Antibiotic Delivery Systems for Oral Infections

Caitlin Bryan
Michele Pisano-Marsh, DMD

1Department of Dental Medicine, Lehigh Valley Health Network
2Research Scholar Program Mentor

Abstract

One of the main causes of oral pain is infection in the mouth. The infections can be intraoral or in pockets between the gums and the teeth. Infection in the gum pockets is called periodontitis. Oral infections can cause pain and tooth loss if left untreated and can have other side effects. Systemic or local delivery of the antibiotics can be used for these infections and there are some advantages and disadvantages to each. Studies comparing the types and method of delivery of antibiotics were analyzed. Antibiotic treatment was found to be most effective when combined with scaling and root planing (SRP). However, it was found that current antibiotic treatments only temporarily treat the problem and are not effective at completely eliminating the infections. New delivery systems and technological advancements in medicine need to be developed to effectively and completely treat these infections.

Keywords

Antibiotics, systemic, local, infections, periodontitis, scaling and root planing (SRP)

Background

The two types of antibiotics prescribed are local and systemic. Systemic antibiotics are usually in pill form and are taken orally. The advantages of systemic antibiotics is that they are less invasive and do not require a doctors application, so the patient can just take them at home. This provides a cost advantage because it is a one-time fee for the prescription and does not require the doctor’s time. Systemic antibiotics can reach deep tissue infections because they deliver through the bloodstream, however this also creates a disadvantage because it is not localized to the site of infection. The systemic antibiotic will travel through the entire body and will cause moderate side effects including diarrhea and vomiting and can cause antibiotic resistance. However, this provides an advantage as the systemic approach does address several infection sites at once.

Local antibiotics are applied directly to the infection site, which gives the great advantage of specificity to that site alone. This makes for fewer side effects because the antibiotics are not traveling through the entire body and helps to avoid bacterial antibiotic resistance. However, this method requires separate applications to multiple sites because it is so specific. This increases the cost, as each application is a separate dose and because it takes up more of the doctors’ time. Another disadvantage to local antibiotics is that they are usually more painful for patients, as many times they are applied through an injection. They are also less efficient than systemic antibiotics at eliminating the bacteria deep within tissue.

Periodontitis is an advanced form of gum disease. Poor dental hygiene, excessive smoking, and a variety of other factors can cause the gums to become so infected that they begin to pull away from the teeth and form small pockets, which can then become easily contaminated with bacteria, causing periodontitis. The bacteria can aggregate and form a biofilm, which acts as a protective barrier around the bacteria. Normal pocket depth is about 1 to 3 mm and any pocket with a probing depth of 4 mm or greater can indicate infection (1). When left untreated, periodontitis damages the soft tissues present in the mouth and destroys the bones and ligaments that support and hold teeth in place.

Although periodontitis is very common - half of people aged 30 or above have the disease - it is still very difficult to treat. This is because there are many different bacteria capable of causing periodontitis (2). Some periodontists take a swab from the patient’s periodontal pockets and send the sample to a lab to be analyzed. The lab returns a detailed description of the types and amount of bacteria causing periodontitis. The report then better helps the doctor to correctly diagnose the patient and prescribe the correct treatment and medication, if necessary.
There are several different ways to combat periodontal infections, not all involving antibiotics. The most common is scaling and root planing (SRP) and involves the periodontist scraping the insides of the pockets in attempt to mechanically extract the bacterial infection and biofilm buildup. Another type of therapy is periodontal surgery, which is more extreme than SRP. Some more technologically advanced surgeries involve lasers with particular wavelengths of light that first target the bacteria to kill them, then stimulate blood flow inside the pocket to initiate healing process. While sometimes these procedures are done alone, often times the SRP and surgeries are combined with antibiotic therapy.

One brand of antibiotic used is Flagyl, a brand name for metronidazole. It is a pill that is taken once to twice daily, usually combined with amoxicillin or doxycycline. Flagyl is known to have very many side effects as most systemic antibiotics do. Some of the major ones include blindness, seizures, and vomiting (3).

The other most widely used antibiotic is Arestin, which uses a local delivery method. Arestin is used directly after SRP and is placed directly in the infected pockets through a cannula, therefore no needles or injections are required (1). Arestin is a revolutionary antibiotic delivery system because the antibiotic, minocycline hydrochloride, is contained in microspheres that slowly degrade over 21 days and therefore gradually release the antibiotic in the infection site (1). Arestin’s side effects are not as drastic as the Flagyl because it is given locally. The most common are headache, pain, infection and flu-like symptoms (1).

Another problem resulting from infections in the mouth is that they affect the ability to locally anesthetize the patient. Local anesthetics are a weak base that, when ionized, work by blocking the sodium ion channels into the nerve (4). This then also blocks the potassium ions from flowing out of the nerve and therefore prevents depolarization. In order for this mechanism to occur, the anesthetic must first enter the nerve in the unionized form (4). If the tissue surrounding the nerve has a low (acidic) pH the anesthesia will not penetrate into the nerve because it will not be in the neutral form.

![Figure 1. “Decay (green) with apical abscess (blue)” Coronation Dental Specialty Group. http://coronationdentalspecialty.ca/services/oral-and-maxillofacial-surgery/extractions/](image)

When there is a large infection in a tooth, as seen in Figure 1, the tooth cannot be restored. The decay (highlighted by the green arrow) is at the bone level, leaving no biological margin for the cavity to be filled. The dark spot (highlighted by the blue arrows) is likely caused because the infection near the crown of the tooth spread through the canals toward the root of the tooth. All the decay in this tooth leaves extraction as the only option for treatment. Even if the tooth could be repaired with a root canal or a filling, all of these treatments require anesthesia to numb.
the tooth prior to any treatment. However, the infection surrounding the tooth lowers the pH of the tissue and local anesthesia can be ineffective. The pH of normal body tissue is 7.41, but in infected tissue the pH may be lowered to 5 or 6 (4). This inhibits the mechanism of the local anesthetic and the patient cannot get numb, preventing proper treatment. There are some methods to combat the pH of the infection including buffering the anesthetic solution with sodium bicarbonate, however this can make the anesthetic less effective. To properly treat the patient, antibiotics must be used to treat the infection prior to the use of anesthesia to return the tissue to a more neutral and normal pH.

Method

To study the effectiveness of antibiotic treatment of oral infections, a literature review was performed. The results from different types and combinations of antibiotics, treatment duration, and combinations with mechanical treatment were all analyzed to discover how well antibiotics treat the infections.

Results

In a systematic review article published by the Journal of the American Dental Association (JADA), results from various studies were compiled, all analyzing the effectiveness of antibiotics in combination with SRP. They found that there was a tendency towards improvement of periodontitis after treating patients with antibiotics and SRP in terms of reducing periodontal probing depth and clinical attachment level (3). They found that wide spectrum antibiotics like amoxicillin with metronidazole and azithromycin were the most effective (3).

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<th>Antibiotic</th>
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<td>Amoxicillin</td>
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Table 1. Results from JADA systematic review (3).

Periodontology 2000, a journal from Denmark, did a similar study, this time focusing on treating Actinobacillus actinomycetemcomitans and Porphyromonas gingivalis which are two of the most prevalent bacteria found in periodontitis. They compiled the results from over 100 studies varying in treatment plans from SRP alone and with antibiotics, antibiotics alone, and periodontal surgery. The different studies within this review had variable results, some with no change in the periodontitis and others with successful treatment. The most successful studies used a combination of antibiotics in conjunction with SRP or surgical treatment (2). However, most studies found that while usually antibiotic therapy helped initially (checked at appointments in a few weeks following the treatment), the periodontitis would sometimes get worse again at appointments several months post-treatment (2). The authors also concluded that while the topical (local) antibiotics do reduce risks, they are not as effective at treating infections in deep pockets.

Discussion
The article in JADA was published more recently than the article in Periodontology and is much more organized and reliable, as they consider bias and had a uniform assessment of each study. Both studies come to the conclusion that antibiotic therapy combined with SRP can help treat periodontitis. Based on the varying success rate of the treatments, current antibiotic therapy is not a guaranteed solution to the problem. These treatments seem to have a temporary effect at stopping the infection from getting worse but fail to completely eliminate bacteria and prevent further infection. Not only do these studies indicate that periodontitis is being inefficiently treated, they also indicate that the antibiotics are not effective to treat the infections causing problems for local anesthesia.

**Conclusion**

The main reason for ineffective treatment is that the local antibiotics cannot penetrate deep enough into the pockets to kill the infection, yet the systemic antibiotics are not localized enough to the infection site. The reason that some of the antibiotics seem to help treat the problem at first, but then worsen over time is most likely due to antibiotic resistance of the bacteria causing the infection. Additionally, the only therapy that addresses the biofilm created by the bacteria is SRP, which is not completely effective.

A more effective antibiotic delivery system needs to be developed to adequately and effectively eliminate all oral infections. The delivery system must be able to: 1. Treat bacteria in deep pockets 2. Eliminate biofilm and 3. Localize the antibiotic to the infection site to prevent antibiotic resistance and side effects. A combination of these three abilities will reduce patient cost and help the doctor effectively and efficiently treat his or her patients.
References