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Infection Rates following Peri-Operative Prophylactic Antibiotics vs. Post-Operative Extended Regimen Prophylactic Antibiotics in Surgical Management of Mandibular Fractures

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Abstract

Purpose: To determine whether or not an extended regimen of prophylactic antibiotics following either open or closed reduction of mandibular fractures is beneficial in lowering the rate of infection in post-operative patients.

Patients and Methods: This study is a retrospective chart review of 150 patients treated operatively for both complicated and uncomplicated mandibular fractures at UNM Health Sciences Center in Albuquerque, NM, between January 1st, 2000 and June 12, 2007. Treatment modalities used were closed reduction with maxillomandibular fixation or open reduction and internal fixation with either wire osteosynthesis or rigid internal fixation. Patients fell into one of two groups: the first group received antibiotics peri-operatively, which consisted of no more than 24 hours of antibiotics in the postoperative period and the second group received extended regimen antibiotics, which consisted of anywhere from 24 hours to 10 days of antibiotics in the postoperative period. 75 patients were included in each group. The type of antibiotic prescribed was at the discretion of the operating surgeon. This study was done using an intention-to-treat analysis. Postoperative infection was diagnosed either subjectively or objectively by the clinician evaluating the patient at follow-up appointments.

Results: In the extended antibiotic group, 8 out of 75 subjects (10.67 percent) developed infection. In the peri-operative antibiotic group, 10 out of 75 subjects (13.33 percent) developed infection. Statistical analysis using chi-square distribution showed that this difference in proportions was not significant (Chi-square=0.06, p=0.8).

Conclusions: This study found that the use of post-operative prophylactic antibiotics does not have a statistically significant effect on post-operative infection rates in surgical management of complicated or uncomplicated mandibular fractures.

Introduction

The original guidelines for timing and use of antibiotics to prevent infection post-operatively were established by Burke and Miles et al's experimental observations. [1,2] They noted that antibiotics must be given within 4 hours after injection of bacteria into a surgical site to prevent the aggressive level of infection that occurs when no antibiotics are administered. These guidelines were set in the 1960's and were generalized for all types of surgeries. Additional studies have proven that a clear benefit does exist when prophylactic antibiotics are used for mandibular fractures. [3,4] A study by Chole and Yee in 1987 showed that infection rates for facial and mandibular fractures was reduced from 42 to 9 percent and 44 to 13 percent respectively in groups treated with antibiotics both pre and post-operatively compared to groups who received no antibiotics. Although these studies helped establish the use of antibiotics for mandibular fractures, they did not establish any guidelines for duration of use. Other recommendations have been made, however, regarding antibiotic administration itself including proper dose, use of narrow spectrum drugs and route of administration. Included in these recommendations was the new suggestion that antibiotics should be used for only a brief period of time, primarily intra-operatively. [5,6]

Studies have been done that have shown that single-dose antibiotic prophylaxis in surgical procedures is equivalent to or better than multiple doses in preventing postoperative infection. [7,8,9] Regarding mandibular fractures specifically, Abubaker and Rollert, in a randomized, double blind and placebo controlled clinical study, showed that extended regimen post-operative antibiotics had no benefit in reducing the incidence of infection in uncomplicated mandibular fractures. In addition, in 2006 Miles, Potter and Ellis in a prospective randomized trial could not prove any statistically significant benefit to the administration of postoperative antibiotics in patients undergoing open reduction and internal fixation of mandibular fractures.

Because to date, there exist no established guidelines for the duration of antibiotics following surgery for mandibular fractures, this retrospective study was designed to help determine whether or not an extended regimen of prophylactic antibiotics following either open or closed reduction of mandibular fractures is beneficial in lowering the rate of infection in post-operative patients.

Methods

Patients

The study sample consisted of patients treated operatively for both complicated and uncomplicated mandibular fractures at UNM Health Sciences Center in Albuquerque, NM, between January 1st, 2000 and June 12, 2007. Patients were either treated by the Plastic Surgery service or the ENT service and admission was not a requirement for inclusion in the study. A minimum of 6 weeks of follow-up data was required for inclusion and no age requirements were used. Patients were chosen using a random number generator. The study sample consisted of a total of 150 patients. 75 patients were assigned for each group. Out of the original group chosen, 19 patients were excluded; 3 because of pre-existing infection, 14 because of lack of adequate follow-up and 2 because of existing antibiotic use at the time of injury. These were all replaced by additional patients using the random number generator. This study was approved by the

Human Research Review Committee at University of New Mexico Health Sciences Center.

Demographic data are summarized in Table 1. Briefly, the sample ranged in age from 4 to 61 years with a mean age of 26.67 years (SD 10.74). 124 patients (82.67 percent) were male and 26 (17.33 percent) were female. 122 patients (81.33 percent) were treated with open reduction and 28 (18.67 percent) were treated with closed reduction. The most commonly used antibiotic used was Ancef (27.33 percent), followed by Clindamycin (26 percent) and unknown (18 percent). 22 patients (14.77 percent) either admitted to or tested positive for drug use and 34 (22.82 percent) either admitted to or tested positive for alcohol use. A total of 18 patients (12 percent) developed a post-operative infection.

TABLE 1
Descriptive Statistics of Study Sample (n=150)

Study Variable	
Age (years)	26.67 ± 10.74*
Gender:	
Male	124 (82.67%)
Female	26 (17.33%)
Type of reduction:	
Open	122 (81.33%)
Closed	28 (18.67%)
Type of Antibiotic:	
Ancef	41 (27.33%)
Augmentin	7 (4.7%)
Cefepime	1 (0.67%)
Cefotaxime	1 (0.67%)
Cefotetan	1 (0.67%)
Clindamycin	39 (26%)
Doxycycline	1 (0.67%)
Imepenim	1 (0.67%)
Keflex	18 (12%)
Penicillin	7 (4.7%)
Unasyn	2 (1.3%)
Zosyn	3 (2%)
Unknown	27 (18%)
Drug use:	
Yes	22 (14.77%)
No	127 (85.23%)
Alcohol use:	
Yes	34 (22.82%)
No	115 (77.18%)
Post-operative infection:	
Yes	18 (12%)
No	132 (88%)

* Mean ± standard deviation

Study Design

Treatment modalities used were closed reduction with maxillomandibular fixation or open reduction and internal fixation with either wire osteosynthesis or rigid internal fixation. Because of the large range of injury types, no attempt was made to control for location of fracture(s) and no data were collected on the type of rigid fixation used. Patients were placed into one of two groups: those treated with antibiotics either (1) peri-operatively, which consisted of no more than 24 hours of antibiotics in the postoperative period or with (2) extended regimen, which consisted of anywhere from 24 hours to 10 days of antibiotics in the postoperative period. Patients were prescribed the type of antibiotic deemed appropriate by the operating surgeon. Patients who were noted to have been prescribed extended regimen antibiotics but did not fill the prescription were kept in their originally assigned group consistent with an intention-to-treat analysis. All patients were given a prescription for chlorhexadine oral rinse post-operatively.

Using a standardized data-collection form we retrospectively abstracted the following study variables from each patient record: (1) age, (2) sex, (3) number of injuries (single vs. multiple), (4) drug or alcohol abuse, (5) method of surgical management, (6) antibiotic type and (7) rates of infection. Postoperative infection was diagnosed either subjectively or objectively by the clinician evaluating the patient at follow-up appointments. No data were collected on the rates of delayed union or non-union.

Statistical Analysis

To detect a difference in infection rate of 2 percent between the two groups, we estimated that 1604 subjects would be needed in each group. This study looked at only 75 patients in each group and therefore can be viewed as a pilot study for future research.

Data management was carried out using Microsoft Excel 2002 (Microsoft Corporation, Redmond, WA). The relationship between infection and treatment was evaluated using the chi-square distribution. The Yates correction for continuity was used. Fisher's exact test was used in cases of heavily skewed or sparse tables. Two-tailed tests and a Type I error rate of 0.05 were employed throughout. Statistical calculations were made with Statgraphics Plus for Windows Version 4.1, (Manugistics, Inc., Rockville, MD).

Results

Table II summarizes the univariate analysis of the association between certain risk factors and treatment modality in an attempt to identify potential confounding variables. Based on this analysis, the two treatment modality samples (peri-operative antibiotics and extended regimen antibiotics) were found to have no significant differences among the risk factors analyzed. Therefore, no risk factors were identified as possible confounding variables.

Table III summarizes the univariate analysis of the association between treatment modality and risk factor versus infection rate. In the extended antibiotic group, 8 out of 75 subjects (10.67 percent) developed infection. In the peri-operative antibiotic group,

10 out of 75 subjects (13.33 percent) developed infection. This difference in proportions was not significant (Chi-square=0.06, p=0.8). Type of reduction (open vs. closed) was not statistically associated with post-operative infection (p=0.57). Of the risk factors analyzed, gender, multiple fractures or alcohol use were also not statistically associated with post-operative infection (p=1.0, 0.67 and 0.80 respectively). Drug use was found to be statistically significant with an infection rate of 37 percent in those admitting to or testing positive for drugs versus an infection rate of 10 percent in those who did not. This difference was further analyzed using Fisher's Exact Test (p=0.02).

TABLE 2
Distribution of Risk Factors by Treatment Modality

	Treatment Modality		
Risk Factor	Peri-operative (n=75)	Extended (n=75)	*p* value
Age (years)	28.07±9.9	27.26±11.56	0.64*
Gender:			
Male	61	63	
Female	14	12	0.83∞
Multiple Fractures:			
Yes	42	44	
No	33	31	0.87∞
Type of reduction:			
Open	63	59	
Closed	12	16	0.53∞
Drug use:			
Yes	10	12	
No	64	63	0.84∞
Alcohol use:			
Yes	13	21	
No	61	54	0.18∞

* T-test
∞ Chi-squared

TABLE 3
Distribution of Infection rate by Treatment Modality and Risk Factor

	Infection		
	Yes	No	*p* value
Treatment Modality:			
Peri-operative	10	65	
Extended	8	67	0.80*
Gender:			
Male	15	109	
Female	3	23	1.0*
Multiple Fractures:			
Yes	9	77	
No	9	55	0.67*
Type of reduction:			
Open	16	106	
Closed	2	26	0.57*
Drug use:			
Yes	6	16	
No	12	116	0.02∞
Alcohol use:			
Yes	5	29	
No	13	103	0.80*

* Chi-squared
∞ Fisher's exact test

Discussion

The mandible is the second most commonly injured facial bone and represents anywhere from 25 to 70 percent of all facial fractures.[10,11] The primary causes of mandibular fractures are vehicular accidents and assault, both very common occurrences in the United States in patients of all ages.[12] Prognosis depends on a number of factors including time to treatment, co-morbid conditions, age, type and location of fracture, alcohol use, socioeconomic status and a complication seen less frequently in recent years, infection. Infection rates have decreased significantly since the use of antibiotics began but is still a major complication and a common cause of mal-union or non-union of repaired mandibular fractures. In his 1996 article, Ellis notes that fibrous union is a common complication of infection associated with rigid internal fixation, which he attributes to a lack of osseous tissue formation caused by an induced hypoxic environment.[13] Although the use of peri-operative antibiotics use in surgical repair of mandibular fractures has been well established, there are still no guidelines for the duration of antibiotic treatment post-operatively. There continue to be many surgeons who prescribe extended regimen antibiotics post-operatively to all patients, thus creating higher costs and a higher chance for the emergence of resistant organisms.

There have been two recent studies that have shown no improvement in post-operative infection rates with the use of extended regimen post-operative antibiotics in the surgical treatment of mandibular fractures. In 2001 Abubaker and Rollert conducted a prospective, randomized, double blind clinical study to evaluate the difference between the effects of a 5-day post-operative course of oral antibiotics versus placebo on the incidence of post-operative infection in uncomplicated fractures of the mandible. This was a preliminary study with only 30 patients. The exclusion criteria included gun shot wounds, complicated fractures, documented immunocompromised medical status, allergy to penicillin, and patients who were not compliant with medication. Patients in both groups were given 2 million U of aqueous penicillin G intravenously every 4 hours from admission through the intra and peri-operative period and for 12 hours post-operatively. Patients in group 1 then received oral Penicillin VK, 500 mg every 6 hours for 5 days. Patients in group 2 received oral placebo using the same schedule. Follow up was performed using a standardized form at 1, 2, 4 and 6 weeks. This study concluded, "The use of post-operative oral antibiotics in uncomplicated mandibular fractures had no benefit in reducing the incidence of infections." The overall infection rate was 13%. It is surprising that the infection rate was this high given that this study excluded many patients who may be at risk for infection including those with complicated fractures, gunshot wounds, and those with immunocompromised status. It should be noted that although they only looked at uncomplicated fractures which may have a lower infection rate overall anyway, a majority of their patients received treatment with open reduction for at least one of their fractures (85% in group 1 and 87% in group 2). In addition, this study did not use an intention to treat analysis. Patients who were not compliant with post-operative antibiotic use and therefore may have been at higher risk for infection because of their noncompliance or socioeconomic status were excluded from the study. Although this may not have affected the main outcome it likely did affect the overall infection rate.[8]

In 2006 Miles, Potter and Ellis conducted a prospective randomized trial of patients treated for mandibular fractures using open reduction and internal fixation. Patients were excluded if: their fracture was infected at the time of treatment, their fractures were the result of a gunshot wound or there was insufficient follow-up (< 5 weeks). A total of 181 patients were included in the final study sample. All patients received pre-operative antibiotics not mandated by study protocol. At the time of surgery the patients were randomized into 2 groups. Group Ab received intra-operative antibiotics which consisted of 2 g cephazolin intravenously (900 mg clindamycin if allergic to penicillin) as well as 2.4 mIU of intramuscular penicillin G benzathine at the conclusion of the procedure. Patients allergic to penicillin received intravenous clindamycin until discharged, and then oral clindamycin for 5 to 7 days. The non-Ab group received intra-operative antibiotics (as above) but did not receive postoperative antibiotics. The overall infection rate was found to be 12 percent. And as in the above study, these researchers stated, "they could not prove any statistically significant benefit to the administration of postoperative antibiotics in patients undergoing open reduction and internal fixation of mandibular fractures." Although of those patients who developed infections, those who received postoperative antibiotics had a longer time between surgery and the development of infection than those who did not receive antibiotics the infection rate between the two groups was not significant. This study also did not use an intention to

treat analysis (patients who were placed in the Ab group originally and did not receive their 2.4 mIU of intramuscular penicillin G at the conclusion of the procedure were then placed into the non-Ab group). In addition, the authors acknowledge that three patients were still placed in the Ab group but did not receive any at the conclusion of the procedure. It is unknown whether this may have had an effect on the overall infection rates for both groups. [9]

Our study results support the above conclusions that the use of post-operative prophylactic antibiotics does not have a statistically significant effect on post-operative infection rates in surgical management of mandibular fractures. Our overall infection rate was 12 percent, which is consistent with the above-mentioned studies and the study by Chole and Yee.[4] All of these rates however are higher than in past studies. [14,15] We found no statistically significant relationship between post-operative infection rate and type of reduction used, gender, multiple fractures or alcohol use. A study by Stone, Dodson and Bays in 1993 found that type of reduction did have a statistically significant effect on post-operative infection rate.[16] This may have been overestimated because three modalities were compared separately (infection rates for closed reduction, open reduction internal fixation and rigid internal fixation were 0 percent, 20 percent and 6.3 percent respectively) and in our study we analyzed open reduction internal fixation and rigid internal fixation as one group. Although it is sensible to conclude that open reduction would result in a higher infection rate, our study may have lacked the statistical power to detect this (81 percent of our sample underwent at least one open reduction). In addition, similar to the above-mentioned study, we did not find an increase in infection rate among patients with multiple versus single fractures. In 2000 Mathog et al. found an increase in non-union secondary to infection in patients with multiple mandibular fractures. [17] Although we did not analyze mal-union or non-union specifically, our sample size would likely not have been large enough to detect a difference as their study consisted of 1432 patients with a non-union rate of 2.8%. Mathog et al. suspected that delay in treatment was a contributing factor to non-union, although past studies showed that in patients receiving antibiotics, a delay in treatment did not increase the risk of infection. [4,14] Our study did not include an analysis of time to treatment.

We did find that drug use had a statistically significant effect, increasing the infection rate post-operatively. This was consistent with past studies. Passeri, Ellis and Sinn in a 1993 study showed that chronic substance abuse could significantly affect outcomes, notably increasing infections and nonunions.[18] It should be noted that our study did not find a significant relationship between alcohol use and infection rate. We may have lacked the statistical power to detect this relationship and in addition, patients may have not been truthful about actual alcohol use and were not included in the alcohol group because their blood level was 0 at the time of presentation.

There are certain limitations that our study poses that should be addressed. First, our sample size may not have been large enough to detect the differences in infection rates necessary to reach statistical significance. As mentioned above, to detect a 2 percent difference, we would have required 1604 patients in each group. Our study had only 75 patients in each group. In that respect, it can be viewed as a pilot study for future research. In addition, we did not group our patients according to specific surgical management or surgeon. This may be necessary for a future study because different surgeons, using specific surgical management and even different operating room staff

may have varied rates of post-operative infection. An important variable that cannot be controlled for in a retrospective chart review is patient compliance. The only proof we had access to was based on the questioning of the patient (and charting of the information) by the surgeon at the follow-up appointment.

In conclusion, our results are consistent with previous studies in that the use of post-operative prophylactic antibiotics does not have a statistically significant effect on post-operative infection rates in surgical management of mandibular fractures. Although peri-operative prophylactic antibiotics have been proven to lower infection rates post-operatively and are in wide use, there seems to be no role for continuation of these antibiotics beyond 24 hours. Larger studies, with improved control of confounding variables may still need to be done to further prove this hypothesis.

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