Systemic Antibiotic Prophylaxis in Maxillofacial Trauma

Subjects: Surgery

Contributor: Femke Goormans, Ruxandra Coropciuc, Maximilien Vercruysse, Isabel Spriet, Robin Willaert, Constantinus Politis

Infection after maxillofacial trauma remains an important complication, with a significant socio-economic impact. While consensus exists that systemic antibiotic prophylaxis reduces the risk of infection in the management of maxillofacial fractures, the type, and duration remain controversial.

Keywords: antibiotic prophylaxis ; anti-bacterial agents ; maxillofacial injuries ; bone fractures ; infections

1. Introduction

Infection after maxillofacial trauma remains an important complication [1], leading to significant morbidity and increased healthcare costs [2]. Overall, infection rates after maxillofacial fractures vary widely across studies and range from 0% to 62% [3][4]. Accurately estimating the incidence and impact of this complication is hampered by the lack of a clear definition, and the variability in outcome parameters renders existing studies difficult to evaluate and compare [5].

Systemic antibiotic prophylaxis is an accepted strategy to prevent infection in daily clinical practice [6]. However, the optimal type and duration remain controversial [7]. An awareness of the need for standardized, evidence-based guidelines has increased in recent years [8]. Furthermore, antimicrobial resistance (AMR) is increasing, and physicians are becoming aware of the importance of limiting antibiotic use [9].

Contemporary guidelines state that antibiotic prophylaxis should be provided for no longer than 24 h [10]. However, these recommendations are mainly based on a handful of clinical studies and uncertainty persists regarding the optimal antibiotic regimen for infection prevention. Previously published systematic reviews often included studies with a significant risk of bias, leading to a misrepresentation of the currently available evidence [1][3][6][7][11][12][13][14][15][16][17]. For these reasons, and on a worldwide scale, heterogeneity in infection prevention protocols still exist. Recent international surveys among maxillofacial trauma surgeons indeed concluded that most surgeons continue antibiotic prophylaxis longer than proposed, which leads to an important overuse of antibiotics [16][17]. Similar issues are currently encountered in infection prevention protocols for long-bone fractures [18][19].

2. Systemic Antibiotic Prophylaxis in Maxillofacial Trauma

2.1. Duration of Systemic Antibiotic Prophylaxis

Prolonged antibiotic prophylaxis does not appear to be beneficial in the prevention of infection. For mandibular fractures, continuing antibiotic prophylaxis for 24 h after wound closure is advised, but not beyond this time frame [20][21][22][23][24][25][26][27][28][29]. For upper and midface fractures, the benefit of continuing antibiotic prophylaxis for 24 h is questioned [22]. For conservatively treated fractures of the middle and upper facial third, there is no evidence for the use of systemic antibiotic prophylaxis at all [30].

2.2. Antibiotic Type and Duration

Although most studies administered β-lactam antibiotics, the antibiotic agents that were prescribed varied widely. In retrospective studies, a wide variety of antibiotics or combinations was often administered without specifying the reasoning for administering the different antibiotic types to different patients [23][24][29][31]. Future trials should be based on a single regimen to avoid possible confounding. Furthermore, the duration of antibiotic prophylaxis varied and none of the studies had the same research question.

2.3. Causal Pathogens

The selection of prophylactic antibiotics for infection prevention should consider the susceptibility of potential pathogens to these antibiotics [32]. Therefore, knowledge of the type of causative pathogens in infection related to the treatment of

maxillofacial trauma is required. When the source of pathogens is skin flora, cefazolin is the antibiotic of choice as it covers Gram-positive cocci (i.e., *Staphylococcal species*) [32]. In maxillofacial trauma surgery, where pathogens may include oropharyngeal flora (*Streptococcal species*; oropharyngeal anaerobes (i.e., *Peptostreptococcus species*)), broad-spectrum antibiotics may be indicated (amoxicillin with clavulanic acid, or cephazolin with metronidazole) [33].

The gold standard for a diagnosis of infection remains the deep tissue cultures, obtained from intraoperative samples [34]. Data on other techniques, such as a culture of sonication fluid from hardware, polymerase chain reaction (PCR), and histopathology (i.e., the presence of polymorphonuclear neutrophils (PMNs)) have not been described with respect to the diagnosis of infection after a maxillofacial trauma. For long-bone fractures, sonication of the osteosynthesis material and subsequent inoculation of sonication fluid has already proven to be useful in diagnosing infection [34]. Using low-intensity ultrasound, sonication is deployed to dislodge the biofilm from the osteosynthesis material. The sonication fluid is then cultured onto bacterial media for further analysis [34]. Sonication may be a way to avoid the contamination of tissue cultures with oral flora, and high-quality studies are needed to substantiate the utility of sonication in the treatment of infection after maxillofacial fractures.

Future trials should thoroughly describe the causal pathogens related to infection after maxillofacial trauma, identified by culture. High quality, uncontaminated, deep tissue and implant samples are essential to validate culture outcomes [35]. Furthermore, to avoid false-negative culture results, it is generally advised to stop antimicrobial therapy two weeks before sampling [35].

2.4. Fracture Type

A mandibular fracture is considered open when the fracture site communicates either intraorally through the mucosa or extraorally through a laceration or avulsive injury of the overlying skin. Therefore, all fractures involving the tooth-bearing areas of the jaws are regarded as open fractures [36]. Any mandibular fracture that does not have extraoral communication and/or involves the tooth-bearing area is considered a closed fracture (e.g., condylar fracture) [36]. Numerous studies have shown that an open fracture is considered a significant risk for infection [23][37][38]. Therefore, not reporting whether the included fractures are open or closed makes the interpretation of the study results almost impossible. As most open fractures are contaminated with microorganisms, immediate antibiotic administration, wound debridement, soft-tissue coverage, and fracture stabilization are necessary [39]. While an immediate antibiotic administration at admission is the standard of care for long-bone open fractures [39], evidence is lacking for maxillofacial fractures and studies have not been able to objectify this benefit [40], possibly due to the limited number of included patients and insufficient follow-up. There is a need for high-quality studies evaluating the benefit of starting antibiotic prophylaxis at admission for open maxillofacial fractures.

2.5. Surgical Treatment

Fracture stability is of the utmost importance in the prevention of infection. Instability leads to ongoing soft-tissue trauma, interruption of neo-vascularity and osteolysis of bone, which creates a supportive environment for bacterial proliferation [41]. However, both surgical therapy (e.g., fracture stability) and the timing of fracture fixation were poorly described [20][22][23][24][25][26][27][29][30][31][37].

Surgical treatment of mandibular fractures is performed using ORIF or CR and maxillomandibular fixation (MMF). Standard MMF methods are either tooth-supported (arch bars, interdental wires, or Ernst ligatures), or bone-supported devices such as intermaxillary fixation (IMF) screws [36]. An open procedure may lead to a four-fold higher rate of infection [23][42].

2.6. Outcome Description

The lack of a uniform definition for infection after maxillofacial trauma also contributed to the scarcity of comparable data. Using inadequate outcome parameters risks underestimating or overestimating the actual number of complications, resulting in misleading study conclusions [5]. The absence of a universally accepted definition of infection after maxillofacial trauma mirrors the situation for fracture-related infection (FRI) in long-bone fractures and prosthetic joint infection (PJI) identified many years ago [43].

To date, the term FRI has not been used to describe infection following maxillofacial trauma. Although general treatment principles may differ, and significant differences exist with respect to the blood supply at the fracture site and the bacterial flora present at the site of injury, the basic diagnostic principles are similar. The definition of FRI is based on clinical, laboratory and radiological features that confirm or exclude the presence of infection. The described confirmatory and

suggestive criteria could also apply to maxillofacial trauma and possibly be utilized to diagnose (and define) infection [5]. The term FRI covers both surgically treated as well as conservatively treated fractures, which is why scholars prefer to use the standardized term of FRI even though it has not yet been widely accepted within oral and maxillofacial surgery practice.

2.7. Implications of Antibiotic Overuse

Antibiotics are a worldwide leading cause of adverse drug reactions and emergency department visits [44]. Prolonged systemic antibiotic prophylaxis can be associated with, rash, diarrhea and *Clostridioides difficile* infection, nausea, vomiting and abdominal pain, malaise, and fatigue [45][46].

Furthermore, prolonged antibiotic prophylaxis could possibly contribute to delayed infectious complications. Zosa et al. described a significantly increased infection risk for patients receiving prolonged antibiotic prophylaxis over seven days [29], and Miles et al. found that patients who received extended antibiotic prophylaxis developed late infectious complications [25].

Finally, the overuse and improper use of antibiotics are considered important drivers for the emergence and spread of AMR [47]. AMR occurs as a natural evolutionary response to antimicrobial exposure, whereby microorganisms acquire the ability to withstand antimicrobial drugs via mutations in chromosomal genes and by horizontal gene transfer [47]. The global spread of AMR may compromise our ability to treat existing and emerging common infectious diseases, as well as undermining many other improvements in health care. Maxillofacial surgeons, like all healthcare workers, should realize that AMR is a global health problem. Antimicrobial stewardship promotes the appropriate use of antibiotics based on internationally accepted guidelines, leading to effective prevention and treatment of infections while avoiding the harmful effects of antibiotic use [47].

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