Topical antimicrobial therapy in the prevention of early childhood caries: a follow-up report

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Abstract

Purpose: The purpose of this study was to assess the efficacy of antimicrobial therapy in the prevention of early childhood caries (ECC).

Methods: The study population consisted of 83 subjects (age: 12 to 19 months ($\bar{x}$=15.6); gender: 40 females and 43 males). Inclusion criteria included: (1) unremarkable medical history; (2) presence of 4 maxillary primary incisors (MPI) with no visible defects; (3) clinically caries free; (4) use of a nursing bottle at naptime and/or bedtime which contained a cariogenic substrate; (5) 2 consecutive ms positive cultures from pooled MPI plaque. The subjects were randomized into 2 groups. The 39 subjects in the experimental group and the 44 subjects in the control group were evaluated every 2 months during the study period. At each evaluation, the subjects had 10% povidone iodine (experimental group) or placebo (control group) applied to their dentition. Treatment failure was defined as the appearance of a white spot lesion(s) on any of the MPI during the study period.

Results: Using the Kaplan-Meier procedure, the estimated percents (±SES) of participants to experience 12 months of disease-free survival were 91±5% for those receiving treatment and 54±9% for those in the control group. Via the log-rank test, the hazard of treatment failure is statistically significantly higher in the placebo group (log-rank statistic 10.28, two-sided *P*=0.0013).

Conclusions: These observations indicate that topical antimicrobial therapy increases disease-free survival in children at high risk for ECC.*(Pediatr Dent 24:204-206, 2002)*

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Early childhood caries (ECC) is a particularly virulent variant of human dental caries that may devastate the primary dentition of infants, toddlers and young preschool children. Bacteriologic studies indicate that ECC is characterized by dense infection of mutans streptococci (ms) on dental surfaces.[1] Accordingly, it is reasonable to conclude that suppression of oral ms populations should reduce risk for ECC. Human [2,3] and animal [4,5] model studies indicate that topical iodine agents can significantly suppress dental levels of ms. In addition, topical iodine agents are approved by the Federal Drug Administration for topical skin and mucosa application in children (Physicians Desk Reference, 2000). This information supports the concept that topical application of an iodine agent to the teeth of children at high risk for ECC should reduce risk for the development of ECC. In this regard, an earlier pilot study[6] provided data to test this concept. That pilot study consisted of 31 subjects and it has since been expanded to include 83 subjects with follow-up findings reported in this paper.

Methods

Institutional Review Board

The methods employed in this study were approved by the Institutional Review Board of the University of Puerto Rico Medical Center.

Population

The study population consisted of 83 babies who were clients of a women, infant and children (WIC) clinic in Puerto Rico. This population was composed of 43 males and 40 females who were 12 to 19 months of age (mean=15.6) at their time of entry into the study. Inclusion criteria were as follows: (1) unremarkable medical history; (2) presence of

4 maxillary primary incisors (MPI) with no visible defects; (3) clinically caries free; (4) use of a nursing bottle at naptime and or bedtime which contained a liquid other than water (NB+); (5) two consecutive positive ms cultures (separated by an 8-week interval) from pooled MPI plaque.

Medical history was confirmed by the WIC clinic's consulting pediatrician. The presence of 4 MPI with no visible defects and caries-free status was established by examining the subjects. Caries diagnosis was based on the criteria of Radike (1972) with the modification that enamel was not scraped from white spot lesions.[7] NB+status was assessed by a questionnaire and interviewing the subject's mother. Nursing bottle contents included cow's milk, cow's milk+ powdered sweetened agents such as sucrose, Ovaltine, Quick, cow's milk+cereal, formula, and fruit juices. A pooled plaque sample was obtained by swabbing the gingival one-third of the 4 MPI with a cotton swab. The samples were placed into vials containing 2 ml of reduced transport fluid (RTF) with glass beads and transported to the laboratory for processing within 4 hours of collection. The samples were dispersed and plated onto Mitis-Salivarius-Bacitracin (MSB) agar as previously described.[8] They were incubated at 37^{0}C for 48 hours under anaerobic conditions and then placed under aerobiosis for 24 h prior to examination. Representative colonies with morphological characteristics of ms were isolated[9] and confirmed to be ms utilizing mannitol and sorbitol fermentation tests.[10]

Design

The study was designed as a randomized double-blind, placebo-controlled clinical trial. Treatment failure was defined as the appearance of a white spot lesion(s) on any of the MPI during the study period. The subjects were randomized into 2 groups. The 39 subjects in the experimental group and the 44 subjects in the control group were evaluated every 2 months during the study period. At each evaluation, they were examined for dental caries and had a 10% povidone iodine solution (experimental group) or placebo solution (control group) applied to their dentition. The placebo was commercial instant tea (without lemon or sweetener) and deionized water.

These agents were placed into coded vials by the laboratory technician so the examiners would be blinded. The agents were applied by swabbing the dentition with a small sterile cotton ball that was saturated with the respective agent and held in a locking cotton pliers. Approximately 0.2 ml of the 10% povidone iodine or the placebo solution was utilized for one application (0.2 ml of 10% povidone iodine contains 2.0 mg of iodine which is not thyrotoxic when delivered bimonthly[11]). In addition, the mothers were questioned at each evaluation to verify the NB+ status of their baby.

Statistical analysis

The probabilities and associated standard errors of the treated and control participants experiencing one year free of white-spot lesions were estimated using the Kaplan-Meier estimator (a survival analysis).[12] The Log-rank test was used to test whether the disease incidence differed between the treatment and control groups. Participants who did not get white spots before the end of the trial (12 months) or before they were lost to follow-up were considered statistically censored at the month of last exam. Participants who discontinued their NB+ feeding habit were considered lost to follow-up at that time. Statistical calculations were performed using SPSS for Windows version 10.05.

Results

Of the 44 participants in the control (placebo) group, 14 (32%) were observed to experience treatment failure; of the 39 treatment (experimental) group subjects, only 3 were observed to experience treatment failure (8%). Using the Kaplan-Meier procedure, the estimated percents (±SES) of participants to experience 12 months of disease-free survival are 91±5% for those receiving treatment and 54±9% for those in the control group. Via the log-rank test, the hazard of treatment failure is statistically significantly higher in the placebo group (log-rank statistic 10.28, two-sided P=0.0013).

Of the control group, 15 participants (34%) were lost to follow-up before treatment failure, discontinuation of NB+ feeding habit, and end of study. The treated group lost 17 participants (44%) prematurely. These percentages are not statistically significantly different (2-sided P=0.50, Fisher's Exact Test).

Discussion

Earlier studies indicate that ECC is microbiologically characterized by dense dental infection with ms.[1] Animal and human studies indicate that accumulation of ms are associated with frequent and prolonged consumption of cariogenic substrates and precede the onset of dental caries.[13,14] These experimental observations support the notion that infants who are colonized by ms and who have caries promoting diets are likely to have a drastic increase in their oral ms populations. Such an increase is associated with a high risk for rampant dental caries. On this basis, it is reasonable to speculate that suppression of ms to non-pathogenic levels may decrease the risk for development of ECC. In this regard, iodine solutions are well known for their ability to suppress ms dental populations when topically applied to the teeth.[2-5]

Collectively, the preceding narrative suggests that periodic topical application of an iodine solution to the dentition of children at high risk for ECC should suppress dental ms levels and, in turn, reduce risk for the development of ECC. Our earlier pilot clinical trial (n=31 subjects)[6] provided an observation that supported this concept thereby justifying the need for a more expanded study. The findings of this study (n=83 subjects) expand and corroborate earlier observations. Stated differently, the experimental results of this clinical trial indicate that topical antimicrobial therapy

significantly increases disease-free survival in children at high risk for developing ECC. It would be important to know if this effect remains after the antimicrobial agent is withdrawn. On this basis, larger and more in-depth clinical trials are warranted prior to introducing 10% povidone iodine therapy as a preventive modality for ECC into clinical practice.

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Abstract of the Scientific Literature

Local Anesthetics for Cardiac Transplant Patients

The purpose of this prospective clinical study was to examine the cardiovascular responses caused by dental local anesthetics in both healthy and cardiac transplant patients. Thirty adult patients were chosen for this study (10 healthy and 20 post-cardiac transplant) with all healthy patients requiring minor oral surgery and all transplant patients requiring gingival surgery. All cardiac transplant patients were at least three months post-transplant and were medicated with cyclosporin along with other immunosuppressant drugs. Prior to dental treatment, all healthy patients (control group) and 10 transplant patients received 4.4ml of 2% lidocaine with 1:80,000 epinephrine, while the remaining transplant patients received 4.4ml of 3% prilocaine with 0.03IU/ml felypressin. Vitals (heart rate, blood pressure and ECG) were recording prior to injection, immediately following injection and 10 minutes following injection. The authors reported that there was no significant change in blood pressure between the two study groups and the control group, nor was any significant change noted in heart rate between the control group and the epinephrine free group. However, there was a significant increase in heart rate in the transplant group 10 minutes after injection of the local anesthetic with epinephrine.

Comments: Although this study was limited to a small number of adult patients, the need to use caution when using local anesthetics containing epinephrine on cardiac transplant patients is certainly relevant for pediatric patients as well. **MM**

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