Scientific Article

Dental Caries Recurrence Following Clinical Treatment for Severe Early Childhood Caries

Robert J. Berkowitz, DDS[1] • Alvin Amante, DMD[2] • Dorota Kopycka-Kedzierawski, DDS, MPH[3] • Ronald J. Billings, DDS, MSD[4] • Changyong Feng, PhD[5]

Abstract: ***Purpose:*** *To determine the relapse rate within one year for a cohort of children treated for severe early childhood caries (S-ECC).* ***Methods:*** *In an earlier report, we assessed the suppressive effect of 10 percent povidone-iodine and the elimination of active caries on salivary mutans streptococci (MS) populations in 77 children with S-ECC; 49 children returned for a 6-month recall exam that occurred 5 to 12 months post dental surgery. Relapse declaration required at least one caries lesion needing a restoration. Contrasts of relapse (R) and non-relapse (NR) to the covariates of gender, race, ethnicity, age, surfaces available for relapse (SAR), time to appointment, and baseline salivary mutans streptococci (MS) counts were statistically evaluated.* ***Results:*** *19 children (39%) were declared R and 30 (61%) were NR. The 2 groups did not statistically differ on: gender, race, ethnicity, age, SAR, baseline salivary MS counts and time to recall appointment. Statistical analyses also showed the covariates had no significant effect on probability of relapse or time to relapse (P>0.05).* ***Conclusions:*** *None of the covariates were related to R. The R rate (39%) observed is consistent with earlier reports. Novel approaches are needed to improve relapse prevention. (Pediatr Dent 2011;33:510-4) Received May 10, 2010 | Last Revision May 4, 2011 | Accepted May 5, 2011*

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Early Childhood Caries (**ECC**) continues to be a significant public health problem that afflicts young children most often in lower socioeconomic groups. Recent NHANES data released in 2007 by the Centers for the Disease Control and Prevention (CDC) show that the prevalence of caries in the primary dentition of US children is on the rise. Almost 28% of 2- to 5-year-old US children were classified as having caries experience in the primary dentition.[1, 2]

The American Academy of Pediatric Dentistry's (**AAPD**) guidelines differentiate S-ECC from ECC as a consequence of a more destructive disease process based on age and number of carious, filled or missing tooth surfaces. The current standard of care for S-ECC includes restoration and extraction of carious teeth, application of topical fluoride, oral hygiene instructions and recommendations regarding feeding behaviors (Oral Health Policies, Reference Manual, AAPD, 2010). Clinical outcomes for S-ECC treated per this standard of care are poor; approximately 40% of children treated for S-ECC will develop new caries lesions within 12 months post dental surgery[3-6]. The present study reports relapse rates data for a cohort of children recently treated for S-ECC in one session under general anesthesia and thus adds additional information regarding outcomes for treatment of this significant oral health problem.

[1]Dr. Berkowitz is a professor and chair and [2]Dr. Amante is a senior resident, Division of Pediatric Dentistry; and [3]Dr. Kopycka-Kedziarawski is an associate professor and [4]Dr. Billings is a professor, Division of Community Dentistry and Oral Disease Prevention, all in the Department of Dentistry, and [5]Dr. Feng is an assistant professor, Department of Biostatistics and Computational Biology, all in the School of Medicine and Dentistry, the University of Rochester Medical Center, Rochester, NY.

Correspond with Dr. Berkowitz at robert_berkowitz@urmc.rochester.edu

Methods

Study design. A retrospective chart review was conducted to determine the relapse rate of new caries lesions and the affect of covariates on the relapse rate for a cohort of children treated for S-ECC based on their 6-month recall visit. These children were enrolled in an earlier study that investigated the time course and duration of suppression of mutans streptococci (**MS**) levels in 77 children with S-ECC following the removal and restoration of carious teeth, application of a 10% povidone-iodine solution (PI), followed by an application of a 1.23% APF foam, and preventive counseling consisting of oral hygiene instruction and recommendations regarding caries promoting feeding behaviors.[7] This investigation is a follow-up study to assess relapse rates during the first year post dental surgery.

The study was approved by the University of Rochester Research Subjects Review Board.

Study population. The study population for this report consisted of 49 children that returned to the Eastman Dental (ED) Pediatric Clinic for routine follow-up care during their first year post dental surgery. Of the 77 children in the original study[7], 28 did not return for a 6-month recall within one year post dental surgery. These 28 children were excluded in this report.

Baseline procedures. The original 77 study participants presented to the Ambulatory Surgical Center of Strong Memorial Hospital at the University of Rochester Medical Center (URMC) for dental surgery under general anesthesia due to S-ECC as part of a study on adjunctive chemotherapeutic suppression of MS.[7] The details of the baseline procedures are presented elsewhere.[7] Saliva was collected prior to dental surgery and the number of colony forming units (CFUs) of MS per ml of saliva was determined. Dental surgery used an aggressive approach.[7,8] After completion of the surgery, 0.2 ml of PI was applied to the

teeth using a cotton ball and immediately wiped away with gauze. Subsequently, 1.23% APF foam was applied to the teeth and immediately wiped away prior to emergence from general anesthesia.

Follow-up procedures. In the original study[7], the subjects were seen at 30 days, 60 days, and 90 days post dental surgery. At all of these follow-up visits a caries exam was performed by the same study examiner that performed the baseline caries exam. At the time of the 90 days follow-up visit, caries lesions were not detected in any of the subjects. The subjects were discharged from the study and placed on the 6 month recall.

One of the authors (AA) performed a retrospective chart review of the 49 subjects that returned within 12 months post dental surgery for a recall visit. Relapse was defined as the presence of at least one new cavitated caries lesion(s) requiring a restoration that necessitated a cavity preparation with a rotary instrument as recorded in the patient's chart.

Forty nine (49) of the 77 subjects returned for a routine 6-month recall visit within first 12 months post dental surgery. Adherence to the 6-month timeline for a routine recall visit varied among the 49 subjects and extended over a range of 5 to 12 months for the group. This variability was largely due to cancellation of originally scheduled appointments and rescheduling of new appointments. The time to relapse was operationalized as occurring at the time of the recall visit when at least one new lesion was identified. The timing of 6-month appointments for children with relapse (**R**) and children without relapse (**NR**) was compared as time to relapse for R and duration of disease-free survival for NR.

Statistical analysis. The relationship of relapse to the patient's age, gender, ethnicity, race, enamel surfaces available for relapse (SAR) post dental surgery, and baseline (pre-dental surgery) MS levels (CFU/ml saliva) was determined. A two-sample *t*-test and Fisher's exact test were used to compare the baseline covariates of relapse and non-relapse groups. All analyses were conducted using SAS® 9.1 (SAS Institute Inc., Cary, NC). The significance level (α) was set at 0.05. We also studied the effects of baseline covariates on the relapse probability by multiple logistic regression and their effects on the time to relapse by the Weibull regression in survival analysis.[9]

Results

Characterization of the subject population. Of the 49 subjects that comprised the study population, having returned for a 6 month recall visit within one year post dental surgery, the gender distribution was 24 females and 25 males; racial distribution was 15 Caucasian and 34 Non-Caucasian; ethnicity distribution was 7 Hispanic and 42 non-Hispanic; mean age was 3.72 years ($\pm$ 0.86); mean SAR post dental surgery was 63.5 ($\pm$11.8); and the mean baseline (pre-dental surgery) $\log_{10}$ MS CFU/ml saliva was 6.17 ($\pm$ 0.90).

Analyses of relapse. No relapse occurred during the first 90 days post dental surgery[7]. Nineteen children (39%) met the study's criterion for relapse and 30 (61%) for no relapse during the follow-up period of 6 month recall appointments that occurred between 5 and 12 months post dental surgery of the original study.

Table 1 summarizes the demographic, baseline MS levels and SAR in the relapse (N=19) and non-relapse (N=30) groups. A two-sample *t*-test showed that there was no significant difference between the two groups in baseline MS levels, SAR and age. Fisher's exact test indicated no significant difference between these two groups with regard to gender, race and ethnicity (all values >0.20).

A comparison of the mean, standard deviation, and median of disease free survival in the relapse group and the mean, standard deviation and median of the elapsed time post surgery to the clinical documentation of relapse in the relapse group is presented in Table 2. Inspection of Table 2 indicates that there was no statistically significant difference in the timing of recall visits for the non- relapse vs. relapse groups (P=0.33; two-sample *t*-test).

Multiple logistic regression was used to assess the effect of the covariates (ie, age, gender, race, baseline MS levels and SAR) on the probability of relapse occurring within 12-months post dental surgery (Table 3). None of these covariates had a statistically significant impact on the probability of relapse during the 12-month study period.

The 19 subjects that relapsed had the relapse detected at different times during the post dental surgery period (range 5 to

Table 1. BASELINE DEMOGRAPHICS OF THE RELAPSE AND NO RELAPSE GROUPS

Variable		Relapse (N=19)	No relapse (N=30)	*P*-value
Baseline $\log_{10}$(CFU)		6.29±1.10	6.08±0.76	0.47†
Number of surfaces (SAR)		64.1±8.6	63.2±16.6	0.77†
Age		3.73±0.74	3.72± 0.91	0.98†
Gender	F	8 (42%)	16 (53%)	0.44*
	M	11 (58%)	14 (47%)	
Race	Caucasian	3 (16%)	12 (40%)	0.11*
	Non-Caucasian	16 (84%)	18 (60%)	
Ethnicity	Hispanic	1 (5%)	6 (20%)	0.22*
	Non-Hispanic	18 (95%)	24 (80%)	

† From two-sample *t*-test. * From Fisher's exact test.

Table 2. COMPARISON OF THE TIME TO RELAPSE FOR THE RELAPSE GROUP AND DURATION OF DISEASE FREE SURVIVAL IN THE NO RELAPSE GROUP

Groups	N	Mean*	SD*	Median*	Range*
Relapse	19	7.4	2.3	6.0	3.0-12.0
No-relapse	30	7.2	1.7	7.0	5.0-12.0

* Measures are months.

Table 3. RESULT OF MULTIPLE LOGISTIC REGRESSION ON THE PROBABILITY OF RELAPSE DURING THE 12 MONTH STUDY PERIOD

Variable	Odds ratio	95% CI of OR	*P*-value
Age	1.28	0.56-2.96	0.56
Baseline $\log_{10}$(CFU)	1.19	0.56-2.51	0.65
Number of surfaces (SAR)	0.99	0.94-1.04	0.66
Gender (M/F)	1.62	0.42-6.16	0.48
Race (non-Caucasian / Caucasian)	4.17	0.90-19.33	0.07

Table 4. RESULT OF WEIBULL REGRESSION ON THE EFFECT OF THE COVARIATES TO THE TIME OF RELAPSE

Variable	Estimate	SD	*P*-value
Age	-0.34	0.57	0.55
Baseline $\log_{10}$(CFU)	-0.61	0.55	0.27
Number of surfaces (SAR)	0.02	0.03	0.52
Gender (M/F)	-0.58	0.99	0.56
Race (non-Caucasian / Caucasian)	-2.03	1.31	0.12

12 months). The effect of the covariates on the time to relapse was studied using the Weibull regression analysis.[9] None of the covariates had a statistically significant association with the time to relapse (time of the 6-month recall appointment) (Table 4).

Discussion

None of the covariates studied were significantly related to relapse; the limited size of the study population (N=49) may have contributed to this finding. The observation that SAR was not associated with relapse has been reported earlier by our group.[8] Baseline MS salivary levels were also not related to relapse. In this regard, it should be pointed out that the main reservoir of MS is the tooth surface and that salivary populations largely reflect spill off from tooth surfaces.[10,11] Although quantifying salivary MS populations facilitates estimation of the density of dental infection[12-15], it does not identify site specific accumulation of these organisms to pathogenic levels on specific enamel surfaces. Accordingly, this may likely explain the lack of relationship between baseline MS saliva levels and relapse observed in this report.

The observation of 39% relapse rate within 12 months post dental surgery is consistent with multiple earlier reports.[3-6] This unacceptable clinical outcome is not surprising, as dental surgery for children with S-ECC has been shown to reduce the magnitude of salivary MS reservoirs but to levels that do not negate caries risk.[16-18] In addition, earlier studies[19-21] clearly indicate that counseling regarding decay promoting feeding behaviors, as practiced by dentists, has produced minimal success. Improvement in long term clinical outcomes for S-ECC may likely be realized through research that places focus on the disease dental caries per se as opposed to surgical treatment as an end in itself.

The subjects in the present report had their S-ECC managed by aggressive dental surgery, a single application of PI and APF foam and preventive education.[7] This approach reduced their baseline salivary MS levels significantly, and the magnitude of the observed suppression appeared to be sustained for 90 days; likewise, none of the subjects developed new carious lesions during the 90 day observation period.[7] However, 19/49 (39%) had relapse detected between 90 days to one year post dental surgery.

The American Dental Association (**ADA**) has published recommendations regarding the use of topical fluoride for prevention of dental caries to the primary dentition.[22] The ADA has recommended the application of fluoride varnish (**FV**) at least twice per year and ideally 4 times per year for children at high risk for caries to their primary dentition per ADA risk assessment guidelines. However no data exist with regard to the efficacy of FV applied 2 or 4 times per year on clinical outcomes for children treated for S-ECC (S-ECC being defined as high risk by ADA risk assessment guidelines[22]). Nevertheless, more recent papers summarized by Weinstein, Spiekerman and Milgrom[23] demonstrate clearly that even multiple and intensive fluoride treatments do not arrest tooth decay in high-risk children.

Improved clinical outcomes for S-ECC may likely be realized through treatment modalities that address the infectious feature of this disease. Suppression of oral reservoirs of MS to non-pathogenic levels is another approach that may be promising. A variety of topical anti-microbial agents have been examined to suppress oral populations of MS.[24-29] In this regard, topical iodine agents appear promising. Iodine is among the most potent of bactericidal agents causing immediate lethality upon bacterial contact. Topical iodine agents are approved by the US Food and Drug Administration for application to the skin of children and iodine has excellent penetrability into dental plaques which is a highly desirable attribute when dealing with biofilms.[30] Iodine's safety, bactericidal and penetrability characteristics make it an excellent agent for oral use.

Earlier studies have demonstrated the prolonged suppressive effects of topically applied iodine (specifically I_2-KI) on oral populations of MS.[31,32] In this regard, it must be emphasized that MS levels are a surrogate marker for dental caries and that the utility of topical iodine in preventing the disease dental caries is the more accurate marker of its therapeutic efficacy.

A pilot study[33] assessed the preliminary efficacy of bimonthly topical PI in a placebo controlled double blind clinical trial in preventing the development of white spot lesions on the primary maxillary incisors of Puerto Rican babies. These babies were all at high risk for ECC as they were all colonized by MS and had decay promoting feeding behaviors. The experimental group had PI applied to their dentition and the control group a placebo solution. Using the Kaplan-Meier procedure, the estimated percents (± SE) of study subjects to experience 12 months of disease free survival was 91(±5%) for those receiving PI (N=39) and 54(±9%) for those receiving the placebo (N=44) (log rank test, P=0.001). These observations indicated that topical PI increases disease free survival in children at high risk for ECC. In addition, it must be pointed out that these children were caries free at their time of entry into the study and therefore likely harbored low oral levels of MS. The question that needs to be answered is whether PI can suppress oral populations of MS to nonpathogenic levels in the setting of a dense MS infection characteristic of S-ECC.[34-39]

A pilot study[40] has addressed the issue of chemotherapeutic suppression of oral MS levels in children afflicted with S-ECC. The study consisted of 21 children, 2-6 years of age, who received treatment for S-ECC in a single session under general anesthesia. Ten children were assigned to the 10% povidone iodine or experimental group and 11 to the saline or control group. After completion of restorative care, either PI or saline was applied to the dentition using a cotton swab; next a 1% sodium fluoride gel was applied to all teeth in both groups. Saliva samples were collected by swab immediately before dental surgery, and after 1 hour, 3 weeks and 3 months post dental surgery. The density of salivary MS infection was determined for each sample.

The results illustrated that MS levels in the PI group were statistically significantly reduced at 1 hour, 3 weeks and 3 months as compared to baseline levels, whereas MS levels in the saline group were statistically significantly reduced only at 1 hour as compared to baseline levels.

In another pilot clinical trial[41] on 25 children with S-ECC treated in one session under general anesthesia, the children were assigned to experimental and control groups. The experimental group received 3 topical applications of PI at bimonthly intervals during the first 4 months of the study and the control group did not receive PI. Examination of the subjects at 6 months post dental surgery demonstrated that 18% of the children in the experimental group had new caries lesions as compared with 63% of children in the control group.

Two very recent studies[42,43] assessed the effect of fluoride varnish (FV) alone as compared to FV + PI. The first study assessed the effect of FV alone (N=428 in FV group) vs. FV + PI (N=186 in FV+PI group) in protecting erupting 1st permanent molars from developing dental caries. The percentages of children with caries-free 1st permanent molars were 79% in the FV group and 88% in the FV+PI group ($P<0.002$). The second study consisted of 172 children (12-30-months-of-age) that received FV alone or FV + PI. The proportion of children with new decayed primary teeth was 41% in the FV + PI group and 54% in the FV group. Multivariate log-binomial regression was used to compare the rate of new decay between the groups, controlling for the number of teeth at baseline and the number of treatment visits. This analysis demonstrated that combined treatment with FV + PI reduced the rate of new tooth decay by 31% over FV alone.

This current study has several limitations. One was the inability to assess the underlying antecedents to relapse. Indeed, one or several variables could have predisposed or adversely affected those children that relapsed (eg, nutrition, oral hygiene, siblings, day care, SES, fluoride exposure, etc). Other issues include the limits of chart audit, the significant loss to follow-up, and the dispersion of the 6-month recall. An unequivocal statistical comparison of the exact time to relapse in the relapse group versus the period of disease free survival in the non- relapse group was not possible. Both groups were evaluated via a routine recall appointment and not under the scrutiny of tighter, more systematic surveillance. Accordingly, the exact date that a caries lesion developed could not be precisely determined, and it is not known if children with no relapse detected at earlier appointments subsequently developed caries lesions within 12 months.

Irrespective of these limitations, our findings coupled with the other earlier reports cited, clearly indicate that clinical outcomes for the management of S-ECC are unacceptable. Well designed and executed randomized clinical trials (RCTs) are indicated to assess the efficacy of FV alone and in combination with PI in improving clinical outcomes for S-ECC. The design of these RCTs should include larger cohorts and at least one year of follow-up for appropriate prospective capture of relapse or caries-free survival. The findings of such RCTs would likely also be of value in guiding primary prevention protocols for children at high risk for ECC.

Conclusions

1. None of the covariates (baseline MS level; surfaces available for relapse; age; gender; race; ethnicity) were statistically related to relapse.
2. The relapse rate (38%) observed in this report is consistent with earlier reports.
3. Novel approaches are needed to improve long term clinical outcomes for the treatment of S-ECC.

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