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ORIGINAL ARTICLE

Effects of gustatory stimulants of salivary secretion on salivary pH and flow: a randomized controlled trial

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OBJECTIVES: To compare salivary pH changes and stimulation efficacy of two different gustatory stimulants of salivary secretion (GSSS).

SETTING: Portuguese Dental Faculty Clinic.

DESIGN: Double blind randomized controlled trial.

SUBJECTS: One hundred and twenty volunteers were randomized to two intervention groups. Sample sized was calculated using an alpha error of 0.05 and a beta of 0.20.

MATERIALS AND METHODS: Participants were randomly assigned to receive a new gustatory stimulant of secretory secretion containing a weaker malic acid, fluoride and xylitol or a traditionally citric acid-based one. Saliva collection was obtained by established methods at different times. The salivary pH of the samples was determined with a pH meter and a microelectrode.

MAIN OUTCOME MEASURES: Salivary pH variations and counts of subjects with pH below 5.5 for over 1 min and stimulated salivary flow were the main outcome measures.

RESULTS: Both GSSS significantly stimulated salivary output without significant differences between the two groups. The new gustatory stimulant of salivary secretion presented a risk reduction of 80 ± 10.6% (95% CI) when compared with the traditional one.

CONCLUSIONS: Gustatory stimulants of salivary secretion with fluoride, xylitol and lower acid content maintain similar salivary stimulation capacity while reducing significantly the dental erosion predictive potential.

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Keywords: gustatory stimulants; saliva; pH; dental erosion; randomized controlled trial

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Introduction

Dental erosion is commonly defined as the chemical wear of the dental hard tissues without the involvement of bacteria (Eccles and Jenkins, 1974). Its aetiology is multifactorial, and the various disease causes are grouped according to acid origin in intrinsic and extrinsic (Gandara and Truelove, 1999). Intrinsic causes include oral cavity exposure to gastric acids due to abnormalities in the gastrointestinal tract (Ismail-Beigi *et al*, 1970; Eccles, 1978; Pope, 1982; Myllarniemi and Saario, 1985; Pace *et al*, 2008) or recurrent vomiting as a result of psychological disorders (Hellstrom, 1977; Knewitz and Drisko, 1988). Extrinsic factors include the unusual or abusive consumption of demineralizing acidic foods and beverages (Eccles and Jenkins, 1974; Smith and Knight, 1984; Asher and Read, 1987; Johansson, 2002; Dugmore and Rock, 2004) and some medicines such as aspirin, vitamin C (Eriksson and ngmar-Mansson, 1986; Meurman and Murtomaa, 1986), iron tonics (James and Parfitt, 1953), acidic oral hygiene products or products with calcium chelators, as well as acidic salivary substitutes and salivary flow stimulants as potential erosive products (Zero, 1996). Nowadays, the prevalence of dental erosion is increasing as modern lifestyle and nutrition habits are believed to favour the incidence of the disease (Zero, 1996).

There is a strong evidence linking exposure of endogenous and exogenous acids to dental erosion, although it is clear that the clinical manifestations are also modified by biological and behavioural factors.

The biological factors related to dental erosion may involve properties and characteristics of saliva, acquired dental pellicle, tooth structure and surrounding soft tissues (Zero, 1996; Lussi *et al*, 2004).

In fact, saliva has been considered as the most important biological factor in dental erosion prevention, due to its ability to act as a protective factor, via acid diluting and buffering, as well as playing an important role in pellicle formation and tooth remineralization (Meurman and Frank, 1991a; Moss, 1998). Therefore, patients with diminished salivary flow have an increased

risk of developing dental erosion (Lussi and Jaeggi, 2006). Thus, in situations where salivation is diminished (like postexercise or xerostomia) (Horswill *et al*, 2006) increasing salivary secretion, and consequently its buffer efficacy, have been referred as an important erosion protection factors and remineralization promoters.

Considering this fact, acidic candies or commercially free available lozenges for gustatory stimulation of salivary secretion have been widely used. However and albeit, usually sugar free, these gustatory stimulants of salivary secretion (GSSS) are composed of different acids (e.g. citric, tartaric or phosphoric), some of which have been proved to have an intrinsic erosive potential (Meurman and Frank, 1991b; Featherstone and Lussi, 2006; Gambon *et al*, 2007).

More recently, a new acidic xylitol-fluoride-containing GSSS (Xerodent^{TM}) (Alpharma, Stockholm, Sweden) has been indicated for use after exercise (Holbrook *et al*, 2003), with the claim that its composition is based on a weaker acid (malic acid) by opposition to stronger acids like citric acid which are commonly present in this class of products. Moreover, Xerodent's fluoride ions and xylitol content could lower the erosive and cariogenic potential of this product (Chunmuang *et al*, 2007; Hove *et al*, 2007a,b, 2008). However, independent studies to assess the real erosive potential and efficacy of salivary stimulation of GSSS are to our knowledge inexistent but needed.

The aim of this randomized controlled trial was to study the erosive potential and salivary stimulation efficacy of an acidic xylitol-fluoride-containing GSSS (Xerodent^{TM}) (malic acid 4.7% w/w), and compare it with a traditional citric acid based acidic GSSS (SST) (Sinclair Pharma Plc., Godalming, UK) (malic acid 4.2% and citric acid 2.1% w/w).

Subjects and methods

Study participants

Patients were recruited between May and July 2007 from a population of students of a Portuguese University through advertisement and were eligible if healthy and above 18. Recruitment was supervised by research assistants.

Exclusion criteria were the presence of systemic conditions that may cause oral dryness and the taking of current xerostomic medication; both records were obtained self reportedly from volunteers.

In total, 120 participants gave their written informed consent and saliva samples were collected at the oral biology research group (GIBO) laboratory. The study protocol was approved by the local University Ethical Committee.

Study protocol and intervention

This randomized controlled study, with two parallel groups, was carried out between September 2007 and May 2008.

Visit 1

During visit 1 exclusion criteria were verified for each participant, they were then randomly allocated to one of two groups named A and B, accordingly to a computer-generated randomization software (GraphPad QuickCalcs Web site: http://www.graphpad.com/quickcalcs/ConfInterval1.cfm, accessed July 2005). Both GSSS were transferred by foreign personnel into two identical opaque flasks labelled A and B containing respectively either the GSSS Xerodent which was considered as the new GSSS group (N) or the GSSS SST which was considered as the control group (C). A code for randomization was kept in an opaque envelope and kept in a safe and opened only at the end of the study. Data were analysed by a third party blinded to the allocation results, which were at that point referred to as treatment A or B in the SPSS worksheet (SPSS, Inc., Chicago, IL, USA). However, pills of N and C have different aspects, smell and taste and therefore masking could not, in our opinion, be guaranteed.

Thereafter, participants were instructed to present themselves between 8 and 11 AM at the laboratory the following weeks. The participants were told to refrain from eating, drinking (except water) for 2 h and should wait at least 1 h after brushing prior to the investigation to minimize effects of diurnal variability in salivary composition. (visit 2 and visit 3) (Dogon *et al*, 1971; Moritsuka *et al*, 2006).

Visit 2

Upon arrival at the laboratory participants were instructed to brush their teeth with a given medium, soft-bristled manual toothbrush (Akzenta, Lugano, Switzerland) and a dentifrice (Aquafresh Extreme Clean, GlaxoSmithKline, Brentford, UK), and wait for 1 h. Mechanical stimulated salivary secretion rate and salivary buffering capacity were measured by methods described as follows.

The participants were told to swallow all saliva present in oral cavity, and a paraffin wax pellet (CRT Buffer; Ivoclar-Vivadent, Stockholm, Liechtenstein) was given to the patient for chewing. A chronometer was started and participants were instructed to collect all their paraffin wax-stimulated salivary secretion in a preweighed 50 ml falcon tube for 5 min. After this procedure the saliva-containing the falcon tube was weighed and stimulated salivary flow rate determined in ml min^{-1}.

The saliva buffer capacity was determined by a modified method from Kitasako *et al* (2005). Briefly, after collecting the stimulated whole saliva, 500 μl of each saliva sample was placed onto a eppendorf (Eppendorf, Hamburg, Germany), and a pH-sensitive microelectrode (electrode INLAB 423; Mettler, Toledo, OH, USA) was used to immediately measure the early pH value within 30 s. Ten microlitres of 0.1 N hydrochloric acid was titrated into the test saliva after removing the cover of the eppendorf, the sample was vortexed and allowed to stabilize for a few seconds and the pH was read. Up to a total of 160 μl of HCl was titrated in order to obtain a pH titration curve for each patient, and to determine the saliva buffering capacity. At 50 μl of titrated HCl, salivary buffering capacities were ranked into one of the following three categories; high buffering capacity (above pH 5.5),

medium buffering capacity (pH 5.5 to pH 4.5) and low buffering capacity (below pH 4.5) (Kitasako *et al*, 2005).

Masticatory stimulation of saliva was performed to determine the individual mechanical-stimulated salivary secretion capacity as this was considered an important baseline characteristic, which was afterwards used to evaluate the homogeneity of salivary function capacity between the two groups. Salivary buffering capacity was determined as it can act as a confounding variable and as it has been widely considered as a major salivary factor with influence on dental enamel protection.

Visit 3

Upon arrival at the laboratory participants were again instructed to brush their teeth with a given toothbrush and dentifrice and wait for an hour. Resting salivary secretion, GSSS-stimulated salivary secretion and erosive potential were determined by methods described as follows. The participants were told to swallow all saliva present in the oral cavity. A chronometer was started and participants were instructed to collect all their unstimulated salivary secretion in a preweighed 15 ml falcon tube during 2 min. After this procedure the saliva-containing falcon tube was weighed and unstimulated salivary flow rate determined in ml min^{-1}. To determine the lozenge-stimulated salivary secretion participants were instructed to swallow all saliva present in the oral cavity, a lozenge of C or N was given to the participant dependent of the attributed group. A chronometer was started and participants were instructed to collect all their accumulated saliva in preweighed falcon tubes at predetermined times (0, 1, 2, 3, 5, 8, 10, 15 and 20 min). After the procedure the saliva-containing falcon tubes were weighed, and lozenge-stimulated salivary flow rate determined in ml min^{-1}. The salivary pH of the samples was determined with a pH meter GLP 22 (Crison, Barcelona, Spain), and a microelectrode, three measures per sample were performed and the mean calculated. The accuracy of the pH meter was checked once every 20 measures using standard buffers to ensure that the readings were correct. Erosive potential was determined as the amount of time of exposition (min) to salivary pH below 5.5. To calculate comparative risk reduction and number needed to treat regarding cases and controls, a secondary dichotomous outcome for evaluation of erosive potential was considered, namely a presence or absence of exposition time for over 1 min.

Objectives

The aims of this study were to compare the effects of the two GSSS on salivary pH and flow variation.

The study hypotheses were:

1. There is a significant difference in the salivary pH variation elicited by the two GSSS.
2. There is a significant difference in the salivary secretion stimulation capacity elicited by the two GSSS.

Outcomes

Primary

The GSSS-induced salivary pH variations were expressed as the mean ± 95% confidence interval of the three pH measures obtained from salivary samples at defined time points.

Time of GSSS-induced pH drop below 5.5 was expressed in minutes as the mean ± 95% confidence interval. To better quantify risk differences of GSSS induced pH drop below 5.5 a contingency table compiling the counts of subjects with pH drops below 5.5 for over 1 min was obtained. Additional analyses were performed to calculate association measures like the absolute risk reduction (ARR) and number needed to treat (NNT).

GSSS-stimulated salivary flow was expressed in ml min^{-1} as the mean ± 95% confidence interval of stimulated salivary flow obtained at different time points.

Overall stimulated salivary flow was also calculated and expressed in ml min^{-1} as the mean ± 95% confidence interval of the total volume of stimulated saliva divided by the total time of each experiment which was 20 min.

Secondary

The secondary outcome was salivary stimulation output defined as the difference between GSSS and basal salivary flow, expressed as ml $min^{-1.}$

Sample size

Although no studies employing GSSS were found in the literature, from a study on the effects of (citric acid based) acidic candies on salivary pH (Jensdottir *et al*, 2006) we expected the control event rate of counts of subjects with pH drops below 5.5 for over 1 min to be of at least 90%.

From there, to compare event rates in the two groups using a Fisher exact test, with the capability of detecting a difference of 25% between groups with a power of 80% and significance level of 0.05, sixty patients per group needed to be enrolled.

Statistics

All data analysis was carried out according to a preestablished plan. Data and analyses were computed using a computer statistical package (SPSS v.15, SPSS Inc., Chicago, IL, USA). Discrete data were analysed using Fisher exact test and direct 95% confidence interval analysis.

Means of salivary flow, salivary pH and time of pH drop below 5.5 were analysed with paired or independent Student's *t*-test or ANOVA and *post hoc* (Tamhane's) tests as appropriate. Two-sided significance tests were used throughout.

Results

Participant follow-up and baseline characteristics

A total of 120 persons were selected for participating in the study (Figure 1). They were randomly assigned to

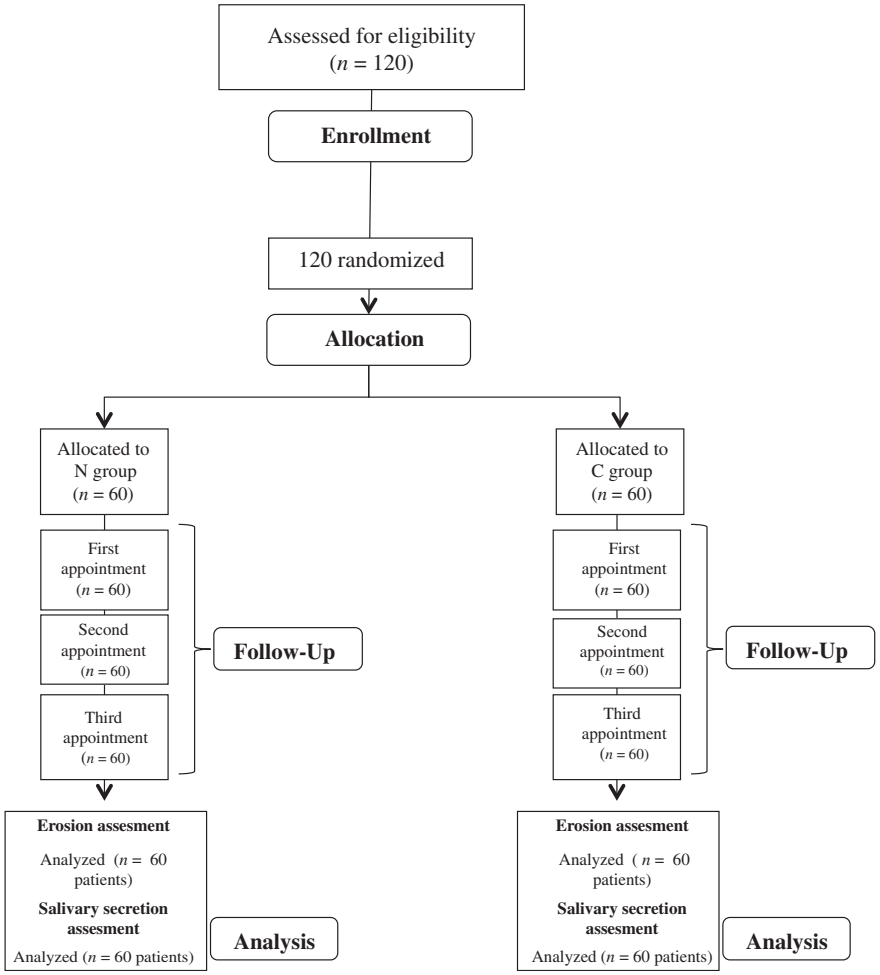

Figure 1 Study design diagram

Table 1 Baseline characteristics, gender distribution and mean ± 95% CI for baseline characteristics

	N	*C*
Gender		
Male	30	23
Female	30	37
Age (years)	21.97 (21.11–22.82)	20.11 (19.26–20.95)
Non-stimulated salivary flow (ml min^{-1})	0.46 (0.38–.053)	0.45 (0.37–0.53)
Mechanical stimulated salivary flow (ml min^{-1})	1.52 (1.27–1.77)	1.30 (1.13–1.48)

one of the two study groups and followed until the end of the study. There were no dropouts. Baseline characteristics of the two groups are depicted in Table 1. Chi-square test and Student's *t*-test were employed for testing differences between categorical and continuous variables respectively. There were no statistically significant differences ($P > 0.05$) between baseline characteristics of the two groups.

Salivary pH variations

Figure 2 shows the results for mean ± 95% confidence intervals of salivary pH changes over time. In both groups the GSSS induced a significant ($P < 0.05$, paired Student's *t*-test) drop in salivary pH levels followed by a slow recovery which for both groups failed to return to basal level after 20 min.

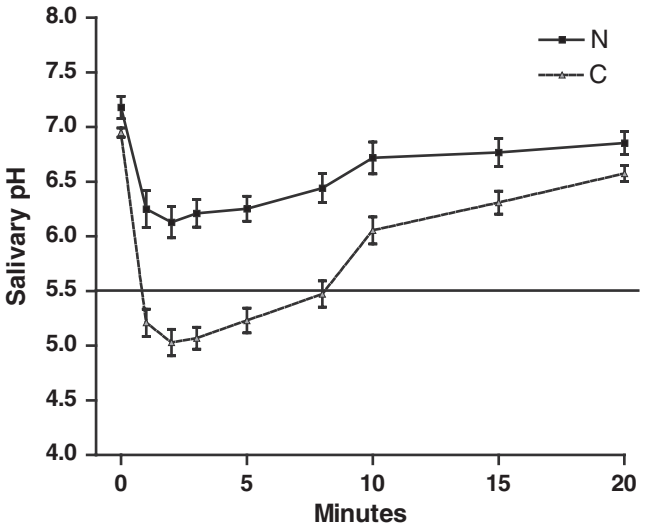

Figure 2 Mean (±95% CI) recordings of salivary pH changes induced by different gustatory stimulants of salivary secretion (GSSS). Traces are typical 60 experiments from 60 subjects. In both groups the GSSS induced a significant ($P < 0.05$, paired Student's *t*-test) drop in salivary pH levels followed by a slow recovery

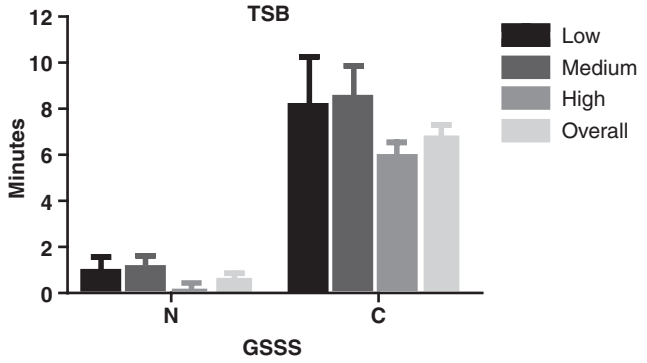

Figure 3 Histograms showing the mean time of salivary pH below 5.5 in minutes (±95% CI) for overall and subgroups based on saliva buffer capacity for each group. When comparing the mean TSB between the two study groups (N and Control) for overall and each salivary buffer capacity subgroup, the N group produced significantly diminished TSB values compared with control ($P < 0.05$ independent T test)

pH drop levels were at all time intervals significantly less ($P < 0.05$, independent Student's *t*-test) accentuated in N group compared with the control. Figure 3 shows the mean time of salivary pH below 5.5 in minutes (TSB) (±95% CI) for overall and subgroups based on saliva buffer capacity for each group. Within each group (N or Control) salivary high buffer capacity produced inferior TSB values when compared with medium or low salivary buffer capacity subgroups, but the differences were not statistically significant (ANOVA plus *post hoc* Tamhane's test $P > 0.05$). When comparing the mean TSB between the two study groups (N and Control) for overall and each salivary buffer capacity subgroup, the N group produced significantly diminished TSB values compared with control ($P < 0.05$ independent T test). Table 2 shows the contingency table for number of participants in each group with TSB values above 1 min. From Table 2 the ARR and NNT were extrapolated with respective 95% confidence intervals to give a quantitative association measure of the reduction in the risk of the GSSS driving the salivary pH for values under 5.5. As comparison of TSB values between salivary buffer capacity subgroups suggested that this secondary variable had little effect by itself on TSB, AAR and NNT are presented only for overall TSB over 1 min values in the two main arms of this study. The N group presented an ARR of 80 ± 10.6 %, 95% CI. For TSB values over 1 min when compared with the control group the NNT was 2 (1.1–1.4 95% CI), meaning that for each two patients who took a N group GSSS an episode of TSB over 1 min was avoided.

Taken together these results suggest that the N GSSS presented a very significant diminished risk for lowering the salivary pH under 5.5 for prolonged times when compared with the control.

Table 2 Frequency distribution for number of participants in each group with salivary pH records below 5.5 for over 1 min. The absolute risk reduction and number needed to treat were extrapolated with respective confidence intervals to give a quantitative association measure of the reduction in erosion potential risk

	pH below 5.5 for over 1 min		
	Present	*Absent*	*Total*
Agonist			
N	9	51	60
C	57	3	60
Total	68	54	120

Salivary secretion

Figure 4 shows the results for mean ± 95% CI of salivary flow changes over time. In both groups the acidic lozenges elicited a significant ($P < 0.05$, paired Student's *t*-test) increase in the salivary flow followed by a progressive decrease reaching basal levels after the 20 min period. The control group elicited a higher salivary output but differences were not significant for any of the time intervals tested ($P > 0.05$ independent T test). Figure 5 shows mean (±95% CI) for basal, GSSS-stimulated and paraffin-stimulated salivary flow for each group. There were no significant ($P > 0.05$, independent Student's *t*-test) differences between the two groups for basal or stimulated salivary flow.

Lozenge-stimulated salivary flow was significantly ($P < 0.05$, independent Student's *t*-test) lower compared with paraffin chewing mechanical-stimulated flow for both groups N and C.

Figure 6 shows the effects of the salivary buffering capacity on the GSSS output for both groups of the study. Within each group (N or Control) salivary high buffer capacity produced superior stimulated salivary output when compared with medium or low salivary buffer capacity subgroups, but differences were statistically significant only for high buffer capacity compared

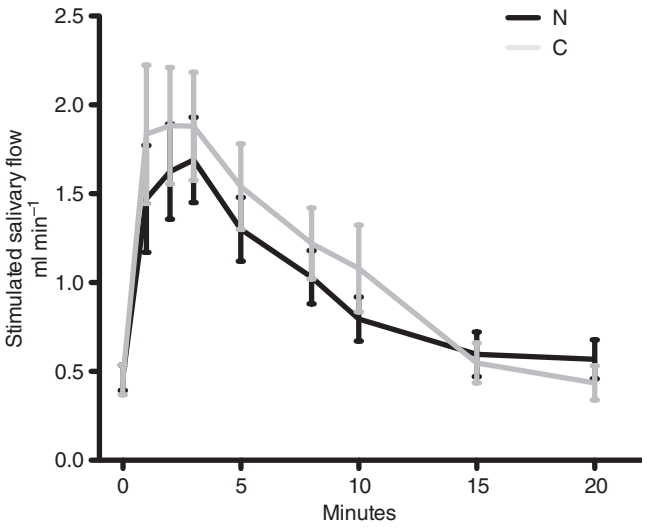

Figure 4 Mean (±95% CI) of salivary flow changes over time during stimulation with gustatory stimulants of salivary secretion. In both groups the acidic lozenges elicited a significant ($P < 0.05$, paired Student's *t*-test) increase in the salivary flow followed by a progressive decrease reaching basal levels after the 20 min period

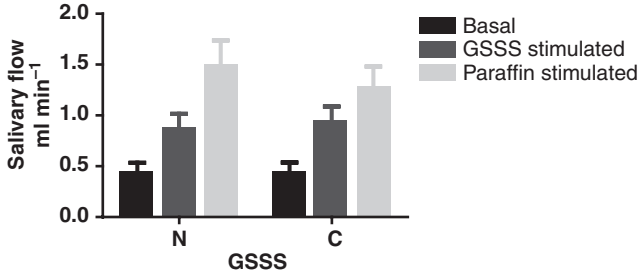

Figure 5 Mean (±95% CI) for basal, gustatory stimulants of salivary secretion-stimulated and paraffin-stimulated salivary flow for each group. There were no significant ($P > 0.05$, independent Student's *t*-test) differences between the two groups for basal or stimulated salivary flow. Note also that lozenge-stimulated salivary flow was significantly ($P < 0.05$, independent Student's *t*-test) lower compared with paraffin chewing mechanical-stimulated flow for both groups

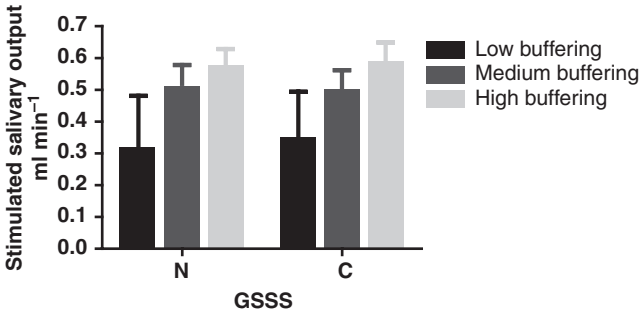

Figure 6 Mean (± 95% CI) stimulated salivary output from gustatory stimulants according to salivary buffering capacity. Between the study arms there were no statistically significant differences when stimulated output was compared for low, medium or high salivary buffering capacity (independent T test, $P > 0.05$)

to low and not to medium (ANOVA plus *post hoc* Tamhane's test $P < 0.05$). Between the study arms there were no statistically significant differences when stimulated output was compared for low, medium or high salivary buffering capacity (independent T test, $P > 0.05$). Taken together the results suggest that N and Control presented a similar capacity in stimulating salivary output.

Discussion

The results of this study show that the use of GSSS induces salivary pH drops which may constitute an increased risk of dental erosion and therefore should be used with caution in patients who still retain their teeth.

However, the results of this study also suggest that the use of a weaker acid-based GSSS containing fluoride and xilitol represent an important reduction in the risk for lowering the salivary pH under hydroxyapatite (HA) critical level of 5.5, for prolonged times when compared with traditional acidic GSSS based on stronger acids. The ARR for the N group of 80% and the NNT of 2 indicate that for every 2 GSSS used of the N type an episode of effective salivary pH drop under 5.5 for over 1 min may be avoided. Moreover, both types of GSSS tested in this trial elicited saliva stimulation with the same magnitude and pattern indicating similar efficacies in saliva stimulation. Thus, the results of this study indicate that GSSS of the N type possess a more favourable risk benefit ratio when compared with the C type GSSS. However, both GSSS presented an inferior capacity for chemical or gustatory saliva stimulation compared with mechanical stimulation.

For the preparation of this study, we conducted a search on Cochrane and PubMed databases for systematic reviews on tooth AND erosion ([MeSH] terms). The Cochrane search retrieved no information. Two meta-analyses on tooth erosion and one systematic review on saliva stimulation were found on PubMed which were not related to GSSS stimulation of salivation. We then conducted an unlimited search on PubMed with the [MeSH] terms tooth AND erosion. For the search on tooth AND erosion we unearthed 1677 references dated from 1979 to 2008; all references were screened for its relevance. Several trials on acidic candies and beverages were identified but no randomized controlled trials related to the use of GSSS and tooth erosion were found. Therefore, to our knowledge, this is the first study on this issue.

Gustatory stimulants of salivary secretion are non-pharmacological stimulants of salivary secretion. Its mode of action is based on gustatory stimulation of salivation. They are sold over the counter and manufacturers claim that its main indication is salivary stimulation for relief of oral dryness in xerostomia. However, the use of acidic candies, lozenges or GSSS has been also advocated in other situations like prolonged physical activity, where dehydration is present and stimulation of salivation would be beneficial (Dugmore and Rock, 2004; Horswill *et al*, 2006; Lussi and Jaeggi, 2008). Moreover, increased salivation would also represent an important defence against dental erosion, as saliva has been widely recognized as an important factor for dental tissue integrity based on its remineralization properties (Amerongen and Veerman, 2002). Nevertheless, GSSS due to its acidic nature may in itself possess an intrinsic potential for dental erosion as it has been suggested to occur with other acidic candies and medicinal products (Giunta, 1983; Duxbury, 1993; Amerongen and Veerman, 2002; Dugmore and Rock, 2004; Gambon *et al*, 2006,2007; Lussi and Jaeggi, 2008).

In this study we have investigated the effects of two GSSS on salivary pH variations. Although salivary pH is not a measure of effective dental erosion, it is correlated with dental erosion potential and decreased salivary pH values have been referred in several studies as being a predictive risk factor for dental erosion (Rees *et al*, 2005; Gambon *et al*, 2007; Hara and Zero, 2008). In this randomized controlled trial, the results show that GSSS used in both groups induce salivary pH drops. However, when the time of salivary pH below 5.5 HA critical level was measured, GSSS of the N type produced significant ($P < 0.05$ Student's *t*-test) reduced values, which corresponded to a significant (Fisher exact test, $P < 0.01$) ARR of 80%, 95% CI (69.4–90.6%) and an NNT of 2.

Therefore, the results of this study show that this type of GSSS presents an important and significant risk reduction in inducing salivary pH drops below the critical HA level of 5.5, suggesting a reduction in dental erosion potential when compared with those used in the control group.

The GSSS used in the study group belong to a new type of salivary stimulants, which include fluoride and xylitol in its composition. Although no randomized controlled trials were found in the literature search on this issue, several *in vitro* studies have demonstrated that the presence of fluoride compounds in enamel potential erosive media can inhibit its erosion effect (Vieira *et al*, 2005; Hove *et al*, 2006,2007a,b,2008; Chunmuang *et al*, 2007; Schlueter *et al*, 2007; Ganss *et al*, 2008; Wiegand *et al*, 2008). The mechanisms behind this effect are not clear but may be related to direct buffering effect from fluoride ions or via fluoride ion participation in ionic force lowering undersaturation balance regarding HA. Moreover similar mechanisms have been demonstrated to occur in the demineralization–remineralization processes occurring in dental decay. Moreover, in another *in vitro* study it was demonstrated that addition of xylitol, fluoride or a xylitol/fluoride combination to an acidic drink or posttreatment with fluoride or a xylitol/fluoride combination can reduce dental erosion (Chunmuang *et al*, 2007). Thus the presence of fluoride and xylitol in the N group GSSS could explain the less pronounced pH drop and dental erosion potential verified. In addition, the N group GSSS are based on a weaker acid composition, which could also explain the weaker effect on pH drop. Moreover, salivary stimulation output was similar in both groups suggesting quantitatively comparable efficacy in saliva stimulation for both groups.

In this study the primary outcome chosen regarding dental erosion risk was the salivary pH drop, this is not a direct measure of effective erosion and this could be viewed as a weakness. Several studies have measured effective dental erosion mainly related to acidic drinks by the use of intra-oral appliances with dental enamel or HA discs or by profilometry among other techniques (Lippert *et al*, 2004; Sakoolnamarka *et al*, 2005; Barbour and Shellis, 2007; Gilchrist *et al*, 2007; Owens and Kitchens, 2007; Thomas *et al*, 2008). More recently, some studies have been conducted where the erosive potential has been evaluated by calculation of under saturation of saliva regarding HA (Jensdottir *et al*, 2005,2006,2007). The main criticism regarding the use of salivary pH variation alone is that despite the fact that salivary pH is considered an important predictor risk factor for dental erosion, it does not account for other interfering factors affecting effective dental erosion such as buffering capacity of saliva. However, in this study we investigated as baseline characteristics the buffering capacity of saliva for every subject by established methods and studied its interactions with the primary outcomes. Within each arm of the study, subjects with low buffer capacity presented a diminished stimulated salivary output and an elevated TSB when compared with subjects with high buffer capacity, although the later was not statistically significant. When comparing the study outcomes between groups N and C for the different buffer capacities same type of associations could be drawn when considering the overall study samples. The relationship between buffer capacity, acid clearance and effect upon salivary pH agrees with previous findings by other authors, namely from studies on acidic candies (Jensdottir *et al*, 2005,2006,2007; Gambon *et al*, 2006,2007). Moreover, despite the protective effects of high buffering, the results of this study show that even in the high buffering subgroup, traditional GSSS such as the ones used in C group still have the ability of producing sustained salivary drops. This was a preliminary study on the effects of this type of GSSS, conducted as a preparative study of a larger trial studying different populations. Subjects employed were healthy and young. It is expectable that even more extreme results could arise in studies employing postphysical activity and dehydration or xerostomic patients with concurrent diminished salivary flow and acid clearance ability.

The fact that the GSSS used in this study had different aspects, smell and taste impaired complete masking. However, the outcomes measured were objective and masking was maintained for the third party who made calculations based on groups defined only as group A or B. Therefore, actions were undertaken to compensate and minimize study weaknesses which did not in our view compromise study quality and validity.

This study was designed as a randomized controlled trial which is recognized as producing the best sound evidence. The study arms shared homogeneity, demographic and functional characteristics, and power calculations ensured that an adequate number of subjects were enrolled.

The results of this study are important and new. Dental erosion is a growing concern in modern civilizations and the structured literature search conducted shows that the number of publications is increasing (Young *et al*, 2008). GSSS for stimulation of saliva are sold over the counter in a considerable number of countries. Up-to-date studies on the erosive potential of these products are lacking. Moreover, further studies with different populations should try to ascertain (from patients' view) the real benefits of using such products as both GSSS used in this study demonstrated a diminished salivary stimulation capacity when compared with mechanical stimulation suggesting that products like fluoride xylitol-containing chewing gums could be more effective and beneficial. In a systematic review chewing gum was referred by patients as being the most effective product in xerostomia relief was concerned (Shiboski *et al*, 2007).

In conclusion, the results of this study demonstrate that common citric acid-based GSSS such as the one employed in the control group of this study induce sustained salivary pH drops which can equate with an increased risk of dental erosion. Moreover, it is strongly suggested that addition of fluoride and xylitol and lowering the acidic nature of this type of GSSS maintains the benefits (similar salivary secretion stimulation capacity) while diminishing in an important way the risk of prolonged pH drop below the HA critical value and therefore its use could be less detrimental and recommended.

Author contributions

Professor António Mata was the PI of the project. He mentored the study design, made the data analysis and wrote the article's final version. Professor Duarte Marques was the study coordinator, supervising all the investigators. He has implemented the study design and also wrote the final version of the article. Dr João Silveira was investigator and contributed to the figures and tables of the article. Dr Joana Marques, Dr Eurico Felino and Nuno Guilherme were investigators of the project.

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