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## Review Antimicrobial prophylaxis in dentistry

### A. Merlos<sup>a,b</sup>, T. Vinuesa<sup>b</sup>, E. Jané-Salas<sup>a</sup>, J. López-López<sup>a</sup>, M. Viñas<sup>b,\*</sup>

<sup>a</sup> Department of Dentistry, Schools of Dentistry and Medicine, University of Barcelona, Feixa Llarga s/n, 08907 L'Hospitalet de Llobregat, Barcelona, Spain <sup>b</sup> Department of Pathology and Experimental Therapeutics, Schools of Dentistry and Medicine, University of Barcelona, Feixa Llarga s/n, 08907 L'Hospitalet de Llobregat, Barcelona, Spain

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#### ABSTRACT

Use of antibiotics both in humans and animals runs along with effects that can contribute to the spread of antibiotic resistance. Although several available guidelines for antibiotic treatment have been published to date, clinical practice in dentistry and particularly in oral surgery is not free from controversies regarding antibiotic prophylaxis. Antibiotic coverage to prevent infectious endocarditis, joint prostheses infections or local infections requires a careful evaluation of the patient condition, associated risks and other aspects that could influence the decision. It is of great relevancy for oral surgeons and for dentists in general to know exactly what they are up against. Here we review the literature regarding prophylactic use of antimicrobials in dentistry.

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#### 1. Introduction

The increasing prevalence of infections caused by multidrugresistant bacteria is now a cause of medical concern and a serious public health problem. This is particularly true in countries in which for several decades the control of antibiotic consumption

\* Corresponding author at: Schools of Medicine and Dentistry,

E-mail address: mvinyas@ub.edu (M. Viñas).

has not been strict enough. At the same time, use of antibiotics for purposes other than human clinics has greatly contributed to the emergence of mechanisms of antimicrobial resistance. A close relationship between induction of antimicrobial resistance in livestock and the emergence of resistant variants in humans has been reported [1–3].

Some of the classic antimicrobial drugs used to treat several types of infection are obsolete since mechanisms leading to antimicrobial resistance have emerged and spread amongst bacterial populations. However, several existing mechanisms of resistance can in some cases affect the efficacy of recently developed drugs. It has been pointed out that the emergence of

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University of Barcelona, University Campus of Bellvitge, Feixa Llarga s/n, L'Hospitalet, Barcelona E08907, Spain. Tel.: +34 934 024 265.

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resistance mechanisms occurs a matter of a few years after initial use of a new antimicrobial and that despite the multiple molecular mechanisms involved in bacterial resistance, withdrawing the antibiotic tends to restore the original phenotype, confirmed both through metagenomic analysis and conventional culture microbiology [4]. Moreover, genomics of the bacterial resistome has permitted the exploration of genes encoding antimicrobial resistance in the past. However, it is feasible that environmental conditions affecting antimicrobial susceptibility have not changed significantly during a long period until the discovery and initial use of antibiotics. It seems clear that in many cases the presence of a gene underlying a given function is necessary but not sufficient to ensure the expression of its function [5].

When analysing causes of the increasing incidence of antimicrobial-resistant bacteria, it has been established that misuse and abuse of antibiotics is one of the main drivers of the emergence of resistant derivatives [6,7]. When a microbe acquires a mechanism that makes it resistant to a drug, the need for further research and investment drives the development of new drugs and then bacteria start a new pathway to become resistant to the new drug. It has been suggested that implementation of policies restricting the use of antibiotics to treat infections in humans and animals under strict supervision of physicians and veterinarians will contribute to diminishing the selective pressure on bacteria in the environment [8]. Such a practice should result in slowing down the rate of emergence of resistant clones. In fact, the speed of development of resistance can be drastically reduced by means of technical interventions. The driver of the process is antibiotic use. It has been demonstrated that genes encoding for resistance already existed before the antimicrobials were discovered and that withdrawing antimicrobials promotes the tendency to recover susceptibility [4].

Health professionals play—or must play—a key role in ensuring appropriate use of antimicrobials. It has been pointed out that dentists can significantly contribute to such a purpose by increasing research efforts, scientific discussions, interaction between basic scientists and clinicians, and eventually reducing (when possible) the use of antimicrobials in their clinical practice [6].

Amongst dentists there has been a 'tradition' to prescribe antibiotics as a prophylactic weapon to prevent post-surgical infections or distant-site infections [9]. Moreover, for many years there has been a routine based on indiscriminate prescription of antimicrobials with lack of scientific evidence, which is considered under the view of basic research as an irresponsible contribution to the misuse of antibiotics on behalf of health professionals [10].

#### 2. Methods

In this paper, we reviewed the published evidence for the use of antimicrobial prophylaxis in dental treatments, particularly in oral surgery. We proceeded to complete a search in the electronic database MEDLINE<sup>®</sup> through PubMed. The search limits established included language (restricted to English) and the period that extended the search dates from 1996 (date in which the term 'Antibiotic prophylaxis' was included as a subject in MeSH) until 2013. The search term combinations were ('Antibiotic prophylaxis' [MeSH] and 'Dentistry' [MeSH]) and ('Antibiotic prophylaxis' [MeSH] and 'Oral surgical procedures' [Mesh]). Duplicate articles or those whose investigation did not correlate with our parameters were ruled out. The second phase was a manual search to identify relevant papers or reviews proceeding from the references of the articles collected in the first phase, with the purpose of considering all articles to avoid missing any relevant contribution owing to a mistaken selection of the search terms. Only those articles published within the indicated period and whose nature was a review, meta-analysis, randomised controlled trial (RCT) or

observational study (case-control or cohorts), as well as publications from official organisations and guidelines, were included. Studies on animals, on humans in which the sample size was  $\leq$ 20 and on humans that did not meet the inclusion criteria were excluded.

#### 3. Results of the literature review

The first search yielded 325 articles collected from the electronic database MEDLINE obeying the search terms. In the second phase, another 19 were added. According to the inclusion and exclusion criteria, only 40 were used, of which 12 were bibliographic reviews, 3 were meta-analyses, 19 were RCTs and 6 were official organisation publications and guidelines. With reference to the contents, literature for and against prescribing antibiotic prophylaxis was found for each entity or pathological state as well as for each surgical procedure.

#### 3.1. Infective endocarditis

A worrying aspect regarding infectious pathology in dentistry is the possibility of triggering infective endocarditis (IE) [11]. IE is an uncommon infection that can be caused either by bacteria or fungi (the latter is the origin in 2–4% of cases) [12]. The most frequently involved bacteria are oral streptococci, with a high incidence of  $\alpha$ -haemolytic *Streptococcus viridians*, and *Staphylococcus aureus* [11,13]. Micro-organisms reach the circulatory system through ruptures in capillaries of the bones/gums and adhere to irregular surfaces, i.e. damaged heart valves, joint or valve prostheses, etc., which often are covered by platelets and fibrin [7]. If bacteria colonise such surfaces after bacteraemia, they can proliferate within a vegetation, with the consequent growth of bacterial or fungal populations, where they grow out and find protection eventually causing valve destruction [7].

Yearly cases of IE range from 3.1 to 7.9 cases/100 000 inhabitants as reported from several countries, USA among them, with an increased incidence with age [14,15]. In Spain, the numbers are 40–60 cases for every 1 000 000 habitants [16]. Despite antibiotic treatment, mortality of IE nowadays is still high (10–20%) [17]; even in optimal conditions when the bacterium is susceptible to the antibiotic prescribed and the dosage is adequate, only a small proportion of cases would be effectively prevented [7,18]. From the 1955 American Heart Association's (AHA) first antibiotic prophylaxis guidelines document, several countries and committees have published new updated versions. In the ninth edition of the AHA document (2007) [7], the list of eligible patients to receive antimicrobial prophylaxis was reduced to those with a high risk of fatal outcome from an IE process, such as valve prostheses carriers, IE background, congenital heart disease (heart defect repaired in the previous 6 months; unrepaired cyanotic congenital heart disease, including palliative shunts and conduits) and cardiac transplant recipients with current cardiac valvulopathy [7]. Native valve diseases such as mitral valve prolapse or bicuspid aortic valves and other heart defects are no longer risk factors for receiving antimicrobial prophylaxis. Thus, antimicrobial prophylaxis is recommended in these defined high-risk patients in any dental surgery procedure that may cause bacteraemia, i.e. manipulation of gingival tissue or the peri-apical area, oral mucosa perforation (biopsies, surgeries, etc.), suture and its removal, and placement of orthodontic bands. Any other procedures such as placement of orthodontic brackets, trial fittings, removal or adjustment of removable prosthodontic or orthodontic appliances, injections in non-infected tissue, oral radiographies, etc., do not require antimicrobial prophylaxis [7]. However, the definition of at-risk patients can be highly variable depending on regions and countries. In South Africa, most (88%) of clinicians were aware of

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