected area involving risk of bacteraemia in patients at elevated risk of endocarditis or other systemic infection complications (Table 1 and 2). The need for prophylaxis is assessed based on general susceptibility to infection (other illnesses and medications increasing susceptibility to infections, presence of foreign bodies) and the level

Endocarditis prophylaxis

Heart conditions that require antibiotic prophylaxis:
- Congenital heart defects, including post surgical correction (except for open ductus arteriosus, which does not require prophylaxis)
- Acquired valvular disease (e.g. in association with ankylosing spondylitis and sequela of rheumatic fever)
- Mitral valve stenosis with significant regurgitation (mixed mitral valve disease)
- Sequela of heart and lung transplantation
- Artificial valve (including homograft valve)
- History of endocarditis
Prophylaxis is not needed in patients with:
- Forum ovale
- Open ductus arteriosus 6 months after closure
- Mitral prolapse without regurgitation
- Status post bypass operation
- Kawasaki disease without valve dysfunction
- Pacemaker
- Heart murmur (harmless) without valvular or congenital dysfunction
- Rheumatic fever without valvular dysfunction

Table 2. *Indications for endocarditis prophylaxis in connection with invasive dental procedures (9,10).*

Antibiotic alternatives

		First-line drugs	Patients allergic to penicillin (other than anaphylactic reaction)	Patients allergic to penicillin (anaphylactic reaction)
Previously healthy patients, patients at increased risk of infection	**Adults**	Amoxicillin 2 g (ENT*)	Cephalexin 1.5 g (STA**) + metronidazole 400 mg	Clindamycin 600 mg (STA)
	Children	Amoxicillin 50 mg/kg (ENT)	Cephalexin 50 mg/kg (STA) + metronidazole 15 mg/kg	Clindamycin 20 mg/kg (STA)
Patients at moderate risk of infection	**Adults**	Amoxicillin 2 g (ENT) + metronidazole 400mg	Cephalexin 1.5 g (STA) + metronidazole 400 mg	Clindamycin 600 mg ± metronidazole 400 mg
	Children	Amoxicillin 50 mg/kg (ENT) + metronidazole 15 mg/kg	Cephalexin 50 mg/kg (STA) + metronidazole 15 mg/kg	Clindamycin 20 mg/kg (STA) ± metronidazole 15 mg/kg
Patients at high risk of infection	**Adults**		Primarily iv medication, hospital treatment	
	Children		Primarily iv medication, hospital treatment	

*ENT: Particularly in cases where a rapidly spreading infection originates from the root canal and enterococci need to be taken into account as well.
**STA: To cover S. aureus in patients colonized with S. aureus in the nasopharynx or in patients with joint prostheses or other endoprostheses or skin wounds

Table 3. *Alternatives to first-line antibiotic prophylaxis in the treatment of odontogenic infection (9,10).*

of infection at the operating site in addition to the invasiveness and extent of the procedure. A single dose of antibiotics is usually sufficient. Severely immunocompromised patients (Table 1) have been shown to be prone to systemic infection of oral origin even with less invasive procedures. Bacterial endocarditis has its own specific risk factors, and there are separate guidelines on antibiotic prophylaxis and its indications in connection with dental procedures (9,10) (Table 2). Preoperative single-dose prophylaxis is also appropriate in generally healthy patients when treating infection foci surgically and if antimicrobial treatment is needed anyway.

How should prophylaxis be used to be of benefit?

There are no randomized, placebo-controlled, double-blind studies available on the impact of immunosuppression on the risk for systemic odontogenic infection complications, as due to ethical reasons patients susceptible to infections cannot be exposed to ineffective treatment of infection. However, there is evidence showing that the risk and degree of bacteraemia is significantly reduced by the intake, higher than normal dose of an antibiotic effective against the most important oral microbes one hour prior to the procedure.

Based on an extensive meta-analysis, antimicrobial agents reduce both ostitis of the oral cavity and infection of surgical wounds in connection with surgical removal of the third molar, but only if the first dose is given prior to the procedure (3). Based on the 16 controlled studies included in the meta-analysis, a course of antimicrobial treatment started postoperatively is less effective than a single dose taken an hour before the procedure, at least in generally healthy patients. Patients with poor tissue response due to an underlying illness or medication are likely to benefit from combining the single-dose prophylaxis with a postoperative antimicrobial course, i.e. so-called perioperative prophylaxis. The total duration of the course depends on the patient's healing capacity, but in most cases it lasts no longer than 5 days. Antimicrobial treatment does not reduce the symptoms of acute pulpitis or prevent flare-up during root canal treatment, which is why prophylaxis is not recommended when treating pulpitis (11).

How to choose the agent for prophylaxis?

The most common pathogens causing purulent oral infections are aerobic and anaerobic streptococci and anaerobic gram-negative bacilli, such as *Prevotella and Fusobacterium* species (6, 12). *Staphylococcus* aureus and other staphylococci are common findings, particularly in infections seen in children and the elderly, but usually infections are due to *S. aureus*. In patients with systemic odontogenic infection, the most commonly cultured bacteria are those belonging to the following genera: *Streptococcus, Actinomyces, Klebsiella, Bacteroides, Prevotella* and *Enterococcus* (7).

In each group of patients, antibiotic prophylaxis should cover the most important pathogens likely to be present and which can cause remote site infections. These always include common oral streptococci and anaerobic bacteria, but *S. aureus* must also be taken into account, if the patient is particularly at risk from infection complications caused by staphylococci (an endoprosthesis susceptible to staphylococcal infections or prior treatment with penicillin, which may have favoured staphylococcal growth). The antimicrobial treatment given to the patient during the preceding month as well as exposure to multi-resistant heath care associated bacteria and carrier status must be charted, and the possibility of selection and enrichment of resistant strains must be taken into consideration when choosing medication. Repeated courses of the same antimicrobial agent within a short period of time is not usually effective due to acquisition and enrichment of resistant microbes. Even if repeated, the impact of single-dose prophylaxis on oral microbiota is likely to be minimal.

CLINICAL RELEVANCE

The main determinants for the need for antibiotic prophylaxis in dentistry are firstly, the medical and immunological status of the patient and secondly, the degree of infection at the operation site and thirdly, invasiveness of the procedure. Minor vascular abnormalities, such as a tricuspid aortic valve, appear to constitute a minimally increased risk for systemic infection complication in immunocompetent patients. Immunocompromised patients are more susceptible to odontogenic infection complications, and antimicrobials play a more important role in their treatment. When treating dental abscesses that require use of systemic antibiotics a 2 g single-dose of amoxicillin is recommended for all patients pre-operatively.

When treating a patient colonized with a multi-resistant health care associated bacterium it is advised to avoid targeting this microbe unnecessarily in order to avoid further resistance which would weaken possibilities for treatment in the future. In general, all use of broad spectrum antimicrobial treatment favours the growth of multi-resistant bacteria. A summary of antibiotic prophylaxis of infection complications of dental origin are presented in Table 3. Amoxicillin is the first-line drug, due to its correct antimicrobial spectrum, its excellent absorption when taken orally as well as its good tissue distribution.

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