ACTA ODONTOLOGICA SCANDINAVICA
VOLUME 78, 2020
NUMBER 01

Acta Odontologica Scandinavica

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ISSN: 0001-6357 (Print) 1502-3850 (Online) Journal homepage: https://www.tandfonline.com/loi/iode20

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To cite this article: Anna Klinge, Dalia Khalil, Björn Klinge, Bodil Lund, Aron Naimi-Akbar, Sofia Tranaeus & Margareta Hultin (2020) Prophylactic antibiotics for staged bone augmentation in implant dentistry, Acta Odontologica Scandinavica, 78:1, 64-73, DOI: 10.1080/00016357.2019.1656819

To link to this article: https://doi.org/10.1080/00016357.2019.1656819

Published online: 04 Sep 2019.

ACTA ODONTOLOGICA SCANDINAVICA
2020, VOL. 78, NO. 1, 64–73
https://doi.org/10.1080/00016357.2019.1656819

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REVIEW ARTICLE

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Prophylactic antibiotics for staged bone augmentation in implant dentistry

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ABSTRACT

Background: The objective of the study was to assess the effect of prophylactic antibiotics on the outcome of bone augmentation and subsequent dental implant placement by combining the recommended quality assessment methods for systematic reviews and primary studies.

Materials and methods: This is a complex systematic review in which systematic reviews as well as primary studies are scrutinised. A search of Medline (OVID), The Cochrane Library (Wiley) and EMBASE, PubMed and Health technology assessment (HTA) organisations as-well as a complementary handsearch was carried out. Selected primary studies were assessed using GRADE. Each study was reviewed by three authors independently.

Results: Abstract screening yielded six potential systematic reviews allocated for full-text inspection. A total of ten primary studies were read in full-text. No relevant systematic reviews regarding the topic of this article were found. The quality assessment resulted in two primary studies with a moderate risk of bias. Of the two studies with a moderate risk of bias, one compared a single dose of clindamycin 600 mg preoperatively with the same preoperative dose followed by four doses of 300 mg every 6 h. The second study compared a single dose prophylaxis of two different types of antibiotic compounds.

Conclusion: In conclusion, the scientific evidence regarding the use of antibiotic prophylaxis for reducing the risk of infection in conjunction with bone augmentation procedures during dental implant placement is very limited. The infection rate as compared to nonusage of prophylactic antibiotics, selection of the most suitable compound, and the optimal duration of prophylactic treatment is still unknown.

ARTICLE HISTORY
Received 8 April 2019
Revised 12 August 2019
Accepted 13 August 2019

KEYWORDS
Antibiotic prophylaxis; bone transplantation; dental implants; systematic review

Introduction

Antibiotic resistance is considered the largest threat to modern health care as many treatment options are dependent on effective antibiotics [1]. Some parts of the world have entered the postantibiotic era where the efficacy of antibiotics can no longer be safely predicted [2]. An important measure to fight this development is restrictive antibiotic utilisation [3]. The stated correlation between increasing rates of antibiotic resistance and antibiotic consumption is unchallenged and well supported [4–7]. The suggestion that short-term antibiotic treatments would pose a reduced risk for antibiotic resistance is not well established [8]. Also a single dose of amoxicillin can select for resistant strains in the oral cavity [9]. For each indication and patient, the potential risk with antibiotic prescription must be weighed against the putative benefits. The antibiotics prescribed in dentistry sum up to approximately 5–10% of the total usage in health care according to reports from Europe and the USA thus contributing to a substantial part of the consumption [10–14].

Insertion of dental implants is a commonly used therapeutic option for replacement of missing teeth and displays excellent success rates [15–24]. When the residual bone volume is insufficient it is common to perform bone augmentation procedures prior to, or in conjunction with, implant placement [25–27].

Considering the large amount of patients subjected to this therapy, the antibiotic used during these procedures may significantly contribute to the overall usage especially if a prophylaxis regimen beyond the day of surgery is prescribed. However, the scientific evidence to support this routine is unclear. A literature review regarding antibiotic prophylaxis in surgery included over 600 references but could not find support for antibiotic prescription beyond the day of surgery for prevention of postoperative infections in any of the studied surgical fields [28]. In the light

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of this, it is reasonable to question whether prolonging the antibiotics beyond the day of surgery during bone augmentation procedures is a motivated procedure.

The number of published systematic reviews has increased significantly in recent years [29,30]. This provides a valuable mean to synthesise current knowledge within a particular field. However, a poorly performed systematic review may be misleading giving the incorrect impression of sound conclusions. It is therefore of great importance that systematic reviews are performed according to high standards and subjected to independent quality control similar to the assessment of original research [31,32]. AMSTAR is a validated and reliable tool that is increasingly being used for evaluation of systematic reviews [33–35]. It has been suggested that when reviewing literature pre-existing reviews should, in concert with the primary study, be incorporated into a complex systematic review [36]. A strict predefined PICO (population, intervention, control and outcome/observation) is mandatory in this process, as well as quality assessment by independent reviewers, resulting in strict inclusion only of systematic reviews of high quality.

The aim of the current study was to assess the available scientific literature regarding the efficacy of prophylactic antibiotics at bone augmentation procedures and subsequent dental implant placement. Including both staged bone augmentation and bone augmentation with simultaneous implant placement.

Table 1. Parameters of interest regarding eligible studies including inclusion and exclusion criteria for both systematic reviews and primary studies.

P	Patients subjected to bone augmentation procedures with or without simultaneous implant placement
I	Antibiotics on day of surgery i.e. short-termed prophylaxis
	Antibiotics more than day of surgery i.e. "extended" prophylaxis
	Head-to-head comparison of different antibiotic compounds or regiments
C	No antibiotic treatment
	Placebo
	Other nonantibiotic treatment e.g. such as antibacterial rinsing
	Other/comparing antibiotic treatment (alternative compound)
	Same compound, different dose/duration
O	Infection (primary)
	Quality of life (primary)
	Pain (primary)
	Implant loss
	Loss of transplant
	Sequestrum/sequestra
	Bone gain assessed by increased volume
	Health economy
	Ethical aspects
Systematic reviews	*Inclusion criteria*
	Systematic review
	Systematic meta-analysis
	Exclusion criteria for systematic reviews
	Exclusion criteria
	Nonsystematic review
	Guidelines
	Letter
	Position paper
	Consensus statements
Primary studies	*Inclusion criteria*
	English abstract
	Randomised control trials (RCT)
	Exclusion criteria
	Animal studies
	In vitro studies
	Any study type except RCT
	Lack of follow-up

Materials and methods

Objective

The objective of the study was to assess the effect of antibiotics on frequency of postoperative infections after bone augmentation in conjunction with dental implant placement, both staged bone augmentation and bone augmentation with simultaneous implant placement.

Criteria for considering studies

The predefined study population, intervention, the comparison of therapies, and outcome parameters for the eligible studies are summarised in Table 1. Additionally, inclusion and exclusion criteria for systematic reviews and primary studies are presented in Table 1.

Search strategies

Two of the authors (AK and ANA) and two information specialists (from Karolinska Institutet University library) performed the literature search. The following databases were searched until October 26, 2015: Medline (OVID), The Cochrane Library (Wiley) and EMBASE (embase.com), PubMed (nonindexed articles). No limitation regarding start year were used. The search was initially performed without any filters for the search of primary studies and then repeated once more with a filter for systematic reviews.

For the detection of recent publications, a complementary search was undertaken in PubMed on August 27, 2018. The additional search did not use any filters and all new findings from both primary studies as well as systematic reviews were screened.

The search terms used for the databases are summarised in Table 2. Search terms used were; e.g. alveolar ridge augmentation, alveolar bone grafting, dental implantation, implant-supported, sinus floor augmentation, sinus floor augmentation, bone graft augmentation, dental implants, antibiotic prophylaxis (Table 2).

Health technology assessment (HTA) organisations were searched regarding the effect of antibiotics versus no treatment or placebo on the outcome of bone augmentation in conjunction with dental implant installation until October 30 2015: National Institute for Health and Care Excellence (NICE), http://www.nice.org.uk/; CADTH, http://www.cadth.ca/; CRD database, http://www.crd.york.ac.uk/CRDWeb/; Kunnskapssenteret, http://www.kunnskapssenteret.no/home?-language=english, and ASERNIP-S http://www.surgeons.org/for-health-professionals/audits-and-surgical-research/asernip-s/publications/. The reference lists of all the eligible studies

Table 2. Search strategy.

Database	Search strategy
Medline (Ovid)	1. Alveolar Ridge Augmentation/ 2. Alveolar Bone Grafting/ 3. Guided Tissue Regeneration, Periodontal/ 4. exp Dental Implantation/ 5. Dental Prosthesis, Implant-Supported/ 6. Sinus Floor Augmentation/ 7. Alveolar Ridge Augmentation.tw,kf. 8. Sinus Floor Augmentation.tw,kf. 9. Bone Graft Augmentation.tw,kf. 10. or/1-9 11. ((bone* or tissue*) adj3 (alveolar or dental or intraoral or intra-oral or jaw or mandible* or maxilla* or oral or periodont* or ridge or sinus or tooth socket) adj3 (augmentation or elevation* or graft* or implantation or osseointegration or preservation or regenerat* or reconstruct* or transplantation)).tw,kf. 12. or/10-11 13. Dental Implants/ 14. ((bone* or tissue*) adj2 (allograft* or allogen* or alloplast* or implant* or heterograft* or substitute* or transplant* or xenograft* or xenogen*) adj3 (alveolar or dental or intraoral or intra-oral or jaw or mandible* or maxilla* or periodont* or oral or ridge or sinus or tooth socket)).tw,kf. 15. or/13-14 16. 12 or 15 17. exp Anti-Bacterial Agents/ 18. Antibiotic Prophylaxis/ 19. (antibiotic* or cephalosporin* or cefazolin or cefuroxime or amox?cillin* or clindam?cin or penicillin* or levofloxacin). tw,kf. 20. or/17–19 21. 16 and 20
The Cochrane Library (Wiley)	#1: ((alveolar or dental or intraoral or intra-oral or jaw or mandible* or maxilla* or oral or periodont* or ridge or sinus or tooth socket) near/3 (augmentation or elevation* or graft* or implantation or osseointegration or preservation or regenerat* or reconstruct* or transplantation)):ti,ab #2: ((allograft* or allogen* or alloplast* or implant* or heterograft* or substitute* or transplant* or xenograft* or xenogen*) near/3 (alveolar or dental or intraoral or intra-oral or jaw or mandible* or maxilla* or periodont* or oral or ridge or sinus or tooth socket)):ti,ab #3: #1 or #2 #4: (antibiotic* or cephalosporin* or cefazolin or cefuroxime or amoxicillin* or amoxycillin* or clindamycin or clindamicin* or penicillin* or levofloxacin):ti,ab #5: #3 AND #4
EMBASE (www.embase.com)	#20: #15 AND #19 #19: #16 OR #17 OR #18 #18: antibiotic*:ab,ti OR cephalosporin*:ab,ti OR cefazolin:ab,ti OR cefuroxime:ab,ti OR amoxicillin*:ab,ti OR amoxycillin*:ab,ti OR clindamycin:ab,ti OR clindamycin*:ab,ti OR penicillin*:ab,ti OR levofloxacin:ab,ti #17: 'antibiotic prophylaxis'/de #16: 'antibiotic agent'/exp #15: #11 OR #14 #14: #12 OR #13 #13: ((bone* OR tissue*) NEAR/2 (allograft* OR allogen* OR alloplast* OR implant* OR heterograft* OR substitute* OR transplant* OR xenograft* OR xenogen*) NEAR/3 (alveolar OR dental OR intraoral OR 'intra-oral' OR jaw OR mandible* OR maxilla* OR oral OR ridge OR sinus OR 'tooth socket')):ab,ti #12: 'tooth implant'/de #11: #9 OR #10 #10: ((bone* OR tissue*) NEAR/3 (alveolar OR dental OR intraoral OR 'intra-oral' OR jaw OR mandible* OR maxilla* OR oral OR ridge OR sinus OR 'tooth socket') NEAR/3 (augmentation OR elevation* OR graft* OR implantation OR osseointegration OR preservation OR regenerat* OR reconstruct* OR transplantation)):ab,ti #9: #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 #8: (guided NEXT/1 tissue NEXT/1 regeneration NEXT/4 periodont*):ab,ti #7: bone NEXT/1 graft NEXT/1 augmentation):ab,ti #6: (sinus NEXT/1 floor NEXT/1 augmentation):ab, #5: (alveolar NEXT/1 ridge NEXT/1 augmentation):ab, #4: 'sinus floor augmentation'/de #3: 'tooth implantation'/de #2: 'alveolar bone grafting'/de #1: 'mandible reconstruction'/de
PubMed* NOT Medline	#6: #5 NOT medline[sb] #5: #3 AND #4 #4: ((antibiotic*[Title/Abstract] OR cephalosporin*[Title/Abstract] OR cefazolin[Title/Abstract] OR cefuroxime[Title/Abstract] OR amoxicillin*[Title/Abstract] OR amoxycillin*[Title/Abstract] OR clindamycin[Title/Abstract] OR clindamycin*[Title/Abstract] OR penicillin*[Title/Abstract] OR levofloxacin[Title/Abstract])) #3: #1 OR #2 #2: ((((bone*[Title/Abstract] OR tissue*[Title/Abstract])) AND (allograft*[Title/Abstract] OR allogen*[Title/Abstract] OR alloplast*[Title/Abstract] OR implant*[Title/Abstract] OR heterograft*[Title/Abstract] OR substitute*[Title/Abstract] OR transplant*[Title/Abstract] OR xenograft*[Title/Abstract] OR xenogen*[Title/Abstract])) AND (alveolar[Title/Abstract] OR dental[Title/Abstract] OR intraoral[Title/Abstract] OR intra-oral[Title/Abstract] OR jaw[Title/Abstract] OR mandible*[Title/Abstract] OR maxilla*[Title/Abstract] OR periodont*[Title/Abstract] OR oral[Title/Abstract] OR ridge[Title/Abstract] OR sinus[Title/Abstract] OR "tooth socket"[Title/Abstract])) #1: ((((bone*[Title/Abstract] OR tissue*[Title/Abstract])) AND (allograft*[Title/Abstract] OR allogen*[Title/Abstract] OR alloplast*[Title/Abstract] OR implant*[Title/Abstract] OR heterograft*[Title/Abstract] OR substitute*[Title/Abstract] OR transplant*[Title/Abstract] OR xenograft*[Title/Abstract] OR xenogen*[Title/Abstract])) AND (alveolar[Title/Abstract] OR dental[Title/Abstract] OR intraoral[Title/Abstract] OR intra-oral[Title/Abstract] OR jaw[Title/Abstract] OR mandible*[Title/Abstract] OR maxilla*[Title/Abstract] OR periodont*[Title/Abstract] OR oral[Title/Abstract] OR ridge[Title/Abstract] OR sinus[Title/Abstract] OR "tooth socket"[Title/Abstract]))

were hand-searched for potential complementary studies. The search was not restricted by language. However, retrieved papers in a language other than English, German, French, or Swedish were excluded.

Study selection

Eligible studies were included in accordance with the inclusion/exclusion criteria. AK (first author) went over the retrieved list of publications and performed a crude exclusion of irrelevant publications based on their title. In case of uncertainty, a study remained included until the next selection step, which consisted of an examination of abstracts. The abstracts were read independently in duplicate by three reviewers, either BL, AK and ST or MH, ANA and BK. Selected primary studies and systematic reviews were read in full-text by three reviewers each, respectively. Any disagreement during the screening process was resolved by discussion in the project group.

Quality assessment

Systematic reviews

No systematic reviews were left for quality assessment, due to out of topic reason. Had there been any systematic reviews to review the quality of the studies would have been assessed according to Mejare 2015 [37], based on AMSTAR assessment items [33].

Primary studies

The quality of the included primary studies was assessed using a protocol for assessment of randomised studies [38]. The quality assessment protocol focus on the risk of bias in individual studies and specific outcomes as well as the overall quality of evidence.

Quality of evidence

The scientific quality of the evidence in the primary studies was graded according to GRADE (**GRAD**ing quality of **E**vidence and strength of recommendations) and set as high, moderate, low, and very low [39] (Table 3). GRADE have 4 steps of evidence grading. The system was developed by the GRADE working group. GRADE is used by e.g. World Health Organization (WHO), NICE, Cochrane Collaboration and British Medical Journal (BMJ).

Table 3. Significance of the four levels of evidence.

Quality level	Current definition
High	We are very confident that the true effect lies close to that of the estimate of the effect
Moderate	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low	Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Data extraction

Systematic reviews

No systematic reviews remained for data extraction due to out of topic reason. Data extraction from the systematic reviews would have been the following: objectives, main results, authors' estimated level of evidence, and knowledge gaps according to authors.

Primary studies

Data was extracted from the primary studies regarding number of included patients, age, gender distribution, length of follow-up, type of intervention, type of control treatment, and relevant treatment outcomes.

Results

Literature search and study selection

The search resulted in 1155 titles after deduplication. The results include both primary studies and systematic reviews ($n = 150$). Search strategy, presented for each database, is shown in Table 1. The search of HTA organisations did not yield any further studies. Flow-charts of the screening process for primary studies and systematic reviews are described in Figures 1 and 2, respectively.

The additional search on August 27, 2018 added 372 new articles: all were screened for both systematic reviews and primary studies.

Systematic reviews

Abstract screening yielded six potential systematic reviews allocated for full-text inspection. The most common reason for exclusion was that the study was out of topic ($n = 4$) (Out of topic means that the study was not within our PICO, e.g. if the article did not mention bone augmentation in association with implants and antibiotics).The second most common reason for exclusion was that the study was not considered a systematic review ($n = 2$) [40–45] (Table 4).

Primary studies

A total of ten primary studies were read in full-text. At this stage another six studies were excluded, yielding four primary studies included for further analysis. Primary studies that were regarded as nonrelevant to the current systematic review were excluded at this stage and reason for exclusion were recorded (Table 5) [46–51]. Reason for exclusion could be e.g. language, not a randomized controlled trial (RCT), or a research question that was not correct.

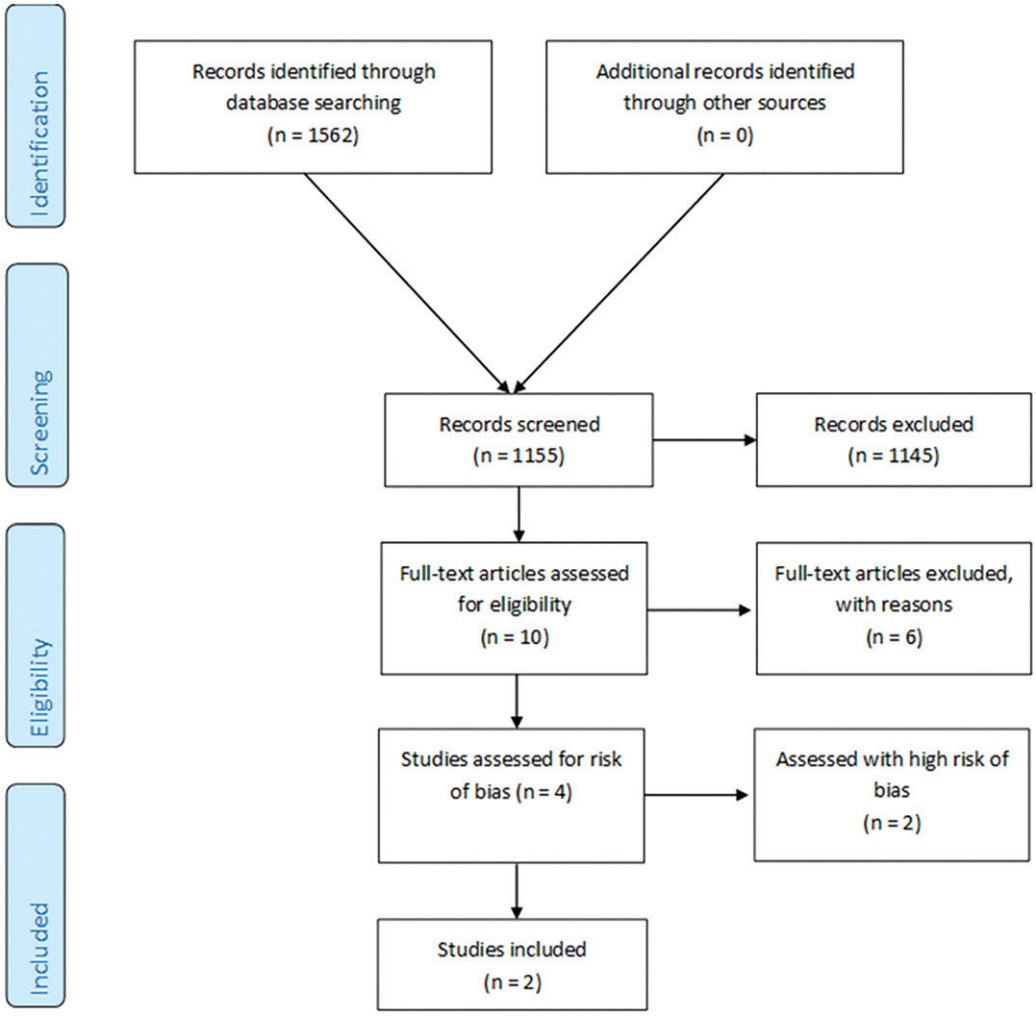

Figure 1. Flow chart, primary studies. From Moher et al. [31].

Quality assessment and data extraction

Systematic reviews

No systematic reviews were left for quality assessment and data extraction due to out of topic reason.

Primary studies

The quality assessment resulted in two studies with a moderate risk of bias, Figure 3 [52,53], and two studies with a high risk of bias [54,55]. The main reason for the two studies being regarded as having a high risk of bias was shortcomings and uncertainties in the randomisation process. The first of the two studies with a moderate risk of bias, Lindeboom et al. [52], compared a single dose of clindamycin 600 mg preoperatively with the same preoperative dose followed by four doses of 300 mg every 6 h.

The second study, Lindeboom et al. [53], compared a single dose prophylaxis of two different types of antibiotic compounds (Table 6). Type of intervention and study population characteristics for studies classified as being of low or moderate risk of bias are also shown in Table 6. Outcome of primary studies classified as being of low or moderate risk of bias are shown in Table 7. In the first study, Lindeboom et al. [52], 2 of 62 patients in the intervention group (600 mg clindamycin 1 h preop.) developed a postoperative infection. In the control group (clindamycin 24 h) 3 of 62 patients developed a postoperative infection at receptor site. In the second study, Lindeboom et al. [53], 4 of 75 patients in the intervention group (2 g penicillin 1 h preop.) developed a postoperative infection. In the control group (600 mg clindamycin 1 h preop.) 2 of 75 patients developed a postoperative infection at receptor site (Table 7). Due to few events, statistical analysis was not applicable. The two studies with a high risk of bias are presented in Figure 4.

Publication bias and heterogeneity

Not applicable due to too few studies available to make a meta-analysis.

Discussion

The results of the present systematic review illustrates that there is a lack of existing scientific evidence on antibiotic

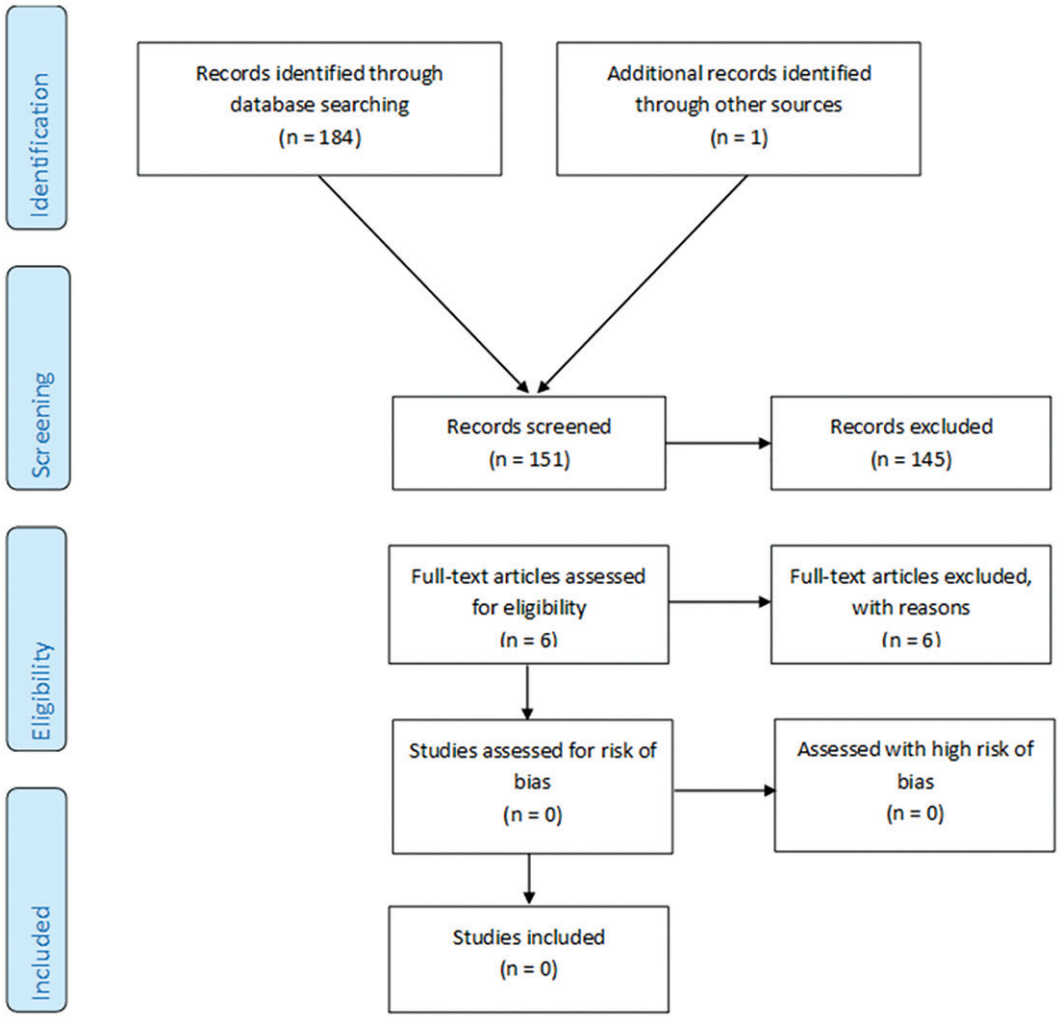

Figure 2. Flow chart, systematic reviews. From Moher et al. [31].

Table 4. Excluded systematic reviews.

Author	Reason for exclusion
Chen et al. [40]	Not a systematic review
Chrcanovic et al. [41]	Out of topic
Esposito et al. [42]	Out of topic
Lang et al. [43]	Out of topic
Sharaf and Dodson [44]	Not a systematic review
Waasdorp et al. [45]	Out of topic

Table 5. Excluded primary studies read in full text.

References	Reason for exclusion
Brennan et al. [46]	Letter to editor
Chuvilkin et al. [47]	Not in English
Cohen [48]	Case series
Eickholz et al. [49]	Not correct research question
Kulshrestha [50]	Not correct research question
Ngeow [51]	Letter to editor

prophylaxis for oral bone augmentation procedures in the alveolar ridge and subsequent dental implant placement.

No data were available on implant placement with simultaneous bone augmentation. Since this procedure is frequently used in implant dentistry, the lack of data for this indication is observable and in need of further research on the subject.

No data was available on any of the other parameters in our PICO, in the included studies.

The study by Lindeboom et al. [52] compared the risk of developing a postsurgical infection at the bone graft receptor site between patients given a single dose of antibiotic prophylaxis and patients receiving a more extended 24-h dose of clindamycin. Although the study showed that there was a difference in risk, albeit not a statistically significant one, the number of postsurgical infections was low in both groups. Therefore the outcome of a statistical comparison between the two groups may be hampered by insufficient power. In addition, Lindeboom et al. [53] found no significant difference in the occurrence of postsurgical recipient site infection when comparing two different antibiotic compounds, penicillin and clindamycin used as a single dose of antibiotic prophylaxis. The result of both the included studies indicates that the wound infection rate when using a single dose of prophylactic antibiotics was low.

There is very limited available evidence on antibiotic prophylaxis on staged bone augmentation with intraoral donor sites and the complete lack of evidence on staged bone augmentation with extra-oral donor bone and implant placement.

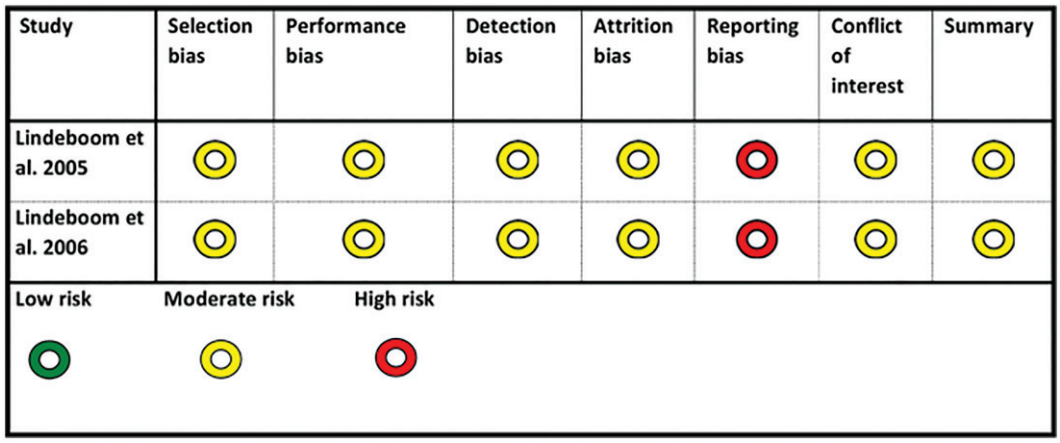

Figure 3. Methodological assessment of included studies.

Table 6. Characteristics and quality assessment of included primary studies with low or moderate risk of bias.

Author Year Country	Population	Study period	Intervention	Control	Risk of bias comments
Lindeboom et al. (2005) The Netherlands	*n*: 124	8 weeks	600 mg clindamycin 1 h prior surgery –placebo capsules every 6 h for 24 h postoperatively	600 mg clindamycin 1 h prior surgery – 300 mg clindamycin every 6 h for 24 h postoperatively	Moderate risk of bias
	Age: 18–59 years Gender (m/f): 50/74 Augmentation: onlay bone graft Smokers: none (exclusion criteria)				No published study protocol Somewhat unclear blinding No reports of loss to follow up
Lindeboom et al. (2006) The Netherlands	*n*: 150	8 weeks	2 g penicillin 1 h prior surgery	600 mg clindamycin 1 h prior surgery	Moderate risk of bias
	Age: 18–67 years Gender (m/f): 52/98 Augmentation: onlay bone graft Smokers: none (exclusion criteria)				No published study protocol Unclear randomization No reports of loss to follow up

n: number of patients; m/f: male/female; g: gram; h: hour; preop: preoperative; postop: postoperative; mg: milligram.

Table 7. Outcome of included primary studies with low or moderate risk of bias.

	Outcome				
	Intervention		Control		
Author Year Country	Postoperative infection	No.	Postoperative infection	No.	Results
Lindeboom et al. (2005) The Netherlands	Clindamycin 600 mg 1 h preop 2 Patients with infection at receptor site	62	Clindamycin 24 h 3 Patients with infection at receptor site	62	RR – 0.67
Lindeboom et al. (2006) The Netherlands	Penicillin 2 g 1 h preop 4 Patients with infection at receptor site	75	Clindamycin 600 mg 1 h preop 2 Patients with infection at receptor site	75	RR – 2.00

No: number of patients; g: gram; preop: preoperative; hr: hour; postop: postoperative; mg: milligram; RR: risk ratio.

Due to the limited number of studies eligible for inclusion in the present systematic review, we were not able to draw a definite conclusion regarding whether prolonged antibiotic prophylaxis is needed to reduce the risk of postoperative infection during bone grafting procedures or if a single dose is equally sufficient. Consequently, there is a gap in our knowledge concerning the efficacy of antibiotic prophylaxis, regardless of length, compared to no use of antibiotics for prevention of potential postoperative infections after bone grafting procedures. Only two primary studies fulfilling the inclusion criteria were considered to be of moderate risk of bias [52,53]. The other eligible primary studies ($n = 2$) were rejected due to a high risk of bias [54,55]. The main reasons for exclusion due to a high risk of bias were an unclear randomisation process and allocation concealment, insufficiently described blinding, and unclear outcome measures.

The core of the systematic review will always be the quality of the included primary studies. Therefore, it is of great importance that RCTs should be designed, performed, and reported in accordance with internationally recognised

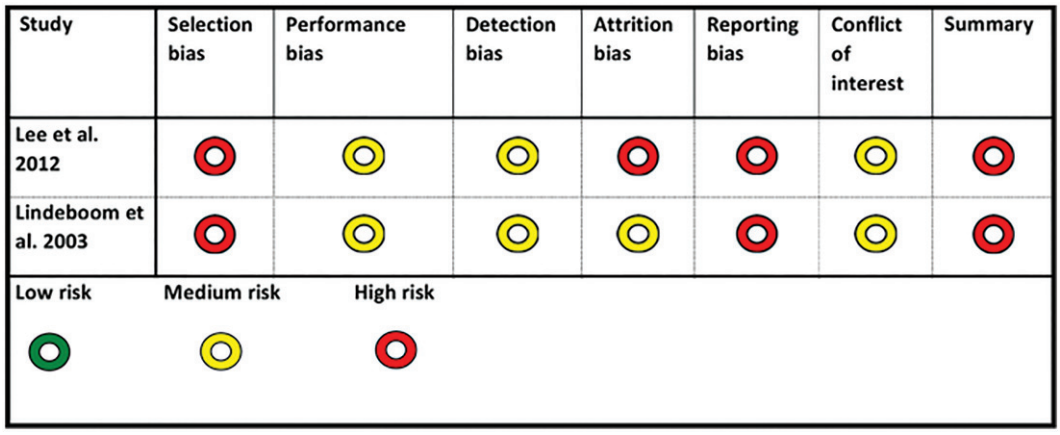

Figure 4. Methodological assessment of excluded studies with high risk of bias.

standards such as the CONSORT statement, in order for accurate conclusions to be drawn [56]. Since the quality of reviews differs significantly, one needs to approach the assessment of systematic reviews in the same way as the current study has approached it [36].

While there are many published systematic reviews on the use of antibiotics in dental implant surgery, we were not able to find any that fulfilled our inclusion criteria. For example, this was the case with a systematic review initially allocated, evaluating survival and success rates of implants placed into fresh extraction sockets, since data of prophylactic antibiotics given in bone grafting procedures was not separately compared [43].

In addition, RCTs on the topic of antibiotics and bone augmentation procedures are lacking. Generally, large numbers of systematic reviews are seen in fields where primary studies are sparse and the results contradictory. This repeated effort to extract and summarise data is probably due to the desire to synthesise solid evidence despite divergent results and/or underpowered primary studies. The phenomenon as such indicates a further need for high-quality research. The results of the present study thus serve to emphasise the fact that one needs to be vigilant about drawing conclusions from such published systematic reviews.

Traditionally, antibiotic prophylaxis has been administered either pre-, peri-, or post-operative to prevent infection developing at the surgical wound site. A placebo-controlled double blind pilot study comparing the prophylactic use of phenethicillin with a placebo in buccal bone-grafting procedures found a high infection rate (40%) at the receptor site in the placebo group. This indicates that antibiotic prophylaxis maybe beneficial in these procedures [53]. These results, however, should be interpreted with caution since the number of patients included in this pilot study was small. It is not known specifically how antibiotics are used in everyday practice. Empiric prophylactic and antibiotic usage varies by country, region, choice of antibiotic, and the duration of the prophylaxis. This is not unexpected considering the weak scientific evidence. Thus, while there is considerable disagreement as to the type and length of the antibiotic prophylaxis, the most common misuse of prophylactic antibiotics is believed to be excessive duration [57].

The WHO suggests that unnecessary use of antibiotics for infections is one of the main etiological factors behind antibiotic resistance [58]. Even a single dose of antibiotic prophylaxis has been shown to induce a selection of resistant strains in the oral microflora [9], illustrating that any dosage and its consequences should be carefully considered. Antibiotic-resistant bacteria have become a major public health crisis and a threat to both global stability and national security [58]. At the same time, it is not possible to develop and manufacture new antibiotics to satisfy the increasing demand, resulting in an irreversible phenomenon that is difficult to manage [59]. The present unnecessary use of common antibiotics may result in both expensive future antibiotics and an increase in bacterial resistance. Therefore, the need for recommendations to limit and optimise the utilisation of antibiotics are needed.

Limitations

The restriction in English language might potentially have resulted in missed relevant studies, which is a limitation in this review.

There were no signs indicating publication bias in the present review, yet there is a possibility that small negative studies might not have been published.

Conclusion

In conclusion, the scientific evidence regarding the use of antibiotic prophylaxis for reducing the risk of infection at bone augmentation procedures and subsequent dental implant placement is very limited. Infection rate has been shown to be low using a single dose of prophylactic antibiotics. However, the infection rate in comparison to nonusage of prophylactic antibiotics, the compound, and the duration of prophylactic treatment is still not known. Therefore, there is an urgent need for further primary RCTs.

Acknowledgments

The authors would like to acknowledge Carl Gornitzki and Gun Brit Knutssön at the Karolinska Institutet library for their skilful assistance.

Disclosure statement

No potential conflict of interest was reported by the authors.

Funding

This work was supported by a special grant from the Swedish Research Council (Dnr 2012-55) in support of National Clinical Research Schools regarding research on infection and antibiotics and to facilitate networking in this area.

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