USE OF SYSTEMIC ANTIBIOTICS IN ACNE

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Systemic antibiotics have remained a mainstay of the treatment program for acne as seen by the dermatologists. In fact, there probably is greater agreement on the value of systemic antibiotics than on any other therapeutic modality used for acne. Tetracycline, in particular, has been the antibiotic of choice and over 10% of all tetracycline that is sold is used for the treatment of acne. Within the last few years, topical antibiotics have been used for acne, but it is my feeling that these will not replace tetracycline in the management of most cases of systemic acne.

There is ample published material relating to the use of systemic antibiotics and, therefore, my purpose in this short presentation is to review only a few of the most significant findings related to the use and complications of antibiotics in the management of patients with acne. As mentioned above, tetracycline has been the prime antibiotic to be used. Erythromycin is probably the second most commonly used antibiotic for acne. In the past, clindamycin was also used quite commonly, but its use has been greatly curtailed since pseudomembranous colitis has been reported as a complication of its use. Other tetracycline derivatives have also been used to a limited extent. While there are reports of clearing of acne with penicillin therapy, there is no evidence to support its efficacy. Likewise, sulfa drugs are ineffective, unless they are used in combination with trimethoprim.

The first question that I want to address is: "How does tetracycline work?" The answer is not completely known. There is no evidence that tetracycline or any of the other broad-spectrum antibiotics have any effect upon the rate of sebum production. The effect is then on the bacterial population follicle. The follicular flora is composed of *Propionibacterium acnes*, staphylococci and micrococci and *Pityrosporum ovale*. Broad-spectrum antibiotics such as tetracycline and erythromycin have been shown to decrease the *P. acnes* population by as much as two to three logs; however, they do not have any effect upon the aerobic staphylococci and micrococci or on *Pityrosporum ovale*. Under in vitro conditions all of these organisms have been found to produce lipases; however, under the in vivo circumstances it has been shown that only *P. acnes* causes triglyceride hydrolysis within the follicle.

A decrease in the free fatty acids accompanies the decrease in the *P. acnes* population. The decrease in the free fatty acids may be the cause of the improvement or it may just be a marker for other activities that may be taking place, for it is known that tetracycline has many other activities on the cells of the body. Be that as it may, when culture techniques are not available the decrease in the free fatty acids is useful in determining whether the *P. acnes* population has been changed by antibiotic therapy.

While most patients do respond to tetracycline therapy, there is a definite minority of patients who do not show an effect from this drug or from any other antibiotic. The obvious question is why is the antibiotic not uniformly useful. One problem that might have to be considered is whether enough antibiotic is being given although it has been shown that one can get a decrease in the bacterial flora and a decrease in the free fatty acids with dosages of tetracycline as small as 250 mg per day. Tetracycline does become concentrated in the follicle and can be identified due to the fact that it is a fluorescent compound. On examination with Wood's light, a greenish-blue fluorescence can be identified at the follicular mouth. This is a useful procedure in determining compliance in patients who might not be taking their tetracycline because it is non-compliance which probably accounts for most of the failures of therapy. Another factor that must be considered is how the drug is taken. This is particularly true with tetracycline, since tetracycline absorption is greatly decreased in the presence of lipids, bicarbonate, calcium, iron etc. For this reason it is essential that tetracycline be taken on an empty stomach. Patients should be advised that their dose of tetracycline should be taken either an hour before or at least an hour after their last meal.

A new approach which should be considered in the antibiotic-resistant patient is the use of "mega" thera-

py as this has been shown to be quite useful. Tetracycline is the drug of choice, as it is unlikely that the patient will be able to tolerate similar dosages of erythromycin. Two to three grams of tetracycline are used, as tolerated, and this has helped many patients with acne. Of course, with dosages of this size, one has to be careful to insure that toxicity does not occur. This requires frequent hemograms as well as examinations for alterations in liver function.

The amount of tetracycline that has been used for the treatment of acne is in itself an excellent indication of the safety of the drug. It is remarkable that the side effects have been as infrequent as they have been. This may be due partially to the fact that in general the dose of tetracycline used for the treatment of acne is often less than that used in conventional antibiotic therapy for infections. The most common side effect has been vaginal candidiasis and even this is not too common. However, there is one serious side effect that the dermatologist should be aware of, and which often times is not diagnosed at the appropriate time. Gram negative folliculitis is a serious complication of antibiotic therapy. It probably arises as a colonization of the skin from the nasal passages and the initial lesions often are found around the nares. Gram negative folliculitis can manifest itself in two forms. The first form consists of small pustular lesions that are usually surrounded by an inflammatory areola. The second form of gram negative folliculitis is manifested by the development of large, succulent deep inflammatory nodules. Gram negative folliculitis should be recognizable as it is heralded by a flare in patients who are otherwise doing quite well on therapy. Under these circumstances, the natural tendency is to increase the dosage of antibiotics. The correct approach to therapy is to obtain a culture and make the necessary adjustments to the antibiotic regimen based upon antibiotic sensitivity data. There are, however, many occasions when the antibiotic sensitivity data is of little help because the antibiotic sensitivity pattern of the gram negative organism is such that one would have to use antibiotics which are too toxic for ordinary use. The synthetic penicillins in high dosages do seem to be effective in gram negative folliculitis and probably are the drug of choice if a specific antibiotic is not indicated on the basis of sensitivity studies. A general awareness of the problem of gram negative folliculitis is most important and will lead to an appreciation of this syndrome.

In closing I want to emphasize once again that broad-spectrum antibiotics are useful agents for the treatment of acne; they probably are the most effective form of therapy that we have for controlling inflammatory acne at the present moment. In severe acne, they are superior to the topical antibiotics although it is certainly possible that topical antibiotics can be used in the approach to minor degrees of the disease.

DISCUSSION

Cunliffe, Leeds: Many people throughout the world probably use different types of tetracycline and I would be interested in your comment as to what the average dose you have given a patient with moderate acne and why do you prefer the straightforward simple tetracycline before the more longeracting ones?

Strauss, Iowa: Most of the patients that I see, which are probably in the grade 2 or grade 3, I start on 500 mg tetracycline or maybe 750. The number that I start on a full gram right off, is relatively small and it involves the patients who have very severe acne. Others prefer to start with a full gram of tetracycline and cut back relatively quickly. I think it is an individual preference and I do not think we have the data to confirm which works more effectively.

Lidén, Umeå: You said that as a side-effect of this mega-therapy you can see polydipsia and polyuria. Is this a pharmacological effect and not an effect of break-down products?

Strauss, Iowa: I do not know.

Lidén, Umeå: When you suspect gram-negative folliculitis, is it sufficient to use an ordinary gram-negative culture technique or is it necessary to use a strictly anaerobic culture technique where you incubate the specimen directly under anaerobic conditions bed side?

Strauss, Iowa: I am submitting my samples to a commercial laboratory and they are probably not using a

strictly anaerobic technique. The major problem in recovering the positive culture is not how strictly aerobic you are, but how quickly the material gets to the lab and whether it dehydrates. I think if you prevent dehydration of the specimen, you recover the organisms in the gram-negative folliculitis.

Plewig, Munich: I would like to comment on the gram-negative infection. I do not see it as frequently in Munich as I did in the United States, probably because we use less antibiotics. We find the organism in high numbers not only in the pustules, but also in the nares, and on the skin surface of the axillae. My patients still have the disease as they had it eight or ten years ago — incurable.

Donsky, Toronto: I feel badly when I hear dermatologists speaking of using tetracycline as our first-line therapy in the treatment of acne. Personally, I prefer to see the use of topical therapy first. Is it not preferable to use a peeling agent, such as salicylic acid with or without sulphur? Then add a benzoyl peroxide preparation in a lower concentration. Increase in concentration as we go on. Same principle with vitamin-A-acid. To the patients that do not do well, we add tetracycline in full dosage.

Strauss, Iowa: Part of the problem may be a difference in the type of patients we are seeing. I am not seeing any primary acne, I am seeing acne that has been through other physicians prior to the time as I am seeing them. They have usually been up that step ladder that you are talking about by the time I see them.