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REVIEW

Effect of Antibiotic Prophylaxis on Surgical Site Wound Infection in Third Molar Surgery: A Meta-Analysis

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ABSTRACT

The objective of this meta-analysis is to assess the impact of antibiotic prophylaxis (AP) on surgical site wound infection (SSWI) throughout third molar surgery (TMS).

A meta-analysis was conducted using examinations that compared AP to placebo for TMS from different languages that satisfied the inclusion criteria. Applying dichotomous random or fixed effect models, the findings of these studies were analysed, and the Odd Ratio (OR) was calculated with 95% confidence intervals (CIs).

A total of 18 studies conducted between 2001 and 2023 were included in the present analysis. These studies initially included 4063 individuals with TMS.

A substantial reduction in SSWI (OR, 0.46; 95% CI, 0.33–0.65, $p < 0.001$) was observed in individuals with TMS who received AP, with no heterogeneity ($I2 = 1\%$) compared to placebo.

Data analysis showed that AP resulted in notably reduced SSWI compared to placebo in individuals with TMS. However, it is important to be cautious when dealing with its values due to the fact that the examinations were conducted by various surgeons with diverse expertise on different types of patients, and the small sample size of many of the examinations chosen for the meta-analysis.

1. Introduction

The surgical extraction of crushed third molars (TMs) is the most commonly performed operation in oral surgery and routine dentistry procedures both globally [1]. The predominant adverse effects after third molar surgery (TMS) include infection and inflammation caused by bacterial contamination due to the specific characteristics and environment of the operation [2]. Postoperative infection manifests in 2% to 12% of individuals [3]. Following the surgical excision of the mandibular TM, approximately 1% of patients may experience severe fascial space cellulitis requiring hospitalization [4]. While rare, particularly serious infections can have expensive and debilitating consequences [5]. The administration of antibiotic prophylaxis (AP) during transmembrane stimulation (TMS) has been a subject of ongoing debate in therapeutic contexts [6]. In his comprehensive analysis of the pathophysiology of pericoronitis and complications following TM removal in the 1960s, Kay presented convincing scientific evidence supporting the necessity of AP for TMS [7]. He showed that a greater proportion of individuals who received transcutaneous magnetic stimulation (TMS) without prior administration of antibacterial prophylaxis developed surgical site wound infections (SSWIs). By contrast, the occurrence of surgical site

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wound infections (SSWI) declined in individuals who received a single dose of penicillin prior to surgery. When a single dose of penicillin reduced the incidence of surgical site wound infection (SSWI) in patients with pericoronitis, the advantage of antibiotic prophylaxis (AP) was much more remarkable. The publication of this study served as the impetus for the extensive prescription of antibiotics for TMS. Although the significance of AP in TMS was called into doubt both before and after the treatment [8]. Longstanding confusion in clinical practice has arisen from the conflicting results of randomized controlled clinical trials (RCTs), with advocates and critics of AP presenting their respective supporting evidence [6]. Despite concerns over the efficacy, risk of allergic and anaphylactic reactions, and possibility of drug resistance, physicians persist in prescribing antibiotics for postoperative complications after transseptal myocardial surgery (TMS) [6]. Numerous published randomized controlled trials (RCTs) have intensified the discussion, with some supporting and opposing the effectiveness of AP [9–11]. Individuals often experience a reduced quality of life and lower productivity due to postoperative Surgical Site-Specific Wound Injuries (SSWI), which are further compounded by devastating pain and significant functional impairment [12]. Hence, medical practitioners have been seeking a pragmatic method to avoid postoperative complications after transcranial magnetic stimulation (TMS) for an extended period. A multitude of randomized controlled trials (RCTs) have investigated the efficacy of AP in decreasing morbidity associated with TMS. However, these studies all had a common limitation: they did not possess sufficient statistical power to detect a substantial disparity between the groups being examined. Seldom did a published clinical trial utilise a sample size that facilitated a robust outcome analysis, mostly because of its significantly smaller scale. This work included a synthetic quantitative analysis of randomized controlled trials (RCTs) on the effectiveness of AP in transcranial magnetic stimulation (TMS). The null hypothesis states that AP was ineffective in preventing surgical complications. The objective of the meta-analysis is to assess the impact of AP on SSWI in TMS.

2. Method

2.1. Design of the examination

The meta-analyses comprised the epidemiological statement and followed a pre-established assessment methodology. In order to gather and analyse data, a diverse range of databases including OVID, PubMed, the Cochrane Library, Embase, and Google Scholar were utilised. These databases were utilized to gather reviews that specifically examined and compared the impact of AP on SSWI in TMS.

2.2. Data pooling

A comparison between AP and placebo approaches for the treatment of TMS identified SSWI as the primary inclusion criterion. No consideration was given to language limitations during the screening process and the selection of tests to be included. No limitations were placed on the potential sample sizes of the examinations that were enlisted. Review, editorial, and letter sections were excluded from this synthesis as they lack an intervention. The complete procedure of study identification is depicted in Fig. 1.

2.3. Eligibility of included examinations

A comprehensive study was undertaken to examine the impact, both beneficial and detrimental, of AP and placebo techniques on the clinical result of TMS patients. The sensitivity analysis only included papers that documented the impact of interventions on the incidence of subsyncopal surgical wound infections (SSWI). Sensitivity and subclass analyses were conducted by comparing the interventional groups to a diverse range of subtypes.

2.4. Inclusion and exclusion criteria

2.4.1. Inclusion criteria

To be included in the meta-analysis, the following criteria were met: a comparison of the outcomes of AP with placebo on SSWI in individuals with TMS. The outcome should be expressed in the suitable output format for statistical analysis.

2.4.2. Exclusion criteria

Non-comparative examinations were not included in the analysis. Furthermore, the present analysis did not include letters, books, review articles, and book chapters.

2.5. Identification of examinations

Using the PICOS concept, a protocol of search techniques was developed and defined as follows: P (population) individuals with TMS; AP (intervention) or “exposure”; C (comparison): the relative effectiveness of AP compared to placebo. O (outcome): SSWI; S (design of the examination): the intended examination was unrestricted.

We conducted an extensive search of the databases PubMed, Cochrane Library, Embase, OVID, and Google Scholar until June 2023 using the targeted

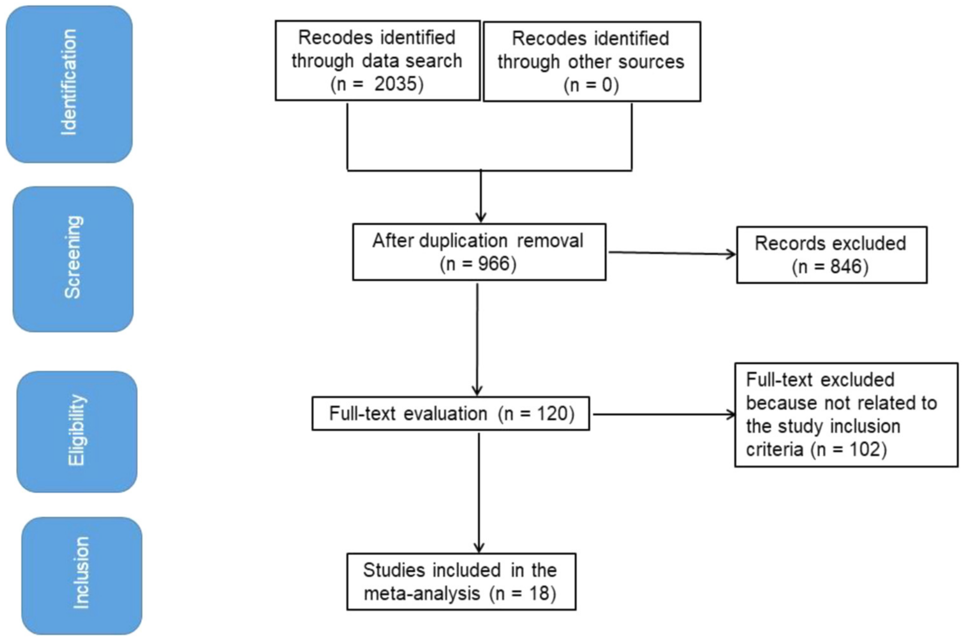

Fig. 1. Schematic diagram of the examination procedure.

Table 1. Database search strategy for inclusion of examinations.

Database	Search strategy
Google Scholar	#1 "third molar surgery" OR "placebo" OR "antimicrobial" #2 "antibiotic prophylaxis" OR "surgical site wound infection" #3 #1 AND #2
Embase	#1 'third molar surgery' /exp OR 'placebo' exp OR 'antimicrobial' #2 'antibiotic prophylaxis'/exp OR 'surgical site wound infection'/ #3 #1 AND #2
Cochrane library	#1 (third molar surgery):ti,ab,kw (placebo):ti,ab,kw (antimicrobial):ti,ab,kw (Word variations have been searched) #2 (antibiotic prophylaxis):ti,ab,kw OR (surgical site wound infection):ti,ab,kw (Word variations have been searched) #3 #1 AND #2
Pubmed	#1 "third molar surgery" [MeSH Terms] OR "placebo" [MeSH] OR "antimicrobial" [All Fields] #2 "antibiotic prophylaxis" [MeSH Terms] OR "surgical site wound infection" [All Fields] #3 #1 AND #2
OVID	#1 "third molar surgery" [All fields] OR "placebo" [All Fields] OR "antimicrobial" [All Fields] #2 "antibiotic prophylaxis" [All fields] OR "surgical site wound infection" [All Fields] #3 #1 AND #2

keywords and related terms outlined in Table 1 (Search methods for various databases). A comprehensive analysis was performed on the titles and abstracts of all the papers included in a reference management system, including with any studies that did not establish a correlation between the specific treatments and clinical results. Furthermore, two authors also act as reviewers to identify suitable examinations.

2.6. Screening of examinations

The volume of data was reduced by employing the following criteria: the surname of the first author of the examination, the period and year of the examination, the country in which the examination was conducted, the gender, the population type that was recruited for the examinations, the total number of subjects, qualitative and quantitative evaluation methods, demographic data, clinical and treatment characteristics, information sources, and outcome evaluations. Two anonymous evaluators evaluated the quality of the methodologies employed in the examinations that were chosen for further investigation, as well as the potential for bias in each examination. Each examination's methodology was independently evaluated by two distinct evaluators.

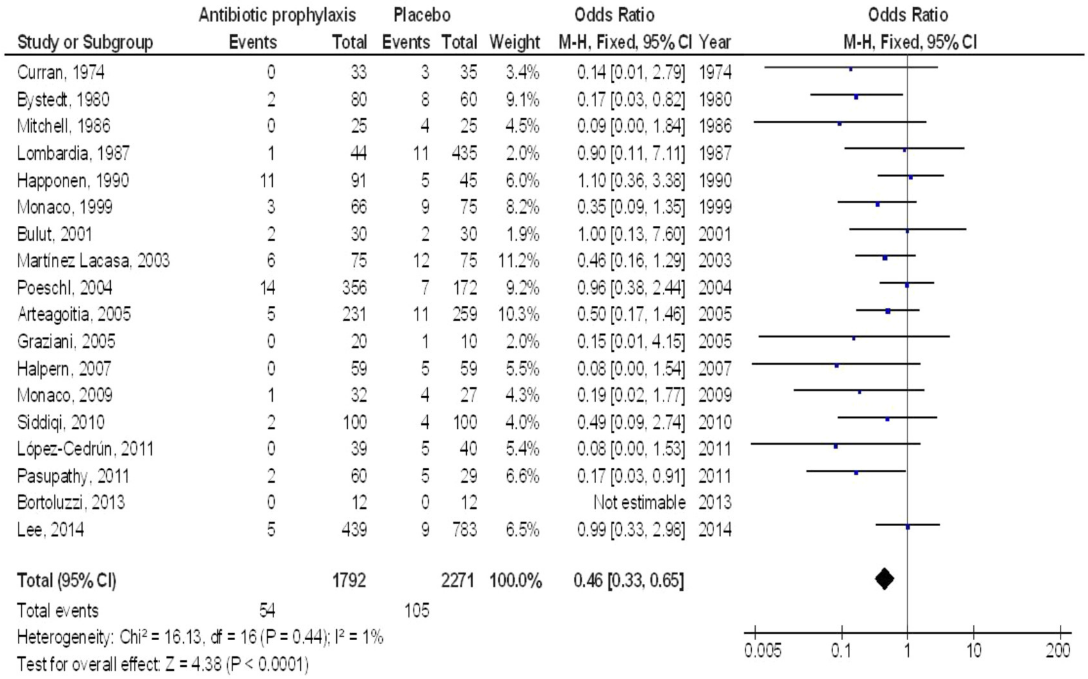

Fig. 2. The effect's forest plot of the AP compared to placebo on SSWI in personals with TMS.

2.7. Statistical analysis

A 95% confidence interval (CI) for the Odds Ratio (OR) was calculated in the present meta-analysis using dichotomous random- or fixed-effect models. The I2 index, shown as a percentage, was calculated as a numerical number ranging from 0 to 100. A value of I2 = 0 implies the absence of heterogeneity, while higher I2 values imply a higher level of heterogeneity. If the correlation coefficient (I2) was equal to or more than 50%, the random effect was selected; otherwise, the fixed effect was chosen [13]. As previously mentioned, subcategory analysis was conducted by categorizing the first assessment into distinct outcome groups. A quantitative analysis of publication bias was conducted using Begg's and Egger's tests. A p-value greater than 0.05 was considered indicative of the presence of publication bias. P-values were calculated using a two-tailed test. Statistical analysis and graphics were generated using Jamovi 2.3 algorithm.

Table 2. Characteristics of examinations.

Study	Country	Total	AP	Placebo
Curran, 1974 [14]	Canada	68	33	35
Bystedt, 1980 [15]	Sweden	140	80	60
Mitchell, 1986 [16]	Germany	50	25	25
Lombardia, 1987 [17]	Spain	479	44	435
Happonen, 1990 [18]	Finland	136	91	45
Monaco, 1999 [19]	Italy	141	66	75
Bulut, 2001 [20]	Turkey	60	30	30
Martínez Lacasa, 2003 [9]	Spain	150	75	75
Poeschl, 2004 [21]	Austria	528	356	172
Arteagoitia, 2005 [10]	Spain	490	231	259
Graziani, 2005 [11]	Italy	30	20	10
Halpern, 2007 [22]	USA	118	59	59
Monaco, 2009 [23]	Italy	59	32	27
Siddiqi, 2010 [24]	New Zealand	200	100	100
López-Cedrún, 2011 [25]	Spain	79	39	40
Pasupathy, 2011 [26]	India	89	60	29
Bortoluzzi, 2013 [27]	Brazil	24	12	12
Lee, 2014 [28]	Korea	1222	439	783
	Total	4063	1792	2271

3. Results

In the meta-analysis, 18 examinations published between 1974 and 2014 were included due to their compliance with the inclusion criteria, which were determined through a review of 2035 pertinent examinations. September 11th, 14th, and 28th The results of these investigations are summarized in Table 2. In the initial phase of the studies, 4063 individuals with TMS were enrolled; 1792 of them were receiving AP, while 2271 were receiving placebo. The sample size ranged from 24 to 1222 individuals.

AP exhibited a statistically significant reduction in SSWI (OR, 0.46; 95% CI, 0.33–0.65, $p < 0.001$) compared to placebo in individuals with TMS, with no heterogeneity (I2 = 1%) as shown in Fig. 2.

The quantitative Egger regression test and the visual explanation of the funnel plot indicated no

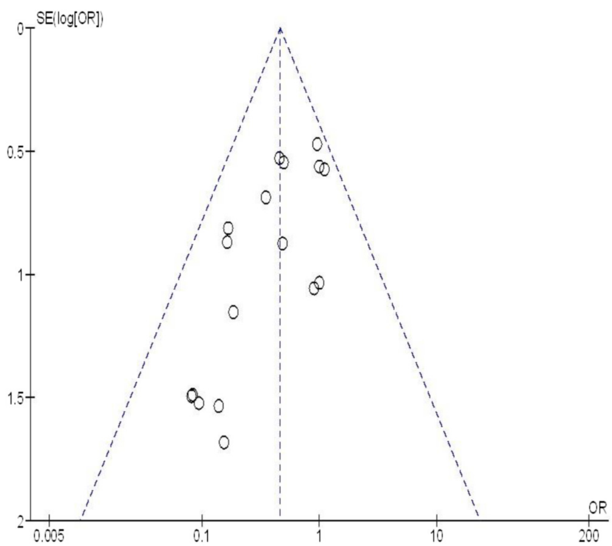

Fig. 3. The funnel plot of the AP compared to placebo on SSWI in personals with TMS.

findings of examination bias (p = 0.86), as depicted in Fig. 3. Nevertheless, the majority of the examinations in question were determined to have inadequate practical quality and without any bias in selective reporting.

4. Discussion

A total of 18 studies conducted between 1974 and 2014 were included in the present analysis. These studies included 4063 individuals who had transcranial magnetic stimulation (TMS) at the beginning of the trials. Among these, 1792 individuals were using AP, while 2271 individuals treated with a placebo [9–11, 14–28]. Data analysis showed that AP resulted in notably reduced SSWI compared to placebo in individuals with TMS. Nevertheless, caution should be exercised while interacting with its values due to the fact that examinations were conducted by different surgeons with varying skills on different types of patients, and the small sample size of many of the examinations chosen for the meta-analysis (8 out of 18 ≥100 patients).

Given that oral surgery is always conducted in a sterile and contaminated setting with a significant colonization of bacteria, and considering that postoperative complications are often caused by bacterial contamination and infections, it would be logical to recommend the use of antibiotics to prevent and decrease the occurrence of postoperative problems. However, there is no consensus on the appropriate administration of antibiotics in transcatheter mutilation surgery (TMS) due to the relatively low incidence of postoperative complications, which are usually not life-threatening. Additionally, some underpowered randomized controlled trials (RCTs) have produced contradictory results. The aim of this quantitative evaluation of randomized controlled trials (RCTs) is to gather all pertinent data and provide suggestions for action planning in transcranial magnetic stimulation (TMS). The clinical pertinence of these findings may not be as readily apparent as their statistical significance in terms of odds ratios. The pain and incapacity caused by TM surgical problems often diminish the quality of life and productivity of people affected [29]. Undoubtedly, these issues incur financial expenses that surpass those of commonly used antibiotics such as amoxicillin. From a cost-effectiveness perspective, it may be justifiable to suggest prophylactic antibiotic treatment for TMS. However, the risks of potential antimicrobial resistance and serious toxic effects are difficult to evaluate and cannot be entirely disregarded in clinical decision-making [30]. The surgeon bears the ultimate responsibility for determining whether or not to provide AP prior to TMS. In order to ascertain whether the benefits of antibiotic treatment outweigh the risks, he must evaluate all likely factors contributing to postoperative complications. The eradication of the blood clot in the extraction socket indicates that the surgical site is no longer associated with a bacterial infection.

Age, gender, and surgical trauma are recognized as contributing variables to the development of postoperative complications [31]. Administering AP only to patients believed to have increased susceptibility to postoperative complications may be advantageous. The optimal scheduling of antibiotic therapy is essential for its capacity to minimize surgical complications. In order to effectively combat germs that contaminate surgical incisions and blood clots, the antibiotic must be present at a therapeutic concentration during the initial incision and prior to the subsequent surgery. Therefore, it is necessary to provide the antibiotic around one hour prior to the surgery [32]. The results of the current investigation reinforced the efficacy of administering antibiotics before surgery in reducing postoperative complications and the ineffectiveness of postoperative dosage. The optimal dose approach for preventing surgical site wound infections (SSWIs) was administering an antibiotic 30 to 90 minutes prior to the initial incision and continuing for 3 to 5 days following the operation. Preoperative use of antibiotics as a single dose had an unpredictable effect on postoperative surgical site wound infections (SSWIs). The administration of an antibiotic dose one hour prior to surgery may be the most economically efficient approach for removing a TM, as the occurrence of surgical site wound infection (SSWI) was lower (6%) among individuals who did not take antibiotics compared to those who did. A broad-spectrum antibiotic, with efficacy against both aerobic and anaerobic bacteria, and a narrow-spectrum antibiotic, with exclusive efficacy against anaerobic bacteria, were used in most of the clinical trials analyzed. While the significance of anaerobic bacteria in postoperative complications has been emphasized [33], both types of bacteria are present in the mouth cavity and within close proximity to TMs [34]. Numerous aerobic and anaerobic bacteria are extremely susceptible to amoxicillin and other penicillin derivatives in the oral cavity. In TMS, they might be the initial option for AP [34].

Notwithstanding our attempts to employ a random effect model to enhance the robustness of the statistical analysis and to use subgroup analysis to distinguish the studies of higher quality from those of lower quality, the findings of this study cannot serve as a rigid reference in clinical practice concerning AP in TMS. While the findings of this study may be the most compelling evidence to date, a carefully designed multicenter randomized controlled trial (RCT) is necessary to reach a definitive conclusion. A definitive clinical trial should consider established risk factors such as age, gender, and smoking. It should also include a clearly defined criteria for including or excluding cases, a standard operating procedure for surgical and antimicrobial treatments, and a dependable approach for evaluating outcomes [35–41].

The meta-analysis included the following limitations: (1) the possibility of assortment bias due to the exclusion of several tests selected for the meta-analysis. Notwithstanding this, the study that was excluded did not fulfill the criteria for being included in the meta-analysis. Additionally, we needed the data to adjust for any influence of variables such as age, gender, and ethnicity on the results. Examining the influence of AP on SSWI in TMS was the primary aim of the study. Incorporating erroneous or insufficient data from a prior analysis may have heightened bias. The nutritional condition of the person, coupled with their ethnicity, gender, and age, likely served as the fundamental factors contributing to discrimination. Owing to inadequate data and certain unpublished research, values may unintentionally be influenced.

5. Conclusions

Data analysis showed that AP resulted in notably reduced SSWI compared to placebo in individuals with TMS. However, it is important to be cautious when dealing with its values due to the fact that the examinations were conducted by various surgeons with varying expertise on different types of patients, and the small sample size of several of the examinations chosen for the meta-analysis (8 out of 18 $\geq$100 individual cases).

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