Ampicillin Concentrations in Human Dental Granuloma after a Single Oral Administration of Talampicillin

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Ampicillin concentrations in human serum and dental granulomas of 31 patients were determined after a single oral dose of talampicillin (equivalent to 500 mg of ampicillin) was administered to each. The specimens were taken at 1.5, 2.0, 2.5, 3.0, and 3.5 h after the administration of talampicillin. The mean peak ampicillin concentrations in serum and dental granulomas occurred at identical times, 2.5 h, and were 8.29 μg/ml (range, 1.81 to 13.20 μg/ml) and 2.94 μg/g (range, 1.14 to 7.16 μg/g), respectively. The mean dental granuloma/serum ampicillin concentration ratio at the peak time (2.5 h) was 0.42 (range, 0.29 to 0.56). Ampicillin concentrations in dental granulomas exceeded most of the MICs for the bacteria commonly isolated from odontogenic infection.

Dental granulomas, commonly found in dental practice, are periapical radiolucent areas in the jawbone at the apices of infected teeth. A dental granuloma occurs when noxious substances from pulpal infection and necrosis escape from the root canal into the periapical tissues, which are stimulated by defensive activity to form a mass of acute inflammatory tissue. This inflammatory hyperplastic tissue is a dental granuloma, which becomes a primary focus of odontogenic infection.

Talampicillin is the phthalidyl ester of ampicillin, which is frequently used prophylactically and in the treatment of infection in dental practice. Talampicillin is hydrolyzed by nonspecific esterases during intestinal absorption, which leads to the release of ampicillin (4). This study was undertaken to determine the ampicillin concentrations in human serum and dental granulomas after a single oral dose of talampicillin.

MATERIALS AND METHODS

Patients. Thirty-one patients who underwent the enucleation of dental granulomas in the mandible were tested in this study. Of the patients, 19 were female and 12 were male. The mean age of the patients was 34 years (range, 23 to 49 years), and the mean body weight was 52 kg (range, 40 to 78 kg). The data from analyses of blood and urine samples from all patients were within normal limits. No patient had any clinical signs of acute inflammation, and none had been receiving any antimicrobial therapy for at least 1 week before the operation.

Sampling and preparation. At 1 to 2 h after breakfast, each patient was given a single preoperative oral dose of talampicillin (equivalent to 500 mg of ampicillin) with 200 ml of water. Specimens of dental granuloma tissue were obtained at 1.5, 2, 2.5, 3, and 3.5 h after administration of the drug. A 3.0-ml sample of blood was also taken from the antecubital vein of each patient. Specimens of dental granuloma and blood were collected once from each patient. The maximum time lag between the collection of the dental granuloma sample and the collection of the blood sample was 3 min.

The dental granuloma specimen was agitated in sterile saline to wash away the blood and was cut into pieces as small as possible. Serum was obtained from blood samples by centrifugation.

The samples were weighed, and parts of 1% phosphate buffer (pH 6.0) were added to the tissue specimen. The mixture was homogenized by a glass homogenizer in an ice bath, stored at 4°C for 18 h to extract ampicillin, and then centrifuged to obtain the supernatant. The supernatant was further diluted with 1% phosphate buffer (pH 6.0) in factors of 1, 5, 10, and 20 for assay purposes. The serum was also diluted with the same buffer in factors of 1, 10, 20, 40, and 60.

Assay. Ampicillin concentration was measured by the paper disk method. The test organism was Micrococcus luteus ATCC 9341. Bacto Penassay Seed agar (Antibiotic Medium 1; Difco Laboratories, Detroit, Mich.) was the assay medium.

Standards for serum and tissue assays were prepared with 1% phosphate buffer (pH 6.0), and five ampicillin concentrations were assayed (range, 0.01 to 0.25 μg/ml). All assays were performed in triplicate. All plates were incubated for 18 h at 37°C, and the resulting growth inhibition zones were measured to a precision of 0.1 mm.

RESULTS

Measurable ampicillin concentrations were found in both the dental granuloma and serum in all cases (Table 1). The peak concentrations of ampicillin in both dental granuloma and serum occurred 2.5 h after administration of talampicillin. The peak concentrations (means ± standard deviations) in the dental granulomas and serum samples were 3.51 ± 1.67 μg/ml (range, 0.53 to 5.36 μg/ml) and 8.29 ± 3.84 μg/ml (range, 1.81 to 13.20 μg/ml), respectively. The ratio of dental granuloma ampicillin concentration to serum ampicillin concentration (mean ± standard deviation) at the peak time (2.5 h) was 0.42 ± 0.10 (range, 0.29 to 0.56).

DISCUSSION

Since the samples could not be collected successively from the same patient, a wide variation was found in
ampicillin concentrations in serum samples as well as in dental granuloma samples. In this study, because outpatients were tested, talampicillin was administrated to nonfasting patients. The water volume at dosing and the elapsed time after breakfast were the only factors which could be controlled. Welling et al. (5) reported that serum ampicillin and amoxicillin concentrations were influenced by different kinds of food. Therefore, although ideally the patients should eat the same meal, it was not possible in this study to control this factor. Although a wide variation was observed, the results of this study are applicable to clinical practice.

Jones (2) has reported that the absorption of talampicillin (250 mg) in a nonfasting patient is lower than in a fasting patient and that the peak time of serum drug concentration in the nonfasting patient is delayed compared with that in the fasting patient (fasting, 4.65 μg/ml and 40 min; nonfasting, 3.26 μg/ml and 60 min). The peak time was further delayed in this study (2.5 h).

Only one report exists on serum ampicillin concentration after talampicillin (equivalent to 500 mg of ampicillin) was given to nonfasting subjects (1). In that study the peak concentration and peak time were 9.63 μg/ml and 2.5 h, respectively. Compared with the results of our study (8.29 μg/ml and 2.5 h), concentration in serum was slightly higher and the peak time was identical.

There is no study on the concentration of antibiotics in human dental granuloma tissue. However, ampicillin concentrations in other oral tissues after a single dose of talampicillin have been reported (1); tissue/serum ampicillin concentration ratios at peak time were 0.50 (gingiva), 0.16 (mandibular bone), 0.34 (dental follicle), and 0.52 (dental pulp). The value for dental granuloma (0.42) was lower than those for gingiva and dental pulp but higher than those for dental follicle and mandibular bone.

The bacteria commonly isolated from odontogenic infection are Streptococcus group A, Peptostreptococcus spp., and Bacteroides spp. Ampicillin concentrations in dental granuloma specimens exceeded most of the MICs for clinically isolated strains of Streptococcus group A (0.025 to 0.78 μg/ml), Peptostreptococcus spp. (0.025 to 0.39 μg/ml), and Bacteroides spp. (0.025 to 25 μg/ml) (3). Since the present results were obtained with a single dose, higher dental granuloma and serum drug concentrations could be achieved in a steady state after multiple dosings.

In summary, ampicillin concentrations in dental granuloma samples after a single oral dose of talampicillin exceeded most of the MICs for clinically isolated Streptococcus group A, Peptostreptococcus spp., and Bacteroides spp. Thus, talampicillin may be a valuable agent for the treatment of odontogenic infections involving periapical infection.

**LITERATURE CITED**


