

Alveolar Osteitis Following Surgical Removal of Mandibular Third Molars

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The purpose of this study was to evaluate two methods that could be used universally to reduce the incidence of alveolar osteitis. In addition, other variables including age and sex of patient, preoperative aspirin use and discomfort, and the use of oral contraceptives were studied. A large controlled prospective study was completed with 952 surgical extraction sites in 476 patients. Postoperative dressings included lincomycin hydrochloride (Lincocin)/absorbable gelatin sponge (Gelfoam), oxytetracycline HCL-hydrocortisone acetate (Terra-Cortril)/absorbable gelatin sponge and absorbable gelatin sponge/saline. Bilaterally impacted mandibular third molars of similar surgical difficulty were selected. Standard accepted surgical technique was used. Patients were seen at one and seven days after surgery or as needed. Lincomycin hydrochloride/absorbable gelatin sponge and oxytetracycline HCL-hydrocortisone acetate/absorbable gelatin sponge were effective in reducing the incidence of alveolar osteitis. Lincomycin hydrochloride/absorbable gelatin sponge is preferred because of the increased morbidity associated with dressings containing petrolatum products. Absorbable gelatin sponge alone is not effective in reducing the incidence of alveolar osteitis. Age and use of oral contraceptives were found in this study to be significant factors related to the incidence of alveolar osteitis.

Alveolar osteitis (AO), more commonly known as "dry socket," is a well known local complication of the extraction or surgical removal of teeth. Alveolar osteitis has "plagued oral surgeons since the practice of exodontia began."¹ The clinical appearance of this disease was first described in 1986.² Numerous papers on AO have been published, yet the etiology and pathogenesis have not yet been fully determined. This syndrome has acquired many names, most of which characterize the clinical picture. The expression dry socket is the earliest name which clearly separates it from other complications of tooth extraction.² The clinical presentation of AO is well known. Most commonly two or three days after tooth removal, the patient returns complaining of intense pain in the alveolus of the extraction site. The alveolus is empty with apparent disintegration of the normal blood clot. This typically occurs after the patient is beginning to feel better. General systemic symptoms such as fever are seldom seen, however lack of proper nutrition and sleep secondary to local complaints contribute to the overall clinical picture. The empty socket is characterized by a denuded sensitive bone surface covered by a grayish-yellow layer of detritus and necrotic tissue.³⁻¹³ The presence of a foul odor is commonly accompanied by gingival inflammation and ipsilateral regional lymphadenopathy. The pain can be localized but more often radiates towards the ear and temporal region. Although rare, maxillary involvement often will radiate to the ocular or frontal regions.¹⁴

Many suggested methods exist for prevention of AO including topical and systemic steroids, topical and systemic antibiotics, matrix forming resorbable materials, antifibrinolytic agents, and various combinations of the above.^{12,15-21} No single method has gained universal success or acceptance, although a large number of practitioners continue to use "their method" often without controlled studies to support its use.

The fear of surgical and postsurgical pain associated with removal of third molars has been a source of great anxiety to many potential patients. Dry socket is a term well known to the general public. Its occurrence often results in pain, intractable to common pain medications,

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and greatly increases the recovery period. Patients who are fortunate to avoid clot breakdown are frequently functioning without discomfort only days after surgery, whereas patients with exposed bone may have a recovery delayed well into the second postoperative week.

The purpose of this study was to compare two methods widely used to reduce the incidence of AO, in a large, controlled study to support or refute their effectiveness and use. Lincomycin hydrochloride in absorbable gelatin sponges and oxytetracycline HCl-hydrocortisone acetate in absorbable gelatin sponges were studied. In addition, specific variables and their relationship to the incidence of AO and treatment were studied to include age and sex of the patient, preoperative aspirin use, discomfort on either side before surgery, discomfort on side of treatment before surgery, and the use of oral contraceptives.

REVIEW OF THE LITERATURE

The reported incidence of AO for all dental extractions is 0.9% to 3.2%.^{11,17,21-23} Following extraction of mandibular third molars the incidence of AO is much higher, ranging from 25% to 30%.^{17,21,22,24-30}

Etiology

Many causes of AO have been listed and studied. These include trauma to the bone during removal,^{5,11,22,31-33} bacteria,^{11,17,23,34-39} circulatory factors,^{9,25,40-42} disease factors,^{11,43} enzyme factors,^{31,44} nutritional factors,⁴¹ (including vitamins⁴⁵⁻⁴⁷ and proteins⁴⁸), poor postoperative care,^{49,50} pericoronitis,⁵¹ saliva,^{42,49,50} stress,⁴⁴ postoperative flushing and curettage of the socket,⁵² mouthwashes,⁵² misuse of gauze sponges,⁴¹ and reduction of blood clotting factors.⁴¹ Some predisposing causes that have been considered to be important are the age of the patient,^{11,53,54} the sex of the patient,¹¹ oral contraceptives,^{55,106} the area of extraction and the number of teeth removed,^{11,21} the month of the year when removed,²¹ the type of anesthesia used,^{42,51} previous incidences of AO,²¹ state of eruption,³² insufficient blood supply to the alveolus,^{29,56-64} postoperative bleeding,^{9,56} foreign bodies in the alveolus,^{6,55,65} and increased fibrinolytic or proteolytic activity in the blood clot.^{30,66-71}

Fibrinolytic Mechanism of AO

Excellent work by Birn¹⁴ explained many of the apparently independent risk factors by the fibrinolytic mechanism for AO.⁵⁵ His research established that trauma is a significant stimulus to fibrinolysis through plasmin activation. Estrogens,^{72,73} bacterial pyrogens,⁷⁴ and other drugs are known to stimulate fibrinolysis.⁵⁵

Fibrinolysis is a normal physiologic process that removes fibrin deposits by enzymatic digestion of the fibrin meshwork into smaller soluble fragments. Fibrin is continually being laid down and removed in the body as injury and repair occur. Local increases in fibrinolysis occur in response to local bleeding. Rises in plasma fibrinolytic activity do not usually occur with this local increase. Minor variations in fibrinolytic activity in individuals and between individuals are normal but gross changes are associated with disease.⁵⁵

Figure 1 illustrates the accepted mechanistic scheme of the fibrinolytic system. Plasmin, the enzyme that hydrolyzes fibrin to soluble fragments, ultimately regulates the degree of fibrinolysis, and is therefore the keystone to fibrinolytic activity.⁵⁵

There are two main categories of fibrinolytic activators—direct and indirect. Enzymes that convert plasminogen to plasmin and are active *in vitro* and *in vivo* are direct activators. Indirect activators increase the amount of an activator enzyme that converts plasminogen to plasmin. Indirect activators are active only *in vivo* because of this intermediate step.⁵⁵

Birn,⁷⁵ and Moody and Southam⁷⁶ reviewed the local differences in fibrinolytic activity between body tissues. The potential fibrinolytic activity varies with bone and uterine tissues having the highest activity in comparison to skeletal muscle, kidney, heart, brain, liver, spleen, lung, and thyroid tissue.

Birn⁷⁷ hypothesized that an increase in fibrinolysis was responsible for dry socket pathology. The fibrinolytic activity of dry sockets was significantly higher than that of normally healing extraction wounds and correlated with the time course of the disease.

Birn⁷⁸ further proposed a scheme for the manner in which trauma causes dry socket. Direct tissue activators are released after trauma to the alveolar bone cells converting plasminogen to plasmin, which digests the fibrin clot, resulting in a dry socket. Further investigation by Birn^{31,79} on the fibrinolytic activity of alveolar bone, however, led to the realization that indirect activators could have a greater role in dry socket than was originally thought.^{75,77}

Birn's work explained not only the mechanism of trauma as one of the risk factors for dry socket, but others as well. There is ample evidence that bacterial pyrogens are indirect activators of fibrinolysis *in vivo*.⁵⁵ In the 1950s several European investigators studied the efficacy of bacterial pyrogens for treating thromboembolic disease.^{74,80,81}

Although bacterial pyrogens and fibrinolytic activity in dry socket have not been postulated to be directly related to each other, this seems quite plausible.⁵⁵ Bacteria are normal inhabitants of the mouth and certain species constantly secrete pyrogens at a basal level. Bacteria thrive on necrotic tissue as cellular defenses are depressed and

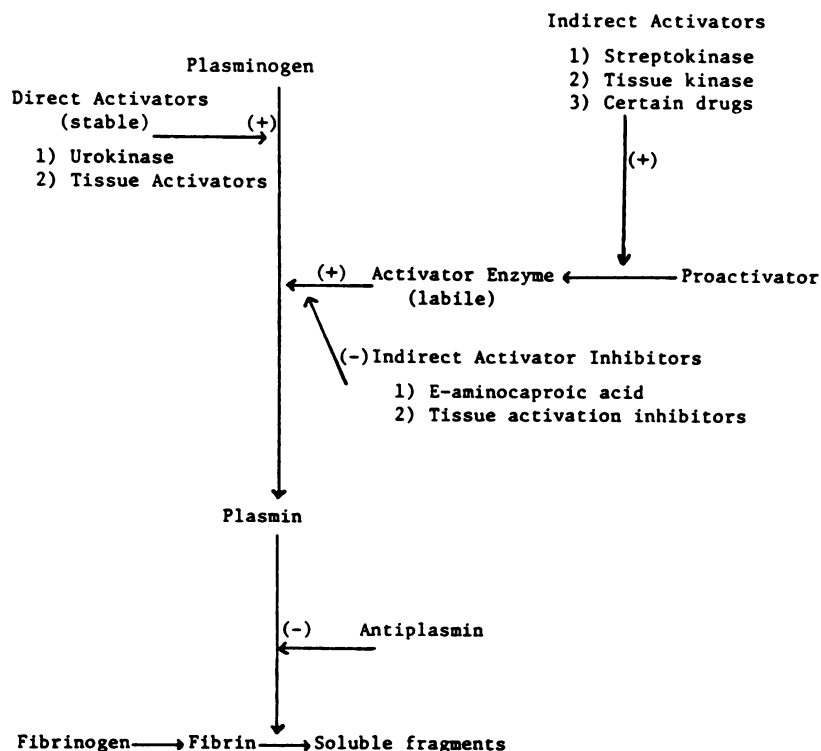


Figure 1 Fibrinolytic system.

the food source is expanded. The number of bacteria increase with dry socket,²⁰ resulting in greater amounts of pyrogens being released into the area. Because pyrogens stimulate fibrinolysis by promoting the conversion of proactivator to activator, more plasmin would be formed, which would lyse the fibrin clot and result in a dry socket. Proper antibiotic therapy could suppress the growth of bacteria and diminish the amount of pyrogens released. Antibiotic failures could be attributed to insufficient dosage or resistant strains of bacteria.⁵⁹

The degree of fibrinolytic activity of common oral bacteria such as *Streptococcus beta hemolyticus*,⁸²⁻⁸⁵ *Staphylococcus*,⁸⁶ or *Bacteroides melanogenicus*⁸⁷ is probably not sufficient to be the cause of dry socket, as the concentration of these bacteria needed for fibrinolysis is such that a rather virulent reaction, accompanied by the characteristic symptoms of infection, redness, swelling, and pus formation, would be expected. These symptoms are not typical of dry socket.^{88,89}

Treponema denticola was postulated by Nitzan as an etiologic agent in AO as it does not inhabit the mouth until late adolescence and AO is rarely seen in childhood.⁸² *Treponema denticola* exhibits a strong plasmin-like fibrinolytic activity,⁸⁷ and when injected subcutaneously into mice, or intramuscularly into guinea pigs, failed to produce abscesses.⁹⁰⁻⁹² The pathogenetic behavior of treponemes is not in accordance with standard criteria of an inflamma-

tory process as they multiply and lyse blood clots without eliciting the clinical symptoms so characteristic of infection, including redness, swelling, and pus formation.⁸²

Age, Sex, and Oral Contraceptives

Alveolar osteitis most frequently occurs in the age group of 20 to 40 years.^{11,25,29} Almost no cases of AO are seen before age 18 or after age 50.^{11,25,29} Lehner²⁹ explains the age distribution in AO by the fact that the highest incidence occurs in the period of time when the third molar, which has a high incidence of AO, erupts and is removed. This explanation is not valid for the total period from 20 to 40 years, when the incidence of AO is especially high. Lehner²⁹ reported 47% of all AO cases occurred in the age group of 25 to 40 years, compared with 39% in the 18 to 25-year group. MacGregor¹¹ reported that the occurrence of AO appears to be age dependent with a peak value in the age range of 30-34 years.¹⁴

Before 1960, Krogh²² and Lehner²⁹ reported there was no difference in the incidence of AO associated with sex. In 1968, MacGregor¹¹ reported a 50% greater incidence of AO in women than men in a series of 4000 extractions. The discrepant results can be explained by a report published by Schow¹ in 1974. Oral contraceptives were not used appreciably before 1960; in Schow's study, 37% of the women were taking oral contraceptives. There was

no significant difference in the incidence of AO between women not taking oral contraceptives and men. Women taking oral contraceptives had a significantly higher incidence of AO (44.6%). Catellani⁵⁵ concluded that the sex of the patient has no bearing on the probability of developing a dry socket, but the use of oral contraceptives played a significant role in increasing the probability. Estrogens, particularly in oral contraceptives, have well-known effects on the coagulation system. Less known, but well studied, are the effects of oral contraceptives on the fibrinolytic system.^{72,73} Ygge⁷² studied plasma fibrinolytic activity in women before and during the use of oral contraceptives and found that when women were taking oral contraceptives they had higher fibrinolytic activity than when not taking oral contraceptives. Hedlin and Monkhouse⁷³ confirmed Ygge's results and demonstrated that an increase in fibrinolytic activity usually begins within 24 hours of administration of the first dose of oral contraceptives. Also demonstrated was a rapid decrease in fibrinolytic activity after oral use of contraceptives was discontinued. This evidence leads to the conclusion that estrogens, like pyrogens, are indirect activators of fibrinolysis and that they contribute to the occurrence of AO by increasing fibrinolysis.⁵⁵ Sweet and Butler¹⁰⁴ previously reported similar data to support studies by Ygge, Monkhouse, and Catellani.

Preoperative Discomfort (Pericoronitis)

It has been shown definitely that extraction of teeth with pericoronitis gives rise to a substantial increase in the number of cases of AO.¹⁴ Numerous authors have reported, and all agree, that the increase in the incidence of AO is caused by the presence of infection which spreads into the alveolar bone and the blood clot.¹⁴

Effects of High-Volume Lavage

Sweet and Butler^{93,94} proposed high volume lavage to flush away a large number of bacteria and other contaminants. Their work with dry socket was comprehensive and compatible with the hypothesis set forth by Birn. Because debris, bacteria, and enzymes have all been implicated in dry socket and or infections of extraction sites, it would seem logical to thoroughly irrigate the surgical area before closure of the wound. High volume lavage was defined as 175 to 350 milliliters. Later studies found little difference when reducing volume to only 60 milliliters.⁹³

Lincomycin Hydrochloride in Absorbable Gelatin Sponges

Only one article has been published using lincomycin hydrochloride in absorbable gelatin sponge for prevention of dry socket. Goldman et al⁸ reported the occurrence of

dry socket was reduced to 1.1% in the patients who received topical lincomycin hydrochloride in absorbable gelatin sponge, as compared with 7.8% when the absorbable gelatin sponge contained saline solution instead of lincomycin hydrochloride. Ninety subjects received absorbable gelatin sponge saturated with sterile lincomycin hydrochloride solution, 300 milligrams per milliliter, and 90 subjects received absorbable gelatin sponges saturated with sterile saline solution. The study was accomplished on a double-blind basis. The reduction in dry sockets was found to be statistically significant at the 5% level.

Oxytetracycline HCl-Hydrocortisone Acetate in Absorbable Gelatin Sponges

Two studies have been published concerning the use of oxytetracycline HCl-hydrocortisone acetate in absorbable gelatin sponge to reduce the incidence of AO. Julius et al⁹⁵ studied 90 impacted mandibular third molars, 45 left and 45 right using 1 milliliter of oxytetracycline HCl-hydrocortisone acetate ophthalmic suspension in an absorbable gelatin sponge square on one side compared with no treatment on the contralateral side. They reported a significant reduction in the total number of cases of AO in the treated sockets, 6.6% as compared with the untreated sockets, 28.8%. A smaller, but still significant reduction was achieved in the soft tissue category. It was concluded that the greatest reduction in AO occurred in the bony impaction category. It was stated that the corticosteroid fraction of oxytetracycline HCl-hydrocortisone acetate did not add to the effectiveness of the preparation in preventing AO. They concluded the protective effect of local oxytetracycline HCl-hydrocortisone acetate therapy increased as trauma associated with the extraction increased.

Rutledge et al⁹⁶ studied 96 mandibular third molars in 48 patients using 0.5 milliliter of oxytetracycline HCl-hydrocortisone acetate ointment in an absorbable gelatin sponge square on one side compared with nothing on the contralateral side. They reported a 0% incidence of AO on the treated side as compared with a 9.2% incidence of AO on the untreated side. No specific statistical analysis was reported. They concluded that oxytetracycline HCl-hydrocortisone acetate in absorbable gelatin sponge was indeed effective in reducing the incidence of AO, but reserved recommendations for its use to patients who might be more susceptible to developing AO. Case reports of myospherulosis associated with its use prompted this qualifying statement.

Myospherulosis

Myospherulosis is an inflammatory, granulomatous lesion, often of iatrogenic origin, which results from the action of lipid substances on extravasated erythrocytes.

Table 1. Covariate Analysis

Treatment	Age (yr)	Incidence of AO (observed)
LH/AGS	<20	8.8%
LH/AGS	20-30	10.7%
LH/AGS	>30	18.1%
OHA/AGS	<20	8.8%
OHA/AGS	20-30	13.2%
OHA/AGS	>30	16.7%
AGS	<20	15.0%
AGS	20-30	15.8%
AGS	>30	38.5%
No treatment	<20	11.0%
No treatment	20-30	20.9%
No treatment	>30	30.0%

LH = Lincomycin hydrochloride; AGS = Absorbable gelatin sponge; OHA = Oxytetracycline-HCl hydrocortisone acetate; AO = alveolar osteitis.

The lesions most often result from the use of petrolatum-based ointments. McClatchie et al first described the lesion in a report of a series of seven Kenyan patients.^{97,98} The lesions occurred in the soft tissues of the proximal limbs and limb girdles. Hutt et al subsequently reported five additional cases from Uganda in patients of similar sex and age, and the lesions were in a similar location.⁹⁹ They observed that all lesions had occurred in areas of the body commonly used by local practitioners for injection of foreign material.

Myospherulosis most often occurs in the oral cavity as nonhealing extraction sites, but may appear as an asymptomatic nodule in the soft tissue. The most common etiologic agent is a petrolatum-based antibiotic ointment used as a postsurgical anodyne dressing, although lesions could occur from the action of any type of exogenous or endogenous lipid on erythrocytes. When curetted from nonhealing sockets, the tissue is brownish-black, tarry in texture, and often associated with a membranous mucoid substance.¹⁰⁰ The use of petrolatum-based ointments is not advised if alternate therapies are available.¹⁰¹ No cases of myospherulosis have been reported with oxytetracycline HCl-hydrocortisone acetate ophthalmic suspension as opposed to the ointment form.

METHODS

A large, controlled prospective study was completed with 476 patients and 952 surgical extraction sites (Table 1). Each patient was instructed on the possible complications of third molar surgery. Healthy patients were selected on the basis of having bilaterally impacted mandibular third molars of similar surgical difficulty. Panoramic radiographs were used to exhibit bilateral symmetry. The degree of

difficulty was not specifically recorded, however partial boney and full boney impactions predominated. Partial boney impaction necessitated the raising of a full thickness mucoperiosteal flap and removal of bone, whereas the full boney impactions required a flap, bone removal, and sectioning of the tooth. Tooth section was accomplished with an electrical handpiece and a #703 straight fissure bur with copious irrigation. Follicular material then was removed gently from the socket. A hand file was used to smooth all sharp boney edges followed by thorough irrigation with normal saline averaging 30 milliliters per socket. Appropriate medicaments were placed at random and the soft tissues reapproximated with 4-0 gut suture; soft tissue closure was not occlusive. Although different surgeons participated in the study, each individual case was completed by the same surgeon, on the same day. Each patient served as his or her own control to aid in data evaluation and control variability. The majority of patients received an intravenous sedation consisting of diazepam and an opioid. Sedative precautions dictated that the patient be without food or drink for at least six hours before surgery. In all cases, local anesthetic with vasoconstrictor was administered with inferior alveolar nerve blocks and buccal infiltration.

Dressings were placed as follows:

1. One hundred control patients with no dressings placed.
2. One hundred patients with lincomycin hydrochloride/absorbable gelatin sponge on one side—no treatment on the other.
3. Eighty-four patients with lincomycin hydrochloride/absorbable gelatin sponge on one side—absorbable gelatin sponge/saline on the other.
4. Ninety-three patients with oxytetracycline HCl-hydrocortisone acetate/absorbable gelatin sponge on one side—no treatment on the other.
5. Ninety-nine patients with absorbable gelatin sponge/saline on one side—no treatment on the other.

Each study group began with 100 patients, however final group numbers varied because of intraoperative complications such as excessive bleeding; other patients were simply lost to follow-up. Medicaments used included lincomycin hydrochloride, 6 milligrams per milliliter in a propylene glycol suspension. One milliliter of the lincomycin hydrochloride solution was used to saturate a 10-millimeter by 10-millimeter piece of sterile absorbable gelatin sponge. The dressing was placed in the socket preselected at random, and the soft tissues were closed as described. The second medicament used was an ophthalmic suspension of oxytetracycline HCl equivalent to 5 milligrams of oxytetracycline and 15 milligrams of hydrocortisone acetate incorporated in mineral oil with aluminum tristearate as an emulsifier per milliliter; 0.5 millili-

ters of the suspension was used to saturate the sterile absorbable gelatin sponge before placement.

Gauze pressure packs were placed intraorally at the end of the surgical procedure, to be kept in place for four to six hours. Extraoral ice packs were applied bilaterally with hand pressure to be used until bedtime, 30 minutes on, then 30 minutes off, alternately. The patients were given a liquid diet for the first 24 hours postoperatively with instructions to advance to a normal diet as tolerated. Normal hygiene and warm saline rinses were not initiated until 24 hours postoperatively. Instructions were also given to avoid smoking, straws, sucking, or spitting. Ibuprofen, 600 or 800 milligrams every six hours as needed for postoperative discomfort was prescribed.

All patients were seen at one and seven days after surgery. Any patients who developed complications were seen as necessary in addition to the scheduled visits. At the postoperative visits, the surgical sites were evaluated for delayed or unusual healing. A liberal definition for diagnosis of AO was adopted, and made as follows:

1. Symptomatic pain in or around the surgical site 36 hours after surgery and requiring an anodyne dressing for relief.
2. Lack of demonstrable clot associated with pain.
3. Delayed healing beyond one week.
4. Wound breakdown any time postoperatively.

The patient were questioned regarding postoperative pain, bleeding, drainage, or loss of material from the extraction sites. Patients who developed AO were treated by placement of a sedative dressing with eugenol into the extraction site; this was replaced at two- to three-day intervals until there was sufficient healing to obviate its use.

The data collected in this prospective study was nominal in nature, ie, AO either occurred or was absent following oral surgery. Therefore, appropriate statistical tests were used to analyze the incidence of AO by treatment groups as opposed to parametric studies that require data continuous in nature. The data was first evaluated by looking at individual teeth, not controlling for variables, and combining across groups. Basic incidence rates of AO were determined for each treatment group studied; no adjustments were made for variables such as age or sex. Comparisons were then performed between treatment groups, again, not controlling for variables. This is the extent of statistical analysis often done for many studies concerning the incidence and reduction of AO. A significance level of $P = 0.05$ was selected before beginning the study.

The statistical analysis then was expanded to control for variables in an attempt to derive more specific information. Analysis by group (McNemar's test¹⁰¹) was done to control all variables by using each patient as his or her

own control. This allowed pairing of each patient and treatment group against himself or herself. In this way, AO on both sides, and AO on neither side could be selected out to allow a direct evaluation of the selected medicament. McNemar's test (group analysis) is a statistical test for paired nominal data which is a variation of the sign test.

Weighted least squares approach on categorical data (Grizzle, Starmer, and Koch¹⁰²) was accomplished to support or refute the results of McNemar's test results. This paired analysis was done to compare between treatment groups.

Statistical analysis then was used to look at covariates.¹⁰³ The variables studied included age and sex of patient, preoperative aspirin use, discomfort on either side before surgery, discomfort on the side of treatment before surgery, and use of oral contraceptives. Incidence rates of AO and significance levels were figured with treatment comparisons, and without taking treatment into account, for each covariate as above.

RESULTS

The overall incidence rates of AO were as follows: lincomycin hydrochloride/absorbable gelatin sponge 11.4%; oxytetracycline HCl-hydrocortisone acetate/absorbable gelatin sponge 12.9%; absorbable gelatin sponge alone 16.4%; no treatment 17%. Only lincomycin hydrochloride/absorbable gelatin sponge compared with no treatment was close to a statistically significant reduction in AO ($P = 0.0504$), when analyzed between groups.

Lincomycin hydrochloride/absorbable gelatin sponge resulted in significantly fewer dry sockets by within-subject comparison than no treatment ($P = 0.0002$). Lincomycin hydrochloride/absorbable gelatin sponge also resulted in significantly fewer dry sockets within-subject than absorbable gelatin sponge alone ($P = 0.0118$). Absorbable gelatin sponge alone did not differ significantly from no treatment ($P = 0.2890$) in reduction of AO. Oxytetracycline HCl-hydrocortisone acetate/absorbable gelatin sponge resulted in significantly fewer dry sockets than no treatment ($P = 0.0212$). The control group showed that side was not important ($P = 0.7906$) in relation to the incidence of AO.

The weighted least squares approach (paired analysis) revealed the following: lincomycin hydrochloride/absorbable gelatin sponge produced a significantly lower proportion of dry sockets than absorbable gelatin sponge ($P = 0.0004$); oxytetracycline HCl-hydrocortisone acetate/absorbable gelatin sponge produced a significantly lower proportion of dry sockets than absorbable gelatin sponge ($P = 0.0126$); no statistically significant difference in proportion of dry sockets existed between lincomycin

hydrochloride/absorbable gelatin sponge and oxytetracycline HCl-hydrocortisone acetate/absorbable gelatin sponge ($P = 0.5368$). The incidence of AO by age group is summarized in Table 1. No significant differences due to age were noted. Preoperative aspirin effect was not significant ($P = 0.1923$). Discomfort effect on either side before surgery was not significant ($P = 0.5120$). Overall treatment effect was significant ($P = 0.0566$), with respect to discomfort on the side of treatment before surgery. Lincomycin hydrochloride/absorbable gelatin sponge produced the greatest reduction of AO when compared with oxytetracycline HCl-hydrocortisone acetate/absorbable gelatin sponge ($P = 0.0287$), taking preoperative discomfort on the side of treatment into account.

Sex effect was not significant ($P = 0.5195$). Males had a 16% incidence rate of AO as compared with 14% for females; the difference was not statistically significant.

Preoperative use of oral contraceptives was borderline significant ($P = 0.0544$). A higher rate of AO for females who used oral contraceptives was observed, 21.5% compared with 11.4% for those females who were not using oral contraceptives.

DISCUSSION

Studies and publications concerning AO, incidence of AO, and reduction of AO are numerous. As in medicine, when the etiology and pathogenesis of a disease entity are not clear cut, the theories of cause and treatment are many and varied. As alluded to earlier, hundreds of papers have been published concerning AO, and its prevention or reduction. Comparison of rates of dry sockets between studies has little meaning because of different diagnostic criteria. In addition, the multitude of contributing factors further obscure incidence rates and their parallel evaluation. Comparison of groups within a study can yield meaningful information that can be extrapolated to other situations. Large numbers of patients and surgical extraction sites, uniform study control, and proper statistical analysis are all vital to the generation of useful data and conclusions.

The incidence of AO in this study is uniformly higher than incidence rates often reported in the literature. This could be due to several factors. First, the third molars selected as acceptable cases for the study were well beyond the scope of undergraduate students, and difficult enough to challenge the graduate residents of oral and maxillofacial surgery. Second, the residents participating in the study as primary surgeons were often near the beginning of their residency training, learning new techniques and acquiring surgical skills through experience. Third, many primary surgeons participated as mandated by rotational requirements. Finally, it is important to note

that a liberal definition of AO was adopted for this study; questionable cases of AO were uniformly diagnosed as such, and treated according to guidelines set forth in the methodology section.

Lincomycin hydrochloride/absorbable gelatin sponge was more effective in reducing the incidence of AO as compared with oxytetracycline HCl-hydrocortisone acetate/absorbable gelatin sponge when reviewing clinical numbers, however, this difference was not statistically significant. Absorbable gelatin sponge neither contributed to, nor reduced the incidence of AO.

Older patients had higher incidence rates of AO than younger patients. Age groups were divided into those less than 20 years of age, those 20 to 30 years of age, and those greater than 30 years of age. This finding is supported by the literature. Lincomycin hydrochloride/absorbable gelatin sponge and oxytetracycline HCl-hydrocortisone acetate/absorbable gelatin sponges were very effective in reducing the incidence of AO in the two older age groups; they were less effective in reducing the incidence of AO in the 20 years and younger age group. Treatment comparisons taking age into account indicated that overall treatment effect was significant ($P = 0.0299$) in reducing the incidence of AO, but individual comparisons between treatment groups were not statistically significant with respect to age.

A slightly higher incidence rate of AO associated with preoperative aspirin use was observed. Only 50 patients recorded preoperative aspirin use as opposed to 682 who did not. Greater numbers are needed to evaluate the effect of preoperative aspirin intake, specifically, the quantity of patients and the dosage of aspirin. It seems plausible that the greater incidence of AO found clinically, might be statistically significant with further investigation.

A slightly higher incidence rate of AO associated with discomfort on either side before surgery was observed, but it was not statistically significant. When looking specifically at discomfort on the side of treatment before surgery, slightly higher rates of AO were observed, but not significantly higher.

A slightly higher incidence rate of AO for males was observed. One hundred twenty-one patients were inadvertently left unspecified with respect to sex, however the incidence rates of AO were reported as percentages. The literature supports the findings reported as the incidence of AO between females not taking oral contraceptives is not significantly different from males.

Use of lincomycin hydrochloride/absorbable gelatin sponge and oxytetracycline HCl-hydrocortisone acetate/absorbable gelatin sponge resulted in a statistically significant reduction in the incidence of AO as compared with the control. This reduction is consistent with the fibrinolytic mechanism of AO set forth by Birn.¹⁴ By decreasing the numbers of bacteria, it is assumed that fewer pyrogens are liberated which stimulate fibrinolysis. Proper antibiotic

therapy may suppress the growth of bacteria and diminish the amount of pyrogens released.⁵⁹

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