Adverse Effects of Clindamycin Associated with Dental Prophylaxis for Infective Endocarditis

Gabriela Ceccon Chianca,[1,2] *Raiane Cardoso Chamon,*[2,3] *Natalia Lopes Pontes Povoa Iorio*[1,2,4]

Universidade Federal Fluminense, Instituto de Saúde de Nova Friburgo, Laboratório de Microbiologia Experimental e Aplicada,[1] *Nova Friburgo, RJ – Brazil*

Universidade Federal Fluminense, Faculdade de Medicina, Programa de Pós-graduação em Patologia,[2] *Niterói, RJ – Brazil*

Universidade Federal Fluminense, Faculdade de Medicina, Departamento de Patologia, Grupo de Pesquisa em Staphylococcus,[3] *Niterói, RJ – Brazil*

Universidade Federal Fluminense, Instituto de Saúde de Nova Friburgo, Programa de Pós-graduação em Odontologia,[4] *Nova Friburgo, RJ – Brazil*

We read with great interest the *Sociedade Brasileira de Cardiologia*'s Perioperative Cardiovascular Assessment Guideline – 2024, especially item 4.4.1 (Dental Procedures) of section 4.4 (Prophylaxis of Infective Endocarditis).[1] The guideline describes in detail, using as references the recommendations of the American and European cardiology societies,[2,3] the dental procedures indicated for prophylaxis for infective endocarditis (IE), prophylaxis regimens to be used before these procedures, and the profile of patients indicated for IE prophylaxis. We would like to congratulate the authors for their attentive look at the Brazilian scenario regarding limited access to dental care in this country, which led to the inclusion, in the Brazilian guideline, of patients with native valve disease among those indicated for IE prophylaxis.

Historically, dentists have prescribed antibiotic prophylaxis before invasive dental procedures for patients at risk of developing IE.[4] This infection, with high morbidity and mortality rates, results from the adhesion and proliferation of microorganisms in the cardiac endothelium, due to exposure of the subendothelial tissue associated with lesions, which generate platelet activation and consequent local fibrin deposition. The main etiological agents of IE are bacteria, especially oral *Streptococcus* species, in low- and middle-income countries, such as Brazil.[1]

The aforementioned guideline[1] recommends the antibiotic clindamycin as an option for prophylaxis in patients with penicillin allergy. This recommendation caught our attention, since the use of this antibiotic as prophylaxis is associated with significant rates of adverse effects, both fatal and non-fatal, related to *Clostridioides difficile* infections,[4] which motivated the removal of clindamycin from the current guidelines recommended by the American and European cardiology societies.[2,5] However, this data was not taken into account in the current guideline of the *Sociedade Brasileira de Cardiologia*,[1] but may be considered in its future revisions.

We acknowledge that the work of Gualandro et al.[1] offers updated knowledge and recommendations on cardiovascular diseases in the perioperative context. We congratulate the team on proposing the fourth update of the guidelines, presenting evidence organized in a way that can be put into practice in the daily exercise of medicine, especially given that the perioperative topic in non-cardiac surgeries is very recent.

Therefore, we present a table containing the prophylaxis regimens to be recommended before dental procedures for patients at high risk of developing IE, taking into account the fatal and non-fatal adverse effects associated with the use of clindamycin as antibiotic prophylaxis for IE (Table 1). We suggest that this table, based on the current recommendations of the American Heart Association[2] and the European Society of Cardiology,[5] be included in future recommendations/guidelines of the *Sociedade Brasileira de Cardiologia* (Table 1).

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Keywords

Dental Prophylaxis; Bacterial Endocarditis; Clindamycin; Drug-Related Side Effects and Adverse Reactions

Mailing Address: Natalia Lopes Pontes Póvoa Iorio •
Universidade Federal Fluminense – Instituto de Saúde de Nova Friburgo – Laboratório de Microbiologia Experimental e Aplicada – Rua Doutor Silvio Henrique Braune, 22. Postal Code 28625-650, Nova Friburgo, RJ – Brazil
E-mail: nataliaiorio@id.uff.br
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Table 1 – Recommended prophylaxis regimens, before dental procedures, for patients at risk of developing infective endocarditis

Individuals with		Antibiotic	Single dose 30-60 minutes before the procedure	
Allergy to penicillin or ampicillin	Impossibility of oral administration		Adults	Children
No	No	Amoxicillin	2 g (oral)	50 mg/kg (oral)
No	Yes	Ampicillin	2 g (IV or IM)	50 mg/kg (IV or IM)
No	Yes	Cefazolin or ceftriaxone	1 g (IV or IM)	50 mg/kg (IV or IM)
Yes	No	Cephalexin[a,b]	2 g (oral)	50 mg/kg (oral)
Yes	No	Azithromycin or clarithromycin	500 mg (oral)	15 mg/kg (oral)
Yes	No	Doxycycline	100 mg (oral)	< 45 kg: 2.2 mg/kg (oral) > 45 kg: 100 mg (oral)
Yes	Yes	Cefazolin or ceftriaxone	1 g (IV or IM)	50 mg/kg (IV or IM)

Clindamycin is no longer recommended due to fatal and non-fatal adverse effects associated with its use. IM: intramuscular; IV: intravenous. a, or another first- or second-generation oral cephalosporin at the equivalent dose for adults or children. b, cephalosporins should not be administered to individuals with a history of anaphylaxis, angioedema, or urticaria to penicillin or ampicillin.

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Reply

***Carolina Zilli Vieira*[1] *and Bruno Caramelli*[2]**

Harvard T H Chan School of Public Health,[1] Boston, Massachusetts – USA

Instituto do Coração do Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo,[2] São Paulo, SP – Brazil

We thank the authors for the suggestion and the need for an amendment to the Guidelines in response to new data and new recommendations published after the publication of the Guideline for Perioperative Cardiovascular Evaluation of the *Sociedade Brasileira de Cardiologia*.[1] The American Dental Association (ADA) recently published in the site changes in the antibiotic prophylaxis prior to dental procedures.[2] The main important change is the removal of clindamycin from the list of antibiotics in dental practice used to prevent infective endocarditis (IE). The use of clindamycin as prophylactic antibiotic has been removed from the American Heart Association in 2021, due to the risk of adverse reactions.[3] In 2023, the European Society of Cardiology (ESC) guidelines adopted similar regulations. To prevent the risk of IE during dental treatment, it has been recommended:[4,5]

1. Adequate and efficient maintenance of oral hygiene

Oral hygiene is important to reduce the risk of gingivitis and periodontitis, as both increase the risk of bacteremia.[5] Patients at increased risk of developing IE should have regular professional dental care and (re)education on the adequate use of a toothbrush, dental floss, and other devices to remove dental plaque.[5]

2. Use of antibiotic prophylaxis before invasive dental and oral procedures

Invasive dental and oral procedures include the manipulation of gingival tissue, periapical region of the teeth, perforation of mucosa, tooth extraction, dental abscess drainage, dental implant procedure, and routine dental cleaning. The use of antibiotic prophylaxis should be highly considered for severe tonsillitis or peritonsillar abscess, even in children.

3. Treatment of infectious diseases caused by pathogens likely to cause IE.
4. Antibiotic prophylaxis before dental surgery

   The prophylactic antibiotic regimen most recommended is oral amoxicillin (adults: 2 grams, children: 50mg/kg) 30-60 minutes before the procedure. Clindamycin is not recommended anymore due to adverse side effects and the risk of secondary infections, especially Clostridioides difficile infection. Intravenous vancomycin should be administered 120 minutes before the procedure. More details can be found in Table 1
5. Antibiotic therapy is not indicated for: (a) anesthetic injections in healthy tissues; (b) dental radiographs; (c) adjustment of removable prosthodontic or orthodontic; (d) shedding of primary teeth; (e) bleeding from trauma in mucosa.

Table 1 – Regimen of antibiotic prophylaxis for dental procedures (single dose 30 to 60 minutes before procedure) according to American Heart Association (AHA, 2024)

Situation	Agent	Adults	Children
Oral	Amoxicillin	2g	50mg/kg
Unable to take oral medication	Ampicillin OR	2g IM or IV	50mg/kg IM or IV
	Cefazolin or ceftriaxone	1g IM or IV	50mg/kg IM or IV
Allergic to penicillin or ampicillin-oral regimen	Cephalexin OR	2g	50mg/kg
	Azithromycin OR	500mg	15mg/kg
	Doxycycline	100mg	<45kg, 2.2mg/kg - >45kg, 100mg
Allergic to penicillin or ampicillin and unable to take oral medication	Cefazolin or ceftriaxone	1g IM or IV	50mg/kg IM or IV

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