

ANTIBIOTIC THERAPY FOR PEDIATRIC DENTAL PATIENTS

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ABSTRACT

The oral pathologies in paediatric patients frequently require the recommendation of adjuvant medication. A lack of knowledge regarding well-defined prescription protocols has been observed in every day practice. The aim of this study was to revise and update the prescription of antibiotics according to the latest guidelines.

We performed electronic research of selected databases: PubMed, Google Scholar, AAPD, from 2010-2020 in order to identify the most frequent antibiotics used in paediatric dentistry.

The antibiotic resistance of bacteria, as well as the side effects that follow the prescription of antibiotics are reported to be in a continuous growth as a result of inadequate use. Prescription of medication, especially antibiotics in paediatric dentistry, must analyze both short and long-term side-effects.

Keywords: antibiotics, medication, prescription, pediatric dentistry

BACKGROUND

Antimicrobial substances

Most of the dental procedures within pediatric dentistry do not represent a risk of bacteremia among clinically healthy patients. The medication in dentistry is mostly prescribed to patients with the purpose of reducing pain and treating bacterial, fungal, viral infections [1,2].

Antimicrobial substances degrade or suppress the growth or the multiplication of microorganisms (bacteria, viruses, fungi, parasites). These substances present a selective toxicity – a lower concentration destroys the microorganisms with-

out causing detriment to the host cells – this ability allows their safe usage [1].

A microorganism's susceptibility to an antibiotic is based on its minimum necessary concentration for that microorganism to stop its dividing – not to be destroyed [1].

Antibiotic prophylaxis is an aid for pedodontic treatments in those situations where there's a risk of bacteremia. This prophylaxis implies the administration of antibiotics before the potentially infectious dental therapy begins [1].

Multiple factors have to be taken into consideration when prescribing antibiotics, such as: the host's (patient's) immune defence mechanisms,

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the severity and the localisation of the infection, as well as the incriminated type of pathogen [3,4].

An effective antibiotic therapy consists of identifying the pathogen through a bacterial culture or a serological test. In the dental practice, this microbiological testing is rarely done [1]. It is, however, indicated post-operative, in recurrent, mistreated or incompletely treated infections, in the treatment of periodontal disease, in immunosuppressed patients or when an osteomyelitis is suspected [1]. From a microbiological perspective, in 50% of cases *Streptococcus viridians* is identified as a bacterial species [5].

Due to the fact that the dental pulp has a terminal type of blood circulation, in case of an infection the inflammation and the immunity are compromised, thus making the root canal a unique bacterial environment [3,4,6].

The spectrum of an antibiotic

It refers to the microorganism species it has an effect on. The antibiotics with a narrow spectrum have an effect on a limited group of microorganisms, whilst those with a broad spectrum have an impact on Gram positive organisms, as well as on a relatively large number of Gram-negative organisms.

Bacteriostatic versus bactericidal

Whilst the bacteriostatic limits the spread of the pathogen throughout the body by stopping its growth and dividing, the bactericidal determines the irreversible destruction of the cells. In the case of bacteriostatic antibiotics, the immune system is let to attack, immobilize and destroy the pathogens. The effects of the bacteriostatic are reversible in the lack of an ulterior immune response, which, therefore, can make the infection reoccur [1,2].

Thus, the action of bactericidal antibiotics is preferred in most of the cases, including oral infections, due to the independent way of action – such as immunocompromised patients [1].

Dosage in children

The dosage in children has to be individualized according to the child's age and bodyweight. A general calculation formula is:

Adult dosage x child weight x K / adult weight
where K stands for a correction coefficient that has different values in regards to the patient's age:

- K=2 for children under one year;
- K=1,5 for children with ages between 1-12 years;
- K=1,25 for children with ages between 12-18 years [5]

In the event that the child's body weight is unknown, the dosage can be calculated regarding its age, starting from the adult's specific dosage:

- 1-3 years old = 1/6 of the adult dosage;
- 3-7 years old = 1/3 of the adult dosage;
- 7-12 years = 1/2 of the adult dosage;
- 12-17 years = 2/3 of the adult dosage [5]

A correlation between the patient's age, the objectives of the pharmacotherapy and the used forms of medication is required.

Different nations, globally, have published their own protocols in order to ensure an efficient and safe usage of medications, both prophylactically and therapeutically in numerous pathologies – after a correct assessment of the systemic spread of the infection, as well as an assessment of the patient's risk factors [8].

METHODS

We performed electronic research of databases: PubMed, Google Scholar, AAPD. We've searched for articles (review, cross-sectional studies, clinical studies, laboratory studies, in English and published / revised in the last 10 years (2010-2020).

The keywords used to search the articles were: antibiotic(s), p(a)ediatric dentistry, antibacterial, antimicrobial and resistance.

Out of a total of 135 articles found, 46 met the criteria of our chosen topic. The other studies were rejected because they lacked relevance and/or specificity in regards to this article's theme. Some of the criteria that wasn't met is related to the language the articles were written in and the date they were published at. Two independent reviewers analysed the articles and made the selection according to the mentioned criteria.

MOST USED ANTIBIOTICS

Dar-Odeh et al. note that in pediatric dentistry amoxicillin is the most frequently prescribed antibiotic, with an indication of administration of 5 days. In case of a penicillin and/or cephalosporins allergy, clindamycin, azithromycin and metronida-

zole have been the most frequent second choice, due to their broad spectrum of action [5,7,8,9] Isla et al. reported a notable efficacy of Metronidazole only on anaerobe species [10]. Easton et al. have proved the superiority of amoxicillin/clavulanic acid over azithromycin, regarding the provided clinical and bacteriologic response [11]. Hong et al. indicate that an exposure of the child to amoxicillin can be the cause of enamel developmental defects, both in the first primary molars, as well as in the central maxillary incisors [12]. Nevertheless, amoxicillin is considered to be the safest and most efficient antibiotic prescribed to children [3,9,11]. According to Isla et al., a minimum total dose of 1g/day of amoxicillin: potassium clavulanate has proved to be efficient on the most frequent bacteria that cause odontogenic infections [10].

Having both a bactericidal and a bacteriostatic action and being well distributed among all the fluids in the organism (except for spinal fluid), Clin-

damycin penetrates bones and abscesses. Furthermore, Nowak et al. mentions that, due to its very good activity against oral pathogens, Clindamycin is the default antibiotic for severe oral infections [1] (table 1).

ANTIBIOTIC PROPHYLAXIS

Indications for antibiotic prophylaxis are: fever over 37.5°C in the last 24 hours (this indicates a systemic response to an infection), trismus, immunocompromised patients/pathological states, wounds/fractures/open lesions, contaminated with extrinsic agents, in avulsed teeth with open or closed apex (as an aiding therapy), in patients with an aggressive form of periodontal disease (combined with a local treatment), in pericoronitis [1,3,7,13,18,19,20].

In the bacterial endocarditis antibiotic prophylaxis in recommended cardiovascular pathologies,

TABLE 1. Dosage of antibiotics in paediatric dentistry

Author	Antibiotic	Children under 12 years	Children over 12 years/ Adolescents	Maximum recommended dose
Skoog Ståhlgrén et al. (2019)	Penicillins G(intramuscular/ intravenous) and V (per os)	20-50 mg/kg/day [14]	1-2 g/day, in 3 or 4 doses per day [14]	3 g/day [14]
AAPD (2019)	Amoxicillin	20-40 mg/kg/day [13]	250-500 mg, in 3 doses per day [13]	2-3 g/day [13]
AAPD (2019), Easton J et al. (2003)	Amoxicillin + potassium clavulanate	20-40 mg/kg/day [11,13]	250-300 mg, 3 times a day or 875 mg twice a day [13]	2 g/day [13]
AAPD (2019), Bakheit AH et al. (2014)	Azithromycin	just one per day: in children older than 6 months = 10 mg/kg/day on the 1st day, then 5 mg/kg/day in days 2-5 [13]	In adults and/or adolescents older than 16 = 500 mg/day on the 1st day, then 250 mg/day in days 2-5. In adults = 500 mg/day for 3 days [13,15]	500 mg/day [13]
AAPD (2019)	Cephalosporins (Cefuroxime)	25-50 mg/kg/day 25-100 mg/kg/day [13]	250-1,000 mg, 4 times a day [13]	4 g/day, for a total period of 10 days [13]
AAPD (2019), Smith MJ et al. (2017)	Clindamycin	10-35 mg/kg/day [16] / 8-20 mg/kg/day [13]	600-1,800 mg 3 times a day [13]	4-8 g/day [13]
AAPD (2019), Wilcox MH et al. (2017)	Cephalosporins (Cefuroxime)	25-50 mg/kg/day [6] / 25-100 mg/kg/day [13]	250-1,000 mg, 4 times a day [13,15]	4 g/day, for a total period of 10 days [13]
AAPD (2019), McFarland LV et al. (2010)	Metronidazole	20-40 mg/kg/day, fragmented every 6 hours [13,18]	500 mg, 3 times a day [18,19]	4 g/day [13]
Vicente D, Pérez-Trallero E (2010)	Tetracycline	In children under 8 years of age, the administration is forbidden. Children over 8 years = 25-50 mg/kg/day. [17]	250-500 mg, 3-4 times a day	2 g/day

according with patient risk: major risk (valvular prosthesis, bacterial endocarditis in past medical records), medium risk (uncorrected valvulopathy, uncorrected septal defects), low risk (corrected cardiac malformations, mitral valve prolapses without regurgitation, acute articular rheumatism in the past (without valvular sequelae)) [20] (table 2).

TABLE 2. Dosage of antibiotics in bacterial endocarditis prophylaxis in paediatric dentistry

Author	Antibiotic	Bacterial endocarditis prophylaxis
AAPD (2019), Bragg L et al. (2014)	Amoxicillin	50 mg/kg, with a maximum of 2 g, 30-60 minutes before the dental procedure [13,22]
AAPD (2019), Bragg L et al. (2014)	Azithromycin	15 mg/kg, with a maximum of 500 mg, 30-60 minutes before the dental procedure [13,22]
AAPD (2019)	Cephalosporins (Cefuroxime)	50 mg/kg, with a maximum of 2g, 30-60 minutes before the dental procedure [13]
AAPD (2019), Bragg L et al. (2014)	Clindamycin	Orally: 20 mg/kg (maximum 600 mg) with 30-60 minutes before the dental procedure; Intramuscular or intravenous: 15 mg/kg (maximum 600 mg), administered 30-60 minutes before the dental procedure; [13,22]

Contraindications for antibiotic prophylaxis are: pain, oedema, erythema, purulent collection, primary teeth luxations, dry alveolitis, plaque-induced gingivitis, eruption gingivitis, pubertal gingivitis, gingivitis as a side effect of oral breathing, primary herpetic gingivostomatitis, viral diseases, at the request of the patients/caregivers [3,7,8,9,13,9,21].

INADEQUATE USE OF ANTIBIOTICS

Several studies show a tendency of over-prescribing antibiotics without a clinical indication, in numerous dental pathologies such as irreversible pulpitis, dental abscess or even for pain management [1,11,24,28,29]. Goel et al. emphasize the importance of four criteria in antibiotic prescription: choosing the appropriate antibiotic, the right dosage, the precise period of administration and choosing, as much as possible, the antimicrobial substance aimed to the pathogen [3]. The administration of antibiotics requires a good comprehension and a correct diagnosis, taking into account

their beneficial effects in comparison with the immediate or late side effects [7].

These unjustified prescriptions are reported to be constantly increasing from year to year [24].

According to a study conducted in UK on 568 patients, Cope et al. reported that more than half of antibiotics (65.6%) were prescribed in situations where there is no sign of infection, and 70.6% were prescribed without considering an operative intervention. Only 19% of antibiotics were prescribed according to the rules in effect [27]. Many dentists prescribe antibiotics, even for the treatment of viral infections (for example: herpes simplex) [23].

Inadequate use of antibiotics, in terms of quantity, timing and duration of treatment, can have important consequences for the child's development. Antibiotics containing sugar (suspensions especially created for easy administration in children – syrups) can cause a number of changes in the oral cavity: the appearance of tooth decay, tooth erosion, and a number of complications, such as pulpal damage (pulpitis) and dental abscess. Proper oral hygiene can prevent the appearance of these pathologies [3] (table 3).

NEGATIVE EFFECTS OF ANTIBIOTICS PROLONGED TREATMENT

An unnecessary prolonged treatment with antibiotics, for up to 21 days, will reduce the ability of the oral microflora to defend itself against pathogenic microorganisms. Colonies of microorganisms will appear that are not normally found in the oral cavity, leading to the appearance of extremely resistant bacterial or fungal infections [23].

In case of too early exposure to antibiotics, they can also affect the intestinal flora, leading to long-term negative effects, such as obesity, superinfections with *Candida albicans*, intestinal transit problems [3]. In terms of microbial resistance to antibiotics, there are approximately 1,030 bacteria worldwide, this number providing the genetic material needed for mutations, rearrangements, and gene transfer [34] (table 4).

BACTERIA RESISTANCE

Prescribing a broad-spectrum antibiotic can significantly damage the microbiome, thus precipi-

TABLE 3. Antibiotics – indications, contraindications

Author	Antibiotic	Indications	Contraindications
Shenoy, E. S et al. (2019)	Penicillin G (intramuscular/ intravenous) and V (per os)	moderate or severe bacterial infections, with the sensitive pathogens [29]	hypersensitivity/anterior allergies (7-10% of the patients) [29]
Abrams EM et al. (2019)	Amoxicillin	infections with sensitive bacterial species (acne, chronic bronchitis, syphilis); in patients allergic to penicillin [30]	In patients with penicillin allergy [30]
Easton J et al. (2003)	Amoxicillin + potassium clavulanate	upper respiratory tract infections, otitis, sinusitis, cutaneous affections [11]	hypersensitivity, in simultaneous administration of disulfiram, in patients with penicillin allergies [11]
Bakheit AH et al. (2014)	Azithromycin	in penicillin allergies, in respiratory-tract infections, otitis media, prophylaxis of group A streptococcal infection and as prevention therapy of bacterial endocarditis in patients undergoing dental procedures who are at high risk for endocarditis, pertussis, mycobacterial infections [25]	liver dysfunctions, hypersensitivity [25]
Campagna JD et al. (2012)	Cephalosporins (Cefuroxime)	in patients with penicillin allergies – with advised skin testing [31]	liver dysfunctions, hypersensitivity [31]
Smith MJ et al. (2017)	Clindamycin	infections with sensitive bacterial species (Streptococcus, Staphylococcus), invasive infections for which optimal dosing is critical [26]	liver dysfunctions, hypersensitivity [26]
Vicente D et al. (2010)	Metronidazole	anaerobic bacteria, some microaerophilic bacteria and protozoa [17]	In patients with liver and/or renal failure [18] Recent research does not confirm a clinically relevant interaction between ethanol and metronidazole [25]
Nowak AJ et al. (2019). Goel D et al. (2020)	Fluoroquinolones	Outside of a clear indication after an antibiogram, no indication in dentistry, especially in the pediatric field [1,3]	
Vicente D et al. (2010)	Tetracyclin	Infections with sensitive bacterial species (acne, chronic bronchitis, syphilis); in patients allergic to penicillin [17]	In children under 8 years of age, the administration is forbidden [17]

itating a superinfection with another pathogen (ex. *Candida albicans*). Therefore, in medical practice, choosing the narrowest spectrum antibiotic that can be efficient on the identified pathogens is recommended [1].

The misuse of antibiotics has led to an increase in the incidence of antibiotic resistance, becoming a global problem that threatens human health [18,27,34]. Since 2014, WHO has categorized antibiotic resistance as a major threat to public health, with hundreds of thousands of people dying each year from highly resistant bacteria [34].

In the past years, the role of the environment in the appearance of super-bacteria has become more important, representing their main source, but also the main transmission path [30]. However, the knowledge related to this subject is quite limited and automatically, the mechanism of formation of super-resistant bacteria is not fully elucidated [34].

There is a clear cause-and-effect relationship between the exposure to antibiotic treatments and

the emergence of antibiotic resistance; the more frequent these treatments are, the higher the risk of resistant infections. In order to minimize this risk, it is mandatory to reduce the prescription of antibiotics when it is not necessary [39]. Another factor that has led to discussions is represented by incomplete treatments, assuming that they conduct to an increase in the incidence of antibiotic-resistant microorganisms a 2016 study entitled “Antibiotic awareness week”, the World Health Organisation recommended that patients always complete antibiotic treatments, even if they feel better after a few days; otherwise, there is a risk of developing antibiotic-resistant bacteria, endangering both them and those around them. However, there are no clinical trials to prove this. Thus, various health organizations, such as the US Centre for Disease Control and Prevention (CDC) and Public Health England, replaced the message sent by the WHO, advising patients to take antibiotics “exactly as prescribed by their doctor” [39].

TABLE 4. The side effects of antibiotics in pediatric dentistry

Author	Antibiotic	Side effects
Shenoy ES et al. (2019)	Penicillin G (intramuscular/ intravenous) and V (per os)	allergic reactions, nausea, vomiting, diarrhoea, fever, rash [29]
Zandbergen D et al. (2016)	Amoxicillin	Nausea, diarrhoea, vomiting and gastrointestinal discomfort, taste alterations, dizziness, headache, a rash on the neck of the face [40]
Gomez R et al. (2012), Easton J et al. (2003)	Amoxicillin + potassium clavulanate	digestive phenomenon (diarrhoea, vomiting, nausea, indigestion), liver toxicity. A modification of the dose in patients with renal pathologies is required [11,34]
Bakheit A et al. (2014)	Azithromycin	Anorexia, dyspepsia, nausea, diarrhoea, colitis, flatulence, dizziness, headache, drowsiness, convulsions, arthralgia, and disturbances in taste and smell, liver dysfunctions, syncope, insomnia, agitation, anxiety, asthenia, paraesthesia, hyperactivity, thrombocytopenia, haemolytic anaemia, interstitial nephritis, acute renal failure, photosensitivity, tooth and tongue discoloration [25]
Campagna JD et al. (2012)	Cephalosporins (Cefuroxime)	Rash, urticaria, anaphylaxis, exacerbation of kidney diseases, colitis [31]
Nowak AJ et al. (2019), Pouwels KB et al. (2019)	Clindamycin	Severe diarrhoea, colitis, thrombophlebitis, hypotension, thrombocytopenia. It is associated with a high risk of infection with <i>Clostridium difficile</i> [1,41]
Nowak AJ et al. (2019), Dar-Odeh N et al. (2018), Pouwels KB et al. (2019)	Fluoroquinolones	Photosensitivity, low glycemic index, QT prolongation (cardiac rhythm pathologies), peripheral neuropathy, chondrotoxicity in the growing bone cartilage [1,24,41]
Nowak AJ et al. (2019), McGowan et al. (2018), Vicente D et al. (2010)	Metronidazole	Gastrointestinal manifestations (nausea, diarrhoea, pain in the epigastrium, discomfort), cephalgia, glossitis, stomatitis and metallic taste. When prescribed in patients with hepatic dysfunctions, its metabolites in the liver are elevated [1,17,36]
Goel D et al. (2020), Becker DE (2011), Vicente D et al. (2010)	Tetracyclin	nausea, vomiting, stomatitis, glossitis, photosensitivity, liver toxicity, renal insufficiency [3,17,37]. Antacids and dairy products lower the intraoral absorption [38]

THE IMPORTANCE OF THE IMPLICATION OF BOTH PARENTS AND CHILDREN

Regarding the compliance of the pedodontic patient, among the strategies listed by Gardiner et al. in order to motivate the child to take the prescribed dose of medication, there are: oral suspensions or various pills / capsules with pleasant taste, different ways to catch their attention or to supervise them (memories, planning, a relationship between doctor and parent) [39].

A well-established plan based on a mutual agreement between the parent and the doctor on the child's medication increases the safety of its correct administration [39].

CONCLUSIONS

The literature reports are showing that every year there's a growing trend of overuse and with-

out therapeutic justification of drugs (especially antibiotics). Amoxicillin is the most frequently prescribed antibiotic, with an indication of administration of 5 days. The misuse of antibiotics has led to an increase in the incidence of antibiotic resistance, becoming a global problem that threatens human health. Choosing the right antibiotic and prescribing it in a conservative and effective way minimizes the potential side effects that can occur. Also, a check-up every 1-2 days can be beneficial to verify the effectiveness of the treatment, but also to detect possible side effects. A correct and well-defined treatment plan, made by mutual agreement between doctor and patient, as well as a good collaboration and communication between them, can be the basis of a well-conducted therapy.

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