Original Article

Treatment of odontogenic infections: An analysis of two antibiotic regimens

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ABSTRACT

Purpose: Retrospective analysis of the efficacy for two commonly used antibiotic regimens in the management of severe odontogenic infections.

Patients and Methods: Evaluation of records of patients admitted to the Oral and Maxillofacial Surgery service at Boston University Medical Center from 2009 to 2014 with severe infections of odontogenic origin (SOI). Patients were divided into two groups based on the administered intravenous antibiotic: 1) Group I: Clindamycin only and 2) Group II: Penicillin and Metronidazole. Variables evaluated included demographic characteristics, ASA status, and anatomic site of infection risk, length of hospital stay, antibiotic failure, and pharmaceutical treatment cost.

Results: 78 patients (46 males and 32 females) were included in the study. There were 57 patients in group I (average age 32.6 years) and 21 in Group II (average age 32.8 years). The average white cell count at time of admission count was higher in Group I (19.3) versus Group II (17.4). Antibiotic failure rate was 3.5% in Group I and 4.7% for group 2 patients.

Conclusion: Clindamycin alone and combination of Penicillin with Metronidazole are both effective pharmaceutical regimens for SOI. Clindamycin therapy resulted in shorter hospital stay and lower net treatment costs with a slightly higher success rate.

1. Introduction

Patients with severe head and neck infections of odontogenic origin (SOI) present a significant challenge to surgeons from both medical and surgical standpoint. Infections from teeth that are limited to the oral cavity or superficial anatomic spaces are primarily managed on an outpatient basis with control of the etiological factor, antibiotics, and surgical incision and drainage if necessary. However, infections involving deep head and neck fascial spaces usually require hospital admission and management as an inpatient since they have the potential to evolve into true medical and airway emergencies. Despite the odontogenic origin of the majority of these infections, the treatment of such infections can be led by various medical or surgical specialties, often subject to individual hospital policies and doctor availability.¹

The aim of this study was to compare the efficacy of two antibiotic treatment regimens in the management of SOI. We hypothesized that results could help clinicians in their decision making process while managing SOI patients with the objectives of being cost-effective and decreasing the use of unnecessary antibiotics which has been shown to promote antimicrobial resistance.

2. Patients and methods

This study involving retrospective record analysis was approved by the institutional review board at Boston University. The inclusion criteria were as follows: 1) Patients with SOI managed by the Oral and Maxillofacial Surgery (OMS) service at Boston Medical Center between 2009 and 2014, 2) Surgery under general anesthesia which involved incision and drainage, removal of the source of infection and drain placement within 24 h of admission, 3) Procurement of culture and sensitivity samples, and 4) Antibiotic therapy with either 3 Clindamycin or Penicillin and Metronidazole. Patients who developed multi organ diseases due to non odontogenic causes were excluded from the study. Patients who were given antibiotics other than the study groups were also not included in the study. For study purposes, all patient records were divided into two groups based on the type of antibiotics administered: 1) Group I: patients treated with intravenous (IV) Clindamycin (600 mg every 8 h), and, Group II: IV Penicillin G (2 million units every four hours) and IV Metronidazole (500 mg every 8 h). Patients were discharged from the hospital when they were found afebrile for a period of 24 h, along with normalization of white blood cell count (WBC), and adequate oral intake (> 1500 calories). Once

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discharged from the hospital, all patients were prescribed oral antibiotic therapy for 7 days. Group I patients were prescribed Clindamycin - 600 mg to be taken every 8 h while patients in Group II received Penicillin VK - 500 mg to be taken every 6 h.

For all patients in either group, average age, gender, American Society of Anesthesiologists (ASA) classification, average WBC on presentation, and the fascial spaces involved were recorded. The degree or severity of risk from infection was classified according to the anatomical sites involved, utilizing the criteria which have been previously published²: 1) Low-risk: infections localized to the buccal or infraorbital spaces; 2) Moderate-risk: infections of the submandibular, submental, sublingual, submasseteric, and/or pterygomandibular spaces; 3) High-risk: infections involving the lateral pharyngeal, retropharyngeal and/or pretracheal spaces. If a patient had involvement of three or more areas of moderate-risk, they were considered to be in the high-risk group. Similarly antibiotic failure was determined by the failure of the patient to respond to the administered drug regimen based on clinical findings, CT scan imaging and culture and sensitivity testing.

3. Results

During the study period, 98 SOI patients were managed by the OMS service at Boston Medical Center. Of these, a total of 78 patients were included in the study. Five of the 98 patients were excluded from the study as their treatment regimen consisted of a Fluoroquinolone which was prescribed due to documented allergy to the antibiotic regimens being evaluated in this study. 15 other patients were excluded due to prolonged inpatient stay secondary to complications arising from medical comorbidities (i.e. Deep Vein Thrombosis, Pulmonary Embolism, Chronic Heart Failure, and hospital acquired pneumonia) which were unrelated to the SOI.

Of the 78 patients included in the study, 46 were males and 32 were females. There were 57 patients in Group I (Clindamycin) and 21 patients in Group II (combination of Penicillin/Metronidazole). There were more male patients in Group I (63.2%) when compared with Group II (47.6%). There was no significant difference between the average ages of the patient sample in both groups. Group I had an average age of 32.6 years while Group II had an average age of 32.8 years. The findings were analyzed using the chi square t tests. The average WBC count at the time of initial presentation was higher in Group I (19.3) vs. Group II (17.4). These differences were not statistically significant (P value < 0.003). Relative to ASA status, 84.7% of the patients in Group I and 76.9% of patients in Group II belonged to either ASA Class I or II. Relative to the risk of infection, 84.7% patients in Group I and 76.1% in Group II reported with moderate risk having involvement of submandibular, sub lingual and submental spaces most commonly. Table 1 summarizes these results. Microbiological assessment of the culture samples revealed findings expected in SOI. Gram-positive microorganisms were found in 75.9% and 66.3% patients for Group I and II respectively. Gram-negative microorganisms were obtained in 21.4% and 42.9% for Group I and II respectively. Anaerobic cultures were seen in 5 21.1% of Group I patients and 37.3% of Group II patients; the remainder were aerobic infections. Table 2 summarizes these findings.

Table 3 was more descriptive in terms of the treatment all the patients received at the hospital. The average number of days of hospital inpatient stay for Group I patients was 5.87 days which was marginally lesser than the average number of days for Group II (6.57 days). Antibiotic failure reports ranged from 3.5% in Group I in comparison to 4.7% in Group II. The overall healthcare costs of treating SOI for our patient in tertiary care healthcare setting was lower in Group I (\$6507.80) when compared to Group II (\$7127.64).

4. Discussion

Historically speaking, SOI of the head and neck region had

Table 1
Group Characteristics.

Characteristics	Treatment Groups (n = 78)	
	Clindamycin Group 1 (n = 57)	Penicillin/Metronidazole Group 2 (n = 21)
Average Age (Years)	32.68	32.42
Gender		
Men	35 (63.2 %)	10 (47.6 %)
Women	21 (36.8 %)	11 (52.4 %)
ASA Class		
Class I	20 (35.3 %)	8 (38.2 %)
Class II	28 (49.4 %)	8 (38.7 %)
Class III	9 (15.3 %)	5 (23.1 %)
Anatomical Risk		
Low	3 (5.2 %)	1 (4.7 %)
Medium	48 (84.7 %)	16 (76.1 %)
High	6 (10.1 %)	4 (19.1 %)

Table 2
Microbiology.

Culture Results	Group 1	Group 2
Gram Positive	75.9 %	66.3 %
Gram Negative	21.4 %	42.9 %
Aerobic	75.1 %	66.1 %
Anaerobic	21.1 %	37.3 %

significant morbidity and mortality associated with them. However, with progression of technology including CT scanning and advanced airway management techniques coupled with major changes in treatment strategies which has included appropriate antibiotic therapy and surgical care delivery in a timely manner, one cannot help but notice the large shift in mortality rate. Williams initially reported close to 50% mortality for treated cases of Ludwig's angina in 1940.³ However, in a subsequent publication, he showed a significant reduction in mortality rate (10%) for similar infections, and this was primarily attributed to application of sound principles of airway management, timely surgical drainage and effective use of antibiotics.⁴ It is understandable that during that era, treating surgeons, dentists, and physicians had minimal resources and limited antibiotic choices. Over the next few decades, scientific development led to a plethora of devices and medications which further led to individual preferences and biases, giving rise to wide controversies in the management of these infections appropriately as discussed in the beginning of this article. Our study shows that Penicillin and Metronidazole or Clindamycin still represent clinically effective and practical antibiotic regimens when used empirically as the first-line therapy.

Any antibiotic regimen used in the management of infection should be based on following basic principles of pharmaceutical therapy which include safety and efficacy of the drug. Rega et al found that greater growth of aerobes was commonly encountered in culture sampling as compared to anaerobes, and gram positive cocci had higher percentage than gram negative rods.⁵ Viridans streptococci, Prevotella, Staphylococci, and Peptostreptococcus were the bacterial strains isolated in most cultures. Similarly, some researchers have found that *Streptococcus anginosus* group and hemolytic streptococci were clearly associated with odontogenic abscesses, while others have shown that Viridans group streptococci (VGS) and Neisseria species may a decisive role in the etiology of SOI with VGS, staphylococci, *Prevotella*, *Peptostreptococcus*, and *Bacteroides* being the most common offending pathogens.^{6,7} These findings are consistent with the microbiological spectrum obtained from the culture samples in our study population.

A combination of Penicillin G and Metronidazole has long been shown to be effective for management of SOI. Penicillin G has greatest

Table 3
Study Variables.

Group	Average Hospital Stay (Days)	Antibiotic Failure (%)	Cost in house (\$)	Antibiotic Cost Out Patient (\$)	Hospital Cost (\$)	Effective Treatment Cost (\$)
Group 1 (n = 57)	5.87	3.5	175.21	52.50	6280	6507.80
Group 2 (n = 21)	6.57	4.7	82.64	16.00	7029	7127.64

activity against gram-positive organisms, gram negative cocci, and non-beta lactamase producing anaerobes, while metronidazole has potent antibacterial activity against anaerobes, including *Bacteroides* and *Clostridium* species. Penicillin derivatives remain effective as an antimicrobial against most major pathogens in orofacial odontogenic infections. Even though Penicillin resistance is a major concern, the combination of Penicillin and Metronidazole was quite effective in SOI as demonstrated by the clinically acceptable failure rate of 4.7% in our study. This is likely due to the fact that Metronidazole acted as supplementary treatment of anaerobic bacteria; we used it in the inpatient course only and patients were discharged on oral Penicillin alone as susceptible anaerobic bacteria are quickly destroyed by a 5 day course of these antibiotics. In a study by Sepannen et al evaluated the type of primary antibiotic administered during hospital stay in two separate studies and found that the use of Penicillin G and Metronidazole remained the highest at 79% of all antibiotics administered for SOI between 1994–1995 (n = 71) and at 80% in 2004 (n = 101) at a medical center in Finland.⁸ The second antibiotic agent that was evaluated was Clindamycin. The spectrum of this medication includes streptococci, staphylococci, and pneumococci; some *Bacteroides* species and other anaerobes, both gram-positive and -negative, are also marginally susceptible. In our study, Clindamycin as a single drug had an acceptable efficacy for the management of SOI with an antibiotic failure rate of 3.5%. This failure rate of Clindamycin was lower than that of Penicillin and Metronidazole, even though Clindamycin has a narrower antimicrobial spectrum. A possible explanation may be the greater prevalence of infections with Penicillin resistant bacteria. Overall, the failure rates for both Clindamycin and Penicillin/Metronidazole were 3.5% and 4.7% respectively, which is well below the critical value of 5%.

If one was to review existing literature, some studies found similar susceptibility rates between penicillin and clindamycin viz., 67% and 60% respectively.⁹ When analyzing the literature for failure rates in the treatment of SOI or head and neck infections, it is often unclear as to how failure was interpreted. It is important to note that in our study, we defined *antibiotic failure* as: 1) poor clinical progress despite a repeat CT scan showing adequate drainage without new collections, and, 2) culture/sensitivity results showed that there were microorganisms outside the prescribed antibiotic spectrum. This way, we were able to differentiate the failure from “*surgical failure*” where there was poor clinical progress and repeat CT scan showed new collections and/or old collection with the surgical drain placed away from the affected site.

A correlation has been suggested between the length of hospitalization and the extent (anatomic) to which the infection has spread, with masticator space being most commonly involved which was found true in our study also.⁶ The average hospital stay for the Clindamycin group was slightly shorter than penicillin/Metronidazole group (5.87 vs. 6.57 days). This extrapolates to lower cost of hospitalization and decreased healthcare cost for the patient on Clindamycin (although the actual cost of Clindamycin itself is higher compared to Penicillin/Metronidazole). In our study, the total hospital cost in group 1 was \$6280 vs. \$7029 for group 2. This amounts to 11.9% less expenditure per patient as compared to group 2. Although such costs will vary significantly between the developed and developing countries, some reports suggest overall hospital costs totaled \$749,382 averaging \$17,842 per person from a study done by Gutta and Jundt in 2012 at a tertiary hospital.¹⁰ Another paper by Ahmed and Abubaker et al showed that over an 8-year period, the hospital costs exceeded \$3.3 million and the charges submitted

were in excess of \$10 million.¹¹ These studies put forth the staggering financial burden on healthcare that can be brought upon due to management of odontogenic infections in the hospitalized patient.

More recently, multiple studies in the medical community advocate for the use of wider spectrum and more potent antibiotics such as Zosyn, Unasyn or third-generation cephalosporins in the management of severe neck infections due to the evolution of resistant bacteria.^{12,13} The results of this study show that Clindamycin and Penicillin/Metronidazole combination still represent a clinically effective first line treatment option for treating SOI, at least for the more common, moderate-risk infections. They should be used empirically until specific culture and sensitivity results are available, while traditional wisdom promotes the use of broader spectrum agent in situations where there is poor clinical progress. Use of culture and sensitivity has been propagated by surgeons all over the world for management of the odontogenic infections; however a large majority of these patients get discharged because they start responding to the surgical drainage in accordance with the empirical antibiotic therapy. Rarely though some patients have a prolonged stay due to either antibiotic failure or surgical failure or both. Patients who stay longer in the hospital have a better chance to improve when the culture and sensitivity results are available, unfortunately a delay in reporting can lead to worsening of symptoms with consequent increase in surgical morbidity and costs of treatment.¹⁴ Benvenuti et al concluded from their study that delaying the antibiotic therapy does not yield better culture results and hence it should be initiated early in the management of severe infections.¹⁵ It seems only prudent that such an approach helps not only in reducing bacterial resistance, but also in minimizing side effects that usually accompany broader spectrum agents. The net effect is decreased burden on the healthcare system.

Based on our results, a reasonable treatment algorithm may be to continue to use Penicillin and Metronidazole or Clindamycin as the empiric first line treatment rather than more potent antibiotics for majority of SOI unless the patient has an allergy to any one of them. The patient could always be switched to a broader spectrum antibiotic if the cultures showed resistance, or the patient failed to improve despite adequate drainage seen on repeat CT scan or if there are other reasons to use a more potent antibiotic (high risk infection, medical comorbidities, etc.).

5. Conclusions

In association with early recognition, prompt surgical drainage, and close monitoring, both Clindamycin and Penicillin with Metronidazole when administered intravenously represent clinically acceptable first-line, empiric medical adjuncts in treating SOI. Broader spectrum and more expensive antibiotics should not be used as initial agents in majority of moderate-risk SOI's, particularly in the wake of rising antibiotic resistance, increased side effects and increased health care costs.

Conflict of interest

The authors declare that they have no conflict of interest associated with this manuscript.

Ethics statement/confirmation of patient permission

This study has been exempted by the Institutional Review Board of

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