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The Optimal Duration of Antibiotic Prophylaxis in Plastic Surgery: A Meta-Analysis of 32 Publications Running Head: Optimal Duration of Antibiotics in Plastic Surgery

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Abstract

Antibiotic prophylaxis administered perioperatively has been shown to decrease the risk for the core measure of post-operative surgical site infection, but specifics of use vary widely among different surgical specialties. This study aimed to perform a meta-analysis of the current literature to determine the optimal duration of antibiotic prophylaxis in the field of plastic surgery.

A systematic literature review was conducted using various terms to locate studies of prophylactic antibiotic use in the field of plastic surgery within the US National Library of Medicine (PubMed). Studies included in the analysis were those with clearly recorded antibiotic dosage, duration and incidence of surgical site infection. Studies were excluded if they included non-plastic surgery procedures or if they did not clearly meet our study parameters. 32 studies were identified. 12 of them involved head and neck surgery, 12 of them involved breast and body surgery, 7 of them involved hand surgery and 1 included multiple types of plastic surgery procedures. The data from each study was divided into one of four duration categories: no antibiotic prophylaxis, single-dose prophylaxis, 24-hour prophylaxis or extended course (24 hr+) prophylaxis. The data was then statistically analyzed for each duration group.

A Forest plot of each of the four categories was created and analyzed using the random effect model. The average percent of events per population for each category was as follows: no prophylaxis was 14.7%, a single dose prophylaxis was 7.7%, 24 hours prophylaxis was 14.1% and extended course of antibiotics was 8.8%. The confidence intervals for each of the four categories overlapped in the combined Forest plot. A comparison of the data for antibiotic prophylaxis demonstrates a possible decrease in post-operative incidents for the single dose prophylaxis and the extended course of antibiotics in comparison to no antibiotics and a 24-hour course of antibiotics. However, as the confidence intervals are wide and overlapping, these findings are not statistically significant. At this time, more research is needed to reach a better understanding of the optimum duration of antibiotic prophylaxis following plastic surgery procedures.

Keywords: Antibiotic prophylaxis; Antibiotic duration; Surgical site infection; Wound infection; Plastic surgery; Meta-analysis

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Introduction

Surgical site infections (SSIs) are one of the largest contributors to complications following surgical procedures. In addition, SSIs are the second most common type of nosocomial infections, with reported rates ranging from 1% to 30% depending on the procedure [1,2]. Patients who contract SSIs are estimated to have re-admission rates up to five times that of patients without SSIs and mortality rates up to twice as high [1,3]. SSIs also impact multiple economic factors including length of stay, readmission rates, and use of both hospital and ancillary services, collectively leading to an overall increase in healthcare related costs [4]. In addition to affecting healthcare expenditures, SSIs may also directly affect physician reimbursement. SSIs are designated as a never event by the Center for Medicare and Medicaid Services, meaning that physicians may not be compensated for procedures in which patients subsequently develop post-operative infections [5,6].

Antibiotic prophylaxis to combat surgical site infection was instituted in the 1960's along with the initiation of a wound classification system by the National Research Council [7]. Since its inauguration, extensive clinical research has been carried out in order to develop standards and guidelines for antibiotic type and duration depending on the procedure being performed. Today, guidelines for the prophylactic use of antibiotics are implemented internationally including within the USA, UK, Canada, Europe, and Australia [8-10]. They exist in multiple surgical fields such as general surgery, colorectal surgery, and obstetrics [2,6,11-13]. Some surgical fields, such as cardiothoracic surgery, do not yet have established guidelines in place for antibiotic prophylaxis, but have multiple studies with suggestions given for evidence-based antibiotic prophylaxis use [14,15]. Additionally, outside of the surgical fields, antibiotic prophylaxis has been a topic of research as well. The American Heart Association produced well-known recommendations for the prevention of endocarditis with dental procedures [16] and guidelines have even been developed for prevention of infections following combat related injuries [17].

Despite these strides, within some subspecialties antibiotic prophylaxis has been less extensively studied and the ideal durations and types are often not specified. A striking example is the field of plastic surgery. Very few studies have been carried out looking at optimal use of antibiotic prophylaxis and practice is largely dependent on physician preference and individual knowledge [7]. The objectives for this study were to seek out and compare studies on the use of antibiotic prophylaxis in the field of plastic surgery. In doing so, we hoped to determine the optimal duration of antibiotic prophylaxis.

Methods

A literature search was performed in the National Library of Medicine using the medical subject headings (MeSH terms) "prophylaxis," "prophylactic antibiotics," "pre-operative antibiotics," "peri-operative antibiotics" and "surgical site infection" combined with various modifiers such as "wound infection," "postoperative complication," "timing" and "duration." To narrow the search field, the article type filter for "clinical trial" was applied. The articles obtained from this search were then reviewed to acquire those that fell within the bounds of our study design. After the initial search, a secondary search was performed using the same terms and modifiers in the top five highest impact plastic surgery journals to ensure the maximum number of studies fitting our criteria had been found. The journals searched included Plastic and Reconstructive Surgery, Journal of Plastic, Reconstructive and Aesthetic Surgery, British Journal of Plastic Surgery, Annals of Plastic Surgery, Aesthetic Plastic Surgery, and Aesthetic Surgery Journal.

Articles dealing specifically with antibiotic prophylaxis in plastic surgery were read for content. Publications were excluded from our study if they included non-plastic surgical procedures, if they did not specify the timing, number, type or duration of antibiotic prophylaxis, if the outcome of surgical site infection was not included, or if the article contained incomplete statistics.

Data was independently extracted from each qualifying study and recorded on a Microsoft Excel spreadsheet. Durations of antibiotic prophylaxis were arbitrarily divided into four groups: no antibiotic prophylaxis, single dose prophylaxis, 24 hour antibiotic course and extended course, which was defined as greater than 24 hours of prophylaxis. Pertinent data points extracted from each study are listed in **Table 1**. In addition, information about the publication such as authors, study design, field and publication venue were recorded. Analysis of the data was conducted using Microsoft Excel. The random effects statistical model was used to calculate outcomes and a Forest Plot was created of the categories.

Results

A quorum diagram detailing the literature search can be viewed in **Figure 1**. A total of 32 randomized controlled trials were identified from the initial 7,069 articles as dealing specifically antibiotic prophylaxis in plastic surgery and included 12,641 patients in all [18-49]. Within the various subdivisions of plastic surgery twelve of the studies investigated head and neck procedures, twelve looked at breast and body surgeries, seven focused on hand and extremity surgeries, and one study included multiple types of plastic surgery procedures. The patients from all studies were divided into the four general prophylaxis groups (no prophylaxis, single dose prophylaxis, 24 hour prophylaxis and extended course prophylaxis). Cumulatively, there were 2,425 patients in the group receiving no antibiotic prophylaxis, 5,033 in the group receiving a single dose of antibiotic prophylaxis, 1,052 in the group receiving 24 hours of antibiotic prophylaxis and 4,104 in the group receiving extended course prophylaxis.

Table 1 Data points extracted from the 32 selected articles.

Data Type
Total number of study participants
Number of participants in each prophylaxis group
Type of antibiotic
Timing of first dose
Total number of doses
Duration of antibiotic course
Cumulative infection rate
Infection rate among each prophylaxis group
Morbidities other than SSI and mortalities

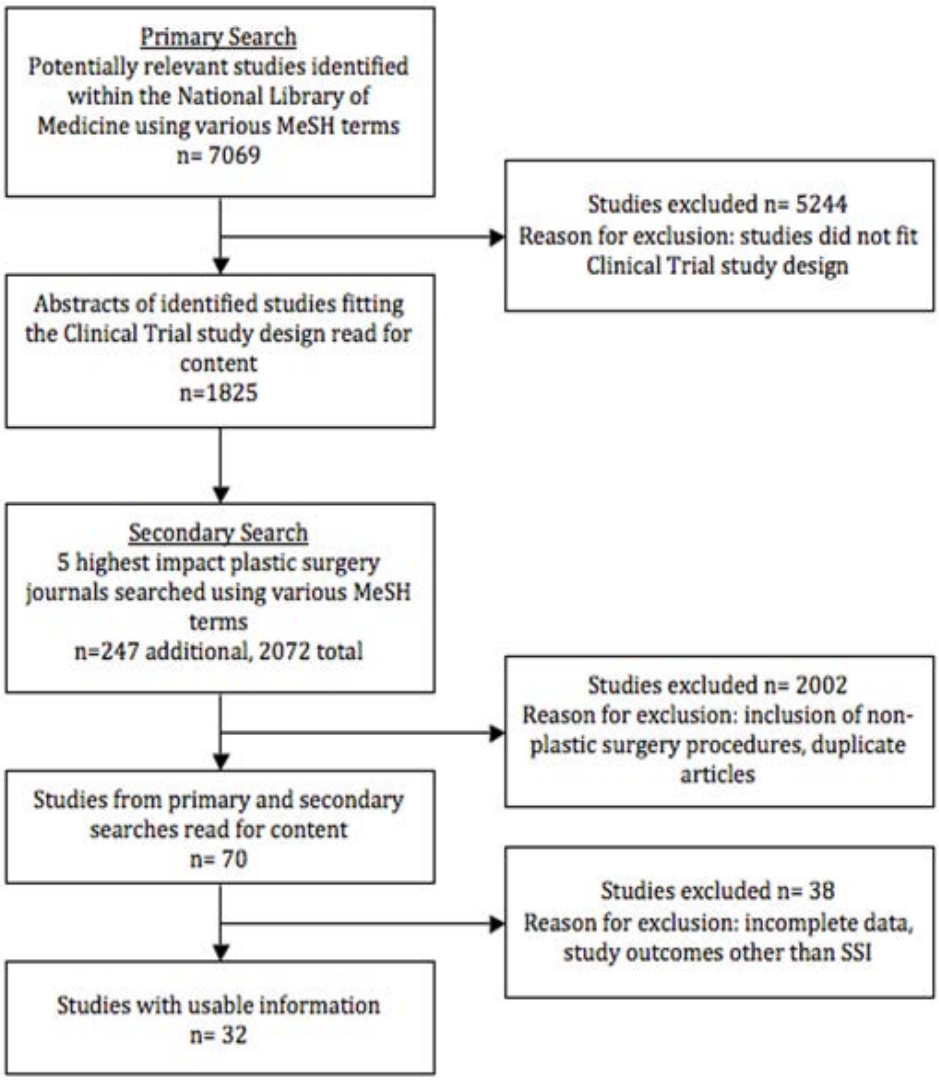

Figure 1 Literature review quorum diagram.

Table 2 Surgical site infection rates for the four durations of antibiotic prophylaxis.

Prophylaxis Duration	Average Adverse Events (%)
No antibiotics	14.8
Single dose	7.7
24 hour antibiotics	14.1
Extended antibiotics	8.8

When analyzed, the varying prophylaxis durations did demonstrate differences in the average number of adverse outcomes **(Table 2)**. However, each category also demonstrated a great deal of variability between studies **(Table 3)**. The results show that are single dose of antibiotics have the lowest incidence at 7.7%, followed closely by the extended course of antibiotic prophylaxis at 8.8%. The 24-hour prophylaxis course demonstrated an average infection rate of 14.1% and the group receiving no prophylaxis predictably demonstrated the highest average rate of infection at 14.9%.

It was curiously observed that the 24-hour prophylaxis group appeared to have significantly higher rates of SSI than either the single dose or extended course groups, closely resembling the group receiving no prophylaxis. Upon analysis of the studies, it was determined that a larger number of hand and extremity surgical procedures were included in the 24 hour group than in either of the other three prophylaxis groups. Many reconstructive hand procedures occur after trauma and can therefore be categorized as contaminated procedures, while elective procedures such as breast reconstruction are categorized as clean or clean-contaminated. It was hypothesized that the larger rate of traumatic events among the hand procedures resulted in higher initial rates of surgical contamination and therefore drove the post-operative rates of SSI up in the 24-hour prophylaxis group.

A Forest Plot of the results depicted similar trends **(Figure 2)**. The variability amongst the studied resulted in large, overlapping 95% confidence intervals. The differences in average rate of SSI indicative there is a slight improvement in outcomes in the

Table 3 SSI rates among each study broken down by prophylaxis group.

No Antibiotic Prophylaxis		Single Dose Antibiotic Prophylaxis		24 Hour Antibiotic Prophylaxis		Extended Course Antibiotic Prophylaxis	
Study	Outcome	Study	Outcome	Study	Outcome	Study	Outcome
Aydin	3.43 %	Clayton	34.33 %	Liu, 2012	19.51 %	Clayton	18.10 %
Veiga-Filho	14.00 %	Mirzabeigi	2.31 %	Aydin	3.13 %	Liu, 2012	15.52 %
Sevin	13.04 %	Danda	9.33 %	Danda	2.67 %	Mirzabeigi	0.00 %
Hall	4.56 %	Khan	0.84 %	Khan	2.62 %	Khan	1.72 %
Ahmadi	29.41 %	Kang	10.71 %	Lovato	13.33 %	Veiga-Filho	2.00 %
Whittaker	14.55 %	Sevin	4.35 %	Liu, 2008	30.77 %	Kang	7.14 %
Kompatscher	3.68 %	Hall	3.22 %	Andrews	7.32 %	Lovato	10.67 %
Stevenson	4.21 %	Ahmadi	17.65 %	Lindeboom	8.06 %	Liu, 2008	18.52 %
Madsen	10.15 %	Lindeboom	9.68 %	O'Grady	18.75 %	Sevin	8.70 %
Amland	20.51 %	Rajan	0.00 %	Carroll	11.43 %	Andrews	10.98 %
Zubowicz	46.67 %	Whittaker	12.50 %	Bentley	60.00 %	Ahmadi	25.00 %
Platt	8.14 %	Kompatscher	3.92 %	Hotz	2.00 %	O'Grady	6.60 %
Sloan	30.00 %	Thomas	5.55 %	Mustafa	13.33 %	Rajan	3.00 %
Worlock	5.88 %	Madsen	4.90 %	Sloan	0.00 %	Whittaker	4.35 %
		Amland	5.06 %	Johnson	18.87 %	Carroll	10.26 %
		Hotz	2.04 %			Stevenson	3.06 %
		Platt	4.47 %			Bentley	6.67 %
						Mustafa	10.00 %
						Madsen	6.57 %
						Zubowicz	0.00 %
						Sloan	2.08 %
						Johnson	25.00 %
						Worlock	7.04 %

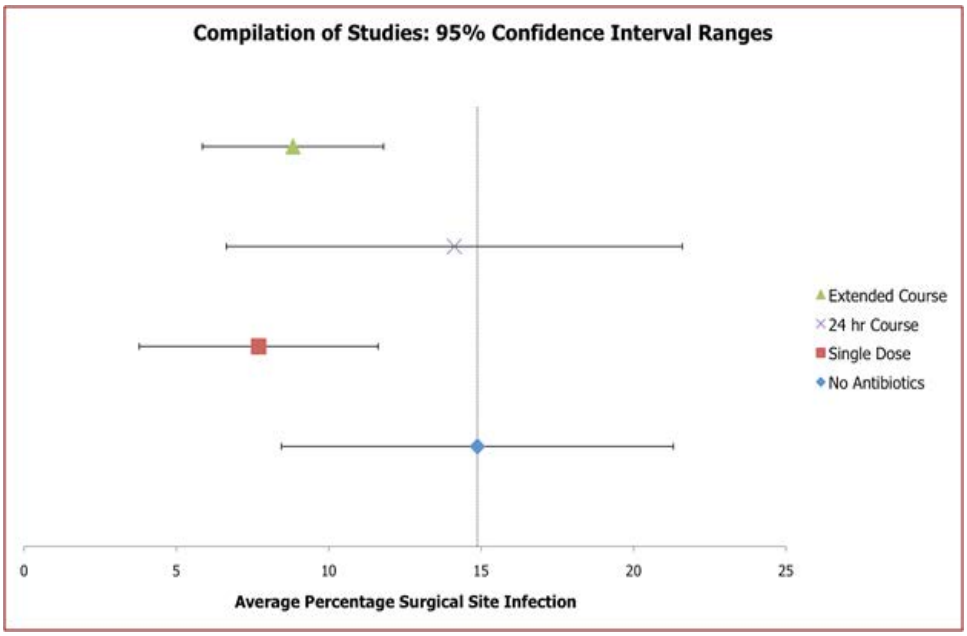

Figure 2 The combined Forest Plot with 95 % confidence intervals for all four antibiotic durations.

single dose and extended dose prophylaxis, but the overlapping confidence intervals render the difference as not statistically significant.

Discussion

In surgery, a great deal of focus has been placed on prevention of complications, particularly ones such as SSIs. Antibiotic

prophylaxis is one area of developing research considered crucially important, but acknowledged by many to be lacking in evidence in some fields [15]. Within the field of plastic surgery in particular, there is yet to be a prospective trial that establishes a concrete, evidence-based standard of care and antibiotic prophylaxis remains a much discussed and studied topic. When used appropriately, antibiotic prophylaxis has been shown to decrease the incidence of SSIs, resulting in improved outcomes as well as economic benefits [50]. Excessive use of antibiotics, however, is strongly discouraged due to the potential for developing resistance as well as for harmful side effects and consequences to patients, such as *C. difficile* colitis [50,51].

At this time, wide variations regarding the use of antibiotics prophylactically are present not only in plastic surgery, but in most surgical fields. A recent international survey found differences to exist between European and North American surgeons' use of antibiotic prophylaxis. Overall, the survey suggested that hesitancy is present for using antibiotics as recommended citing that many surgeons continue the prophylaxis for multiple days over the recommended prophylaxis durations following surgery [52]. This study is not alone in illustrating a need for stronger adherence to guidelines regarding prophylactic antibiotics [53].

Some important limitations to this study should be pointed out. Firstly, we acknowledge the limitation of grouping all surgical procedures, within the various subdivisions of plastic surgery, solely based on four general prophylactic antibiotic groups. The broad inclusion criterion was to allow clinical heterogeneity; however, prophylactic antibiotic treatments should be used on a case-by-case basis. Future investigation may be warranted in further stratifying based on wound type or procedure being performed. Lastly, the possible introduction of selection bias as well as other biases carried over from the studies, in which this meta-analysis examined, should be recognized.

In the shifting political and financial aspects of healthcare, guidelines and adherence to prophylaxis will likely become even more significant. Due to the changing economics and policies of medicine, as well as to the responsibility of physicians to their patients, it is crucial that the body of evidence-based literature in plastic surgery regarding antibiotic prophylaxis be improved.

Conclusion

This meta-analysis underlines the conflicting reports regarding the efficacy of antibiotics in different plastic surgery procedures and emphasizes the variability among usage currently present in the plastic surgery literature. When the data was compiled and analyzed, large, overlapping confidence intervals were demonstrated on Forest plot. These intervals illustrate the lack of cohesiveness among the current literature and indicate the need for a greater number of subjects in the study populations in order to determine whether or not significant differences exist.

Recent studies indicate that antibiotic prophylaxis use in plastic surgery is increasing, emphasizing a growing demand for concrete scientific evidence and guidelines [54]. The growing use along with the results of this study demonstrates a need for increased (and improved) research regarding the subject of antibiotic prophylaxis in the field of plastic surgery.

Conflicts of Interest and Sources of Funding

None declared.

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