Collaborative WHO xylitol field studies in Hungary

An overview

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The essential aim was to assess the caries-reducing potential of partial substitution of dietary sucrose by xylitol. The evaluation was carried out in comparison with systemic fluoride in milk or drinking water and restorative treatment solely. The scope of the studies included longitudinal analysis of caries increment, surveillance of sucrose consumption and rate of its substitution by xylitol, monitoring of the intake and excretion of fluoride, microbiological assessments of the salivary aciduric flora, represented predominantly by lactobacilli, yeasts, and *Streptococcus mutans*, determination of the oral hygiene development, and assay of the carbohydrate to protein ratio of dental plaque. These studies were presented in the form of separate reports, referred to in the ensuing text by their Roman numerals. In this context, we also attempted to discuss the interrelations between substudies.

The background and the general planning of this field study are essentially covered in the first reports (I and II). The trial was carried out in institutionalized children, predominantly orphans but also hearing- and sight-impaired or blind subjects, all aged between 6 and 12 years at the base-line examination of the longitudinal caries trials (I and VII). The subjects were located in 11 institutions with fairly uniform diet. A high incidence of caries in these children further influenced our decision to carry out the study in these conditions. We were also aware of the risk of a high number of dropouts, calculated to 15% per year. For this reason, the protocol demanded a 2-year study, although provision was made for a 3-year trial. The protocol further stated that the children admitted to the institutions during the 1st year study should be included in the trial for a 2-year period.

The proportion of dropouts proved to be lower than expected—that is, 10% per year. A 3-year field study was thus carried out in initially 990 subjects, 689 of these comprising the final material included in the longitudinal study of caries increment (I). Evaluation of caries incidence was complicated owing to age-, sex-, institution-, and group-dependent differences at the base-line examination. All essential variables were then studied in single age class subgroups and analyzed over base-line prevalence and number of permanent teeth (I). The DMFS incidence and the increment rate expressed as the ratio between caries incidence and the tooth surface population at risk were significantly ($p < 0.001$) lower in the xylitol group ($n = 278$) than measured in the fluoride ($n = 266$) and control ($n = 145$) groups. Caries was thus reduced between 25% and 45% in the former group in comparison with the two latter groups.

The major part (67%) of the material of the 2-year trial (VII) consisted of the above material and included additionally the new subjects admitted to the institutions within the 1st year of the 3-year study. The initial number of subjects was 1219; the final material consisting of 976 children (base-line age, 6–12 years). Existing base-line differences as to age and caries prevalence were largely eliminated owing to the combined influence of new subjects, dropouts, and, in particular, the experimental regimen having equilibrated existing differences in caries prevalence in 2/3 of the present material during the 1st year of the 3-year study (I)—that is, the pre-study period of the latter investigation (VII). The xylitol regimen ($n = 399$) resulted in a 37% lower caries increment and a 40% lower incidence than registered in the control group ($n = 221$). The development was similar, although less distinct, between the xylitol and fluoride

($n = 356$) groups ($p < 0.001$; covariance analysis with base-line prevalence, number of permanent teeth, and visible plaque index as covariants).

The dietary analysis was carried out in 280 subjects from 8 institutions (II). The study indicated that the frequency of sucrose consumption was high and that the intake increased over the weekend in comparison with weekdays. Surprisingly, the consumption of the xylitol-containing sweets (14–20 g/day) was paralleled by frequent use of sucrose. The low caries increment registered in the longitudinal trials (I and VII) was evidently not due to the absence of sucrose.

The intake and excretion of urinary fluoride was monitored at all institutions in 380 subjects. The highest exposure and excretion of fluoride occurred at two of the three institutions belonging to the fluoride group; however, the next highest was an institution in the control group (II). This was also reflected by a low caries incidence in the latter subgroup (I).

The microbiological substudies included longitudinal analyses of the salivary lactobacilli and yeasts (III) and cross-sectional salivary *S. mutans* (IV) at the end of the 3-year trial. In the former study ($n = 291$) high counts of the aciduric flora prevailed throughout the study. Some improvement occurred during the study, however, mainly in the xylitol group. We consider that the high counts of the aciduric flora reflected the frequent consumption of fermentable carbohydrates (II and III).

At the end of the trial salivary *S. mutans* was quantified in 390 children (IV). Zero and low values included 83% of the subjects in the xylitol group. The comparative values were 42% and 53% in the fluoride and control groups, respectively. The results clearly indicate the association between the dietary (xylitol) regimen and low *S. mutans* levels, as further discussed in the final section of this overview.

The oral hygiene conditions were evaluated longitudinally at yearly examinations. The visible plaque index based on the total number of permanent teeth was determined in 688 subjects. The oral hygiene conditions were generally poor. A definite, although delayed, improvement was found in the xylitol group. We conclude that the acceptable conditions in this group are only partly due to xylitol-induced effects on plaque. We believe, however, that the overall implementation of the oral hygiene measures gradually reached a level at which removal of plaque was facilitated by the dietary regimen in the xylitol group. The findings, especially the relationship among oral hygiene (V), the caries trials (I and VII), and the associated studies (III and IV), will be discussed at an institutional level in the final section.

Dental plaque was also analyzed cross-sectionally and longitudinally ($n = 83$) as to the carbohydrate to protein ratio (VI). Reference values obtained 15 months after the end of the study were used to replace missing base-line values. A low carbohydrate to protein ratio was measured in the xylitol and fluoride groups. In contrast, a high ratio was found in the control group. We hesitate to draw firm conclusions; although the subjects in the xylitol group originated from four institutions, the fluoride and control groups were represented solely by a limited number of subjects from two institutions only. Our results suggest, however, the potential value of parallel quantitative and qualitative assessment of plaque.

*Comparison of studies at institutional level**

The evaluation at an institutional level was hampered by the fact that parts of the substudies, covering the frequency of consumption of sucrose (II), longitudinal analysis of the salivary aciduric flora and yeasts (III), and the carbohydrate to protein ratio of dental plaque (VI), were not carried out at all institutions. Generally, observations were available from at least eight institutions. For this reason, the ensuing comparisons were grouped into 2 entities covering the findings from 11 to 8 institutions, respectively. It should also be noted that the total number of subjects was low at some of the institutions, such as 1 VÖR and 3 HUN institutions accommodating a total of 37 and 29 children only (the institutions are identified

* Analysis by Kaisu Pienihäkkinen.

Table 1. Ranking of caries prevalence and incidence indices (I), and associated observations (II–V) at an institutional ($n = 11$) level

Group	Code no. and institution	Caries prevalence				Caries incidence				Fluoride (in urine)	Aciduric flora (final)*	Yeasts (final)*	*S. mutans* (final)	VPI (base line)	VIP (final)
		Base line	Final	$D_{2\text{-}4}S$ (final)	$D_{3\text{-}4}S$ (final)	$\Delta D_{1\text{-}4}MFS$	$Rate_{1\text{-}4}$	$\Delta D_{2\text{-}4}MFS$	$Rate_{2\text{-}4}$						
Xylitol	1 VÖR	3	6.5	3	3	8	8.5	6	6	9	9.5	1	2	4	6
	2 AGA	7	2	4.5	6	3	3	1.5	1	8	9.5	11	4	2	2
	3 HUN	8	8	6	4.5	6	7	10	10	11	6	8.5	3	9	3
	4 VAK	10	1	2	1.5	2	2	1.5	4.5	5	2	8.5	1	8	8
	5 NAG	11	3	1	1.5	1	1	3	2	10	1	5	5	6	1
Fluoride	6 FOT	3	5	7	7.5	7	5	7	7	7	4	2.5	11	5	11
	7 KOM	5	9	10	10	9	8.5	8	8	2	9.5	10	8	10	5
	10 ZAM	6	6.5	4.5	4.5	4	4	5	4.5	1	7	7	6	3	9
Control	8 ACS	9	11	11	11	10	11	11	11	4	9.5	4	10	11	4
	9 ALS	3	10	8	7.5	11	10	9	9	6	3	6	9	1	10
	11 BOG	1	4	9	9	5	6	4	3	3	5	2.5	7	7	7

* Not included in paper III; tables available on request ($n = 388$).

Table 2. Ranking of caries increment (I) and associated observations (II–V) at an institutional ($n = 8$) level

Group	Code no. and institution	Caries indicence				Sucrose, total, WD*	Sucrose, total, WE†	Sucrose, weighted mean‡	Fluoride (in urine)	Aciduric flora (final)	Yeasts (final)	*S. mutans* (final)	VPI (base line)	VPI (final)
		$\Delta D_{1\text{-}4}MFS$	$Rate_{1\text{-}4}$	$\Delta D_{2\text{-}4}MFS$	$Rate_{2\text{-}4}$									
Xylitol	1 VÖR	7	7.5	5	5	8	4.5	8	6	7.5	1	1	3	5
	2 AGA	2	2	1	1	2	7	5	5	7.5	8	3	1	2
	3 HUN	5	6	8	8	5	4.5	4	8	4	6	2	7	3
	5 NAG	1	1	2	2	1	2	1	7	1	4	4	5	1
Fluoride	6 FOT	6	4	6	6	6	6	6	4	2	2.5	8	4	9
	7 KOM	8	7.5	7	7	3	8	7	2	7	7	7	8	4
	10 ZAM	3	3	4	4	4	1	2.5	1	5	5	5	2	8
Control	11 BOG	4	5	3	3	7	3	2.5	3	3	2.5	6	6	6

* WD = weekdays.
† WE = weekends.
‡ Sucrose in liquid form at meals not included.

by code number and the three first letters of their name). The largest institutions were 5 NAG and 6 FOT, with 90 and 141 subjects, respectively. In some of the substudies the control group was represented by a low number of subjects and one institution only (II, III, and VI).

The comparisons at an institutional level were carried out by ranking, with the best result, such as the lowest caries increment and the lowest CFU values of *S. mutans*, denoted as 1 (highest ranking); the worst findings were assigned 11 or 8, respectively. Unless otherwise stated, all these calculations were based on tables appearing in the individual reports (I–VI).

There was fair agreement between the main caries trial and the substudies (Tables 1 and 2). This was evident at examining the ranking lists (Tables 1 and 2) as an entity, particularly at the institutions with the lowest (5 NAG and 4 VAK) and highest (8 ACS and 9 ALS) caries increment.

At 5 NAG and 4 VAK the caries indices covering increment and rate and the final prevalence consistently yielded a very high ranking (Tables 1 and 2). These findings are striking in view of the very low ranking of these institutions at the base-line examination (Table 1). The associated observations matched the caries development—for example, with regard to consumption frequency of sucrose (Table 2) and the counts of *S. mutans* (Table 1). The range of the CFU values of *S. mutans* was narrow, all these institutions being ranked high in the entire xylitol group (IV). Despite the xylitol regimen the oral hygiene conditions in the 4 VAK subgroup ranked low throughout the study (V). This result, however, was due to sight-impaired or blind children with difficulties in maintaining an acceptable oral hygiene level (I and II).

The institutions 8 ACS and 9 ALS ranked fairly consistently lowest for caries (Table 1). This observation was paralleled by high counts of *S. mutans* at both institutions (Table 1). At the former institution the oral hygiene conditions improved markedly during the study, although this was not reflected in the aciduric flora (Table 1).

The consumption of sucrose, notably the weighted mean frequency excluding sugar in solution at meals (II), was reflected in high counts of the aciduric flora at institutions (1 VÖR, 2 AGA, and 7 KOM) where conventional sweets were routinely distributed (Table 2).

Part of the observations requires further explanation of the background factors. In the fluoride group the highest urinary fluoride levels were measured at 10 ZAM (with naturally fluoridated water) and 7 KOM (milk fluoridation), to be followed by 11 BOG (control group (!) with suboptimal level of fluoride in the drinking water). Caries increment and rate, although moderate at 10 ZAM and 11 BOG, were high at 7 KOM and also at 6 FOT. At the latter institution the measured low urinary fluoride level was due to suspension of milk fluoridation for 3 months (II). In contrast to the 7 KOM institution, with milk fluoridation initiated at the commencement of the 3-year trial, fluoridation of milk at 6 FOT was started 2 years before the present study (I).

General conclusions

We conclude that the two caries trials (I and VII) unconditionally show the practical value of partial substitution of sucrose by xylitol in solid sweets and, additionally, through the unsupervised use of a xylitol-containing dentifrice, as a caries-preventive measure. These results are obtained in field study conditions, far from ideal with regard to consumption of sucrose- and xylitol-containing sweets (II).

In addition, the treatment effect in the xylitol and fluoride groups is achieved in comparison with a control group consisting predominantly of rural children with lower prevalence and incidence of caries than generally observed in comparative urban materials (I). We believe that the observed differences would have been even more striking if compared with a control group composed of urban—for example, Budapest—children.

We further conclude that the associated substudies (II-VI) generally support and add to the value of this series of concerted studies.