Stomatologija. Baltic Dental and Maxillofacial Journal, 26: 57-67, 2024

The role of antibiotic prophylaxis for healthy patients in tooth extraction and implantation procedures: A systematic review

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SUMMARY

Background and Objectives. Prophylactic antibiotics are frequently prescribed following outpatient oral surgical procedures to minimize the risk of surgical site infections. However, the overuse of antibiotics contributes to microbial resistance and increases the likelihood of adverse side effects. This highlights the need for a rational approach in assessing the necessity and appropriate dosing of antibiotics after outpatient oral surgeries. The primary aim of this study was to systematically analyze the literature on the use of prophylactic antibiotics in outpatient oral surgery.

Materials and Methods. Scientific articles were selected following PRISMA guidelines. The review included randomized controlled trials (RCTs) published in English between 2013 and 2023. Data searches were conducted on PubMed, ClinicalKey, and Cochrane Library databases.

Results. A total of 15 RCTs involving 3,032 participants were included in this review. Of these, six studies reported no statistically significant differences between groups in terms of post-operative outcomes. In contrast, six studies focusing on tooth extraction reported significant differences in pain, swelling, trismus, and bleeding between the groups. Additionally, three studies on dental implant procedures revealed significant differences concerning implant failure rates, flap closure, and pain levels. Despite these findings, the overall evidence did not demonstrate statistically significant benefits of prophylactic antibiotics in reducing post-operative infectious complications. Furthermore, no evidence was found to support the importance of timing in the administration of prophylactic antibiotic therapy.

Conclusions. The findings of this systematic review do not support the routine use of prophylactic antibiotics for healthy patients to prevent post-operative infections in outpatient oral surgical procedures. Further research is needed to establish clear guidelines on the necessity and optimal timing of antibiotic use in such cases.

Keywords: antibiotic, prophylaxis, tooth extraction, dental implant.

INTRODUCTION

The discovery of antibiotics in the early 20th century significantly changed medical practice, providing new opportunities for the treatment and prevention of infectious diseases. In 1928, British microbiologist Alexander Fleming, while observing staphylococcal colonies in a Petri dish, noticed a mold that formed a clear zone free of bacterial colonies. This revolutionary discovery marked the beginning of penicillin, the first antibiotic, and led to the production of antibiotics in the mid-20th century, which increased the average lifespan by about 20 years (1). Antibiotics work by inhibiting bacterial growth or killing bacteria and are used to treat various bacterial infections. They can also be prescribed prophylactically to prevent infections after surgical procedures (2). The National Health Service (NHS) in the United Kingdom emphasizes that antibiotics should only be prescribed when necessary—in cases of infections that would not resolve or would complicate without antibiotics (3).

Despite significant benefits of antibiotics, their overuse has led to serious problems due to the

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development of bacterial resistance. According to the World Health Organization (WHO), infections caused by antibiotic-resistant bacteria contribute to millions of deaths each year, and this number is rising (4). Additionally, irrational use of antibiotics increases the risk of side effects. These side effects can range from mild, such as nausea and diarrhea, to severe allergic reactions.

In Lithuania, dental practitioners and outpatient oral surgeons commonly prescribe amoxicillin and clindamycin as first-line antibiotics due to their broad spectrum of activity (5). These antibiotics work through bacteriostatic or bactericidal mechanisms: amoxicillin inhibits bacterial cell wall synthesis, while clindamycin prevents protein synthesis, thereby stopping bacterial replication (6, 7). In dental practice, antibiotics may be prescribed before surgery, after it, or during both periods to reduce the risk of postoperative infections. Prophylactic antibiotic therapy is especially important for patients with immunosuppressive conditions, such as HIV, undergoing chemotherapy, neutropenia, anemia, or autoimmune diseases.

Surgical wounds, according to the classification adopted by the U.S. Centers for Disease Control and Prevention in 1985, are divided into four categories. Based on microbial contamination, most oral surgical procedures are classified as clean-contaminated wounds, with an infection risk of 5-15%. Proper prophylactic antibiotic administration can reduce this risk to 1%. Various studies indicate that the complication rate in tooth extraction and implantation cases can be as high as 10%. These procedures are most common in outpatient oral surgery practise. Mucositis, peri-implantitis, and early implant rejection are identified as the most common postoperative complications and can be associated with surgical wound contamination (8, 9).

The use of antibiotics in oral surgery plays a crucial role when dealing with inflammatory diseases and post operational complications. However, no less important is the rational use of antibiotics which ensures effectiveness, reduces the risk of adverse effects and antimicrobial resistance induced by overuse. The aim of this systematic literature review is to assess and evaluate the need of prophylactic antibiotic therapy in tooth extraction and implantation procedures for healthy patients without comorbidities.

MATERIAL AND METHODS

This systematic review was conducted according to the PRISMA statement (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) (10).

Eligibility Criteria

According to the Participants Intervention Comparison Outcome Study design schema (PICOS), the study included randomized clinical trials conducted with human patients without systemic diseases undergoing tooth extraction or dental implantation, comparing the infection rates of surgical wounds with prophylactic antibiotics or placebo.

Exclusion criteria were case report and series, literature reviews, studies on animals, studies on patients with systemic diseases or genetic syndromes.

Information Sources and Search Strategy

The search for scientific publications was performed by a single researcher in electronic databases such as PubMed, ClinicalKey, and Cochrane Library. Scientific articles published from 2013 to 2023 were searched.

The search in the PubMed database utilized the following keyword combination: (Antibiotic Prophylaxis) AND ((Tooth Extraction) OR (Dental Implant)). The search strategy was accordingly adapted for the ClinicalKey and Cochrane Library databases. The limitations were applied as follows: articles in English, studies no older than 10 years, and a minimum participant number greater than 10.

Study Selection

The study selection process was carried out in three stages. In the first stage, articles were evaluated based on the title of the scientific publication, leading to the exclusion of those older than 10 years and publications that were not randomized clinical trials. In the second stage, abstracts were reviewed, and publications that did not meet the eligibility criteria were excluded, including those unrelated to tooth extraction or implantation, as well as non-English articles. In the third stage, publications that met the criteria from the first and second stages were analyzed in full text. After analyzing the full text, publications examining non-oral antibiotics were excluded. The number of excluded publications was recorded.

Data Extraction and Management

Characteristics and data of included studies that were considered eligible were extracted. The following variables were recorded for each reviewed article: author, publication year, characteristics of study participants (sample size, age, and gender), intervention (tooth extraction or implantation, along with the number of procedures performed), and ap-

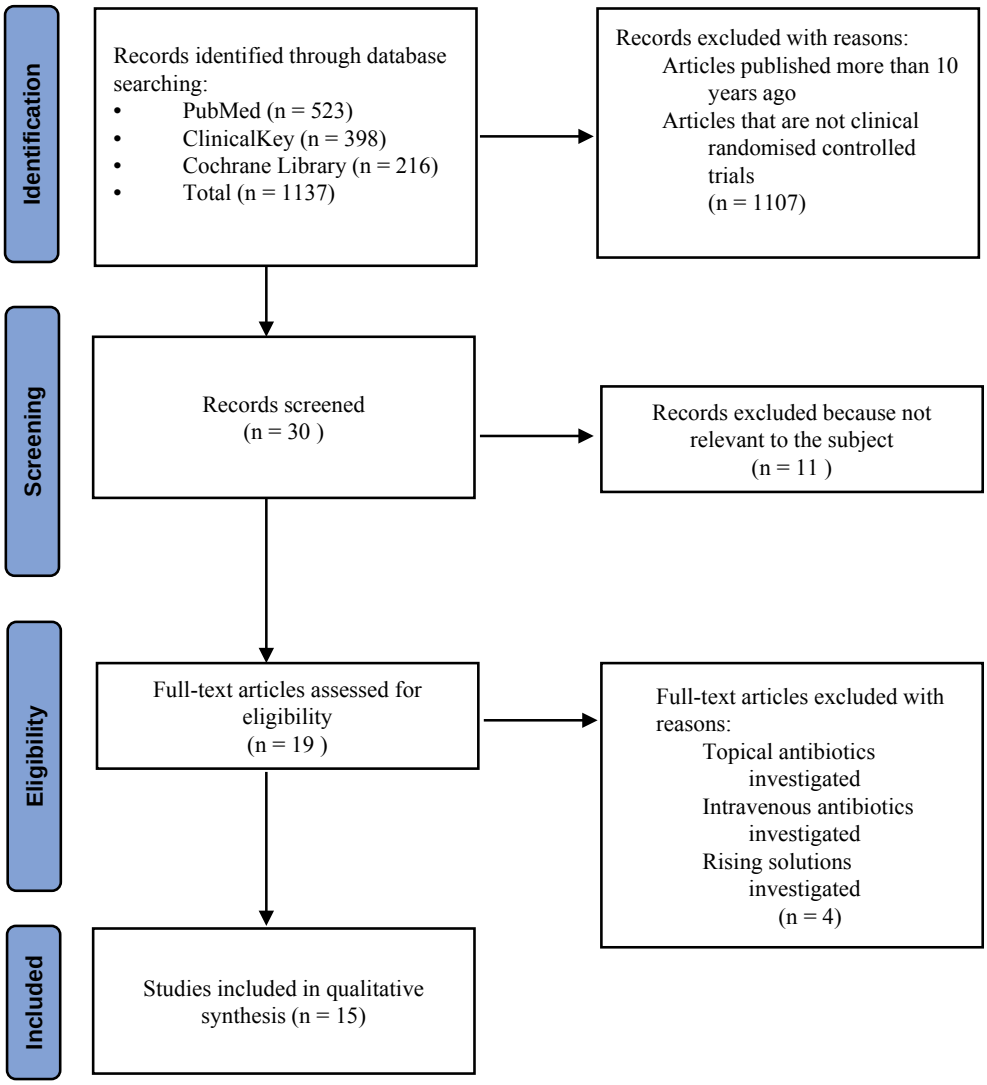

Fig. 1. PRISMA flow diagram

plied antibiotic therapy (types of antibiotics, timing of administration, and dosage). The selected scientific publications assessed local and systemic signs of infection (pain, swelling, trismus, purulence, erythema, bleeding, fever, osteomyelitis, fistula, peri-implantitis, alveolitis, wound dehiscence), specific signs (early implant rejection, implant mobility), and manifestations related to antibiotic side effects (gastrointestinal irritation, nausea, vomiting, diarrhea, allergic reactions).

Quality Assessment

The selected publications were evaluated for the risk of bias. Articles were categorized into groups based on the level of bias risk: low, unclear, and high risk. The bias risk of the publications was assessed according to "The Cochrane Collaboration" guidelines for assessing bias in randomized trials. For this purpose, six criteria were used and evaluated according to the risk level: low risk (+), high risk (-), and unclear risk (?).

RESULTS

Study Selection

Publications were selected according to the PRISMA methodology (Figure). A total of 1, 137 scientific publications were found. Out of these, 1, 107 publications were excluded because they were older than 10 years or were not randomized clinical trials. Among the remaining articles, 11 were excluded due to titles or abstracts that did not meet the review criteria. After analyzing the remaining publications in full text, an additional 4 articles were excluded because they examined topical, intravenous antibiotics, or mouth rinses. In the final selection stage, out of the 15 selected publications, 8 were about tooth extraction, and 7 were about dental implantation (11-25).

Study characteristics

All included publications are randomized clinical trials. Eight of the included studies describe tooth extraction surgeries, while the remaining seven focus on dental implantation surgeries. The characteristics of the included studies are summarized in Table 1.

Participants. The systematic literature review involved 3, 032 participants without comorbidities who underwent tooth extraction or implantation procedures. The number of participants in the studies ranged from 50 to 474. The gender distribution was approximately 48% male and 52% female; however, the authors Sidana *et al.* (16) and Xue *et al.* (25) did not provide information on gender. The average age ranged from 21 to 57 years; age data were also not provided by the authors Sidana *et al.* (16), Janas-Naze *et al.* (23), Nolan *et al.* (24), and Xue *et al.* (25). Participants with immunodeficiency diseases, diabetes, pregnant or breastfeeding women, as well as those who underwent radiotherapy, chemother-

apy, or those who had taken antibiotics prior to the procedure were excluded. Some authors included smoking patients. All studies were conducted by randomly dividing the participant groups into approximately equal parts.

Antibiotic therapy. The distribution of studies based on prescribed medications: in 12 publications, participants were prescribed amoxicillin (11-16, 18-20, 22, 24, 25), in 1 publication amoxicillin with clavulanic acid (17), in 2 publications clindamycin was prescribed (21, 23), in 1 study ibuprofen was used (16), and in 1 publication no medication was prescribed (15). In 10 studies, control group participants received a placebo (11-13, 17, 19-22, 24, 25) while in 3 studies, the timing of different antibiotic administrations was compared without a control group (14, 18, 23).

The distribution of studies based on the timing of antibiotic administration regarding surgical procedures: antibiotics were given before surgery (11, 13-21, 24), after surgery (14, 16, 19, 22, 23), and during both (12, 14, 18-20, 22, 25).

When evaluating the effectiveness of prophylactic antibiotic therapy in tooth extraction surgeries, the authors compared participant groups based on surgical wound suppuration and alveolitis. Symp-

Table 1. General characteristics of the selected studies (continued on the next page)

No.	Study	Intervention: type of surgery	Patients	Study design	Groups	Type of medicine/placebo and dosage	Patients	Gender (M/F)	Mean age
1.	Momand *et al.* 2022 [11]	Implantation	474	RCT	1	Amoxicillin 2 g 1 h before surgery	238	121/118	57
					2	Placebo	235	118/117	57
2.	Kirnabeur *et al.* 2022 [12]	Tooth extraction	50	RCT	1	Amoxicillin 2 g 1 h before surgery and 1,5 g per day after surgery for 3 days	50	21/29	21
					2	Placebo	50	21/29	21
3.	Yanine *et al.* 2021 [13]	Tooth extraction	154	RCT	1	Amoxicillin 2 g 1 h before surgery	77	22/55	21
					2	Placebo	77	25/52	21
4.	Tabrizi *et al.* 2022 [14]	Implantation	450	RCT	1	Amoxicillin 2 g 1 h before surgery	150	79/71	47
					2	Amoxicillin 2 g 1 h before surgery, 500 mg after surgery every 8 h for 5 days	150	75/75	46
					3	Amoxicillin 500 mg after surgery every 8 h for 5 days	150	76/74	49
5.	Kashani *et al.* 2019 [15]	Implantation	447	RCT	1	Amoxicillin 2 g 1 h before surgery (in case of allergy - clindamycin 600 mg 1 h before surgery)	224	109/114	56
					2	No antibiotic	224	95/129	50
6.	Sidana *et al.* 2017 [16]	Tooth extraction	171	RCT	1	Ibuprofen 400 mg after surgery 3 times per day for 3 days	47	-	-
					2	Amoxicillin 500 mg after surgery 3 times per day for 3 days and ibuprofen 400 mg after surgery 3 times per day for 3 days	50	-	-
					3	Amoxicillin 500 mg 1 h before surgery and ibuprofen 400 mg after surgery 3 times per day for 3 days	42	-	-
					4	Chlorhexidine rinse 15 minutes before surgery, rinse 2 times per day after surgery and ibuprofen 400 mg after surgery 3 times per day for 3 days	32	-	-
7.	Arteagoitia *et al.* 2015 [17]	Tooth extraction	118	RCT	1	Amoxicillin 2 g with clavulanic acid 125 mg 2 hours before surgery	60	32/32	25
					2	Placebo	58	26/28	31
8.	El-Kholey *et al.* 2014 [18]	Implantation	80	RCT	1	Amoxicillin 1 g 1 h before surgery	40	16/24	32
					2	Amoxicillin 1 g 1 h before surgery, 500 mg after surgery every 8 h for 3 days	40	14/26	30

RCT – randomized clinical trial; M – males; F – females.

toms such as fever, swelling, bleeding, limited mouth opening, trismus, erythema, pain, and the need for analgesics were also assessed. Pain was evaluated using the Visual Analog Scale (VAS), while other signs were assessed clinically.

In evaluating the effectiveness of prophylactic antibiotic therapy in dental implantation surgeries, the authors compared general signs of infection, such as fever, pain, swelling, wound suppuration, and the formation of fistulas, as well as specific signs: early implant rejection, mobility, and peri-implantitis. Pain was assessed using VAS, while other signs were assessed clinically. Peak peri-implantitis and osteomyelitis were diagnosed radiographically.

Quality Assessment

After assessing the risk of bias using the Cochrane risk of bias tool, it was determined that out of the 15 selected articles, 1 article met the criteria for high risk (15), and 4 articles were rated as having unclear risk (14, 17, 18, 23) (Table 2).

Results of tooth extraction studies

The results of tooth extraction studies are summarized in Table 3.

Table 1. General characteristics of the selected studies (continued from the previous page)

No.	Study	Intervention: type of surgery	Patients	Study design	Groups	Type of medicine/placebo and dosage	Patients	Gender (M/F)	Mean age
9.	Tan *et al.* 2013 [19]	Implantation	329	RCT	1	Amoxicillin 2 g 1 h before surgery	81	41/40	48
					2	Amoxicillin 2 g 1 h immediately surgery	82	47/35	47
					3	Amoxicillin 2 g 1 h before surgery, 500 mg after surgery 3 times per day for 3 days	86	47/39	46
					4	Placebo	80	47/33	45
10.	Milani *et al.* 2015 [20]	Tooth extraction	80	RCT	1	Amoxicillin 1 g 1 h before surgery and amoxicillin 500 mg daily after surgery for 7 days	30	26/54	23
					2	Amoxicillin 1 g 1 h before surgery and placebo daily after surgery for 7 days	30		
					3	Placebo 1 h before surgery and daily after surgery for 7 days	20		
11.	Santamaría Arrieta *et al.* 2022 [21]	Implantation	62	RCT	1	Clindamycin 600 mg 1 h before surgery	31	14/17	49
					2	Placebo 1 h before surgery	31	8/23	47
12.	Mariscal-Cazalla *et al.* 2021 [22]	Tooth extraction	92	RCT	1	Amoxicillin 750 mg before and after surgery	30	12/18	27
					2	Amoxicillin 750 mg after surgery	32	14/18	24
					3	Placebo before and after surgery	30	11/19	24
13.	Janas-Naze *et al.* 2022 [23]	Tooth extraction	278	RCT	1	Clindamycin 150 mg every 8 h for 5 days	92	42/50	-
					2	Clindamycin 300 mg every 8 h for 5 days	92	48/44	-
					3	Clindamycin 600 mg every 12 h for 5 days	94	54/40	-
14.	Nolan *et al.* 2013 [24]	Implantation	55	RCT	1	Amoxicillin 3 g 1 h before surgery	27	11/16	-
					2	Placebo	28	8/20	-
15.	Xue *et al.* 2015 [25]	Tooth extraction	192	RCT	1	Amoxicillin 500 mg (in case of allergy - clindamycin 300 mg) 1 h before surgery, 500 mg after surgery 3 times per day for 3 days	96	-	-
					2	Placebo	96	-	-

RCT – randomized clinical trial; M – males; F – females.

Kirnbauer *et al.* conducted a split-mouth study involving 50 patients who underwent the extraction of 100 wisdom teeth. Patients in the experimental group were administered amoxicillin before the procedure and for three days afterwards, while patients in the control group received a placebo. The results showed that post-operational bleeding from the wound was more frequent in the experimental group but there were no significant differences comparing other signs(12).

Yanine *et al.* studied 154 patients who had 154 impacted teeth removed. The need for analgesics was significantly higher in the control group. However, no differences in other potential complications between the groups were identified (13).

Arteagoitia *et al.* analyzed 118 patients and additionally evaluated the level of C-reactive protein in the blood. The experimental group received amoxicillin with clavulanic acid prior to the extraction of teeth. The control group more frequently experienced mucosal edema, limited mouth opening, and pain upon intraoral and extraoral palpation (17).

In Mariscal-Cazalla *et al.*'s study 92 patients participated. Postoperative pain and the need for analgesics were significantly higher in the control group after the extraction of impacted mandibular molars. Differences in other signs were not statistically significant (22).

Janas-Naze *et al.* included 278 patients who were given different doses of clindamycin. Patients that received antibiotics within longer intervals experienced trismus and pain more frequently, but no differences in other criteria between the groups were found (23).

Xue *et al.* examined 192 patients, additionally evaluating gastrointestinal side effects. Postoperative pain on the tenth day was significantly higher in the control group (25). In the studies conducted by Sidana *et al.* (16) and Milani *et al.* (20), no significant differences were found between the experimental and control groups.

Results of tooth implantation studies

The results of tooth implantation studies are summarized in Table 4.

Table 2. Summary of risk of bias assessment for randomized study (Cochrane risk-of-bias tool)

Study	Random sequence generation	Allocation sequence concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Overall
Momand *et al.* 2022 [11]	Low	Low	Low	Low	Low	Low	Low
Kirnabeur *et al.* 2022 [12]	Low	Low	Low	Low	Low	Low	Low
Yanine *et al.* 2021 [13]	Low	Low	Low	Low	Unclear	Low	Low
Tabrizi *et al.* 2022 [14]	Low	Low	High	Low	Low	Low	Unclear
Kashani *et al.* 2019 [15]	Low	High	High	High	Low	Low	High
Sidana *et al.* 2017 [16]	Low	Low	Low	Low	Unclear	Low	Low
Arteagoitia *et al.* 2015 [17]	Low	Unclear	Low	Low	Unclear	Low	Unclear
El-Kholey *et al.* 2014 [21]	Low	Unclear	High	Low	Low	Low	Unclear
Tan *et al.* 2013 [19]	Low	Low	Low	Low	Low	Low	Low
Milani *et al.* 2015 [20]	Low	Low	Low	Low	Unclear	Low	Low
Santamaría Arrieta *et al.* 2022 [21]	Low	Low	Low	Low	Low	Low	Low
Mariscal-Cazalla *et al.* 2021 [22]	Low	Unclear	Low	Low	Low	Low	Low
Janas-Naze *et al.* 2022 [23]	Low	Low	High	Low	Low	Low	Unclear
Nolan *et al.* 2013 [24]	Low	Low	Low	Low	Low	Low	Low
Xue *et al.* 2015 [25]	Low	Low	Low	Low	Low	Unclear	Low

P – patient; Imp – implant.

Table 3. Summary of the results of the included tooth extraction studies

No.	Study	Procedure	Patients	Groups	Dosage	Evaluating criteria	Outcome
1.	Kirnabeur *et al.* 2022 [13]	Extraction of impacted or partially impacted third molars	50	1	Amoxicillin 2 g 1 h before surgery and 1,5 g per day after surgery for 3 days	Surgical site infection, swelling, limited mouth opening, bleeding, pain, need for analgesics	Significantly more bleeding occured in Group 1.
				2	Placebo		
2.	Yanine *et al.* 2021 [13]	Extraction of impacted mandibular third molars	154	1	Amoxicillin 2 g 1 h before surgery	Surgical site infection, need for analgesics	The need for analgesics was significantly higher in Group 2.
				2	Placebo		
3.	Sidana *et al.* 2017 [16]	Extraction of erupted teeth affected by caries or periodontitis or third molars	171	1	Ibuprofen 400 mg after surgery 3 times per day for 3 days	Pain, swelling, signs of infection, fever, alveolitis	Statistically insignificant difference.
				2	Amoxicillin 500 mg after surgery 3 times per day for 3 days and ibuprofen 400 mg after surgery 3 times per day for 3 days		
				3	Amoxicillin 500 mg 1 h before surgery and ibuprofen 400 mg after surgery 3 times per day for 3 days		
				4	Chlorhexidine rinse 15 minutes before surgery, rinse 2 times per day after surgery and ibuprofen 400 mg after surgery 3 times per day for 3 days		
4.	Arteagoitia *et al.* 2015 [17]	Extraction of impacted mandibular third molars	118	1	Amoxicillin 2 g with clavulanic acid 125 mg 2 hours before surgery	Dehiscence, intraoral erythema, intraoral edema, intraoral abscess, extraoral erythema, alveolitis, limited mouth opening, intraoral tenderness upon palpation, extraoral tenderness upon palpation, CRP	Group 2 had significantly greater intraoral edema, more limited mouth opening, higher postoperative pain and increased tenderness on intraoral and extraoral palpation.
				2	Placebo		
5.	Milani *et al.* 2015 [20]	Extraction of impacted mandibular third molars	80	1	Amoxicillin 1 g 1 h before surgery and amoxicillin 500 mg daily after surgery for 7 days	Mouth opening, edema, pain	Statistically insignificant difference.
				2	Amoxicillin 1 g 1 h before surgery and placebo daily after surgery for 7 days		
				3	Placebo 1 h before surgery and daily after surgery for 7 days		
6.	Mariscal-Cazalla *et al.* 2021 [22]	Extraction of impacted mandibular third molars	92	1	Amoxicillin 750 mg before and after surgery	Infectious complications inflammation severity, pain	Group 3 had significantly higher pain and need for analgesics.
				2	Amoxicillin 750 mg after surgery		
				3	Placebo before and after surgery		
7.	Janas-Naze *et al.* [23]	Extraction of impacted mandibular third molars	278	1	Clindamycin 150 mg every 8 h for 5 days	Posoperative inflammatory parameters, posoperative pain, clindamycin concentration in saliva	Group 3 had significantly higher pain and trismus.
				2	Clindamycin 300 mg every 8 h for 5 days		
				3	Clindamycin 600 mg every 12 h for 5 days		
8.	Xue *et al.* [25]	Extraction of impacted mandibular third molars	192	1	Amoxicillin 500 mg (in case of allergy - clindamycin 300 mg) 1 h before surgery, 500 mg after surgery 3 times per day for 3 days	Bleeding, gastrointestinal reaction, ulcers, fever, posoperative pain, pain during swallowing, swelling, limited mouth opening	Group 2 had significantly higher pain.
				2	Placebo		

In the study by Momand *et al.*, which included 474 patients, who received 757 dental implants, no statistically significant differences were found between the groups in regards with early implant rejection and wound infection (11). Similarly, in Tabrizi *et al.*'s study with 450 patients, no statistically significant differences were observed in postoperative infections between the experimental and control groups (14).

In the study by Kashani *et al.*, which included 447 patients receiving a total of 963 dental implants, significantly more implant rejections were observed in the control group, where patients did not receive antibiotics ($p < 0.001$). (15).

El-Kholey's study, which included 80 patients with 90 implants, evaluated parameters such as wound dehiscence, apical peri-implantitis, wound suppuration, and early implant rejection. However, no significant differences were observed between the groups (18).

In the study by Tan *et al.*, involving 329 patients with 329 implants, surgical wound dehiscence occurred significantly more frequently in the control group ($p < 0.001$). No significant differences were found in the occurrence of pain, swelling, bleeding, bruising, suppuration, or implant stability (19). Santamaria Arrieta *et al.*'s study, which included 62 patients with 62 implants, reported no significant differences between groups in terms of early implant rejection or signs of infection (21). Nolan *et al.*'s study, involving 55 patients, found that postoperative pain was significantly more frequent

Table 4. Summary of the results of the included tooth implantation studies

No.	Study	Procedure	Patients	Groups	Dosage	Evaluating criteria	Outcome
1.	Momand *et al.* 2022 [11]	Implantation	474	1	Amoxicillin 2 g 1 h before surgery	Early implant rejection, posoperative infection	Statistically insignificant difference.
				2	Placebo		
2.	Tabrizi *et al.* 2022 [14]	Implantation	450	1	Amoxicillin 2 g 1 h before surgery	Infection	Statistically insignificant difference.
				2	Amoxicillin 2 g 1 h before surgery, 500 mg after surgery every 8 h for 5 days		
				3	Amoxicillin 500 mg after surgery every 8 h for 5 days		
3.	Kashani *et al.* 2019 [15]	Implantation	447	1	Amoxicillin 2 g 1 h before surgery (in case of allergy - clindamycin 600 mg 1 h before surgery)	Early implant rejection	Significantly more rejected implants in Group 2
				2	No antibiotic		
4.	El-Kholey *et al.* 2014 [18]	Implantation	80	1	Amoxicillin 1 g 1 h before surgery	Wound dehiscence, apical periimplantitis, wound infection, early implant rejection	Statistically insignificant difference.
				2	Amoxicillin 1 g 1 h before surgery, 500 mg after surgery every 8 h for 3 days		
5.	Tan *et al.* 2013 [19]	Implantation	329	1	Amoxicillin 2 g 1 h before surgery	Pain, swelling, bruising, bleeding, wound dehiscence, implant stability	Significantly more wound dehiscence in Group 4
				2	Amoxicillin 2 g 1 h immediately surgery		
				3	Amoxicillin 2 g 1 h before surgery, 500 mg after surgery 3 times per day for 3 days		
				4	Placebo		
6.	Santamaría Arrieta *et al.* 2022 [21]	Implantation	62	1	Clindamycin 600 mg 1 h before surgery	Early implant rejection, radiological signs of infection, implant stability, suppuration, appearance of fistulas, osteomyelitis, fever, postoperative pain, localized inflammation, bleeding, extraoral and intraoral erythema	Statistically insignificant difference.
				2	Placebo 1 h before surgery		
7.	Nolan *et al.* [24]	Implantation	55	1	Amoxicillin 3 g 1 h before surgery	Swelling, wound dehiscence, suppuration, pain	Significantly higher paini n Group 2.
				2	Placebo		

in the control group (p = 0.01), although no other significant differences were observed in the evaluated parameters (24).

DISCUSSION

Tooth extraction surgeries

Eight out of the fifteen included studies were related to tooth extraction, involving 1, 135 participants without comorbidities. Six studies showed significant differences between groups in terms of inflammatory and infection signs (12, 13, 17, 22, 23, 25). In four studies, pain was statistically greater in the control group, which did not receive antibiotics (17, 22, 23, 25). It is worth noting that in two of these four studies, smoking participants were included, which could have influenced the results (13, 22). The studies conducted by Yanine *et al.* (13) and Mariscal-Cazalla *et al.* (22) revealed a statistically significant increase in the demand for analgesics among participants in the experimental groups compared to those in the control groups. Notably, the inclusion of smokers in these studies may have impacted the results.

In some studies, such as those by Kirnbauer *et al.*, Sidana *et al.* and Milani *et al.*, no statistically significant differences were found between the experimental and control groups regarding pain assessment (12, 16, 20). Post operational bleeding rate was higher in the experimental group in one study (12). Other studies did not identify any statistically significant differences between the groups.

The incidence of postoperative infections such as alveolitis and wound suppuration, were not statistically significant different in none of the eight tooth extraction studies. However, in the study by Arteagoitia *et al.* (17), greater swelling and limited mouth opening were observed in the control group. In the study by Janas-Naze *et al.*, increased trismus was found in the experimental group, where antibiotics were less frequently administered after the procedure (23). The majority of assessed infection or inflammation criteria did not differ between the groups. In separate studies, statistically significant differences were noted in the occurrence of individual signs. The study by Janas-Naze *et al.* found that less frequent administration of antibiotics (every 12 hours) was associated with greater trismus and pain compared to more frequent administration (every 8 hours) (23). No differences were observed in other studies. There were no statistically significant differences between the groups comparing adverse effects of antibiotic intake, such as nausea, vomiting, or diarrhea.

No statistically significant differences were observed evaluating impact of different dosage of prophylactic antibioticotherapy. Seven of the eight studies examined only the extraction of impacted third molars, which ofter require incision and osteotomy (12, 13, 17, 20, 22, 23, 25), while the study by Sidana *et al.* included cases of various tooth extractions (16).

It is important to note that some of the evaluated symptoms are influenced by the traumatic nature of tooth extraction procedures, which can contribute to varying degrees of symptom presentation. Therefore, without ensuring the homogeneity of dental extraction procedures in the included studies, the results should be interpreted with caution.

Tooth implantation surgeries

In this review of seven dental implantation studies involving 1, 897 patients without comorbidities, three studies showed significant differences between the experimental and control groups regarding implant rejection, pain, and wound dehiscence (15, 19, 24). In the study by Kashani *et al.*, a higher number of early implant rejections was found in the control group, possibly due to the lack of antibiotic use (15). In Tan *et al.*'s study, wound dehiscence occurred more frequently in the control group four weeks after implantation; however, this difference disappeared after eight weeks (19). Other studies did not report any statistically significant differences between the groups in the assessment of wound dehiscence.

In Nolan *et al.*'s study, pain was significantly greater in the control group, note that smoking may have had an influence on this result (24). In other studies, no statistically significant difference was found between the groups when evaluating pain.

In all seven publications on dental implantation, no differences were found between the groups regarding postoperative infection criteria. Different doses of prophylactic antibiotics or the timing of their administration did not affect the assessed criteria.

Similarly to the results concerning dental extraction procedures, the findings related to dental implantation should be interpreted cautiously, considering the traumatic nature of the procedure. The impact of prophylactic antibiotic use on post-operative complications—such as pain, swelling, trismus, and bleeding—should be evaluated alongside the potential effects of the procedure's invasiveness, duration, and technique.

Other Systematic Reviews

The results of this review align with the findings of studies related to postoperative infections in the

article by Singh Gill *et al.* (26) and the influence of prophylactic antibiotic administration timing in the article by Roca-Millan *et al.* (27). Roca-Millan *et al.* also identified a lower rate of implant rejection in the experimental groups, consistent with the results from one study in this review. The systematic literature review by Romandini *et al.* showed that a 3 g dose of amoxicillin prior to implantation statistically reduces early implant rejection—this finding does not align with the results of this review (28).

Limitations

Not all studies included in the review were double-blinded, which may increase subjectivity into the results. The inclusion of smokers may have affected the intensity of pain and other postoperative factors. The follow-up periods in the studies ranged from 7 days to 6 months, however after this time, the effect of antibiotics on the evaluated outcomes become less relevant. The invasiveness of the surgeries performed during the studies also varied: some involved single implantations (14, 19, 21), while others ranged from one to three implants (11, 18, 24), or even up to ten implants (15). Additionally, augmentation was performed only in some studies (11, 13, 15), while in others, it was a criterion for exclusion (18, 19, 21, 24). Besides, authors did not elaborate on differences of duration, technique and intraoperative complications that could impact the post-operative morbidities. The small number of studies on different antibiotic dosages complicated the assessment of results.

CONCLUSIONS

Within the limits of this review the results of the studies do not support the hypothesis that prophylactic antibiotic therapy reduces the risk of infectious complications after tooth extraction or dental implantation procedures in healthy patients. The results also do not support the hypothesis that timing and dosage of prophylactic antibiotics significantly influence the occurrence of infectious complications in patients without comorbidities.

Author Contributions: Conceptualization, A.K.; methodology, A.K., D.K., P.G, A.G., J.Ž.; software, A.K. and P.G.; validation, A.K., D.K., P.G, A.G., J.Ž.; data curation, A.K., D.K., P.G., A.G., J.Ž.; writing – original draft preparation, A.K., D.K., P.G., A.G., J.Ž.; writing – review and editing, A.K., D.K. and P.G.; supervision, A.K. and P.G. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Conflicts of Interest: The authors state no conflict of interest.

REFERENCES

1. Hutchings MI, Truman AW, Wilkinson B. Antibiotics: past, present and future. Curr Opin Microbiol. 2019;51:72-80. doi:10.1016/j.mib.2019.10.008
2. Suda, K. J., Henschel, H., Patel, U., Fitzpatrick, M. A., & Evans, C. T. (2017). Use of Antibiotic Prophylaxis for Tooth Extractions, Dental Implants, and Periodontal Surgical Procedures. Open forum infectious diseases, 5(1), ofx250.
3. Dammling C, Abramowicz S, Kinard B. Current Concepts in Prophylactic Antibiotics in Oral and Maxillofacial Surgery. Oral Maxillofac Surg Clin North Am. 2022;34(1):157-167. doi:10.1016/j.coms.2021.08.015
4. European Centre for Disease Prevention and Control. Antimicrobial consumption in the EU/EEA (ESAC-Net) - Annual Epidemiological Report 2021. Stockholm: ECDC; 2022.
5. Kasradze S. The need for prophylactic antibiotic therapy in patients without comorbidities undergoing outpatient oral surgery procedures. [Master's thesis] Kaunas LUHS 2023.
6. Girskis D. The practice of Lithuanian dentists and maxillofacial surgeons in using antibacterial prophylaxis during the surgical removal of lower jaw third molars. [Master's thesis] Kaunas LUHS 2017.
7. Sauvage E, Terrak M. Glycosyltransferases and Transpeptidases/Penicillin-Binding Proteins: Valuable Targets for New Antibacterials. Antibiotics (Basel). 2016;5(1):12. Published 2016 Feb 17. doi:10.3390/antibiotics5010012
8. Yue Yi EK, Siew Ying AL, Mohan M, Menon RK. Prevalence of Postoperative Infection after Tooth Extraction: A Retrospective Study. Int J Dent. 2021;2021:6664311. Published 2021 Jun 8. doi:10.1155/2021/6664311
9. Lee CT, Zhang S, Leung YY, Li SK, Tsang CC, Chu CH. Patients' satisfaction and prevalence of complications on surgical extraction of third molar. Patient Prefer Adherence. 2015;9:257-263. Published 2015 Feb 10. doi:10.2147/PPA.S76236
10. Moher, D.; Liberati, A.; Tetzlaff, J.; Altman, D.G. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. Int. J. Surg. 2010, 8, 336–341.
11. Momand, P, Becktor, JP, Naimi-Akbar, A, Tobin, G, Götrick, B. Effect of antibiotic prophylaxis in dental

implant surgery: A multicenter placebo-controlled double-blinded randomized clinical trial. Clin Implant Dent Relat Res. 2022; 24(1): 116- 124.
12. Kirnbauer, B., Jakse, N., Truschnegg, A., Dzidic, I., Mukaddam, K. & Payer, M. (2022). Is perioperative antibiotic prophylaxis in the case of routine surgical removal of the third molar still justified? A randomized, double-blind, placebo-controlled clinical trial with a split- mouth design. Clinical Oral Investigations, 26(10), 6409–6421.
13. Yanine, N., Sabelle, N., Vergara-Gárate, V., Salazar, J., Araya-Cabello, I., Carrasco-Labra, A., Martin, C., & Villanueva, J. (2021). Effect of antibiotic prophylaxis for preventing infectious complications following impacted mandibular third molar surgery. A randomized controlled trial. Medicina oral, patologia oral y cirugia bucal, 26(6), e703–e710.
14. Tabrizi, R., Mobin, F., Dehghanpour, M., & Torabi, Z. S. (2022). Comparison of three antibiotic protocols for prevention of infection in dental implant surgery: A randomized clinical trial. Journal of cranio-maxillo-facial surgery : official publication of the European Association for Cranio-Maxillo-Facial Surgery, 50(4), 293–297.
15. Kashani, H., Hilon, J., Rasoul, M. H., & Friberg, B. (2019). Influence of a single preoperative dose of antibiotics on the early implant failure rate. A randomized clinical trial. Clinical implant dentistry and related research, 21(2), 278–283.
16. Sidana, S., Mistry, Y., Gandevivala, A., & Motwani, N. (2017). Evaluation of the Need for Antibiotic Prophylaxis During Routine Intra-alveolar Dental Extractions in Healthy Patients: A Randomized Double-Blind Controlled Trial. The journal of evidence-based dental practice, 17(3), 184–189.
17. Arteagoitia, I., Ramos, E., Santamaria, G., Barbier, L., Alvarez, J., & Santamaria, J. (2015). Amoxicillin/clavulanic acid 2000/125 mg to prevent complications due to infection following completely bone-impacted lower third molar removal: a clinical trial. Oral surgery, oral medicine, oral pathology and oral radiology, 119(1), 8–16.
18. El-Kholey K. E. (2014). Efficacy of two antibiotic regimens in the reduction of early dental implant failure: a pilot study. International journal of oral and maxillofacial surgery, 43(4), 487–490.
19. Tan, W. C., Ong, M., Han, J., Mattheos, N., Pjetursson, B. E., Tsai, A. Y., Sanz, I., Wong, M. C., Lang, N. P., & ITI Antibiotic Study Group (2014). Effect of systemic antibiotics on clinical and patient-reported outcomes of implant therapy - a multicenter randomized controlled clinical trial. Clinical oral implants research, 25(2), 185–193.
20. Milani, B. A., Bauer, H. C., Sampaio-Filho, H., Horliana, A. C., Perez, F. E., Tortamano, I. P., & Jorge, W. A. (2015). Antibiotic therapy in fully impacted lower third molar surgery: randomized three-arm, double-blind, controlled trial. Oral and maxillofacial surgery, 19(4), 341–346.
21. Santamaría Arrieta, G., Rodríguez Sánchez, F., Rodriguez-Andrés, C., Barbier, L., & Arteagoitia, I. (2023). The effect of preoperative clindamycin in reducing early oral implant failure: a randomised placebo-controlled clinical trial. Clinical oral investigations, 27(3), 1113–1122.
22. Mariscal-Cazalla, M. D. M., Manzano-Moreno, F. J., García-Vázquez, M., Vallecillo- Capilla, M. F., & Olmedo-Gaya, M. V. (2021). Do perioperative antibiotics reduce complications of mandibular third molar removal? A double-blind randomized controlled clinical trial. Oral surgery, oral medicine, oral pathology and oral radiology, 131(3), 286– 294.
23. Janas-Naze, A., Torbicka, G., Chybicki, D., Lipczyńska-Lewandowska, M., & Zhang, W. (2022). Comparative Efficacy of Different Oral Doses of Clindamycin in Preventing Post- Operative Sequelae of Lower Third Molar Surgery-A Randomized, Triple-Blind Study. Medicina (Kaunas, Lithuania), 58(5), 668.
24. Nolan, R., Kemmoona, M., Polyzois, I., & Claffey, N. (2014). The influence of prophylactic antibiotic administration on post-operative morbidity in dental implant surgery. A prospective double blind randomized controlled clinical trial. Clinical oral implants research, 25(2), 252–259.
25. Xue, P., Wang, J., Wu, B., Ma, Y., Wu, F., & Hou, R. (2015). Efficacy of antibiotic prophylaxis on postoperative inflammatory complications in Chinese patients having impacted mandibular third molars removed: a split-mouth, double-blind, self-controlled, clinical trial. The British journal of oral & maxillofacial surgery, 53(5), 416–420.
26. Singh Gill A, Morrissey H, Rahman A. A Systematic Review and Meta-Analysis Evaluating Antibiotic Prophylaxis in Dental Implants and Extraction Procedures. Medicina (Kaunas). 2018;54(6):95. Published 2018 Dec 1.
27. Roca-Millan E, Estrugo-Devesa A, Merlos A, Jané-Salas E, Vinuesa T, López-López J. Systemic Antibiotic Prophylaxis to Reduce Early Implant Failure: A Systematic Review and Meta-Analysis. Antibiotics (Basel). 2021;10(6):698. Published 2021 Jun 10. doi:10.3390/antibiotics10060698
28. Romandini M, De Tullio I, Congedi F, et al. Antibiotic prophylaxis at dental implant placement: Which is the best protocol? A systematic review and network meta-analysis. J Clin Periodontol. 2019;46(3):382-395. doi:10.1111/jcpe.13080

Received: 06 01 2024
Accepted for publishing: 23 09 2024