EFFECTS OF XYLITOL AND STIMULATED SALIVARY FLOW ON CALCULUS ACCUMULATION IN GASTROSTOMY TUBE-FED PATIENTS: A PILOT STUDY

A Thesis

by

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ABSTRACT

This pilot study was initiated to investigate whether xylitol and/or stimulated salivary flow would have an effect on the accumulation of calculus in gastrostomy tube-fed patients. Following stringent inclusion criteria and 33% patient drop-out, four patients completed at least one of the two interventions after an initial baseline period. Intervention #1 consisted of using Dr. John's® sugar-free lollipops (Product #NMF100) three times a day for five minutes each over a period of eight weeks. Intervention #2 utilized Dr. John's® xylitol-containing sugar-free lollipops (Product #NMXF100, 1 gram of xylitol per lollipop) three times a day for five minutes each over a period of eight weeks. Intra-oral photographs of the buccal surfaces of the maxillary first permanent molars were used to determine the amount of calculus formed pre- and post-interventions. Calculus levels were determined using the Calculus Score Method and by percentage of surface area covered by calculus using Elements® software. No significant differences were found comparing either post-intervention calculus levels to pre-intervention baseline calculus levels. Also no significance was found between Intervention #1 and #2. The extremely low patient enrollment and high percentage of patient drop-out render this pilot study inadequate in drawing significant conclusions.

ACKNOWLEDGEMENTS

I have been so fortunate to work with a team who exemplifies great attitude and a passion for treating children with special health care needs. I want to thank the Baylor Oral Health Foundation and my committee members Drs. Carolyn Kerins, Susan McGuire, Kavita Viswanathan, and Larry Bellinger for their support and patience throughout the entire process. I especially want to thank the dental team at Texas Scottish Rite Hospital for Children (TSRHC), led by clinic manager Maria Anderson, for their unwavering willingness to help and keep spirits high when patient compliance could have easily bogged us down. A very special thank you to my Committee chair, Dr. Carolyn Kerins, for all of her hard work in getting the study off the ground. A strenuous IRB proposal and approval process took months to finalize and I appreciate the mentorship and guidance she provided from beginning to end. Also, many thanks to Dr. Richard Adams and Melinda Valentine at TSRHC for their help in identification of possible study participants.

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TABLE OF CONTENTS

Page

ABSTRACT ii

ACKNOWLEDGMENTS iii

TABLE OF CONTENTS iv

LIST OF FIGURES v

LIST OF TABLES vi

CHAPTER I INTRODUCTION 1

CHAPTER II SUMMARY AND CONCLUSIONS: EFFECTS OF XYLITOL AND STIMULATED SALIVARY FLOW ON CALCULUS ACCUMULATION IN GASTROSTOMY TUBE-FED PATIENTS, A PILOT STUDY 7

Materials and Methods 7
Results 17
Discussion 24
Conclusions 27

REFERENCES 28

LIST OF FIGURES

FIGURE		Page
1	Flow Sheet for Visits 1-5: Sequence and Description of Visits	12
2	Example of Standardized Intra-Oral Photographs of a Study Patient using Elements® Software for Surface Area Calculation	16
3	Calculus Accumulation on Maxillary Right and Left First Permanent Molars in Patient #1	18
4	Calculus Accumulation on Maxillary Right and Left First Permanent Molars in Patient #2	19
5	Calculus Accumulation on Maxillary Right and Left First Permanent Molars in Patient #3	20
6	Calculus Accumulation on Maxillary Right and Left First Permanent Molars in Patient #4	21

LIST OF TABLES

TABLE Page

1 Calculus Scores Using the Calculus Score Method 22

2 Percentage Surface Area of Calculus Coverage on the Buccal Surface of the Maxillary Left and Right First Permanent Molars Using Elements® Software 23

CHAPTER I

INTRODUCTION

Pediatric Dentistry is an age-defined specialty that provides both primary and comprehensive preventive and therapeutic oral health care for infants and children through adolescence, including those with special health care needs.[1] The pediatric dentist must be comfortable and competent in treating patients who are challenged by physical or mental complexities. Over the years, many of these complexities have shown to be associated with specific oral diseases and conditions. One such association is the increase of calculus accumulation and periodontal disease in patients fed by gastrostomy tube (GT).[2,3,4]

Gastrostomy is a surgical procedure that places a tube through the abdomen wall into the stomach in order to administer feedings for individuals who:

1. have difficulty swallowing;
2. are categorized as failure to thrive;
3. have inadequate caloric intake;
4. have feeding disorders;
5. are severely disabled with poor nutritional status; or
6. have upper gastrointestinal tract obstruction.[5]

While a variety of feeding therapies exist to help transition the child from GT-fed to eating by mouth[6], the reality is that many of these children suffer such severe

neurological impairments that this transition is simply not realistic. Children suffering from cerebral palsy (CP) and spina bifida are commonly using a GT for years and may never complete the transition to exclusive mouth feeding. It is reported that nearly 90% of children with CP suffer from gastrointestinal disorders, including dysphagia and aphagia.[7,8,9]

In addition to these difficulties in swallowing, patients who are GT-fed often report issues with sialorrhea (drooling).[10,11,12,13] This sialorrhea is not associated with excess saliva production, rather the child is unable to swallow normal outputs of saliva because of their dysphagia. In fact, patients who are primarily GT-fed lack sufficient salivary flow since they do not experience the positive effects of food stimulation orally. Children with CP have been shown to have a 50% reduction in salivary flow rate compared to a control group.[14] In order to alleviate some of the physical and psychosocial issues with sialorrhea, some GT-fed children are treated with anticholinergics, botulinum toxin A injections, or surgically tying off of the salivary ducts in order to decrease the quantity of saliva.

Poor oral hygiene is frequently reported in children fed by GT and can be explained by the various symptoms of their medical complexities or the adverse effects of treating them.[3,15,16] These include oral defensiveness, lack of sufficient salivary flow due to the loss of food stimulation orally, loss of adequate quantities of saliva due to pharmaceutical or surgical treatment of sialorrhea, difficulty in brushing due to dyskinetic movements, presence of pathological oral reflexes (biting and vomiting), and inability to

use a toothbrush. Saliva plays an important role in maintaining oral health with its antimicrobial activity, lubrication, and buffering properties.[17] A decrease in salivary flow rate and prolonged exposure to a stagnant pooling of saliva that cannot be swallowed is associated with increased calculus deposits and a shift in the oral bacterial population toward more pathogenic species.[2,18,19]

Calculus is a calcified or calcifying mass that forms and attaches on the surface of natural teeth and dental prostheses.[20] Dental calculus is composed primarily of mineral as well as inorganic and organic components and ordinarily consists of mineralized bacterial plaque.[21] Dental calculus provides an opportune environment for additional bacteria to live and multiple and plays a major role in initiating and maintaining periodontal disease.[20,21]

In healthy individuals, calculus formation is correlated with plaque accumulation. In GT-fed individuals who are not eating by mouth, there is comparatively little plaque accumulation. Dicks and Banning (1991) demonstrated that even with stringent oral hygiene parameters, calculus accumulation could be decreased, but was still accumulated in higher quantities in GT-fed patients. Although the patients fed by GT had less plaque accumulation, they still produced more calculus than their counterparts not fed by tube.[22] Anecdotally, many dental personnel report they have noticed that patients who are concomitantly undergoing feeding therapy or consume some food by mouth (even pureed food) seem to produce less calculus when compared to those fed exclusively by GT.

The health concerns associated with increased calculus accumulation for these patients do not end with the oral cavity. A recent study demonstrated this calculus is significantly related to aspiration pneumonia.[19] The risk of developing aspiration pneumonia is of great concern to the clinicians treating these patients.[6] Pneumonia is a potentially life-threatening complication and a real threat for these children with increased levels of pathogenic bacteria in the form of calculus and stagnant pooling of saliva in their mouths. Combine that with the fact that 89% of GT-fed patients experience aspiration events and it seems all too easy for this risk to become a reality.[23] During dental cleanings, extreme caution must be taken when removing debris to prevent bacteria laden particles of calculus from being aspirated by the patient. Most children fed by GT exhibit oral defensiveness. The level of anxiety and resistance expressed by these patients often necessitates the use of restraints and mouth props, increasing the risk for aspiration.

With the identification of increased calculus deposits and risk to periodontal disease and aspiration pneumonia, the medical and dental research communities have investigated potential pharmacologic and non-pharmacologic approaches to treating GT-fed patients. Many pediatric dentists treating these medically complex children have found the only way to minimize the health risks at this time may be to see them more frequently for dental cleanings. Whereas a healthy child is commonly seen every six months for a professional cleaning, the children fed by GT are being placed on two- or three-month professional cleaning intervals. This presents additional time commitment

and financial hardship issues for the families of these children and uses a larger amount of the funds provided by the federal government who support some of these children through special programs.

Xylitol, a dietary sugar substitute, has become an emerging area of study in the dental field ever since it was shown to inhibit the development of dental caries.[24] Recent studies indicate that xylitol may also have the ability to disrupt the adhesive properties that oral bacteria utilize to form biofilms on the dentition that manifest as plaque and calculus. The microbes produce water-insoluble glucans (WIGs) that allow them to stick to tooth surfaces, as well as each other, in order to create a growing biofilm that mineralizes and becomes dental calculus. Xylitol has been shown to decrease the synthesis of WIGs in *S. mutans* and some of the other bacteria implicated in calculus formation.[25] Bacterial adhesion to a glass surface simulating the smooth surfaces of teeth has shown to be inhibited by realistic concentrations of xylitol that can be found in the saliva when xylitol-containing products have been consumed.[26] More recently, the sugar substitute's role in decreasing calculus accumulation has been supported in veterinary literature.[27] Clarke (2006) found a reduction in plaque and calculus accumulation in cats by the simple addition of xylitol to their drinking water.

While the mechanisms of action are not well understood, the advantages of xylitol as an additive in foods and dental dentifrices are well documented.[28] It is suspected that xylitol may alter the quality and/or quantity of saliva and oral microflora; these components have shown to have a direct impact on calculus formation and

organization.[17] Specifically, statherin and cystatin are salivary proteins that have shown to inhibit calculus formation and bacterial growth, respectively.[29] It has not been studied whether xylitol is able to up-regulate the actions of these proteins.

While the dental community has been aware of the increased calculus deposits in GT-fed patients for many years, to date there have not been any studies that examine the potential role that xylitol could have in the reduction of calculus in human subjects. Therefore, the aim of this study is to investigate the effects that increased salivary stimulation and xylitol have on calculus deposition in children who are primarily GT-fed. Studying these relationships may lead to a better understanding of the mechanisms involved in calculus accumulation in this distinct patient population.

CHAPTER II

SUMMARY AND CONCLUSIONS: EFFECTS OF XYLITOL AND STIMULATED SALIVARY FLOW ON CALCULUS ACCUMULATION IN GASTROSTOMY TUBE-FED PATIENTS, A PILOT STUDY

Texas Scottish Rite Hospital for Children (TSRHC) in Dallas, Texas treats thousands of outpatient children with special needs and medical complexities in the dental department each year. Many of these children suffer eating disorders for which a GT was placed to administer feedings. The relationship between increased calculus levels, periodontal disease and aspiration pneumonia in patients primarily fed by GT has been well documented in the children treated at TSRHC. A previous pilot study showed an association with decreased calculus deposits in children who experienced increased salivation following mastication exercises and the application of a flavoring agent to the buccal mucosa.[30] In order to study the effects of xylitol on the accumulation of calculus in GT-fed pediatric patients, a prospective, randomized crossover clinical trial was conducted in the dental clinic at TSRHC.

Materials and Methods

Approval for access to patient information was obtained from the Institutional Review Board at the University of Texas Southwestern Medical Center and site specific

approval from TSRHC. Patient recruitment began with a generated search in hospital records for any GT-fed patients between the ages of 6 and 17 who had a documented visit to the dental clinic within the last two years. A total of ninety-two patients were identified to fit the search parameters and were cleared by their feeding therapist and pediatrician as healthy enough to qualify for the proposed experimental protocols without significant risk to their health. These patient files were then reviewed to identify any of the following exclusion criteria:

1. Consume more than one meal per day by mouth
2. Have had an episode of aspiration pneumonia in the last two years
3. Take medications or have had surgery to control salivary flow
4. Inability to tolerate oral stimulation
5. Lack historical compliance with regularly scheduled dental recall visits
6. Lack historical findings of heavy calculus production throughout the mouth, especially the buccal surfaces of maxillary molars

Thirty-four patients were cleared of these criteria, and the principal investigator contacted the parents/legal guardians to ascertain their level of interest in participation. Twenty-two patients were unable to be reached as the contact information for the parent/legal guardian was either disconnected or they did not respond to repeated attempts to schedule a screening appointment. Four parents expressed understanding and interest in the study, however, they could not commit to the study protocol due to travel hardships. During the screening process, two patients were identified to exhibit severe gingival hyperplasia due to prolonged use of phenytoin that did not allow for sufficient inspection of the buccal

surfaces of the maxillary first permanent molars. The remaining six patients did not meet any of the exclusion criteria, their parents and caregivers understood the importance of oral health, and they agreed to enroll in the study by signing the necessary consent forms. Procedures and possible discomforts, risks and benefits were explained fully to the parents/guardians; a licensed translator at TSRHC was provided for those parents who did not speak English. Due to the unexpectedly low number of study participants, this investigation continued as a pilot study.

At the initial screening, all six patients had not received a dental prophylaxis in the last three months. It was decided for each of these patients to utilize the screening appointment as the first of a total of five study visits. Dicks and Banning (1991) determined that 99% of the calculus in GT-fed patients formed within the first 60 days following prophylaxis. The study protocol used this time interval as the length of time to evaluate a patient's baseline calculus as well as the effects of the two study interventions. A longer wash-out period of 84 days was used in between study interventions to lower the chances of residual effects from the first intervention on the second intervention. Total length of study participation for each subject was thirty-six weeks.

Sequence of Visits

At the first visit, patients received a dental prophylaxis including hand-scaling, rubber cup polish, flossing, and fluoride treatment; scaling of the maxillary permanent first molars was completed by the principal investigator and all remaining treatment was provided by the same registered dental hygienist throughout the study. Patients were

scheduled to return in eight weeks, and parents were asked to continue with the patient's routine medication, dietary, and oral hygiene habits throughout the study. A diary calendar was provided to each study family to keep track of visits, intervention schedules, and to note any questions or concerns. The diary was reviewed at each subsequent visit.

At the second visit, 0.5mL samples of whole saliva were collected from under the tongue using a sterile pipette or by spitting directly into an ice-cooled vessel and transported to Baylor College of Dentistry in an ice chest to store in the appropriately cooled 28° F freezer of Dr. Ibtisam Al-Hashimi's Salivary Dysfunction Laboratory. Samples will remain stored for future investigation. Prior to completing the dental prophylaxis, standardized intra-oral photographs (obtained by a Canon PowerShot G16 digital camera, Tokyo, Japan) of the buccal surfaces of the right and left maxillary first permanent molars were taken by the principal investigator and served as the pre-intervention baseline calculus formation photographs for the study. The dental cleaning procedures were carried out in the same manner as the first visit. Using computer block randomization, patients were then randomly assigned to one of two experimental protocols (Intervention #1 or #2).

Intervention #1

Study patients utilize Dr. John's® sugar-free lollipops (Product #NMF100, Grand Rapids, MI), three times a day for five minutes each, switching from the left to right sides using the aid of a one-minute sand timer over a period of eight weeks.

Intervention #2

Study patients utilize Dr. John's® xylitol-containing sugar-free lollipops (Product #NMXF100, 1 gram of xylitol per lollipop) three times a day for five minutes each, switching from the left to right sides using the aid of a one-minute sand timer over a period of eight weeks.

Patients were then scheduled to return in eight weeks for the third visit.

At the third visit, salivary sampling was completed and stored as previously mentioned. Intra-oral photographs were taken in the same manner as the previous visit to evaluate the effects of the first assigned treatment intervention. The same dental prophylaxis was completed and patients were scheduled to return in twelve weeks to allow for a sufficient "wash-out" period with no assigned interventions.

Following the "wash-out" period, patients returned for their fourth visit. Salivary sampling, intra-oral photographs and a dental prophylaxis were all completed in the same manner as previous visits. Patients were then assigned to the second treatment intervention, whichever they did not get assigned to previously. Patients were scheduled to return in eight weeks.

At the fifth and final visit, the last salivary samples, intra-oral photographs and dental prophylaxis were completed for the study. The patients and their parents/guardians were thanked for their commitment to the study and were encouraged to maintain their three-month intervals for dental cleanings at TSRHC. See Figure 1 for a review of study visits.

Figure 1. Flow Sheet for Visits 1-5: Sequence and Description of Visits

Visit 1: Baseline Cleansed Surfaces

- Dental prophylaxis including hand-scaling, rubber cup polish, flossing, fluoride
- Instructed to proceed with routine medications, oral hygiene, and dietary habits
- Diary calendar provided to keep track of visits, intervention schedules, and to note any questions or concerns

⬇8 weeks

Visit 2: Pre-Intervention Baseline Calculus Formation

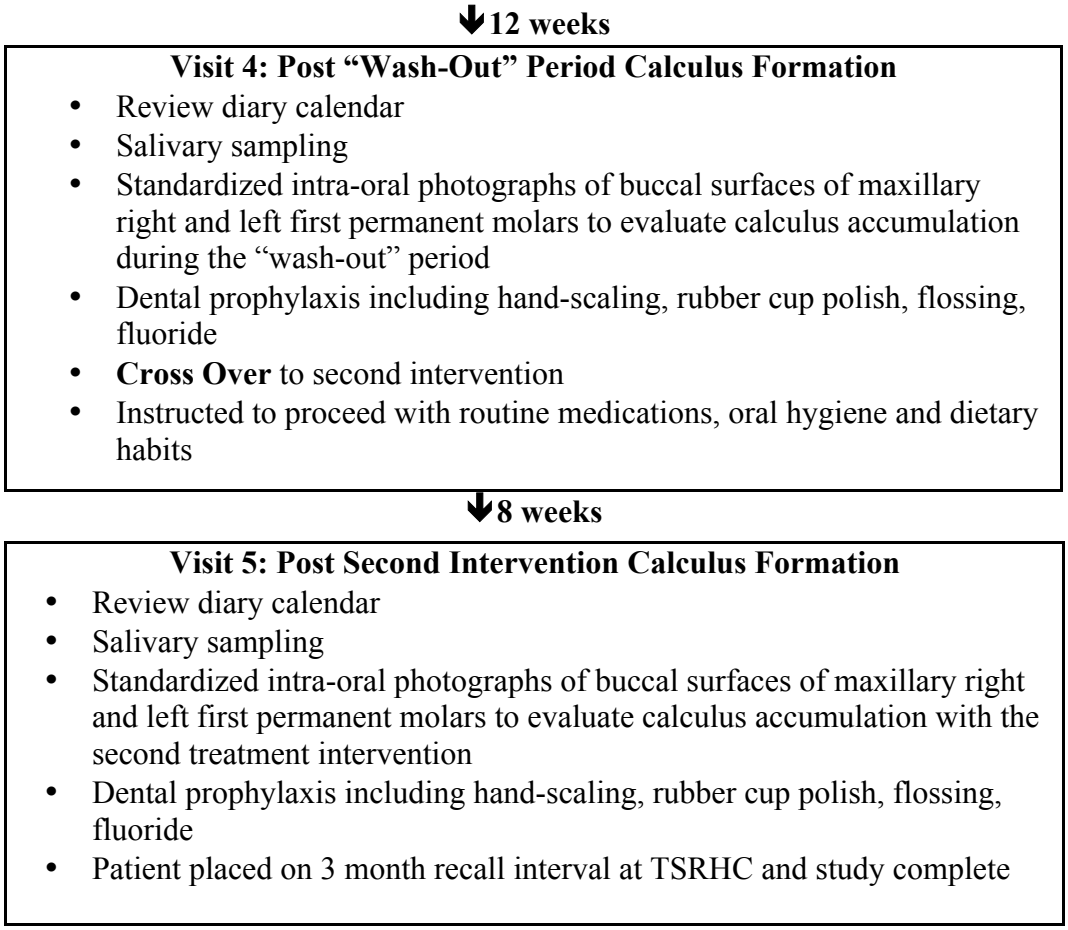
- Review diary calendar
- Salivary sampling
- Standardized intra-oral photographs of buccal surfaces of maxillary right and left first permanent molars to evaluate calculus accumulation with no treatment intervention
- Dental prophylaxis including hand-scaling, rubber cup polish, flossing, fluoride
- Assignment of First Intervention (determined by computer block randomization)
- Instructed to proceed with routine medications, oral hygiene and dietary habits

⬇8 weeks

Visit 3: Post First Intervention Calculus Formation

- Review diary calendar
- Salivary sampling
- Standardized intra-oral photographs of buccal surfaces of maxillary right and left first permanent molars to evaluate calculus accumulation with the first treatment intervention
- Dental prophylaxis including hand-scaling, rubber cup polish, flossing, fluoride
- Patient enters “wash-out” period prior to starting second treatment intervention
- Instructed to proceed with routine medications, oral hygiene and dietary habits

Figure 1. continued.



Descriptive Analysis: Calculus Score Method

Pre-intervention baseline calculus formation, post-Intervention #1, and post-Intervention #2 photographs were viewed by three standardized, calibrated examiners blinded to the interventions. Raters were three registered dental hygienists who received instructions at the same time and completed the assessment on their own score sheet. The Calculus Score Method, adapted from the Simplified Oral Hygiene Index (Greene and Vermillion, 1964) was used for scoring.[31] The rating system is as follows:

0 = No calculus present

1 = Supragingival calculus covering not more than 1/3 of the exposed tooth surface

2 = Supragingival calculus covering more than 1/3 but not more than 2/3 of the exposed tooth surface or the presence of individual flecks of subgingival calculus around the cervical portion of the tooth

3 = Supragingival calculus covering more than 2/3 of the exposed tooth surface or a continuous heavy band of subgingival calculus around the cervical portion of tooth or both

Scores for the post-intervention photographs for both interventions were compared with the scores for the pre-intervention baseline calculus formation photographs and each other for each patient to determine whether either intervention was effective in decreasing the calculus deposition using Wilcoxan-Signed Rank test.

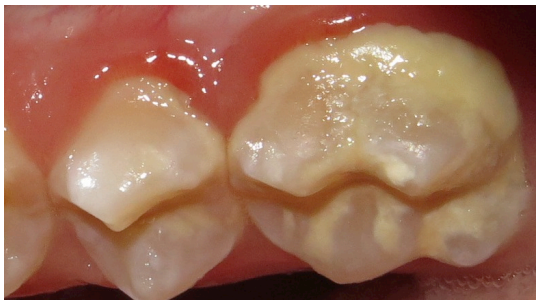
Quantitative Analysis: Percent Surface Area of Calculus Accumulation

A software program, Elements®, was used to quantify the amount of calculus accumulation in the following manner: Photographs were viewed on a computer screen and the buccal surface of the maxillary right and left first permanent molar was traced by the principal investigator. Following the initial tracing of the total buccal surface area, tracings of all areas of calculus deposition were completed on the same photograph (Figure 2). The computer calculated and stored surface area measurements to be analyzed at the completion of the study. The surface area occupied by calculus was calculated as a percentage of the total surface area traced for the buccal surface. The principal investigator performed this same procedure for all pre-intervention baseline calculus accumulation, post-Intervention #1 calculus accumulation, and post-Intervention #2 calculus accumulation photographs. The surface area percentages of both interventions were compared with the percentages of the pre-intervention baseline calculus formation photographs and each other for each patient to determine whether either intervention was effective in decreasing the calculus deposition. Data was analyzed by paired t-test.

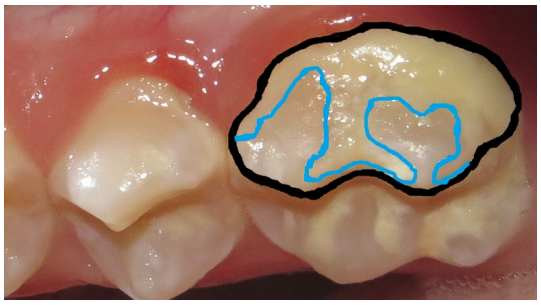
Figure 2. Example of Standardized Intra-Oral Photographs of a Study Patient using Elements® Software for Surface Area Calculation.

A. Standardized photograph of calculus accumulation on the maxillary left first permanent molar
B. Elements® tracing of the total buccal surface area and the portion of that surface area occupied by calculus deposits

A



B



Results

At the onset of the study, six patients were enrolled and completed pre-intervention baseline calculus measurements after the first eight-week interval. When patients were placed on a lollipop intervention, two were unable to continue with the study due to parental concern with swallowing difficulties in the first week of intervention. One patient suffered unrelated serious medical issues and had to be released from the study following their first intervention (Intervention #1); one was unable to adhere to the study schedule and was released following the "wash-out" period having only completed Intervention #2 and one patient completed both interventions but failed to return for evaluation after the second intervention (Intervention #2). Therefore, only one patient made it through the entire study completing evaluations of both Intervention #1 and #2.

Descriptive Analysis: Calculus Score Method

Three calibrated, blinded examiners viewed on the same computer screen randomly ordered intra-oral color photographs of each participant's pre-intervention baseline calculus accumulation and any post-intervention calculus accumulation photographs that were completed (Figures 3-6). They assigned scores of 0-3 (Calculus Score Method) depending on the level of calculus on the buccal surface of the maxillary right and left first permanent molars. Each examiner rated each picture individually.

Figure 3. Calculus Accumulation on Maxillary Right and Left Permanent Molars in Patient #1.

A, B. Pre-Intervention (Baseline)
C, D. Post-Intervention #1 (Placebo lollipop)
E, F. Post-Intervention #2 (Xylitol lollipop)

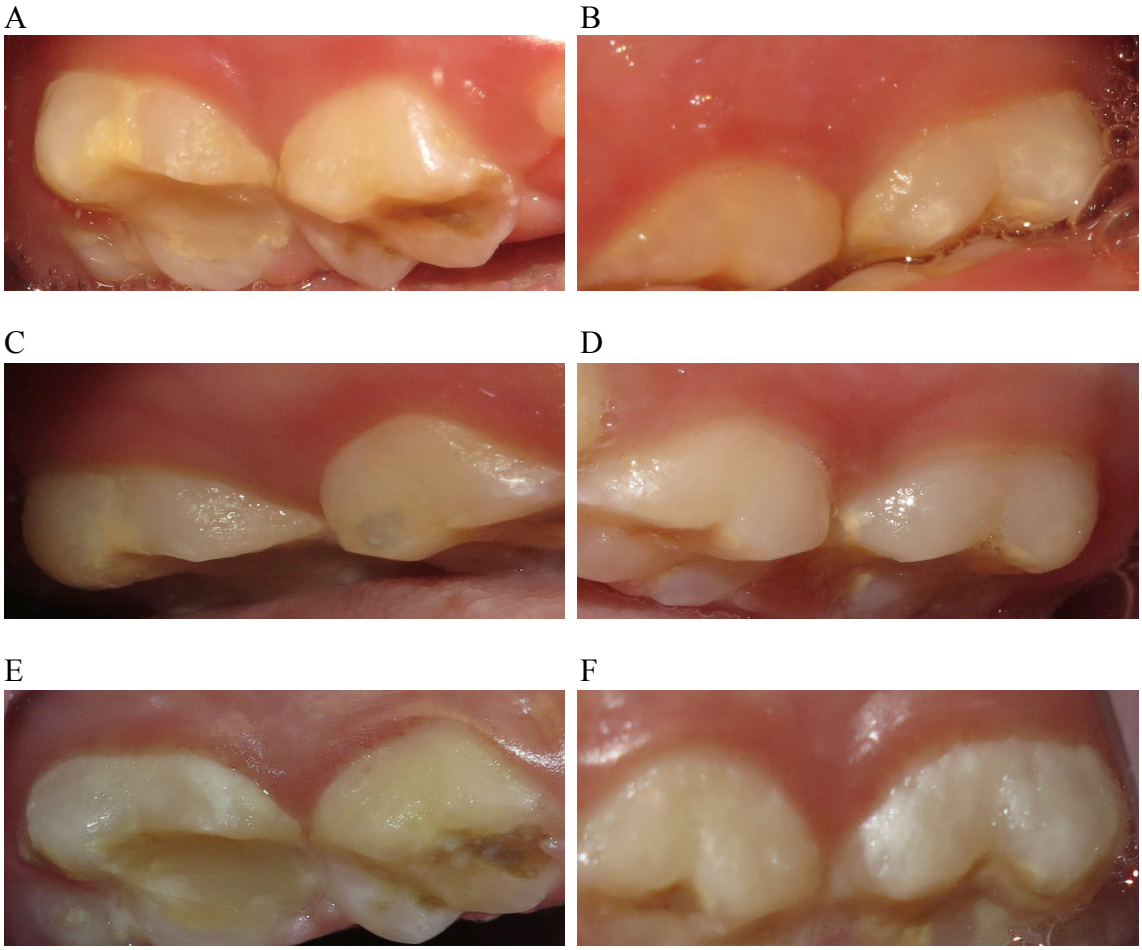


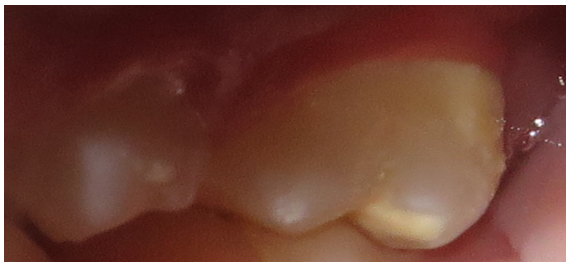
Figure 4. Calculus Accumulation on Maxillary Right and Left Permanent Molars in Patient #2.

A, B. Pre-Intervention (Baseline)

C, D. Post-Intervention #1 (Placebo lollipop)

A

B



C

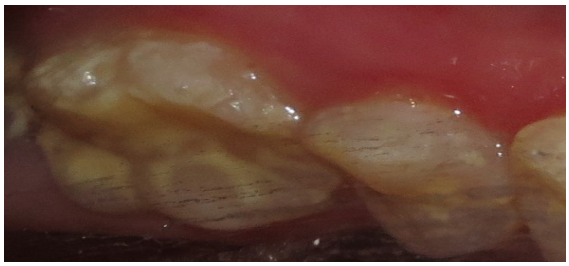
D

Figure 5. Calculus Accumulation on Maxillary Right and Left Permanent Molars in Patient #3.

A, B. Pre-Intervention (Baseline)

C, D. Post-Intervention #2 (Xylitol lollipop)

A



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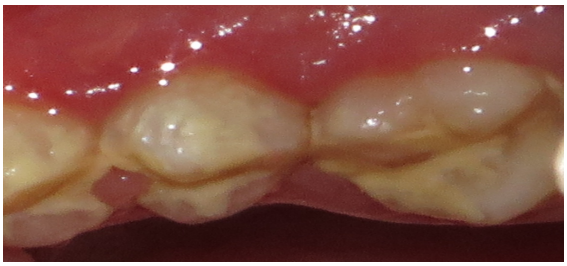

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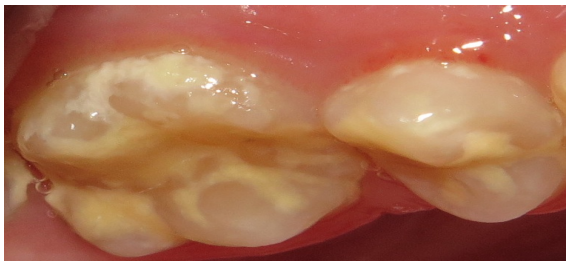

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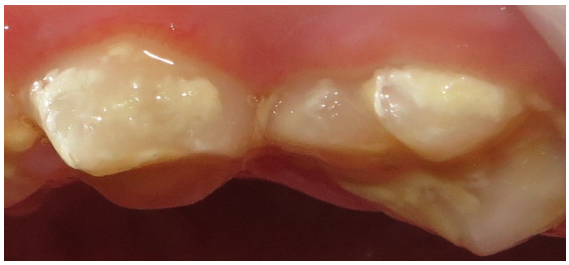
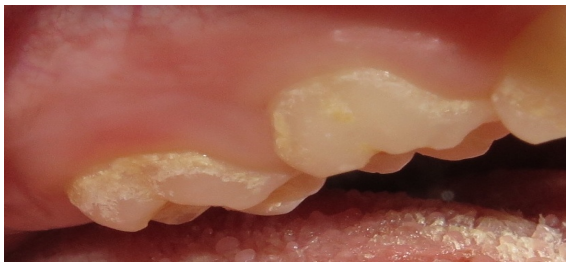


Figure 6. Calculus Accumulation on Maxillary Right and Left Permanent Molars in Patient #4.

A, B. Pre-Intervention (Baseline)

C, D. Post-Intervention #1 (Placebo lollipop)

A



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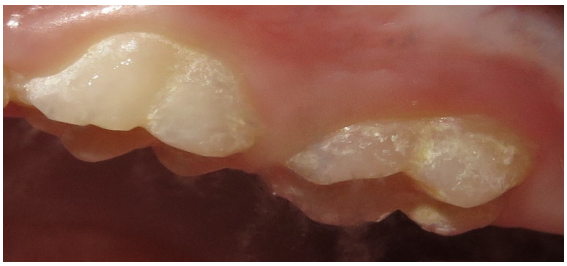
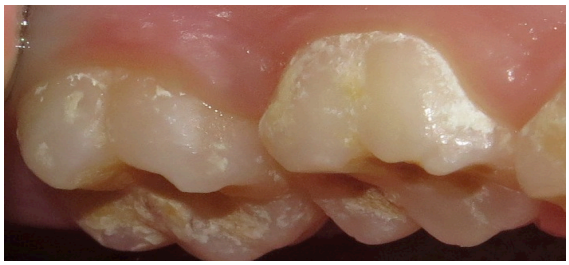


C



D

When all photographs were rated, the principal investigator collected the sheets and reviewed the ratings. A rating was acceptable when at least two examiners were in agreement. All scores met this acceptability requirement and no further review was needed. The scores are summarized in Table 1.

Table 1. Calculus Scores Using the Calculus Score Method.

Patient	Pre-Intervention Baseline Calculus Score		Post-Intervention #1 Calculus Score (Placebo lollipop)		Post-Intervention #2 Calculus Score (Xylitol lollipop)	
	Left	Right	Left	Right	Left	Right
1	2	1	1	0	2	3
2	0*	2	0*	3		
3	2	1			3	2
4	3	2	1	2		
Average	2.33±0.58	1.50±0.58	1.00±0.00	1.67±1.53	2.50±0.71	2.50±0.71

*Score not used in statistical analysis

Due to a lack of calculus on the maxillary left first permanent molar of patient #2 at baseline, these scores were not used in statistical analysis. When the scores were analyzed, no strong trends or significant differences could be found for baseline compared to Intervention #1 ($Z=-1.134$, $p=0.257$) or baseline compared to Intervention #2 ($Z=-1.633$, $p=0.102$). Intervention #1 compared to Intervention #2 also showed no significant difference ($Z=-1.34$, $p=0.180$).

Quantitative Analysis: Percent Surface Area of Calculus Accumulation

The principal investigator traced digital color photographs of the buccal surface of the maxillary left and right first permanent molars using the Elements® software, and the percentages of surface area covered by calculus at baseline and following all

interventions completed were calculated. The values for the percentage surface area covered by calculus are summarized in Table 2.

Table 2. Percentage Surface Area of Calculus Coverage on the Buccal Surface of the Maxillary Left and Right First Permanent Molars Using Elements® Software.

Patient	Pre-Intervention Baseline Calculus		Post-Intervention #1 Calculus (Placebo lollipop)		Post-Intervention #2 Calculus (Xylitol lollipop)	
	Left	Right	Left	Right	Left	Right
1	39.04	17.77	5.49	2.96	18.76	18.93
2	0.00*	17.61	0.00*	53.49		
3	38.06	2.66			33.91	27.34
4	44.47	32.64	7.64	7.01		
Average	40.52±3.45	17.67±12.24	6.57±1.52	21.15±28.07	26.34±10.71	23.14±5.95

*Measurement not used in statistical analysis

Due to a lack of calculus on the maxillary left first permanent molar of patient #2 at baseline, these scores were not used in statistical analysis. No strong trends or significant differences could be found for baseline compared to Intervention #1 ($t=1.130$, $p=0.32$) or baseline compared to Intervention #2 ($t=-0.38$, $p=0.97$). Intervention #1 compared to Intervention #2 also showed no significant difference ($t=-10.616$, $p=0.06$).

Discussion

This pilot study was initiated to investigate whether xylitol and/or stimulated salivary flow would have an effect on the accumulation of calculus in gastrostomy tube-fed patients. The results of this prospective, randomized crossover clinical trial were analyzed; though lack significant meaning since only one patient was able to complete both interventions. While an additional three patients were able to complete one of the two study interventions, the lack of enrollment and large standard deviations observed prevent the identification of any possible outliers or reaching significant differences.

The only trend that appears somewhat promising is the reduction in calculus accumulation observed following Intervention #1 compared to baseline for patients #1 and #4. However, the results observed in patient #2 prevent this conclusion and the lack of patient number render it impossible to consider patient #2 an outlier. Surprising to the study team, the trend in calculus accumulation appears to increase following Intervention #2 compared to baseline. Again, lack of patient number prevents any significance or strength to this trend.

While calculus accumulation measurements failed to provide significant results, perhaps the salivary samples collected will show a change in the quality of the saliva in these GT-fed patients. With the addition of more study patients, it would be interesting to note whether concentrations of statherin and/or cystatin, salivary proteins involved in calculus reduction[29], change significantly with either intervention. Additionally, if a significant difference were found in the continuation of this study, it would be important

to investigate any changes in the bacterial make-up of the calculus exhibited in these patients. It has been reported that xylitol has the ability to decrease the synthesis of WIGs, used for tooth adherence, in many of the common bacterial species found in human calculus.[25]

The overlying issue with the current pilot study is the difficulty in obtaining an adequate patient enrollment and completion of the crossover study. It seems that a number of changes would be necessary to secure enough study patients. Investigators have considered loosening the exclusion criteria but are limited by minimizing medical risks and the addition of more study variables. The most appropriate change may be to include those GT-fed patients who have a more controlled salivary flow with the help of medications or salivary duct surgery. Twenty-five possible study participants were excluded due to this history. Investigators also encourage the continuation of this study to be multi-centered. TSRHC is limited in numbers of GT-fed children and exhibits a high rate of non-compliance and patient cancellations/"no-shows" for scheduled appointments. The study team predicts an association between these high rates of non-compliance with TSRHC offering free services, but this has not been proven. The team believes adding Children's Medical Center in Dallas, TX as an additional study site may allow for adequate patient enrollment to be reached.

The study team acknowledges there may be some controversy in the results of the study due to inadequacies in the study protocol and method of calculus measurement. In terms of using a lollipop intervention as a vehicle for xylitol delivery, we are aware that patients were unable to consume the entire lollipop in five minutes. This makes it

difficult to quantify how much of the 1 gram of xylitol was consumed. Also, the heightened behavioral issues with the medically compromised and special needs patients used in the study made obtaining high quality photographs of the molars very difficult. While using a percentage of surface area seen in the intra-oral photographs minimizes error, it is still logical to believe any buccal surface area not clearly shown in the photographs could create skewed measurements. Using surface area measurements to quantify calculus accumulation does not incorporate the depth or density of the observed calculus. This may produce large variability in results depending on how calculus deposition occurs in each patient. The most accurate measurement of calculus deposition would involve collecting, drying, and weighing samples at each interval. However, this protocol may be found too difficult to accomplish in the desired patient population due to behavioral issues and health risks. At this time, the study team hopes to continue with the current methods of calculus measurement with a greater enrollment number to identify any possible trends before measurement techniques are revised.

Conclusions

Periodontal disease and aspiration pneumonia as a result of increased calculus accumulation is a difficult reality for many GT-fed children. It is important to continue to investigate both pharmacological and non-pharmacological interventions that may decrease the deposition of dental calculus in this unique and medically fragile patient population.

In conclusion:

1. No strong trend or significant difference was identified in calculus accumulation following the use of Dr. John's® sugar-free lollipops (Product #NMF100) three times a day for five minutes each over a period of eight weeks.
2. No strong trend or significant difference was identified in calculus accumulation following the use of Dr. John's® xylitol-containing sugar-free lollipops (Product #NMXF100) three times a day for five minutes each over a period of eight weeks.
3. These results need to be validated in a larger patient population.
4. Pediatric dentists must understand the major health risks to GT-fed children associated with increased calculus deposition.

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