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Caries-Preventive Effect of Salt Fluoridation in Preschool Children in The Gambia: A Prospective, Controlled, Interventional Study

Rainer A. Jordan[a] Andreas Schulte[b] Alexander C. Bockelbrink[d] Sarah Puetz[d] Ella Naumova[c] Lars G. Wärn[e] Stefan Zimmer[a]

Departments of [a]Operative and Preventive Dentistry, [b]Special Care Dentistry, and [c]Biological and Material Sciences in Dentistry, at [d]School of Dentistry, Faculty of Health, Witten/Herdecke University, Witten, Germany; [e]Swedent Clinic, Kotu, The Gambia

Keywords

Caries experience · Caries prevention · Fluoridated salt

Abstract

The aim of this study was to investigate the anticaries effect of fluoridated salt in a communal feeding program for preschool children. In the Gambian city of Brikama, drinking water had a low fluoride content (0.1 mg F^-/L) and young children did not use toothpaste for oral hygiene. Its 2 preschools served as clusters for the trial. Random allocation of the kindergartens was performed by one person not involved in the study, and the clinical examinations were carried out using the envelope method. Meals were prepared with fluoridated salt (250 mg F^-/kg salt) in the intervention group but not in the control group. According to the inclusion criteria (complete primary dentition and informed consent from legal guardian), 441 children aged 3–5 years were enrolled. The children were examined by calibrated persons according to WHO criteria, allowing the calculation of $d_3$mft scores. The primary end point was the mean difference in the incidence of caries cavities ($\Delta d_{3/4}$mft) after 12 months. After 12 months, the mean caries incidence per person was 1.29 $d_{3/4}$mf teeth (95% CI: 0.96; 1.62) in the test group (n = 304 children) and 3.83 $d_{3/4}$mf teeth (95% CI: 2.94; 4.72) in the control group (n = 137 children). Thus, the caries-prevented fraction was 66.3%. No signs of harm due to the intervention were observed. The use of fluoridated salt in a communal feeding program and in an environment with negligible availability of fluoride from other sources yields a considerable caries-preventive effect.

Fluoridated salt has been available in many European (e.g., Switzerland, Germany, France, Austria) and Latin-American countries (e.g., Colombia, Jamaica, Mexico) for many years and is still on sale there [Pollick, 2013]. Some decades ago, epidemiological studies from Hungary and Switzerland indicated that fluoridated salt contributed distinctly to a reduction in caries prevalence [Tóth, 1973; Marthaler and Steiner, 1981]. Later, cross-sectional epidemiological studies from Germany and Austria demonstrated that kindergarten and school children living in households where fluoridated salt was used had significantly lower mean dmft or DMFT values than children from families that did not use fluoridated salt [Schulte et al., 2001; Pieper et al., 2007, 2012; Wagner et al., 2014; Winter et al., 2016]. In these studies, either children or parents were asked whether they used fluoridated salt for

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E-Mail karger@karger.com
www.karger.com/cre

Prof. Dr. A. Rainer Jordan
Institute of German Dentists
Universitaetsstrasse 73
DE–50931 Cologne (Germany)
E-Mail r.jordan@idz-koeln.de

preparing meals. However, the number of meals prepared with fluoridated salt per week or month was not taken into account. To the best of our knowledge, to date only one prospective study has been published where the caries-preventive effect of fluoridated salt was investigated [Wennhall et al. 2014]. Prospective clinical studies on the biokinetics of fluoridated salt proved that the consumption of meals or salted snacks yields a statistically significant increase in salivary fluoride concentration for about 30 min [Björnström et al., 2004; Hedman et al., 2006; Kaiser et al., 2006]. These studies do not allow for estimation of the caries-preventive potential of fluoridated salt because in all Western countries the population benefits also from fluoride delivered by toothpastes, dental varnishes, rinsing solutions, or gels. Thus, it is of great scientific interest to investigate also with the aid of prospective studies whether fluoridated salt has a real caries-preventive effect and, if so, to estimate the size of this effect. Additionally, such studies would be valuable because numerous prospective studies have been conducted showing a caries-preventive effect of fluoridated water, toothpastes, rinsing solutions, gels, and varnishes. Thus, many of these studies could be included in systematic reviews and meta-analyses which are able to demonstrate an evidence-based caries-preventive effect of these ways to deliver fluoride [Marinho et al., 2003, 2013, 2015; Iheozor-Ejiofor et al., 2015].

The main objective of this prospective, controlled, interventional study was to investigate whether fluoridated salt has a significant caries-preventive effect in preschool children living in an urban region of The Gambia. Another aim of this study was to estimate the potential size the caries-preventive effect of fluoridated salt.

Materials and Methods

This was a prospective, controlled, interventional study to evaluate the relative caries-preventive effect of fluoridated table salt in communal feeding of preschool children after 12 months. This population was chosen since communal feeding in Brikama is restricted to preschools. The study protocol was approved by the Witten/Herdecke University Institutional Review Board (No. 106/2010) and by the Department of State for Health and Social Welfare of the Republic of The Gambia in the form of a memorandum of understanding. All participants and parents or legal guardians gave written informed consent with the aid of a native speaker before the study-related procedures were performed. As the illiteracy rate is about 55% [CIA, 2016], a signature was replaced by a dactylogram where necessary. The study was conducted in line with the Declaration of Helsinki and registered with ClinicalTrials.gov (NCT02585882). Figure 1 shows the study participant flow.

Sample Size

Sample size calculation was performed with G*Power 3 [Faul et al., 2007]. Basic data for sample size calculation was the mean dental caries experience of preschool children in urban parts of The Gambia, which was reported to be 2.09 dmft teeth (SD: 1.92) [Lietz and Gängler, 2002]. An effect measure of caries prevention by fluoridated table salt of 35% was assumed according to the relevant literature [Tóth, 1973]. An alpha error was set at 0.05, and the study power at 80%. A target sample of 130 subjects for each study arm (test and control group) was calculated.

Study Population

Eligible participants were children aged from 3 to 5 years living in urban Gambia with preschool attendance at the co-operating kindergartens. The inclusion criteria for participating in this study were (1) complete primary dentition and (2) informed consent from a parent or legal guardian. The only exclusion criterion was refusal to participate in the study.

Study End Points

Primary End Point

To measure the caries-preventive effect of salt fluoridation, the difference in the incidence of cavitated carious teeth ($\Delta d_{3/4}$mft) after the study-related intervention was chosen as the primary end point [WHO, 2013]. Using the primary study end point, the relative preventive dental caries effect was calculated according to the following formula: 100 – ($\Delta d_{3/4}$mft (test group)/$\Delta d_{3/4}$mft (control group)) ×100.

Secondary End Points

The first secondary end point was the difference in the incidence of teeth with white spot lesions (ΔG_{2-4}), with G_2 denoting slight white spot formation (<1.5 mm diameter with intact surface), G_3 denoting excessive white spot formation (>1.5 mm diameter with intact surface), and G_4 denoting white spot formation with cavitation into enamel [Gorelick et al., 1982]. Only the most severe clinical finding per tooth was registered. That means that one tooth could display a cavitated or an initial carious lesion but not both.

The other secondary end point was the difference in the incidence of total carious teeth (ΔTCT (= G_{2-4} + $d_{3/4}$mft)). Total carious teeth were calculated as a weighted sum score according to the following weights: G_2: 1 point; G_3: 2 points; G_4: 3 points; $d_{3/4}$t and ft: 4 points; tooth with pulpitis, ulcer, fistula, or abscess due to caries: 5 points; and missing tooth (mt): 6 points.

Safety End Point

For quality control, a fluoride concentration measurement of the table salt was performed as a safety end point at t_0, $t_{0\,+\,6\text{ mths}}$, and $t_{0\,+\,12\text{ mths}} = t_1$. For this purpose, packages with fluoridated salt which were provided for the study were randomly selected. Measurements were executed using an Orion Ionplus Fluoride Electrode (Thermo Electron, Beverly, MA, USA) after standardized calibration for low-level measurement. The analysis was undertaken in triplicate per sample, and a mean was calculated for each measurement point. The threshold limit value was set at 0.1 ppm F^-.

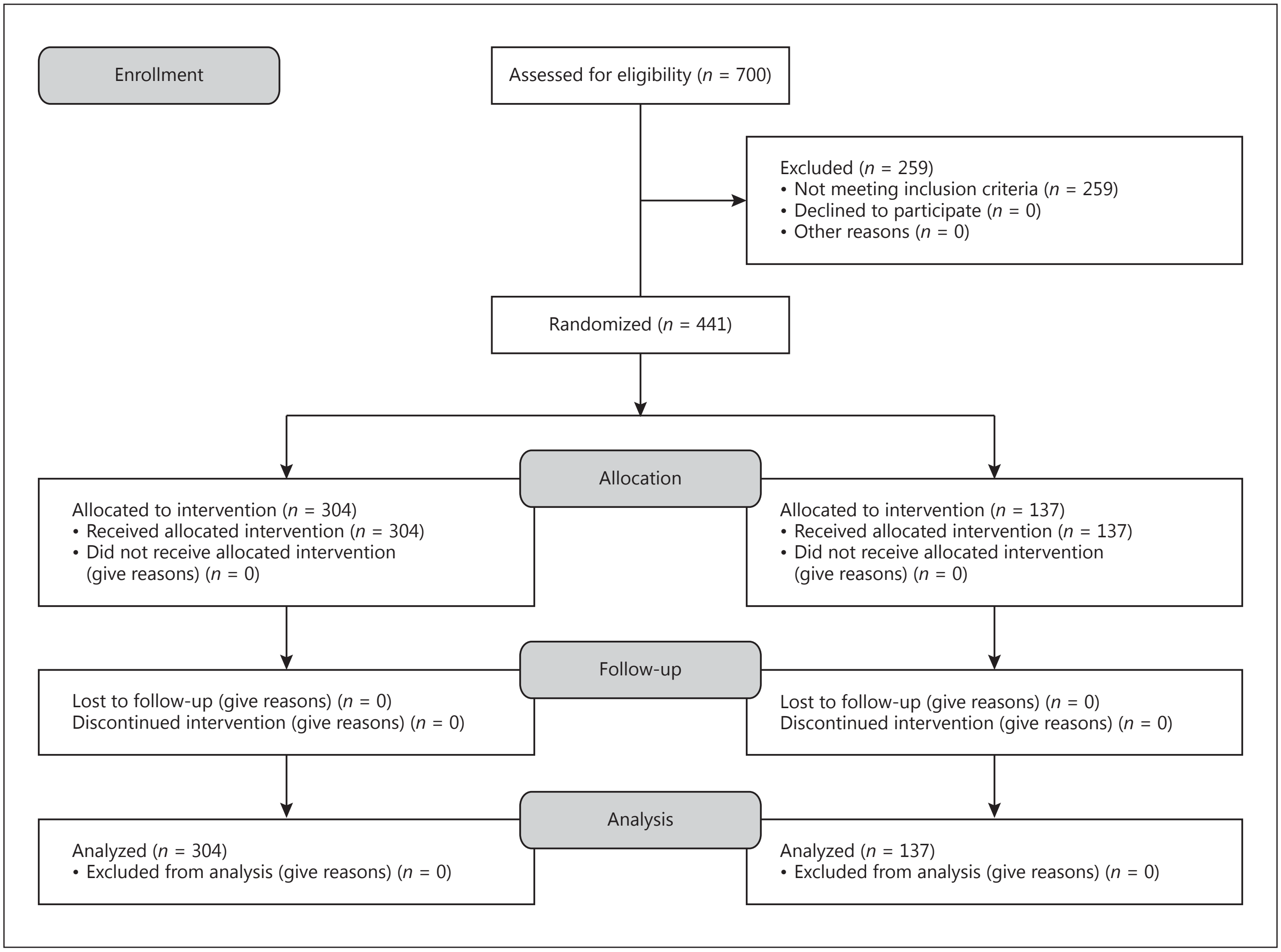

Fig. 1. Flowchart of the participants throughout the study.

Participants and Investigators

Participants were screened, recruited, and included in the study at 2 public preschools in Brikama, West Coast Region, The Gambia, in March 2012. As The Gambia is part of the Commonwealth since 1965, the (pre-)school system is harmonized throughout the country according to British example. Brikama is the administrative center of the most populated West Coast Region of the country. Therefore, preschools were selected for representative reasons of the urban area. The screening and dental examinations took place during regular teaching time in an affiliated dental station. Two investigation teams performed the study-related examinations. A team consisted of two dentists of which one was the clinical investigator, and the other served as the study nurse. All were equally calibrated in clinical dental caries screening. Interexaminer Cohen's reliability K was 0.82 [Cohen, 1960] for cavitated carious lesions, indicating an almost perfect match against the expert (R.A.J.) [Landis and Koch, 1977]. Since the population which was used for calibration showed only a small number of initial lesions, its diagnosis was further checked by using clinical pictures. Interexaminer reliability was calculated only for the primary study end point.

Randomization and Allocation Concealment

As the intervention procedure was bound to the communal preschool feeding, an individual randomization of subjects to the study arms was not feasible. Instead, one preschool was chosen for intervention and the other preschool served as control. The assortment of intervention was performed according to a random selection (envelope method) by a person who apart from this was not involved in the study (L.G.W.). All preschool children meeting the inclusion and exclusion criteria were primarily allocated to the test group and the control group, respectively.

Interventions

Natural fluoride availability in the Gambian West Coast Region had been determined in advance of this interventional study to evaluate general fluoride availability [Jordan et al., 2008a]. In the study region, the fluoride concentration in drinking water was determined to be 0.1 mg/L. In this region, traditional oral hygiene for children does not comprise (fluoride) toothpastes until religious maturity at the age of about 12 years. Instead, children's traditional oral hygiene measures consist of wiping out the oral cavity with a slurry mixture of ashes and sand [Jordan et al., 2008b].

The study-related intervention of administration of fluoridated table salt (MarkenJodSalz + Fluorid; Südwestdeutsche Salzwerke AG, Heilbronn, Germany) was organized during once-daily communal preschool feeding. According to the manufacturer's declaration, the fluoride concentration of the fluoridated table salt was 250 mg/kg. The central preschool kitchen was instructed to flavor the meals with a calculated amount of fluoridated table salt. The amount was set with 0.4 mg fluoride per capita per day for a period of 12 months. The study intervention period was executed between September 2012 and August 2013. The calculation for the total flavoring table salt amount was as follows:

- Number of subjects in the intervention preschool, including subjects not included in the study but taking part in the communal preschool feeding ($n = 450$).
- Fluoride concentration of fluoridated table salt: 25 mg F^- per 100 g salt.
- In total, 720 g of fluoridated table salt daily for the preparation of the communal preschool feeding, i.e., 1.6 g of fluoridated table salt per capita per day, which complied with recent World Health Organization (WHO) recommendations of salt intake [WHO, 2012].

Meals of the control group were prepared without fluoridated table salt. Before starting the intervention, all subjects received a dental examination at t_0. Teeth were cleaned with an electric toothbrush (Vitality precision clean; Oral-B, Schwalbach, Germany) before inspection without using toothpaste. Teeth were then dried with cotton rolls (Cotton rolls for kids; Roeko, Langenau, Germany) and hand-bellows (Delamax, Berlin, Germany). Dental caries inspection was performed visually with the aid of dental mirrors and blunt probes in natural light under sun protection according to recent recommendation for epidemiological field studies [WHO, 2013]. Since complete plaque removal was checked after toothbrushing, white spots could be reliably detected. They were classified as initial carious lesions only if present at typical predilection sites. With respect to available field hygiene measures, disposable dental instruments were used (Nordenta, Hamburg, Germany). After completion of the intervention, all subjects were dentally examined again at t_1 in exactly the same manner as at t_0.

Study Settings

Subjects of the test group were preschool children at the "Kindergarten Wattenscheid in Gambia", Brikama-Kabafita, West Coast Region, The Gambia. Subjects of the control group were preschool children at the "Kindergarten Bottrop in Gambia", Brikama, West Coast Region, The Gambia.

Study Hypothesis

We used a null hypothesis (H_0), assuming no statistical difference in $\Delta d_{3/4}$mft at t_1 between the test and the control group.

Statistical Analysis

Demographic data were compared as intergroup comparison using the Wilcoxon rank-sum test with $p < 0.05$ for statistical significance. Analyses of the study end points were performed using 95% confidence intervals. IBM SPSS software (version 21; International Business Machines Corp, Armonk, NY, USA) was used for computing statistical analysis.

Table 1. Demographic characteristics of the subjects in the test and control groups at t_0

	Test group	Control group
Mean age, years	4.7[a]	4.9[a]
Female, *n* (%)	184 (60.5)[b]	90 (65.7)[b]
Male, *n* (%)	120 (39.5)[b]	47 (34.3)[b]
Total, *n*	304	137

[a] Intergroup comparison with $p = 0.04$. [b] Intergroup comparison with $p = 0.3$.

Results

Three hundred and four eligible subjects were recruited and allocated to the test group according to the study protocol, and 137 eligible subjects were recruited and allocated to the control group. There was no protocol deviation during the intervention and all subjects finished the study (Fig. 1). Statistical analysis was therefore intention-to-treat. Demographic data of the subjects at t_0 are presented in Table 1.

In terms of the primary study end point ($d_{3/4}$t), 33.0% were caries-free in the test group and 25.9% were caries-free in the control group at t_0. Baseline caries experience in the test and control groups was 3.35 and 2.74 $d_{3/4}$mf teeth, respectively, and 4.65 and 5.41 $G_{2–4}$ teeth with white spot lesions, respectively. Weighted total carious teeth (TCT index) were 23.95 in the test group and 23.26 in the control group at baseline (Table 2); 26.7% were caries-free in the test group and 16,8% were caries-free in the control group at t_1. Postintervention caries experience in the test and the control group was 4.63 and 6.57 $d_{3/4}$mf teeth, respectively, and 8.14 and 7.70 $G_{2–4}$ teeth with white spot lesions, respectively. Weighted total carious teeth were 36.80 in the test group and 47.74 in the control group at t_1 (Table 3).

Primary End Point

The mean caries incidence per person was 1.29 $d_{3/4}$mf teeth at t_1 in the test group and 3.83 $d_{3/4}$mf teeth in the control group. As the 95% confidence intervals between the test and the control group did not overlap, the difference in caries incidence was found to be statistically sig-

Table 2. Caries experience in the test and control groups at t_0 (primary and secondary study end points)

Index (t_0)	Test group	Control group
$d_{3/4}mft^a$	3.35 (2.83; 3.86)	2.74 (1.76; 3.72)
$G_{2-4}{}^b$	4.65 (4.17; 5.14)	5.41 (4.33; 6.49)
TCT^c	23.95 (21.51; 26.39)	23.26 (18.14; 28.39)

Data are presented as mean values (95% CI). [a] $d_{3/4}$, decayed with cavitation into dentine; m, missing; f, filled; t, teeth, according to WHO [2013]. [b] G_{2-4}, teeth with white spot lesions from slight white spot formation (2) to white spot formation with cavitation into enamel (4) according to Gorelick et al. [1982]. [c] TCT, weighted sum score according to the following weights: G_2, 1 point; G_3, 2 points; G_4, 3 points; $d_{3/4}f$, 4 points; tooth with pulpitis, ulcer, fistula, or abscess due to caries, 5 points; m, 6 points.

nificant. After 12 months, 2.54 teeth could be prevented from caries by fluoridated salt communal preschool feeding, resulting in a prevented fraction of 66.3% (Table 4). The relative risk for developing dentine caries was reduced by 22 percentage points in the test group as compared to the control group (Table 5).

Secondary End Points

At t_1, the mean incidence of teeth with white spot lesions per person, including grades G_{2-4} of the Gorelick index, was 3.48 in the test group and 2.28 in the control group. As the 95% confidence intervals between the test and the control group were overlapping, the difference in the incidence of white spot lesions was found to be not statistically significant (Table 4).

The incidence of total carious teeth in the test group as measured by the TCT index was 34.70 at t_1, while that in the control group was 38.80. Again, as the 95% confidence intervals between the test and the control group were overlapping, the difference in the incidence of weighted total carious teeth was found to be not statistically significant (Table 4).

Safety End Point

The mean fluoride concentration of the table salt used was 261 mg/kg F^- at t_0, 250 mg/kg F^- at $t_{0+6\,mths}$, and 244 mg/kg F^- at t_1.

A post hoc power calculation of the primary study end point revealed a study power of 99.9% (tails: 2; effect size: 0.67 [mean test group: 1.29; mean control group: 3.83; SD control group: 3.00]; alpha error: 0.05; sample size test group: 304; sample size control group: 137) [Faul et al., 2007].

Table 3. Caries experience in the test and control groups at t_1 (primary and secondary study end points)

Index (t_1)	Test group	Control group
$d_{3/4}mft^a$	4.63 (4.04; 5.23)	6.57 (5.52; 7.61)
$G_{2\_4}{}^b$	8.14 (7.45; 8.83)	7.70 (6.56; 8.83)
TCT^c	36.80 (34.10; 39.50)	47.74 (42.78; 52.70)

Data are presented as mean values (95% CI). See Table 2 for explanation of superscript letters.

Table 4. Caries incidence in the test and control groups (primary and secondary study end points)

Index (t_1--t_0)	Test group	Control group
$\Delta d_{3/4}mft^{a,*}$	1.29 (0.96; 1.62)	3.83 (2.94; 4.72)
$\Delta G_{2-4}{}^{b,\#}$	3.48 (2.70; 4.27)	2.28 (0.62; 3.94)
$\Delta TCL^{c,\#}$	34.70 (31.80; 37.60)	38.80 (32.84; 44.77)

Data are presented as mean values (95% CI). See Table 2 for explanation of superscript letters. * Primary study end point. # Secondary study end points.

Table 5. Proportions (%) of dentine caries-free individuals in the test and control groups at t_0 and t_1

Index	Test group	Control group	RR (95% CI)
$d_{3/4}$ (t_0)	33.0	25.9	0.90 (0.80; 1.04)
$d_{3/4}$ (t_1)	26.7	16.8	0.88 (0.79; 1.01)

$d_{3/4}$, decayed with cavitation into dentine; RR, relative risk; 95% CI, 95% confidence intervals.

Discussion

In the present study, the prevented fraction of cavities was 66.3% ($d_{3/4}$mf teeth 1.29 vs. 3.83). This is in accordance with findings of Tóth [1973], who found a prevented fraction of 53% in 4- to 6-year-old Hungarian children 10 years after the introduction of fluoridated salt when compared to a control group. The prevented fraction in the Hungarian study in 7- to 11-year-olds was 48%, and 49% in 12- to 14-year-olds.

An age group that was also comparable to that of the present study was examined in a retrospective study in a socially deprived area in Clermont-Ferrand (France). In a univariate analysis, the 4- to 5-year-old children whose parents reported using fluoridated salt showed a 29% lower caries experience than the children who did not use it (dt 1.11 vs. 1.57). However, a greater part of the population also consumed other fluoride products such as toothpaste and fluoride supplements (from 0 to 2 years of age) and brushed their teeth regularly [Tubert-Jeannin et al., 2009]. Therefore, the data from Clermont-Ferrand are not comparable to the present data from The Gambia, where almost no background fluoridation was present.

Wennhall et al. [2014] presented another prospective intervention study assessing fluoridated salt in 12- to 14-year-old children. In contrast to our study, fluoridated table salt did not reduce the number of new caries lesions or slow down the proximal progression rate after 2 years. Beside some methodological differences, fluoridated salt was offered by table salt jars during communal school meals and by free supply in the homes. The authors stated a lack of consistent compliance and a high dropout rate. Additionally, the schoolchildren were advised to brush their teeth twice daily with fluoride toothpaste. The results of both prospective studies are barely comparable, which might explain the contrary outcomes.

Caries-preventive effects from salt fluoridation are also reported from other countries. In Mexico, a caries-preventive effect of 43.7% (DMFT 2.47 vs. 4.39) was found in 12-year-olds after 9 years of salt fluoridation (250 mg F^-/kg) in two consecutive cross-sectional studies [Irigoyen and Sánchez-Hinojosa, 2000]. A similar study from Jamaica showed a caries-preventive effect of 83.9% in 12-year-olds (DMFT 1.08 vs. 6.72) after the consumption of fluoridated salt (250 mg F^-/kg) for 8 years [Estupiñán-Day et al., 2001]. Since the studies from both Mexico and Jamaica were consecutive cross-sectional studies, effects other than salt fluoridation might have contributed to the caries reduction. An epidemiological study on 9-year-olds in France showed a caries reduction in deciduous teeth of 35.5% (dft 0.91 vs. 1.41) for those children who had consumed fluoridated salt from the age of 5–6 years in comparison to those who had not. Since the number of children analyzed was too small, no significant difference could be found for permanent teeth [Fabien et al., 1996].

In their meta-analysis, Yengopal et al. [2010] showed a mean caries prevention of 0.98 DMFT in 6- to 8-year-olds, 2.13 DMFT in 9- to 12-year-olds, and 4.22 DMFT in 13- to 15-year-olds. No prevented fraction was reported. Only comparative studies (evidence level III-2 and III-3) could be included in this analysis, since to date no randomized controlled trials are available for the effect of fluoridated salt. Based on this fact, Espelid [2009] analyzed the effect of fluoridated salt in his literature review and stated that "In particular new research is needed concerning possible caries-preventive effects of fluoridated milk and salt."

As shown by Björnström et al. [2004], the consumption of popcorn prepared with table salt containing 250 mg F^-/kg resulted in a 16-fold increase of the fluoride concentration in saliva (from 0.021 to 0.338 mg/L F^-) and in a 3-fold increase of the fluoride concentration in supragingival plaque (from 4.0 to 12.2 mg F^-/kg) after 30 min. In saliva, the concentration decreased rapidly but still remained elevated after 120 min (0.051 mg F^-/kg). In plaque, the fluoride concentration further accumulated after 30 min and reached the highest level after 120 min (20.6 mg F^-/kg) when the observation stopped. It might be speculated that the fluoride accumulation in plaque is more important for caries prevention than its presence in saliva because a plaque-covered tooth surface is where caries can occur. Bearing this in mind, it seems important that the fluoride concentration is highly elevated for 2 h after the consumption of fluoridated salt. The popcorn was prepared with 6.0 g of salt, resulting in an average amount of 1.5 mg of fluoride. In the present study, only 0.4 mg of fluoride was ingested per subject per day. However, the volunteers in the popcorn study were adults (21–27 years of age), and therefore the ingestion per body weight might have been even higher in the present study. Nevertheless, since fluoride acts primarily locally and not systemically, it is unclear whether this ratio is of any importance [Limeback, 1999]. More important might be the prevailing time of the food prepared with fluoridated salt in the oral cavity. In the popcorn study, the volunteers were instructed to eat the snack within 30 min. This is comparable to the time that the children in the test kindergarten needed to consume their lunch, which was the only meal prepared with the fluoridated salt.

In vitro data have already shown that low fluoride concentrations of 0.1 mg/L result in a caries-preventive effect [Amjad and Nancollas, 1979]. These concentrations were considerably exceeded in saliva and plaque in the popcorn study and stayed elevated for a prolonged period. Other studies confirm that fluoride concentrations exceed 0.1 mg/L in saliva [Macpherson and Stephen, 2001] or saliva and plaque [Kaiser et al., 2006] after the consumption of food which was prepared with table salt containing 250 ppm fluoride. The consumption of fluoridated salt results in a systemic fluoride intake. In order to prevent fluorosis, it should not be used when water fluoridation is available. In combination with the use of fluoride toothpaste, there is no elevated risk of developing dental fluorosis. In comparison to water fluoridation, the fluoridated salt has advantages and disadvantages. One disadvantage is that it does not reach everyone. On the other hand, as compared to water fluoridation, fluoridated salt allows for the freedom of choice whether to use it or not.

In the present study, 2.54 cavitated teeth were prevented in the test group in comparison to the control group ($d_{3/4}$mf teeth 1.29 vs. 3.83). However, the increment of white spot lesions was higher in the test than in the control group ($G_{2–4}$ 3.48 vs. 2.28) after 12 months. When taking both results into account, it must be argued that the 2.54 cavitated teeth were obviously not totally prevented, but in part seemed to be arrested at an earlier caries stadium. In fact, when performing a net calculation, only 1.34 cavitated teeth were completely prevented (sound instead of cavitated). An additional 1.2 teeth were arrested at the incipient stage, though these were not cavitated lesions (white spot lesions instead of cavitation). This consideration suggests that fluoride might not completely stop the caries process but rather slow down its progression.

In the present study, the Gorelick index [Gorelick et al., 1982] was used to assess initial enamel lesions. This very specific index with 3 categories was found to be suitable to quantify these lesions under the field conditions prevailing in The Gambia as the ICDAS and ICCMS epidemiology tool was not yet published when this study started in 2012. Other more often used indices like the ICDAS [Pitts, 2004] could not be used due to the absence of technical infrastructure such as artificial light and compressed air.

No reliability test for the diagnosis of initial enamel lesions was performed, and the clinical circumstances were not optimal (examination under field conditions). Therefore, an underestimation of initial enamel lesions cannot be excluded. However, since the circumstances were the same in both groups, this should not have influenced the prevented fraction for this kind of lesion. It must be kept in mind that the primary study end point was caries incidence as measured by $d_{3/4}$mft, e.g., cavitated carious lesions.

In order to describe the total caries incidence more clearly in one value, a novel total caries teeth index (TCT index) was introduced as the third study end point. This index was calculated as a weighted sum score, with small initial carious lesions (G_2) accounting for 1 point and the worst consequence of caries (missing tooth) accounting for 6 points. The new index was built based on Chosack's caries severity index for primary teeth [Chosack, 1986].

The strength of the present study is that, to our knowledge, this trial is the first controlled interventional study to assess the efficacy of fluoridated table salt in an infrastructural environment without further fluoride background. It allows, therefore, for the calculation of a net anticaries effect of fluoridated salt. Another strength is that the effect of cooking with fluoridated salt could be investigated without noteworthy background fluoridation. However, this is also a weakness of the study since the results cannot be transferred to more developed economies as described by the country classification of the United Nations (UN), where fluoride products are available and used in many forms. In the UN classification, The Gambia is described as a developing economy. While malnutrition has a high prevalence among preschool children in rural regions of The Gambia [FAO, 2010], no malnutrition is observed in the urban region where the present study took place. The diet of the included children consists of rice, chicken, vegetables, and fruits, which was also the composition of the daily lunch prepared in the kindergartens. Overall, dietary habits should not have influenced the study outcome since there was no obvious difference between the test and the control kindergartens. Breastfeeding, as another possible confounder, was not assessed in that study but usually stops before the age of 3 years.

A methodological weakness is that the 441 participants could not be individually randomized. This was due to logistic reasons. It was not possible to individually attribute meals cooked with or without fluoridated salt, but it was possible to attribute the 2 included kindergartens in total to one of the two groups. Since the 2 kindergartens had different sizes, the test (n = 304) and the control (n = 137) group were very unequal. However, since the results for the primary end point ($\Delta d_{3/4}$mft) showed a statistically significant difference and a clinical relevance, this unequal distribution seems to be acceptable. The limitations of the randomization process also affected the examiner blindness. Since the test and the control group were represented by 1 public preschool each, it was not possible to guarantee examiner blindness. In the preschool that received fluoridated salt, the program was very popular, and therefore it could not be arranged that no one talked to the examiners nor was it possible to hide the pallets with the salt packages from the examiners who lived in the housing area of the preschool. Although the effect of social desirability is well known, there are no data available to allow a quantification of the bias arising from this phenomenon when examiner blinding is not possible. However, it must be assumed that some overestimation of the caries-preventive effect of the fluoridated salt cannot be excluded.

Instead of using a composed caries index, incipient and cavitated carious lesions were separately reported. This was done for two reasons. First, complete calibration was only possible for established lesions since the population which was used for calibration showed a small number of initial lesions only. A more intensive calibration was therefore carried out on the basis of clinical pictures. Second, initial lesions might not end up with invasive treatment. However, differentiation should be made between lesions that require invasive treatment and those that do not. Therefore, it was decided to define cavitated lesions as the primary study end point and incipient lesions as the secondary end point.

In view of the primary end point of the study (dentinal caries), the observation period of 1 year was very short. However, from an earlier study it was known that caries was developing very fast in that region of The Gambia and that dentinal decay could already be observed after 1 year [Lietz and Gängler, 2002]. In a recent study by Bernabé et al. [2016], a linear dose-response relationship between sugar intake and caries development was shown, and there is no doubt that the reason for the high caries increment observed in the present study was caused by frequent sugar intake. However, a reduction of sugar intake in the observed community does not seem to be realistic. Therefore, caries prevention by fluoride administration is an alternative. The study of Bernabé et al. [2016] demonstrated that fluoride reduced the association between sugar intake and caries.

From a research perspective, a randomized controlled trial in a high-income country would be desirable in order to know the effect of preparing food with fluoridated salt where fluoridated water is not available. It is known that a population-based preventive measure has only a limited value if a high level of oral health is already reached [Jones et al., 1997]. However, even in high-income countries, there is still a part of the population with a high caries burden, and since fluoridated salt is cheap and easily accessible to all people, it has the potential to be an effective public health measure even in high-income countries.

It is known that sodium chloride is an essential mineral source for humans but may cause cardiovascular diseases if consumed in too high amounts [Mozaffarian et al., 2014]. The WHO recommends a maximum daily intake of 5 g [WHO, 2012]. In the present study, the daily amount of ingested sodium chloride was 1.6 g for preschool children, which complies with the WHO recommendations. However, the concept of salt fluoridation is not bound to a high intake of sodium fluoride. The only reason for using sodium chloride as a fluoride carrier is the fact that it is consumed within narrow confines all over the world. If the salt consumption lowers, the fluoride concentration could be elevated to keep the same caries-preventive effect. Finally, salt fluoridation is recommended by the WHO where water fluoridation is not feasible for technical, financial, or sociocultural reasons, which is the case in many developing countries like The Gambia [Petersen and Ogawa, 2016].

In conclusion, the use of fluoridated salt to prepare the communal feeding of preschool children in The Gambia resulted in a considerable caries-preventive effect and should therefore be promoted, at least in populations with a high caries burden.

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Author Contributions

The authors made the following contributions to this manuscript: R.A.J. was principal investigator and wrote the manuscript. A.S. wrote the manuscript. A.C.B. was local tutor and organized the field work. S.P. developed the study protocol and carried out the data processing. E.N. was responsible for table salt quality check and fluoride measurements. L.G.W. was local supervisor and responsible for the allocation concealment. S.Z. was responsible for quality assurance and writing the manuscript.

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