MILK – A VEHICLE FOR FLUORIDES: A REVIEW

Leite – um veículo para flúor: revisão

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Abstract

The aim of this review is to give an overview of 50 years experience of milk fluoridation and draw conclusions about the applicability of the method. Fluoridated milk was first investigated in the early 1950s, almost simultaneously in Switzerland, the USA and Japan. Stimulated by the favourable results obtained from these early studies, the establishment of The Borrow Dental Milk Foundation (subsequently The Borrow Foundation) in England gave an excellent opportunity for further research, both clinical and non-clinical, and a productive collaboration with the World Health Organization which began in the early 1980s. Numerous peer-reviewed publications in international journals showed clearly the bioavailability of fluoride in milk. Clinical trials were initiated in the 1980s. Some of these can be classed as randomised controlled trials, while most of the clinical studies were community preventive programs. These evaluations showed clearly that the optimal daily intake of fluoride in milk is effective in preventing dental caries. Fluoridation of milk can be recommended as a caries preventive measure where the fluoride concentration in drinking water is suboptimal, caries experience in children is significant, and there is an existing school milk program.

Keywords: Caries prevention; Fluoride prevention; Milk fluoridation; Caries reduction; Community programs.

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Resumo
O objetivo desta revisão é um relato panorâmico de 50 anos de experiência em fluoretação do leite e comentar conclusões sobre a aplicabilidade do método. O leite fluoretado foi inicialmente estudado no início de 1950, quase simultaneamente na Suíça, nos EUA e no Japão. Estes resultados favoráveis estimularam o estabelecimento da Fundação Borrow do Leite Dental (subsequentemente Fundação Borrow), na Inglaterra, uma oportunidade excelente para pesquisas adicionais, tanto clínica como não clínica, e uma colaboração muito produtiva com a Organização Mundial da Saúde, no início de 1980. Numerosas publicações em revistas internacionais demonstraram claramente a disponibilidade biológica do flúor no leite – estudos clínicos foram iniciados em 1980. Alguns destes estudos podem ser classificados como pesquisas controladas aleatoriamente, enquanto a maioria dos estudos clínicos foi programa comunitário de prevenção. Os resultados mostram claramente que a ingestão diária adequada do flúor pelo leite é eficaz na prevenção da cárie dentária. Fluoretação do leite pode ser recomendada como medida preventiva para a cárie dentária onde a concentração de flúor na água potável seja abaixo do recomendado (subótima), onde a prevalência de cárie em crianças seja significante e onde exista um programa de leite escolar.
Palavras-chave: Prevenção da cárie; Flúor; Fluoretação do leite; Redução da cárie; Programas comunitários.

Introduction

Dental caries - based on a recent review of the World Health Organization (WHO) – has decreased considerably in several countries and regions: the burden of the disease is, however, still considerable in many populations. The benefits of fluoride prevention are presently reaching only about 20 % of the world population. Dental caries is a public health problem in some groups of countries with high income, as well as in countries of Asia and South America.

The beneficial effects of fluoride in the prevention of dental caries are scientifically proven facts: increased acid resistance of dental enamel, inhibition of acid production by plaque bacteria, promotion of remineralisation of incipient enamel lesions, etc. Fluorides may be used individually (tablet, toothpaste, mouthrinse), in a professional way (varnish, gel), or by organizing community-based fluoride programs (drinking water, salt, milk).

The fluoridation of drinking water, which began in America in 1945, was the first community program in this respect. The idea of milk fluoridation emerged – simultaneously with salt fluoridation (1955) – in Switzerland (Ziegler, 1953) (1), in Japan (Imamura, 1952) (2) and in the USA (Rusoff, 1955) (3). Based on contemporary investigations, fluoride added to milk does not change its taste or other characteristics, is absorbed well, although slower than from fluoridated water. It has been considered advantageous that fluoride is added to an important nutrient for infants and small children, and that its consumption is not mandatory for everybody, only for those who need it most and agree to receive it. The caries preventive effect of fluoride can even be enhanced by the milk vehicle, due to the cariostatic properties of its mineral content, milk proteins and fats.

Early clinical investigations

The first results were reported by Imamura (2) after a five-year study of Yokohama schoolchildren. Milk or soup, containing 2.0 to 2.5mg sodium fluoride, was consumed at lunch-time, 150 to 180 days per year, by 167 children. Compared with the control group, 29 to 34% caries reductions were observed in the permanent dentition.

In the USA (Baton Rouge, Louisiana) Rusoff and co-workers (3) reported, in 1962, on 3.5 years’ results in 129 (65 test and 64 control) children. In children consuming fluoridated milk at school meals, 35% less caries was recorded than in the control children; in those who were 6 years old at the beginning, the reduction was even larger at 70%.

In Winterthur, Switzerland, Ziegler and Wirz (1) used 0.22 % sodium fluoride solution, prepared by pharmacies in plastic bottles, for the fluoridation of household milk; added by the parents to the milk of the children. Participants were 749 test and 553 control children who were 9 to 44 months old at the start of the program. In 1964, after six years, caries reductions were 17% for the deft index and 30% for the defs index in the primary dentition, and 64 % for DMFT and 65 % for
DMFS in permanent molars. The proportion of caries-free children increased significantly in the fluoridated milk group.

**The Borrow Foundation**

The establishment of a charity foundation in England by Edgar Wilfred Borrow (1902-1990) for the promotion of milk fluoridation in order to prevent dental caries in children, brought important progress in the field of research and clinical studies.

E.W. Borrow (Figure 1), a wealthy farmer and mechanical engineer in south England, constantly interested in the technical aspects of fluoridation of milk, set up a foundation in 1971, named the ‘Borrow Dental Milk Foundation’, for the above purposes. The aims, summarized in 12 points, were mainly “to promote and support research of fluoridated milk for human consumption by the help of grants, equipment, lectures, scientific publications, and to disseminate knowledge about this method”.

![Figure 1 - Edgar Wilfred Borrow – the founder of ‘The Borrow Foundation’](image)

The aims of the original ‘Trustees’ deed’ were extended in 1993 to include “the support of activities on health promotion and education,… and on healthy nutrition, including milk and milk products”. The name of the foundation was changed in 2002 to ‘The Borrow Foundation’ (www.borrow-foundation.org).

In recognition of his humanitarian services, E.W. Borrow received an Honorary Doctorate from Lousiana University, USA, in 1983. The authors of this present review are two of the five ‘trustees’ of The Borrow Foundation.

The results of clinical and basic research studies, supported by The Borrow Foundation, have made the creation and extension of milk fluoridation programs possible in numerous countries of the world. Based on discussions initiated in the 1980s between The Borrow Foundation and the World Health Organization (WHO), the Bulgarian milk fluoridation program was initiated, and a ‘Memorandum for Understanding’ was signed by The Foundation and WHO in 1991; this has been renewed every three years. As a result of this collaboration, a book was published in 1996.
summarizing the studies of basic and clinical research into milk fluoridation. A new, revised edition is expected to be published in 2008 as a WHO document (4, 5).

The aim of the present review is to summarize briefly the results of basic research and community studies published in these monographs (4, 5).

**Theoretical considerations**

Concerning the pathomechanism of fluorides, it is accepted that elevated fluoride ion concentrations at the dental plaque/enamel border decrease the rate of demineralisation, increase remineralisation, and reduce acid production of dental plaque. However, the use of milk as a vehicle, generated questions concerning possible chemical reactions between milk and fluoride ions, bioavailability of systematically administered fluoride in milk, and interactions involving fluoride in the oral cavity (enamel, saliva, plaque and caries).

The results of basic studies on milk fluoridation have been published in more than 100 peer-reviewed papers, with increasing frequency in the last 20 years. Based on these studies, according to recent knowledge, the greater part of fluoride added to milk, forms a soluble complex with the protein fraction of milk, from which the fluoride can be liberated in ionic form, so that it is bioavailable. The absorption of fluorides with simultaneous food consumption is slower than for fluoride without food. The proportion absorbed depends on the calcium content of the diet and also on the chemical formulation of the fluoride agent, since Villa et al. (6) observed better absorption with sodium monofluorophosphate, than with sodium fluoride.

Marthaler in 1978 (7) proposed that regular measurements of fluoride excreted in urine by children participating in systemic fluoride programs was advisable. Since then, monitoring volume and concentration of fluoride in urine has been included in clinical investigations and community preventive programs. The analysis of 24 hour urine excretion is presently the best marker of the bioavailability of fluorides. A WHO document, published in 1999, offers detailed guidelines for the method and calculations: based on these, the optimal fluoride concentration in milk and the appropriate intake of fluoride can be determined.

The systemic effect of fluorides in milk is supported by numerous experimental data. However, by the 1980s, the opinion as to how fluoride acts to prevent dental caries was going through a change: even with the use of systemic fluoride agents, topical effects were considered more important. The consumption of fluoridated milk incorporated into dental enamel inhibited demineralisation and promoted remineralisation.

The results point to the fact that 30-60 minutes after the intake of fluoridated milk, both the levels of fluoride in whole saliva and dental plaque increase as a consequence of the presence of fluoridated milk in the mouth and increased concentrations of fluoride in salivary secretions following the absorption of ingested fluoride. Thus, fluoride in milk acts both systemically and topically, in the same way as fluoride in water.

**Clinical examinations**

Long-term human studies with fluoridated milk on children, undertaken in about twelve countries have been reported in numerous peer-reviewed papers. Only some of these studies can be classified as RCTs (randomised controlled trials) according to the criteria used in evidence-based medicine; the others can be classed as community-based programs. In the following paragraphs, the main features of the evaluations of these milk fluoridation programs in different countries of the world will be summarized, but without the detailed numerical results which can be found in the relevant literature (1, 2) (Table 1).
**Table 1 - List of published reports of studies into the effectiveness of milk fluoridation**

<table>
<thead>
<tr>
<th>Study</th>
<th>Year of study</th>
<th>Authors</th>
<th>Caries prevention in:</th>
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<tr>
<td></td>
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<td>Primary teeth</td>
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<td>Permanant teeth</td>
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<tr>
<td>Yokohama, Japan</td>
<td>1952 – 1956</td>
<td>Imamura</td>
<td>1959</td>
</tr>
<tr>
<td>Baton Rouge, USA</td>
<td>1955 - 1959</td>
<td>Rusoff et al</td>
<td>1962</td>
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<tr>
<td>Winterthur, Switzerland</td>
<td>1958 - 1964</td>
<td>Wirz</td>
<td>1964</td>
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<tr>
<td>Agudos, Brazil</td>
<td>1976 - 1979</td>
<td>Lopes et al</td>
<td>1984</td>
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<tr>
<td>Louisiana, USA</td>
<td>1982 - 1985</td>
<td>Legett et al</td>
<td>1987</td>
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<td></td>
<td></td>
<td>Atanassov et al.</td>
<td>1999</td>
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<tr>
<td>Codegua, Chile</td>
<td>1994 - 1999</td>
<td>Marito et al</td>
<td>2001</td>
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<tr>
<td>Voronezh, Russia</td>
<td>1994 - 2004</td>
<td>Pakhomov et al</td>
<td>2005</td>
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<td>Beijing, China</td>
<td>1997 - 1999</td>
<td>Bian et al</td>
<td>2003</td>
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<tr>
<td>Knowsley, UK</td>
<td>1997 - 2001</td>
<td>Ketley et al</td>
<td>2003</td>
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<td>Volgograd, Russia</td>
<td>1998 - 2002</td>
<td>Maslak et al</td>
<td>2004</td>
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<td>Araucania, Chile</td>
<td>1999 - 2002</td>
<td>Weitz and Villa</td>
<td>2004</td>
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**Scotland: Glasgow**

Due to the strong criticism of the early clinical studies (for example, small numbers of participants, lack of baseline examinations, etc.), Stephen et al. (8, 9) initiated in Glasgow, in 1976, a double blind clinical trial on 4 ½ and 5 ½ year old schoolchildren. The group of test children consumed 200 ml milk each school day (about 200 days per year), containing 1.5 mg fluoride, while the control group received plain milk. The results published in 1984, after five years, reported a 36 % reduction in DMFT and a 48 % reduction in DMFS values for the first permanent molars which were not yet erupted at baseline in the test group compared with the control group. Fluoride excretion in urine was monitored constantly during the study.

This evaluation (together with the Volgograd program by Maslak: see later) is one of the programs accepted as an RCT by the Cochrane Centre for Systematic Reviews.
Hungary: Fót

In the ‘Children’s City’ of Fót, a milk fluoridation program was initiated by Bánóczy, Zimmermann et al. (10) in 1979, involving about 1000 children aged 2 to 18 years. The results were published after 2, 3 and 10 years (1982-1992) (11-13). The children drank for breakfast milk or cocoa, containing 0.4 mg fluoride for kindergarten children and 0.75 mg fluoride for the schoolchildren. The sodium fluoride solutions were prepared by the Pharmacy of Semmelweis University in closed glass bottles, then added to the milk in the kitchen of the home, stirred thoroughly for 15 minutes, and consumed within 30 minutes by the children.

After five years, in the test group (165) children compared with a control group, a considerable caries reduction was observed in both the primary and permanent dentitions. In 7 to 10 year old children, these percentage reductions were 54 % in DMFT and 53 % in DMFS values. The reduction in the total permanent dentition was 60 % for DMFT, and 67 % for DMFS, respectively; the highest reductions were found in the children who had consumed fluoridated milk from 2 to 3 years of age. The difference between the caries prevalence of the test and control groups was, in spite of loss of children from the study, still statistically significant after 10 years.

Israel: Bethlehem

Zahlaka et al. (14) reported in 1987 the results of a study on 273 children who were aged 4 to 7 years at baseline and who had consumed fluoridated milk for three years. The fluoridated milk was produced from milk powder, and the dissolved milk contained 1 mg fluoride per litre. A 63 % caries reduction was observed in both the primary and permanent dentitions.

USA: Lousiana, Baton Rouge

In the second Lousiana community program, begun in 1982, schoolchildren consumed fluoridated milk, containing cocoa and sugar, for lunch for two or three years. After two years, a significant caries reduction was observed in the permanent dentition: however, due to the loss of children, three year results could not be evaluated. The organisers of the experiment, Leggett (15), planned also to establish a research institute for milk fluoridation which, however, could not be realised.

Bulgaria: Asenovgrad

One of the most extensive milk fluoridation programs, which is still functioning, was initiated by Pakhomov et al. (16) in Bulgaria in 1988 with the support of WHO. The objective was to see if such a program was feasible under everyday life conditions. Bulgaria seemed to be an excellent choice for this community-based program due to the regular consumption of milk and milk products (for example, yoghurt) by children.

The city Asenovgrad in south Bulgaria was selected as the test community and the nearby city of Panaguriche as the control community; later, Karlovo became the control community. The fluoridated milk was produced and transferred from the Plovdiv dairy, in plastic bags, containing 1 mg fluoride per day. About 3,000 children aged 3 to 10 years entered the program in Asenovgrad (Figure 2).
The caries examinations at baseline and after 3 and 5 years were performed by dentists calibrated by a WHO epidemiologist. Urine monitoring was carried out regularly. After five years, mean dmft values were 52% lower in the test group children aged 6 ½ years and 40% lower in the 8 ½ year olds. The reduction in mean DMFT in these two age groups were 89% and 79% — statistically highly significant. After 10 years of the program, Atanassov et al. recorded further significant differences in the proportion of caries-free children and in mean DMFT values of the test and control groups.

The fluoridated milk program has been extended steadily to other parts of Bulgaria; in some communities there is a preference for fluoridated yoghurt.

South America: Brazil, Peru and Chile

From Brazil, Lopes et al. (17) reported in 1984 a small milk fluoridation study lasting 16 months. However, due to the short period, the results were not significant.

In Peru, a milk fluoridation program, controlled by the University of Trujillo, started in the 2000s, based on the government program ‘vaso di leche’, which provides one glass milk for children each day. The children received their milk in the ‘Mother’s clubs’, where the fluoride solution prepared by the pharmacies was added to the fresh milk brought in by farmers, stirred thoroughly for 15 minutes, and consumed shortly after (Figure 3). However, the program was stopped after a few years because of the expanding salt fluoridation program in that country and the migration of children: no evaluation was made.

Figure 3 - Peru program: fluoridated milk – after stirring- distributed at the ’mothers club’
Chile: Codegua and Araucania

The Chilean milk fluoridation programs possess two features which differ from other programs. First, instead of using sodium fluoride they use sodium monofluorophosphate which, according to Villa et al. (6) has good bioavailability and other advantages and, second, the fluoride is added to powdered milk.

Codegua program

The community program which started in Chile in 1994 is based on the ‘national nutrition complementing program’ (PNAC) which has been in existence for more than 50 years. Under this scheme, every Chilean child, from birth to two years of age, receives two kilograms of milk powder every month, while children aged 2-6 years receive monthly one kilogram of milk powder with cereals. The PNAC program covers 90 % of the child population, and was used by Marino et al. (18) for their fluoridated milk pilot program in the rural area of Codegua (test) and La Punta (control).

Children between 0 and 6 years of age consumed for four years daily, 0.25, 0.5 or 0.75 mg fluoride mixed into the milk powder, according to their age-group. Fluoride-containing toothpaste was available and urine monitoring for fluoride excretion was performed regularly. After five years, the proportion of caries-free children was higher in Codegua than in the control La Punta, and mean dmfs values showed significant reductions in children in Codegua compared with children in La Punta. However, examinations performed three years after cessation of the program showed very small differences, pointing to the necessity of continuous maintenance of caries preventive programs.

Araucania program

In the IXth region of Chile, a new program started in 1999 with about 35,000 children aged 6 to 14 years, who were participants of the national powdered milk program (see above). In the community of Araucania, 6, 9 and 12 years old children received milk powder containing sodium monofluorophosphate, while the control children received milk powder without added fluoride. The control children were already participating in a community preventive program in which they received applications of APF gel. Examinations showed, historically, reductions in caries of 24 to 27 % in children aged 9 and 12 years, which was similar to the results of the fluoride gel program.

Because the fluoride gel program was difficult to administer, the milk-powder fluoridation program has now been introduced into the majority of the Chilean regions as part of the caries preventive program for 6-14 year old children living in rural communities. While the main cities in Chile receive optimally fluoridated water as a public health measure, milk fluoridation is provided in the rural areas where water fluoridation is technically not possible, in order to ensure equity (19).

China: Beijing

Due to the increasing caries prevalence in some parts of China, a milk fluoridation program was introduced between 1994-1997 for Chinese kindergarten children in a district of Beijing. An evaluation showed no effect, probably due to the high amount of sugar (7-10 %) added to milk (20).

In the second phase of the program, therefore, no sugar or only small amount of sugar was added to the pasteurized milk which contained 2.5 ppm fluoride and which was consumed everyday in kindergartens. In addition, children brought home milk for weekends in boxes. Dentists calibrated to WHO standards examined the children after 21 months, recording also arrested caries. The mean dmft value in the test group showed a 69 % reduction compared with the control. These results showed that fluoridated milk, when consumed daily, is able to prevent caries in the primary dentition and stop active dentinal caries from progressing – probably due to the topical effect of fluoridated milk.

United Kingdom: Knowsley, Wirral

Knowsley program

In the UK, a milk fluoridation program was launched in 1997 in Knowsley by Ketley et al. (21) where 4,060 3 to 5 year old children (mean age 4.7 years), consumed daily milk containing 0.5 mg fluoride; the control children in Skelmersdale drank plain milk. The number of days the children received milk was about 180 days per year. Caries evaluation was made, based on BASCD (British Association for the Study of Community Dentistry)
criteria. After four years, no statistically significant differences in dmft and dmfs values of the two groups were found. The DMFT and DFS values were slightly, but not statistically significantly, smaller in the 7 to 9 year old children of the test group, than in the control. The assumption for these results was that the dose of fluoride in the milk was too low and that the period of consumption was not long enough to show an effect.

**Wirral program**

In the Wirral region, examinations, using BASCD criteria, were made by Riley et al. (22) on 5,700 children, who were 5 years old when they entered the fluoridated milk program. Data for the four permanent molars were compared between 773 children who had been drinking fluoridated milk for six years at least, and 2,052 children from Shefton, who had received milk without added fluoride. Caries prevalence in the test group was 13 % less in the primary dentition and 16 % less in the permanent dentition. The mean DMFT value showed a reduction of 31 %, and the mean DFS a 37% reduction, compared with the control.

**Russia: Volgograd and Voronezh**

Milk fluoridation programs in Russia started in 1993 as a collaboration between the WHO and The Borrow Foundation, in a multicentric form, with the participation of Voronezh, Maykop and Smolensk, later on in Volgograd and in several communities in Tatarstan (Figure 4). evaluating three year results in 1999 for 15,000 participating children, reported caries reductions between 55 and 68% (5).

![Figure 4 - Measurement of the fluoride solution in the Russian program](image-url)
Volgograd program

Maslak et al. (23) in a three year study, investigated the effect of fluoridated milk in children who were caries-free at 3 years of age. In this double-blind evaluation, undertaken by examiners calibrated according to WHO criteria, on 75 test and 91 control children, they found statistically significant reductions both in dmft and DMFT values, in longitudinal, as well as in cross-sectional comparative analyses.

According to the evaluation by the Cochrane Centre for Systematic Reviews, this study, as well as that of Stephen et al from Scotland, is accepted as an RCT and as evidence for the effectiveness of milk fluoridation.

Voronezh program

The effect of the 10 year milk fluoridation program was evaluated on 15,000 kindergarten children in two horizontal comparative analyses. Pakhomov et al. (24) compared data from 335 test and 175 control children after three years, and revealed a statistically significant reduction in dmft values and an increase in caries-free children in the test group. In a second analysis, data from 3, 6, 9 and 12 year old children were compared cross-sectionally with baseline data, and a statistically significant caries reduction was observed. Urinary fluoride monitoring showed that the daily consumption of 200 ml milk containing 2.5 ppm fluoride is an effective caries preventive method and that the fluoride intake corresponded to physiological norms.

Thailand: Bangkok

A well-organized milk fluoridation program for children started in Thailand five years ago, with the help of the Royal Dairy and supported by the royal family. An evaluation is in progress. In the coming year, the project will be extended to include all schoolchildren in Bangkok, and new programs are starting in four other cities in Thailand (Figure 5 and 6).

Figure 5 and 6 - Thailand program: schoolchildren consuming fluoridated milk during a break
Conclusions

Summarising: the effectiveness of milk fluoridation in preventing dental caries is supported by about 16 studies reported in numerous papers. Of these, eight demonstrated caries prevention in primary teeth and 11 in the permanent dentition (Table 1) Two studies showed no effect in either dentition. After cessation of a pilot milk fluoridation program, caries incidence increased. Two RCTs showed caries reductions, and evaluations of the several community programs pointed to the feasibility of the method under real life conditions.

Based on the performed studies, it seems that to obtain good results with milk fluoridation, even in the primary dentition, the programs should start early, possibly before the age of four. In order to protect the permanent molars, the consumption of fluoridated milk is necessary after their eruption too. The introduction of milk fluoridation programs should be considered where the fluoride content of drinking water is low, where a regular school milk system is working and where the children are able to consume the fluoridated milk for at least 200 days in a year.

References


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