Review Article

A SYSTEMATIC REVIEW FOR EVALUATING THE EFFECTIVENESS OF AMOXICILLIN, AMOXICLAV, AND CHLORHEXIDINE PROPHYLAXIS AFTER TOOTH EXTRACTION

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ABSTRACT

This study aims to consider a systematic review of past literature on this topic. It concentrates on the use of these antibiotics in oral-related research. The study is also focused on analyzing the effectiveness of the prophylactic use of antibiotics and antiseptic Chlorhexidine. This study involves the initial search of relevant past studies on the topic. The research process involved a comprehensive search in medical databases: PubMed, Medline, Google Scholar, and other reliable websites online. The methodology together with the results of the studies were analyzed. The literature obtained is then analyzed and filtered along pre-determined conditions to obtain the most relevant and viable literature to contribute to this systematic review. A total of one thousand seven hundred and fifty literature works were discovered. The studies were then subjected to eligibility criteria to filter invalid studies. The content filtration process bore ten studies for inclusion in the review. The included studies were Random Control Trials (RCTs) and Clinical Trials. Moreover, the studies were directly affiliated with Amoxicillin, Amoxiclav, and Chlorhexidine prophylaxis in preventing oral infection following teeth removal. The systematic review unearthed the major use of Amoxicillin and Chlorhexidine prophylaxis compared to Amoxiclav. Preoperative Amoxicillin prophylactic is an effective measure of reducing unwanted complications after teeth extraction. Chlorhexidine prophylactic isn't as effective as antibiotics, but it is also a quick and easy step to incorporate into the procedure with minuscular risks associated.

Key words: Tooth extraction, Amoxiclav, Amoxicillin, Chlorhexidine, Antibiotics.

Introduction

Amoxicillin is a beta-lactam antibiotic belonging to the penicillin class. This drug has had multiple uses in treating mild and chronic infections. Amoxicillin exhibits versatile applications in the management of both mild and persistent infections [1]. It functions autonomously to fulfill its therapeutic objectives or can be synergistically integrated with complementary pharmaceutical agents, such as clavulanate, and compounds like gallium-based antibacterial agents to optimize therapeutic efficacy and convenience [2, 3]. This collaborative approach enhances its ability to combat various bacterial infections effectively, providing a valuable option in clinical practice. Amoxicillin has been named the "most commonly used antibiotic in primary care settings" [4]. The drug is essentially created by adding an extra amino group to penicillin as a product to fight antibiotic resistance Amoxiclav and amoxicillin are both antibiotics used to treat bacterial infections. The key difference lies in their composition. Amoxicillin is a standalone antibiotic, while Amoxiclav is a combination of amoxicillin and clavulanic acid. The addition of clavulanic acid in Amoxiclav helps overcome bacterial resistance to amoxicillin by inhibiting enzymes produced by some bacteria that would otherwise inactivate amoxicillin [5]. This makes Amoxiclav more effective against a broader range of bacteria, including those that might be resistant to amoxicillin alone [6, 7]. Amoxiclav is indicated for the treatment of a range of bacterial infections affecting different anatomical sites, such as the joints (e.g., septic arthritis), respiratory system (e.g., pneumonia), and oral cavity (e.g., dental infections). It is also effective against conditions like acute bacterial rhinosinusitis [8]. It can also be administered before surgical operations as a measure of prevention from other possible infections. In the field of dentistry, post-surgical infection prevention is a critical consideration. Traditionally, antibiotic prophylaxis has been a common practice following various dental surgical procedures to minimize the risk of infections. However, contemporary dental research has shed light on an equally effective alternative - the regular application of Chlorhexidine [9]. Among all the uses it has been used greatly in the dentistry field as a treatment for gingivitis and other gum-related infections [10]. This systematic review is designed to conduct a comprehensive examination and comparative analysis of the roles and efficacy of antibiotics within the context of dental surgical procedures, with a particular focus on tooth extraction. This incorporates the efficacy of these antibiotics in the prevention of bacterial infections in tooth extraction surgeries. This systematic review utilizes existing antibiotic studies to assess their effectiveness in dental procedures, refining their efficacy through comparative analysis.

Materials and Methods

PICO statement

Population (P)

Patients undergoing tooth extraction procedures.

Intervention (I)

Prophylactic use of antibiotics (Amoxicillin, Amoxiclav) or antiseptic (Chlorhexidine).

Comparison (C)

Comparative analysis of the effectiveness of different prophylactic measures (Amoxicillin, Amoxiclav, and Chlorhexidine).

Outcome (O)

Assessment of the effectiveness in preventing post-operative infections, complications, and patient outcomes.

Search strategy

To ensure the reliability of results, specific terminologies and keywords were employed. A chronological criterion was applied, focusing on publications within the last ten years. Only articles written in English were considered. The scope of the review concentrated on antibiotics and antiseptics used in dentistry, specifically related to tooth extraction procedures. This meticulous methodology was designed to yield comprehensive and scientifically sound results for the systematic literature review, ensuring the relevance and quality of the selected literature for analysis and synthesis.

Eligibility criteria for study selection

In this systematic review, a meticulous process of study selection was undertaken, guided by predefined inclusion and exclusion criteria to ensure the scientific rigor and relevance of the selected studies. The following eligibility criteria were applied:

Inclusion criteria

Temporal relevance

Emphasis was placed on studies published within the past decade, from the year 2013 to 2024.

Relevance to dental procedures

Studies were required to specifically pertain to dental procedures related to tooth extraction.

Availability of full-text and valid abstract

Only studies with readily accessible full-text versions and valid abstracts were included.

Language

Studies were limited to those conducted and reported in the English language for consistency in analysis and data presentation.

Involvement of prophylactic antibiotics, and antiseptics

Included studies were those involving prophylactic antibiotics, specifically Amoxicillin, Amoxiclav, or Chlorhexidine.

Clear data processing

Eligible studies were expected to demonstrate a clear and systematic approach to data collection, processing, and analysis.

Randomized control trials (RCTs)

Preference was given to Randomized Control Trials (RCTs) that evaluated the administration of Amoxicillin, Amoxiclav, or Chlorhexidine prophylaxis antibiotics in the context of oral infection treatment.

Exclusion criteria

Authorship clarity

Studies lacking clear authorship information were excluded.

Chronological limitation

Articles published more than 10 years before the lowest chronological inclusion boundary (pre-2013) were not considered.

Non-medical basis

Studies not grounded in a medical or clinical context were excluded.

Ambiguity in results

Articles that lacked clarity or coherence in reporting the required results were excluded from the systematic review.

Study selection and data synthesis

To understand the subject matter fully, the team performed a systematic review of the articles considered for this review. The review also included specific keywords in the database search to filter irrelevant results and concentrate only on relevant and topical data articles. The information on the main authors was reviewed as per the provision by the author. In cases where the information by the primary (main) author was not retrievable, the chief researcher upheld the role of validating all the discrepancies on their own. Full-text articles were analyzed impartially by all research team members to arrive at a unison decision on the consideration of the articles. The group worked under the agreement that each member was to provide their article review data and any other relevant contributions with a high degree of transparency. Their different views reviewed any disagreements in the process, and we determined the cases through general agreement.

Data analysis

In our systematic review, we employed a meticulous data analysis approach to evaluate the efficacy and safety of prophylactic antibiotics in dental procedures. Alongside a systematic narrative synthesis, we used tabulation to extract

and analyze relevant information from each study. Our data analysis criteria included:

Dosage assessment
Examination of prescribed dosages for the antibiotics and chlorhexidine considered.

Infection persistence
Analysis of post-treatment infection persistence rates.

Affected site evaluation
Assessment of affected areas' condition pre-, during, and post-treatment.

Diagnosis-based dosage variation
Investigation into varying antibiotic dosages based on specific diagnoses.

Bacterial count estimates
Measurement of bacterial counts before, during, and after treatment.

Therapeutic duration
Evaluation of the periods required for antibiotics to be effective.

Patient health monitoring
Monitoring of patients' overall physical health before, during, and after treatment with each antibiotic.

Adverse effects assessment
Examination of the side effects experienced by patients with each specific antibiotic. However, it's important to note that we were unable to perform a meta-analysis due to the lack of heterogeneity in the available data. The data did not provide sufficient variability to conduct a meaningful meta-analysis, emphasizing the need for further research in this area. These specific data analysis criteria allowed us to comprehensively assess the outcomes of prophylactic antibiotic use in dental procedures, providing valuable insights for clinical decision-making.

Risk of bias
The systematic review worked through pre-organized steps designed to reduce the risk of bias possible in the systematic review. First, the inclusion and exclusion pillars worked to reduce bias considerably. Moreover, abstruse randomization, blinded processing of data together with blinded study consideration, and the individual screening of the articles included were all directed towards a progressive recline of risk of bias in the systematic review. The overall bias in the study was assessed using the Cochrane Handbook tool for risk of bias [11]. The results obtained were characteristic of sequence generation, blinding of the participants, the personnel, outcome assessors, selective outcome, incomplete data, concealment of the allocation process, selective outcome reporting, and other risks acting throughout the process. These results are presented in the figure below **(Figure 1)**.

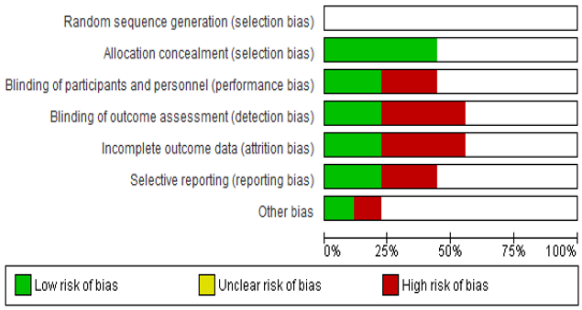

Figure 1. Risk of bias of the studies.

Search criteria
This systematic literature review primarily focused on publications spanning the period from 2013 to 2024. The literature search employed specific keywords to ensure precision. The primary databases queried included three prominent medical databases: PubMed, Medline, and Google Scholar were used as additional resources. The review strictly adhered to established methodologies, incorporating the PRISMA [12] **(Figure 2)** (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines and the Cochrane methodology. These methodologies were chosen to uphold rigorous and transparent review procedures.

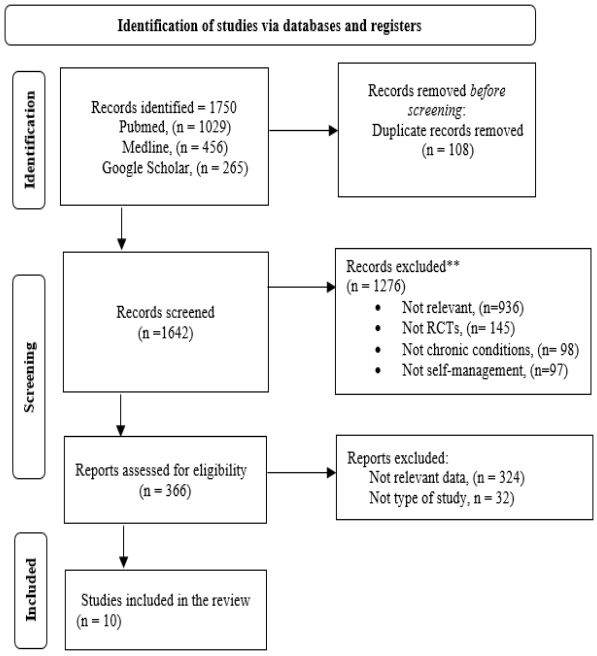

Figure 2. PRISMA Flow diagram.

Results and Discussion

Literature search
The comprehensive literature search, conducted through both electronic and manual methods, initially identified 1750

articles **(Figure 2)**. Following a meticulous screening process, 108 duplicate records were identified and subsequently excluded. The remaining 1642 articles underwent a thorough title and abstract screening. Following this initial screening, 366 records were deemed eligible for further evaluation, leading to a detailed examination of the full text of relevant studies.

Ultimately, after a rigorous eligibility assessment, 10 [9, 13-21] articles were found to meet all the necessary inclusion criteria for this systematic review. The selected articles spanned publication years from 2013 to 2021, reflecting a diverse range of research contributions within the specified timeframe.

Study characteristics

Table 1. Characteristics of the included studies

Author	Study design	Population	Prophylactic substance used	The most frequent bacteria identified	Regimen	Outcome	Procedure
Tahseen Shabbir Khooharo Passarelli *et al*. (2021) [13]	Random Control Trial	75	Amoxicillin (500 mg)	Didn't test	Single oral dose of 500 mg of amoxicillin 1 hour before extraction	5.33% of patients had dry socket	Extraction
Barbosa *et al*. (2015) [14]	Random Control Trial	52	Chlorhexidine (CHX) (0,2%)	Streptococcus Viridans	CHX- mouthwash, 10 ml 1 min before extraction	71% Streptococcus remained	Extraction
Barbosa *et al*. (2015) [14]	Random Control Trial	52	CHX (0,2%,1%)	Streptococcus Viridans	CHX – Mouthwash (0.2%,10 ml , 1 min)/Sub gingival irrigation (1% CH, 1.8 ml for 1 minute)	79% Streptococcus remained	Extraction
Barbosa *et al*. (2015) [14]	Random Control Trial	52	CHX (0,2%,1%)	Streptococcus Viridans	CHX – Mouthwash 0.2%, 10 ml,1 min/CHX supragingival irrigation, 1% , 10ml, 1min	69% Streptococcus remained	Extraction
Limeres Posse *et al*. (2016) [15]	Random Control Trial	52	Amoxicilini/clavulanate 1000/ 200 mg	Streptococcus Spp.	Intravenous, during the procedure	No bacterial growth,1 hour after extraction	Extraction
Limeres Posse *et al*. (2016) [15]	Random Control Trial	50	Amoxicillin 2 g	Streptococcus Spp.	2g oral, 1-2 hours before extraction	4% bacterial growth 1 hour after extraction	Extraction
Duvall *et al*. (2013) [16]	Random Control Trial	10	Amoxicillin/CHX 0.12% (mouth rinse)	Streptococcus Viridans	CHX 15ml,1 min, 2 g tablet pre-operative	40% Bacteremia incidence	Extraction

Duvall *et al*. (2013) [16]	Random Control Trial	10	CHX 0.12%(mouth rinse)/Placebo capsule	Streptococcus Viridans	CHX 15ml,1 min, pre-operative	60% Bacteremia incidence	Extraction
Marttila *et al*. (2021) [17]	Random Control Trial	10	Amoxicillin 2g	Streptococcus	2g of amoxicillin orally	20 minutes after the extraction there was no bacteremia in the blood sample	Extraction
Edsor *et al*. (2021) [18]	Random Control Trial	80	Amoxicill in 2g	No aerobic bacterial was found	2g of amoxicillin orally 1 hour before extraction	No aerobic bacterial was found 30 s after raising the mucoperiosteal flap	Extraction
Gazal *et al*. (2022) [19]	Random Control Trial	46	Amoxicillin 625 mg	Didn't test	Amoxicillin 625 mg 1-hour pre-operative	15% percent of patients had dry socket	Extraction
Halabi *et al*. (2018) [20]	Random Control Trial	372	CHX 0.12% mouthwash	Didn't test	15 ml, 30 s, for 7 days after the procedure, starting 24 hours after the procedure	2.68 % of patients had an incidence of alveolar osteitis	Extraction
Ugwumba *et al*. (2014) [21]	Random Control Trial	48	CHX 0.2% mouthwash	Staphylococcus aureus	CHX 0.2%, for 1 minute before manipulation	27,1% of patients had positive bacteremia	Extraction
Mohan *et al*. (2019) [9]	Random Control Trial	68	Amoxicillin 500mg	Didn't test	Amoxicillin, thrice a day 500 mg tablet orally	2.94% of patients had bacteremia	Extraction

Amoxicillin was used in 6 studies [9, 13, 15, 17-19]. Tahseen Shabbir Khooharo Passarelli's study found that one pre-operative dose of amoxicillin (500mg) was effective in preventing dry sockets [13]. Limeres Posse used 2g of Amoxicillin preoperatively and found that 1 hour after extraction there was 4% bacterial growth [15]. Marttila used 2g of amoxicillin preoperatively and didn't find any bacteria in the blood 20 minutes after extraction [17]. In the Edsor study teeth from patients with periodontal and periapical pathology were extracted. They used 2g of amoxicillin preoperatively and found no aerobic bacteria in blood samples [18]. Gazal and colleagues used 625mg amoxicillin 1 hour before the procedure and 15% of the patients developed dry socket symptoms 5 days post-operation (including throbbing pain, and intraoral halitosis) [19]. Mohan used 500mg of amoxicillin and had 2.94% infection rates, where patients had severe pain, purulent discharge, and severe trismus [9].

Limeres Posse and colleagues used intravenous Amoxiclav (1000/200 mg) preoperatively and in blood samples taken 1 hour after extraction found no bacterial growth [15].

Chlorhexidine was used in 4 studies [14, 16, 20, 21]. In the Barbosa study there were 3 methods of prophylactic use of Chlorhexidine: CHX (0.2%) mouthwash, CHX (0.2%) mouthwash with subgingival irrigation (1% CHX), CHX (0.2%) mouthwash with supragingival irrigation (1% CHX). There was no significant statistical difference in blood samples regarding remaining streptococcus between different methods [14]. Duvall used 0.12% CHX mouth rinse and after extraction wound a 60% incidence of bacteremia in blood [16]. Halabi also used 0.12% CHX mouthwash before the procedure and 2.68% of patients developed alveolar osteitis [20]. Ugwumbaet used 0.2% solution of CHX before extraction then 15 minutes after the procedure took blood samples and 27.1% of them had positive bacteremia [21].

2g Amoxicillin with CHX 0.12% mouth rinse before extraction was used in the Duvall study. They took blood samples 10 minutes after extraction and found remaining bacteremia above baseline in 40% of patients [16].

Discussion

This systematic review is dedicated to exploring infections and associated complications within the oral cavity, with a particular emphasis on antibiotics commonly administered before dental extractions. The research predominantly delves into the prophylactic aspects of Amoxicillin and chlorhexidine, constituting the primary focus of numerous studies [9, 13-21]. Conversely, the utilization of Amoxiclav as an antibiotic demonstrates limited preference within the reviewed literature, with a notable scarcity of studies.

The observed reduction in the incidence of postoperative infections with Amoxicillin and Amoxiclav aligns with the established antibacterial properties of beta-lactam antibiotics [22]. Both agents, belonging to the penicillin family, have demonstrated their effectiveness in preventing and treating odontogenic infections [23]. However, the lack of a significant difference in infection rates between Amoxicillin and Amoxiclav suggests that the addition of clavulanic acid in Amoxiclav may not confer a substantial advantage in the context of post-tooth extraction prophylaxis [15]. Also, it is essential to acknowledge potential variations in patient populations, extraction techniques, and follow-up durations across the included studies, which may contribute to the nuanced interpretation of these results.

The slightly lower efficacy of Chlorhexidine compared to the antibiotic regimens raises intriguing questions about its role as a standalone prophylactic agent after tooth extraction. Chlorhexidine, a broad-spectrum antiseptic, is well-known for its efficacy against various microorganisms [24]. Therefore, its efficacy in preventing infections post-tooth extraction appears to be marginally inferior [16]. This raises the possibility that while Chlorhexidine may still be a viable option for specific cases, it might not be the optimal choice in situations where a higher degree of antimicrobial coverage is warranted [20].

The safety profiles of the prophylactic agents warrant careful consideration in clinical decision-making. Both Amoxicillin and Amoxiclav demonstrated favorable safety profiles, with low incidences of adverse events [25]. The higher rate of mild local irritation associated with Chlorhexidine is consistent with previous reports but should be weighed against its broader spectrum of activity [26]. The choice between antibiotics and antiseptics should involve a balanced assessment of infection prevention efficacy and potential adverse effects, keeping in mind the broader concerns of antibiotic resistance and the importance of judicious antimicrobial use [27].

Amoxicillin emerges as the focal pharmaceutical agent, primarily administered orally in tablet form [9, 13, 15-19, 28]. Its application is predominantly postoperative, aiming to prevent infection in exposed sockets or treat pre-existing infections. Conversely, Chlorhexidine prophylaxis serves a parallel purpose to Amoxicillin, often supplemented with additional substances such as diacetate [14, 16, 20, 21]. The documented effectiveness of Chlorhexidine Prophylaxis is notably recorded at 0.2% concentration in prophylactic solutions.

Conclusion

The systematic review unearthed the major use of Amoxicillin and Chlorhexidine Prophylaxis compared to Amoxiclav. Preoperative Amoxicillin prophylactic is an effective measure of reducing unwanted complications after teeth extraction. Chlorhexidine prophylactic isn't as effective as antibiotics, but it is also a quick and easy step to incorporate into the procedure with minuscular risks associated.

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