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Review Article

Is antibiotics overuse justified when immediate intervention is not possible? A rapid evidence review

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Abstract

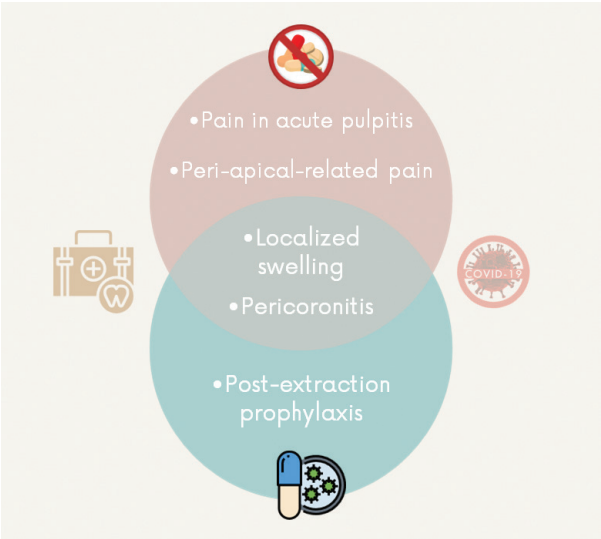
Introduction: This review revisits clinical use of antibiotics for most common acute oro-dental conditions; we aim to provide evidence governing antibiotics use when access to oral healthcare is not available, as during the ongoing outbreak of the severe acute respiratory syndrome coronavirus 2.

Materials and methods: In this rapid review, articles were retrieved after conducting a search on PubMed and Google Scholar. Relevant publications were selected and analyzed. Most recent systematic reviews with/without meta-analyses and societal guidelines were selected. Data were extracted, grouped, and synthesized according to the respective subtopic analysis.

Results and discussion: There was evidence supporting the use of antibiotics in common oro-dental conditions as temporary measure when immediate care is not accessible, such as in case of localized oral swellings as well as to prevent post-extraction complications. No sufficient evidence could be found in support of antibiotic use for pain resulting from pulpal origin.

Conclusion: Antibiotic use may be justified to defer treatment temporarily or reduce risk of complications in case of localized infection and tooth extraction, when no access to immediate dental care is possible.

Graphical abstract:



Keywords

antibacterial agents, antibiotics, COVID-19, drug misuse, odontogenic infection.

Introduction

In the recent decades, the rise of antimicrobial resistance has called for major reform in antibiotic use practices. Many studies have been conducted to quantify and decrease abuse of antibiotics for conditions that can be managed without. In 2016, the Center for Disease Control and Prevention (CDC) reported that around 9.5% of all antibiotics prescriptions was attributed to the dental field (Center for Disease Control 2016). In fact, there is worldwide over-prescription of antibiotics in dentistry for conditions lacking evidence for benefit, especially for some endodontic conditions (Segura-Egea et al. 2017).

Refined guidelines have stressed on the importance of immediate interventional management and only limiting systemic antibiotics prescription to a number of conditions, mainly when there are signs of spreading or systemic involvement of the orofacial infection or when immediate intervention is not possible (AAE 2017a, b; Segura-Egea et al. 2018). Nevertheless, despite the general decline in antibiotic prescriptions in the last decade, Durkin et al. recently showed that around 14% of antibiotic prescriptions by general dentists in the United States were inappropriate (Durkin et al. 2018). This may hold true and even higher in other areas of the world.

However, in the current outbreak of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) worldwide (Lai et al. 2020), and the general discourage of contact and severe limit of elective medical and surgical procedures to managing more serious situations only, access to dental care may be reduced. This also extends to any period of crisis: large-scale civil unrest, wars, natural disasters, and other disease outbreaks. Indeed, many patients would even prefer to decrease visits to health care facilities and postpone any lengthy treatment. Eventually, medical treatment for dental conditions that necessitate dental/surgical intervention mainly consists of over-the-counter analgesics and antimicrobial agents. In such a time, therefore, is empiric antibiotic prescription temporarily justified? What acute conditions may benefit from antibiotics to relieve symptoms and medical risk until further treatment is possible?

Consequently, in this manuscript, we revisit the usefulness of antibiotic prescription in some most-common acute dental conditions in times when immediate access to oral health care is not possible. The clinical significance of such a topic extends from establishing modest clinical guide for dental practitioners, as well as to emergency physicians who may be seeing an increase in dental emergencies during the current crisis.

Materials and methods

A search was conducted on PubMed and Google Scholar using the keywords and MeSH (medical subject headings) terms "antibiotics" and "dentistry" for literature published in the last 10 years (from January 1, 2010 to November 20, 2020). Results were navigated individually, and relevant publications were identified through their titles and abstracts (Fig. 1). Then, further 35 articles were extracted and analyzed, 10 of which were deemed pertinent and consisted of most recent systematic reviews, Cochrane reviews, and societal guidelines on the current topic, and conclusions were drawn out. Only recent systematic reviews with/without meta-analyses and societal guidelines were selected.

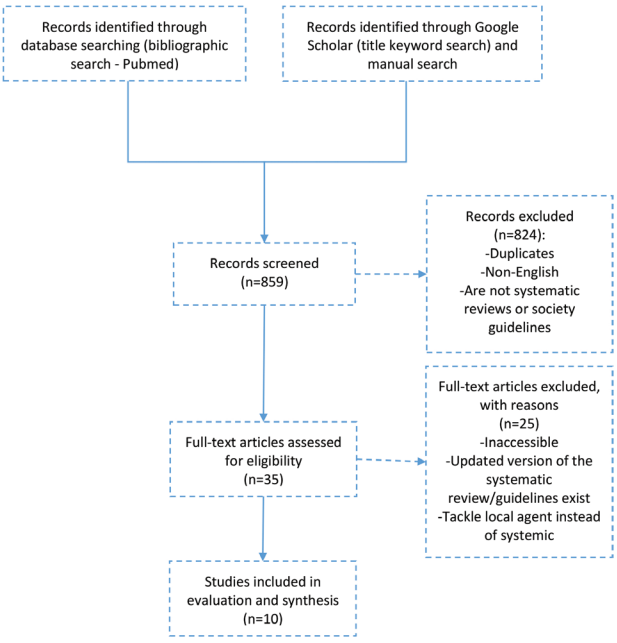


Figure 1. Literature search methodology utilizing PRISMA framework. The search was performed through PubMed and Google Scholar.

Results

The resultant 10 publications included three Cochrane systematic reviews, 4 systematic reviews with/without meta-analyses and 3 societal guidelines or position statements. Included publications with main characteristics are summarized in Table 1.

Table 1. Outline of evaluated publications with main conclusions pertinent to our review and reported limitations

Authors	Type	Year	Condition For Antibiotic Use	Conclusion For Using Systemic Antibiotics	Reported Limitations
Cervino G et al.	Systematic review	2019	Complication prophylaxis following third molar extraction	In favor of use, yet more emphasis on clinician-related factors in influencing post-operative sequelae than antibiotic use	- Unclear bias risk in multiple reviewed studies - Inability to evaluate different regimens
Keenan A et al.	Cochrane systematic review	2019	Pain reduction in irreversible pulpitis	Insufficient evidence with or against the use of antibiotics	Conclusion largely based on a single low-power RCT
Tampi MP et al. (*American Dental Association*)	Systematic review and meta-analysis	2019	Urgent management of symptomatic irreversible pulpitis, symptomatic apical periodontitis, and localized acute apical abscess	- Both a benefit and harm on the outcome of pain and intraoral swelling - Large potential harm from antibiotic use	- Lack of large, robust RCTs - Lack of accurate estimates quantifying the direct impact of dental antibiotic prescribing on health outcomes
Cope AL et al.	Cochrane systematic review	2018	Symptomatic apical periodontitis and acute apical abscess in adults	Insufficient evidence with or against the use of anitbiotics	High risk of bias in one out of two studies
Aminoshariae et al.	Systematic review	2016	Prevention of infection or pain during endodontic treatment	Ineffective if antibiotics are administered pre- or post-operatively	Possible unintended bias: - Empirical regimens were used in most of the reviewed studies - Larger research group is needed
Ramos E et al.	Systematic review and meta-analysis	2016	Prevention of dry socket and infection after third molar extraction	Significant reduction of dry socket and infection risk	Generalizability across reviewed studies as no adjustment is possible for clinician specialty, experience, intra-operative time, procedure complexity, antibiotic regiment and others
Lodi et al.	Cochrane systematic review	2012	Prophylaxis following tooth extraction	Possible reduction of pain, risk of dry socket and infection	High risk of bias in majority of assessed studies (13)
Lockhart PB et al. (*American Dental Association*)	Clinical guidelines	2019	Urgent management of pulpal and periapical-related dental pain and intraoral swelling	Recommended antibiotics use in case of no immediate access to dental care in case of risk of systemic involvement Not recommended if direct access to dental care is available	Low-quality and limited evidence on efficacy, benefits and harms of antibiotics use in the target population
American Association of Endodontists	Position statement	2017	Endodontic infections	Ineffective in treating localized swellings when indicated intervention is performed Clinical judgement based is warranted as no sufficient evidence with or against in case of absence of intervention	No available clear evidence for indication and regimen of antibiotics in such cases
Segura-Egea JJ et al. (*European Society of Endodontology*)	Position statement	2018	Endodontic infections	No indication in cases of symptomatic irreversible pulpitis, pulp necrosis, symptomatic apical periodontitis, chronic apical abscess and acute apical abscess without systemic involvement in healthy individuals with no risk factors	Largely based on non-systematic reviews of literature

Discussion

Acute pulpitis

In a recent systematic review and meta-analysis by Aminoshariae and Khulild which assessed available randomized controlled trials evaluating the benefit of antibiotics in endodontic infections and pain, the researchers reported absence of evidence to support or reject the use of antibiotics in irreversible pulpitis. They analyzed one well-designed trial but with a small power; this trial showed that there was no significant difference in pain relief between individuals with untreated irreversible pulpitis who did or did not take antibiotics in addition to analgesics (Aminoshariae and Kulild 2016). Conversely, Hoskin and Veitz-Keenan as well reported no evidence for antibiotic use in reducing pain in patients with acute pulpitis (Hoskin and Veitz-Keenan 2016).

In a recent systematic review and meta-analysis, Tampi et al. found, after the analysis of 3 trials on the efficacy of systemic antibiotics the urgent management of symptomatic irreversible pulpitis, with or without apical periodontitis, that pain scores were not in favor of antibiotic use up to the 3rd day after the symptom start; in contrast, pain was reported as increased when antibiotics were used. However, surprisingly, they reported slightly better

pain scores in antibiotics group on the 7th day. Nevertheless, they reported increased harm as well along with the same outcome (Tampi et al. 2019).

Finally, Lockhart et al. issued clinical practice guidelines on antibiotic use for urgent management of pulpal and periapical-related dental pain and intra-oral swelling. They recommended against the use of antibiotics for pain reduction in patients with no access to oral healthcare. However, they stated that, in the event that patients have no access to oral healthcare, "clinicians and patients may not find this recommendation acceptable or feasible for implementation given that patients may have high expectations for receiving an antibiotic" (Lockhart et al. 2019).

Localized swelling

Recent recommendations have advised against the use of antibiotics in treating localized swellings, given necessary intervention takes place (AAE 2017b; Segura Egea et al. 2017; Segura-Egea et al. 2018). However, few tackled the indication of antibiotics in case of no immediate access to oral health care.

In cases of pulpal necrosis with localized acute apical abscess, Lockhart et al. suggested that patients with no immediate access to interventional procedures receive antibiotic regimen to avoid risk of possible progression of the infection systemically (Lockhart et al. 2019); however, they did not recommend the use of antibiotics in cases of pulpal necrosis with symptomatic apical periodontitis without swelling.

Regarding pain, a Cochrane review in 2019 evaluated the available randomized controlled trials comparing the effect of the use of antibiotics vs placebo in cases of apical periodontitis and acute apical abscess on pain swelling. There were no statistically significant differences in participant-reported measures of pain or swelling at any of the time points assessed within the review. The review reported no studies that provided antibiotics without endodontic treatment (Cope et al. 2018).

Another type of localized infection that may lead to acute episode of pain is pericoronitis around a semi-erupted tooth. Mild to moderate cases of pericoronitis may be managed with chlorhexidine mouthwash and oral hygiene; in severe pericoronitis, antibiotics in addition to the mouthwash may be necessary (Wehr et al. 2019).

Surgical procedures

Adjunct antibiotics may be provided to certain interventions: pre-operative prophylactic antibiotics, e.g., for immunocompromised patients undergoing surgical procedure, or post-operative to reduce the likelihood of complications and infection, as in extraction, soft-tissue injury, or other conditions.

A Cochrane review conducted in 2012 concluded that antibiotics may reduce pain, risk of dry socket and infection following third molar extraction. However, they did not encourage systematic antibiotic use in healthy patients undergoing third molar extraction (Lodi et al. 2012). In two more recent systematic reviews, both Ramos et al. and Cervino et al. provided a similar conclusion that systematic antibiotics do reduce risk of post-operative infection and alveolar osteitis in patients undergoing third molar extractions (Ramos et al. 2016; Cervino et al. 2019).

Moreover, the use of chlorhexidine, both as gel or mouthwash, is reported to significantly reduce the risk of alveolar osteitis following third molar extraction, with gel being slightly superior to the mouthwash formulation (Daly et al. 2012; Rodríguez Sánchez et al. 2017; Teshome 2017; Zhou et al. 2017).

Therefore, in times of limited access to oral health care, it may seem rational that urgent third molar extractions may be supplemented with antibiotics and chlorhexidine mouthwash or gel to reduce risk of complications and hence avoid a second encounter with the patient, or worse, avoid patient show-up in flooded emergency departments. While there is no enough evidence for antibiotic use following urgent, simple, non-third-molar extractions, principles of third molar management may be generalized to other extractions, and clinicians are advised to follow-up closely with patients in all cases.

Clinical relevance and limitations

Non-traditional antibiotic therapy and prophylaxis may be justified for some acute dental conditions and discouraged for others, as summarized in Table 2. This may help dental and emergency medicine practitioners when evaluating dental emergencies in times of crisis and in areas with no access to care, when definitive dental procedures are not readily accessible.

Limitations of this review are mainly related to its nature. Being a rapid review of evidence, evaluated evidence was limited to the past 10 years. Furthermore, extensive quality assessment of the included reports was not possible (Khangura et al. 2012); to reduce such biases, we attempted to follow a systematic approach in all the study

Table 2. Summary of therapeutic and prophylactic antibiotics use in acute dental conditions when immediate interventional management is difficult

Condition	Antibiotic Use
Acute spontaneous dental pain with no signs of infection	Not recommended
Acute dental pain upon mastication with no signs of infection	Not recommended
Localized swelling	Recommended if no access to immediate intervention *Instruct patient to present to urgent services in case of progression*
Pain in site of semi-erupted third molar/tooth	Recommended in severe cases
Urgent tooth extraction	Recommended to reduce complication risk if follow-up is not possible

phases, and limitations were inferred from each report as was directly evident.

Conclusion

In times of outstanding crises as well as in areas of little access to dental care, temporary measures may include an unconventional approach to dental care. Our review identifies some most common acute dental conditions and the usefulness of systemic antibiotics use. These suggestions are based on scarce evidence and are suggested exclusively in times of limited oral health access; these are only intended for temporary management until standard treatment can be delivered. We strongly recommend following established and indicated definitive treatment approaches whenever possible.

Conflict of interests

The authors declare no conflict of interests.

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