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The effectiveness of using the toothpastes with a different fluoride content on the early childhood caries (ECC) reduction – systematic review

Skuteczność stosowania past do zębów o różnej zawartości fluoru w redukcji próchnicy wczesnego dzieciństwa (ECC)– przegląd systematyczny

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Keywords

dental caries, early childhood caries, fluoride, toothpaste

Summary

Introduction. Scientific evidence indicates the anti-caries benefits of using the 1000-1500 ppm fluoride toothpastes compared to ≤ 600 ppm in permanent dentition, while there is a small number of studies regarding effectiveness of fluoride toothpastes in children with primary dentition.
Aim. The purpose of this study was to present the results of a systematic review of the literature on the effectiveness of early childhood caries (ECC) prophylaxis using low and standard toothpastes, in the age group of 1-6 years.
Material and methods. The methodology was in line with the guidelines from PRISMA. Article search was performed independently by two reviewers, in six electronic databases. Narrative analysis of the mean caries increment was performed to assess the effect of fluoride toothpaste on dmft and dmfs indices.
Results. Nine studies out of 136 originally identified articles were included in the systematic review. The results of the analysis comparing effect of 1000-1500 versus ≤ 600 ppm fluoride toothpastes for tooth (dmft) and surface level (dmfs) confirmed the evidence of association between level of fluoride content and ECC increment.
Conclusions. This systematic review, despite some limitations, indicate a greater efficacy of toothpastes containing 1000-1500 ppm F compared to those with low fluorine content in the prevention of ECC.

Słowa kluczowe

próchnica zębów, próchnica wczesnego dzieciństwa, fluorek, pasta do zębów

Streszczenie

Wstęp. Dowody naukowe wskazują na większe korzyści przeciwpróchnicowego działania wynikające ze stosowania past do zębów zawierających 1000-1500 ppm fluoru w porównaniu z pastami o zawartości fluoru ≤ 600 ppm w uzębieniu stałym, natomiast istnieje niewielka liczba badań dotyczących skuteczności past z fluorem u dzieci z uzębieniem mlecznym.

Cel. Celem niniejszej pracy było przedstawienie wyników przeglądu systematycznego literatury na temat skuteczności profilaktyki próchnicy wczesnego dzieciństwa (ECC) przy użyciu past do zębów o standardowej zawartości fluoru, w grupie wiekowej 1-6 lat.
Materiał i metody. Metodologia przeglądu jest zgodna z wytycznymi PRISMA. Wyszukiwanie artykułów zostało przeprowadzone niezależnie przez dwóch recenzentów w sześciu elektronicznych bazach danych. Przeprowadzono analizę narracyjną średniego przyrostu próchnicy w celu oceny wpływu pasty z fluorem na wskaźniki puwz i puwp.
Wyniki. Dziewięć badań spośród 136 początkowo zidentyfikowanych zostało włączonych do przeglądu systematycznego. Wyniki analizy porównującej efekt stosowania past do zębów z 1000-1500 ppm fluoru w stosunku do tych zawierających ≤ 600 ppm na poziom wskaźnika zębowego (puwz) i powierzchniowego (puwp) potwierdziły dowody związku między poziomem zawartości fluorków a przyrostem ECC.
Wnioski. Ten przegląd systematyczny, pomimo pewnych ograniczeń, wskazuje na większą skuteczność past do zębów zawierających 1000-1500 ppm F w porównaniu do tych o niskiej zawartości fluoru w zapobieganiu ECC.

Introduction

According to the modified definition, Early Childhood Caries (ECC) is the presence of one or more decayed (non cavitated or cavitated lesions), missing (due to caries) or filled tooth surfaces in any primary tooth in a child under the age of six (1).

WHO (World Health Organization) data from 2015 show that, ECC is one of the most widespread diseases worldwide among children under 6 years of age (1). In Poland, it is found in over 76% of preschool children, including about 54% of 3-year-olds (2).

WHO and FDI (World Dental Federation) recommend regular monitoring of children's oral health and control of the effectiveness of the implemented programs of health promotion and prevention of oral diseases in special risk groups, i.e. children and pregnant women (1, 3).

The complex pathomechanism of caries is a classic example of interactions between the external environment (frequent supply of large amounts of sugars), microorganisms (dysbiosis of the oral bacterial flora, contributing to the dominance of cariogenic species) and a susceptible host (especially when presence of enamel defects) (4).

Proper nutrition, oral hygiene and the use of preventive agents containing fluorides are the pillars for the caries prevention (4). Fluorine affects the original mineralization of the organic matrix and pre-eruptive maturation of tooth enamel (5).

The main role of fluorine in caries control is its post-eruptive action based on inhibiting demineralization and supporting remineralization, with different effects depending on its concentration. Constant presence of fluoride in low concentrations (< 50 ppm), resulting from the use of standard fluoride toothpastes enables the reposition of mineral compounds lost during the repeated acid attacks resulting in the formation of less susceptible crystals with a fluorapatite-like coating (formation of fluorohydroxyapatite) (5). The use of fluoride gels, foams and varnishes delivers a higher fluorine ion concentrations (> 100 ppm), which additionally ensures the formation of calcium fluoride (CaF_2) which is a reservoir of fluoride ions released during the attack of bacterial acids on the tooth (5). Fluorine is also involved in the reduction of the impact of caries-forming bacteria by: the reduction of acid production, reduction of bacterial plaque deposition on the tooth surface, inhibition of carbohydrate metabolism in bacterial cells (5).

There is no definite consensus on the recommended age of 1000 ppm fluoride toothpaste introduction for 1-6 years old children related to the risk of fluorosis.

WHO, FDI (World Dental Federation), AAPD (American Academy of Pediatric Dentistry), AAP (American Academy of Pediatrics), ADA (American Dental Association) and EAPD (European Academy of Pediatric Dentistry) (similarly to Polish experts) recommend for young children, brushing their teeth twice a day using a toothpaste containing 1000 ppm of fluoride from the moment of the eruption of the first primary tooth until the 6 years of age (3, 6-8). Trace/grain of rice amounts of the toothpaste is recommended to the age of 3 years (2 years – EAPD), and then the size of a peas to the age of 6 years (3, 6-8). On the other hand, CDC (United States Health and Human Services Centers for Disease Control and Prevention) recommends the use of toothpastes containing 1000 ppm of fluorine only from the age of 2 and previously – a paste without fluorine (CDC) (9). The use the toothpastes containing 1000 ppm F from the moment of the first tooth eruption is recommended in some countries in cases of high risk of caries, while in all children in the others (1).

The above recommendations are based on scientific evidence that indicates the benefits of using the toothpastes with a higher content of fluoride (1000-1500 ppm) compared to those with its lower content (≤ 600 ppm) mainly in permanent dentition. This is the result of a small number of studies regarding effectiveness of low and standard fluoride content toothpastes in children with primary dentition (10-13).

Aim

Because the aim of this investigation was to assess the effectiveness of early childhood caries prophylaxis using toothpastes with fluoride concentrations ≤ 600 ppm and ≥ 1000 ppm, we focus on group under-6-year-olds.

Material and methods

This systematic review aims to answer the following research question: Which toothpastes, with fluoride concentrations ≤ 600 ppm or 1000-1500 ppm, are more effective in ECC reduction?

The methodology of this systematic review was in line with the guidelines from PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) for conducting this type of analysis, and the recommended individual stages were followed (14).

Selection criteria

Randomized and cluster-randomized clinical trials assessing the effectiveness of fluoride toothpastes in caries reduction in young children, were included. The intervention had to involve a toothpaste with a certain concentration of fluorine (≤ 600 ppm or 1000-1500 ppm) in the test group compared to the control group not using such a toothpaste, using a toothpaste with a different fluorine concentration or a non-fluoride toothpaste, or using a placebo. There were no restrictions regarding fluoride agent, abrasive system and pH of toothpaste, as well as the presence or absence of fluoridated water. Accepted studies included those in which the primary outcome was caries increment in primary dentition, compared to the initial state, measured by the change in the average values of the dmft/dmfs indices which are the sum of the number of decayed, missing and filled (due to caries), primary teeth or tooth surfaces, divided by the number of participants. The criteria for including the studies were also the age (1-6 years) and good health (no chronic systemic diseases and allergies) of the participants (regardless of initial level of caries), as well as minimum study duration of 12 months.

Systematic and narrative reviews were excluded.

Search strategy

A many-sided search for appropriate articles from the last four decades was based on a search strategy included controlled vocabulary and free terms and was performed (up to and including September 2020, updated until February 2021) for each of six electronic databases: MEDLINE via PubMed, EMBASE, The Cochrane Register of Controlled Trials (CENTRAL/CCTR), WEB OF SCIENCE, LILACS and SCOPUS.

The used MeSH terms were: ”dental caries”, “early childhood caries”, “fluoride”, “toothpaste”, and “prevention.” The following strategy was developed for MEDLINE and adapted for the other databases: (“fluorides” [MeSH Terms] OR “fluorides” [All Fields] OR “fluoride” [All Fields]) AND (“toothpastes” [MeSH Terms] OR “toothpastes” [All Fields] OR “toothpaste” [All Fields]) AND (“dental caries” [MeSH Terms] OR “dental” [All Fields] AND “caries” [All Fields]) OR (“dental caries” [All Fields]) AND (“prevention and control” [Subheading] OR “prevention” [All Fields] AND “control” [All Fields]) OR “prevention and control” [All Fields] OR “prevention” [All Fields]), (“toothpastes” [MeSH Terms] OR “toothpastes” [All Fields] OR “toothpaste” [All Fields]) AND early ([All Fields] AND “Childhood” [Journal] OR “childhood” [All Fields]) AND (“dental caries” [MeSH Terms]) OR (“dental” [All Fields] AND “caries” [All Fields]) OR “dental caries” ([All Fields] OR “caries” [All Fields]) AND (“prevention and control” [Subheading] OR (“prevention” [All Fields] AND “control” [All Fields]) OR (“prevention and control” [All Fields] OR “prevention” [All Fields]).

No restrictions were placed on the language or date of publication when searching the electronic databases. Additional sources included two international registers of ongoing trials (Current Controlled Trials and Clinical-Trials.gov) and polish national database for dissertation abstracts. Reference lists of accepted papers and previously published systematic and narrative reviews of fluoride toothpastes were screened to detect any trials that met the inclusion criteria.

Two independent examiners (MS, MJK) were carried out handsearching of all articles published in the following dentistry journals: Acta Odontologica Scandinavica, Archives of Oral Biology, British Dental Journal, Caries Research, Community Dental Health, Community Dentistry & Oral Epidemiology, European Archives of Paediatric Dentistry, European Journal of Oral Sciences, International Dental Journal, International Journal of Dentistry, Journal of the American Dental Association, Journal of Clinical Pediatric Dentistry, Journal of Dental Research, Journal of Dentistry for Children, Journal of Public Health Dentistry and Pediatric Dentistry.

Selection of studies and data extraction

All the potentially eligible articles were imported to a reference management system (Mendeley Desktop) to enable identification and removing duplicate studies.

Two researchers independently assessed the titles and abstracts to exclude articles not related to the topic and the selection criteria. Clearly ineligible articles were rejected. For studies that required more information to determine relevance or in cases where abstracts were unavailable, full texts of papers, were obtained.

The same researchers then independently reviewed the full-text version of the remaining articles to assess their eligibility for inclusion. Disagreements among the reviewers were resolved by consensus after consulting a third researcher (AJ). All excluded studies (with the reasons for exclusion) were documented (Appendix).

The trials that met all the inclusion criteria were processed for data extraction. Information were abstracted from the studies using a data extraction form and gather, in the tables, in accordance with the guidelines outlined by the Cochrane Collaboration (14). The data included: characteristics of study (methods, interventions), participants, adverse effects, and main outcomes.

Assessment of risk of bias in included (individual) studies

All studies included in the review were assessed independently for risk of bias, as part of the data extraction process, using The Cochrane Collaboration's tool (15).

The following domains were assessed: random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias) and outcome assessors (detection bias), incomplete outcome data (attrition bias) and selective outcome reporting (reporting bias). Baseline balanced and free of contamination or co-intervention were also assessed. Each domain was classified as having low, high or unclear (uncertain) risk of bias.

Studies were categorized (the overall risk of bias of each study) as being at low (if all domains were at low risk of bias), high that weakens results' confidence (if at least one domain was at high risk of bias), or unclear risk of bias (if at least one domain was at unclear risk of bias).

For this review, possible sources of bias, included: blinding (low risk of bias even if only single blinding of outcome assessors), selective outcome reporting (low risk of bias when the outcomes included caries increment at surface and tooth level), baseline balance (low risk of bias when data showed baseline balance towards age, socioeconomic status and caries levels) and contamination (low risk of bias when solutions to avoid contamination between groups were included).

Data synthesis and analysis

Narrative analysis of the mean caries increment between the test and the control groups, was performed to assess the effect of fluoride toothpaste on the number of decayed, missing owing to caries and filled teeth (dmft) and dental surfaces (dmfs). It was carried out for comparison of low (≤ 600 ppm) and standard (1000-1500 ppm) fluoride toothpastes and for surface and tooth level (tab. 1 and 2).

Results

Search, study selection and characteristics of included studies

Figure 1 shows study identification process in the form of PRISMA flow diagram. After removing duplicates, the electronic search retrieved 1627 records. The search of other (non-electronic) sources as well as for ongoing trials revealed one additional report. The remaining records were screened based on the title, abstract and keywords and 1492 records were eliminated based on improper study design or outcome. 136 reports were considered potentially eligible to the present systematic review and the full-text articles were obtained for further assessment. Nine articles corresponding to nine studies were included in the present systematic review. No additional relevant clinical trial was identified after updating the electronic search in February 2020. Table 1 and 2 show details of included studies (16-24) in short version. Publication years of included studies ranged from 1989 to 2010. 1-6 years old participants of all included trials were brushing teeth with fluoride toothpaste twice a day. This activity was supervised or assisted by preschool/school staff or parents at home in all studies. The oral health education was part of the intervention in seven of them (tab. 1 and 2). The interventions differed across studies; test groups used different fluoride concentrations, whereas control groups received either a placebo or no fluorine toothpastes (tab. 1 and 2). Study duration ranged from 20 to 60 months. Mean baseline dmft/dmfs indices for both groups had similar values in all trials (tab. 1 and 2). The water resources in five studies (20-24) were not fluoridated or the fluoride levels were below the optimal concentration (0.35 ppm). One study (19) reported an optimal level of fluoride in drinking water, while such an information was not provided in another three (16-18). Excluded trials with the reasons of exclusion are available in appendix.

Risk of bias in included studies

The included studies were weighted by risk of bias, but were not selected for analysis (all studies that met inclusion criteria were included in systematic review). Table 3 shows the risk of bias in each of nine studies included in the review, according to seven domains. The most frequent high risk of bias were in the selective reporting domain (21-23) and incomplete outcome data (17, 18), followed by baseline imbalance (23).

Some aspects, such as allocation concealment and sequence generation, have not been reported adequately and therefore were judged as unclear in seven (16-19, 21, 23, 24) and in six (16-18, 21, 23, 24) studies, respectively. Six studies (16-18, 20, 21, 24) have also failed to provide enough information on baseline balance and three studies (18, 20, 21) – on free of contamination. Six studies (16-20, 24) were free of selective outcome reporting and six (16, 19-23) – of incomplete outcome data. The domain considered to have the lowest risk of bias was blinding, uncertain in two (18, 20).

Overall risk of bias

No study was assessed at low risk of bias for all domains (low risk of bias overall). Five studies (17, 18, 21-23) were assessed as being at high risk of bias for at least one domain (high risk of bias overall). Four studies (16, 19, 20, 24) were assessed as being at unclear overall risk of bias (at least one domain judged to be at unclear risk of bias and no domains at high risk of bias).

The overall risk of bias for these nine studies, as a group, is high.

Results of individual (included) studies and synthesis of results

Nine studies, recruiting children between 1 and 6 years of age, evaluated the caries-preventive effect of different

Tab. 1. Characteristics of included studies. Effect of low fluoride toothpastes (< 600 ppm) on ECC increment: surface and tooth index (dmfs/t)

Author, year	Design/ age	Follow up [mos]	Group	n	FTP [ppm]	dmft (mean ± SD)		dmfs (mean ± SD)		Caries outcome	Adverse effect	Risk of bias
						Before	Increment	Before	Increment			
Winter et al. 1989 (16)	RCT/ 2 yrs	36	Test	477	550/no HP	0	1.72 (2.53)	0	2.52 (4.827)	NS	NR	Unclear
			Control	428	1055/no HP	0	1.45 (2.53)	0	2.29 (4.827)			
Sonju-Clasen et al. 1995^ (17)	CRCT/< 7 yrs	22	Test	46	250/no HP	1.0 (2.2)	1.2 (2.2)	2.0 (5.5)	2.9 (5.1)	NS	NR	High
			Control	50	1450/no HP	1.2 (2.8)	0.8 (1.4)	2.4 (6.6)	1.7 (3.2)			
Davies et al. 2002 (20)	RCT/1 yr	48-60	Test	1176	440/HP	0	2.49 (3.16)	ND	ND	NS	NR	Unclear
			Control	1186	No FTP/HP	0	2.57 (3.16)	ND	ND			
Andruske-viciene et al. 2008 (18)	RCT/ 3-7 yrs	36	Test	152	500/HP	1.33 (2.12)	0.77 (0.62)	1.42 (1.85)	0.88 (1.11)	S	NR	High
			Control	133	ND/no HP	1.59 (2.22)	1.41 (0.92)	1.86 (2.77)	1.92 (0.92)			
Vilhena et al. 2010 (19)	RCT/4 yrs	20	Test	250	550/HP	ND	ND	5.24 (5.37)	2.05 (2.79)	NS	NR	Unclear
			Control	270	1100/HP	ND	ND	5.05 (4.89)	2.08 (2.34)			

mean dmft/dmfs index – the average value of the dmft/dmfs index (for a group of examined people) is the sum of the number of teeth (t) or tooth surface (s) with the current carious lesion, the number of teeth removed due to caries (m) and the number of filled teeth (f)

(mean) caries increment (dmft/s) – (average) caries growth measured by the change in the number of teeth/surfaces with caries lost due to caries and filled in compared to the initial state

SD – standard deviations; RCT – randomized control trials; CRCT – cluster randomized controlled trials; FTP – fluoride toothpaste; HP – oral health program; ND – no data; S – significant; NS – no significant; NR – not reported

^effective sample size originally n = 89

Tab. 2. Characteristics of included studies. Effect of 1000-1500 ppm fluoride toothpastes on ECC increment: dmfs/t index

Author, year	Design/age	Follow up [mos]	Group	n	FTP [ppm]	dmft (mean ± SD)		dmfs (mean ± SD)		Caries outcome	Adverse effect	Risk of bias
						Before	Increment	Before	Increment			
Winter et al. 1989 (16)	RCT/2 yrs	36	Test	428	1055/no HP	0	1.45 (2.53)	0	2.29 (4.827)	NS	NR	Unclear
			Control	477	550/no HP	0	1.72 (2.53)	0	2.52 (4.827)			
Sonju-Clasen et al. 1995^ (17)	CRCT/< 7 yrs	22	Test	50	1450/no HP	1.2 (2.8)	0.8 (1.4)	2.4 (6.6)	1.7 (3.2)	NS	NR	High
			Control	46	250/no HP	1.0 (2.2)	1.2 (2.2)	2.0 (5.5)	2.9 (5.1)			
Davies et al. 2002 (20)	RCT/1 yr	48-60	Test	1186	1450/HP	0	2.15 (2.96)	ND	ND	S	NR	Unclear
			Control	1176	No FTP/HP	0	2.57 (3.16)	ND	ND			
You et al. 2002 (21)	RCT/ 3 yrs	24	Test	457	1100/HP	ND	ND	6.24 (8.06)	4.07 (5.30)	S	NR	High
			Control	395	placebo/no HP	ND	ND	6.24 (7.95)	4.85 (6.12)			
Rong et al. 2003 (22)	RCT/ test 2.9 (0.39)* control 3.0 (0.34) yrs*	24	Test	258	1100/HP	2.98 (3.39)	ND	5.24 (7.08)	2.47 (4.09)	S	NR	High
			Control	256	0/no HP	ND	ND	5.96 (7.74)	3.56 (5.30)			
Jackson et al. 2005 (23)	RCT/** 5.63 (5.61-5.66) yrs	21	Test	181	1450/ HP	ND	ND	7.34 (10.54)	2.43 (5.25)	S	NR	High
			Control	189	ND/no HP	ND	ND	5.41 (10.45)	2.76 (5.23)			
Fan et al. 2008^^ (24)	RCT/test 4.23 (0.134)* control 4.19 (0.149) yrs*	24	Test	329	1500/HP	ND	ND	3.54 (5.34)	2.75 (4.33)	S	NR	Unclear
			Control	328	placebo/HP	ND	ND	3.60 (6.07)	4.73 (5.17)			
Vilhena et al. 2010 (19)	RCT/4 yrs	20	Test	270	1100/ HP	ND	ND	5.05 (4.89)	2.08 (2.34)	NS	NR	Unclear
			Control	250	550/ HP	ND	ND	5.24 (5.37)	2.05 (2.79)			

mean dmft/dmfs index – the average value of the dmft/dmfs index (for a group of examined people) is the sum of the number of teeth (t) or tooth surface (s) with the current carious lesion, the number of teeth removed due to caries (m) and the number of filled teeth (f)

(mean) caries increment (dmft/s) – (average) caries growth measured by the change in the number of teeth/surfaces with caries lost due to caries and filled in compared to the initial state

*mean age (SD)

**mean age, years (95% CI)

SD – standard deviations; RCT – randomized control trials controlled trial; CRCT – cluster randomized controlled trials; FTP – fluoride toothpaste; HP – oral health promotion; ND – no data; S – significant; NS – not significant; NR – not reported

^ effective sample size originally n = 89

^^dfs

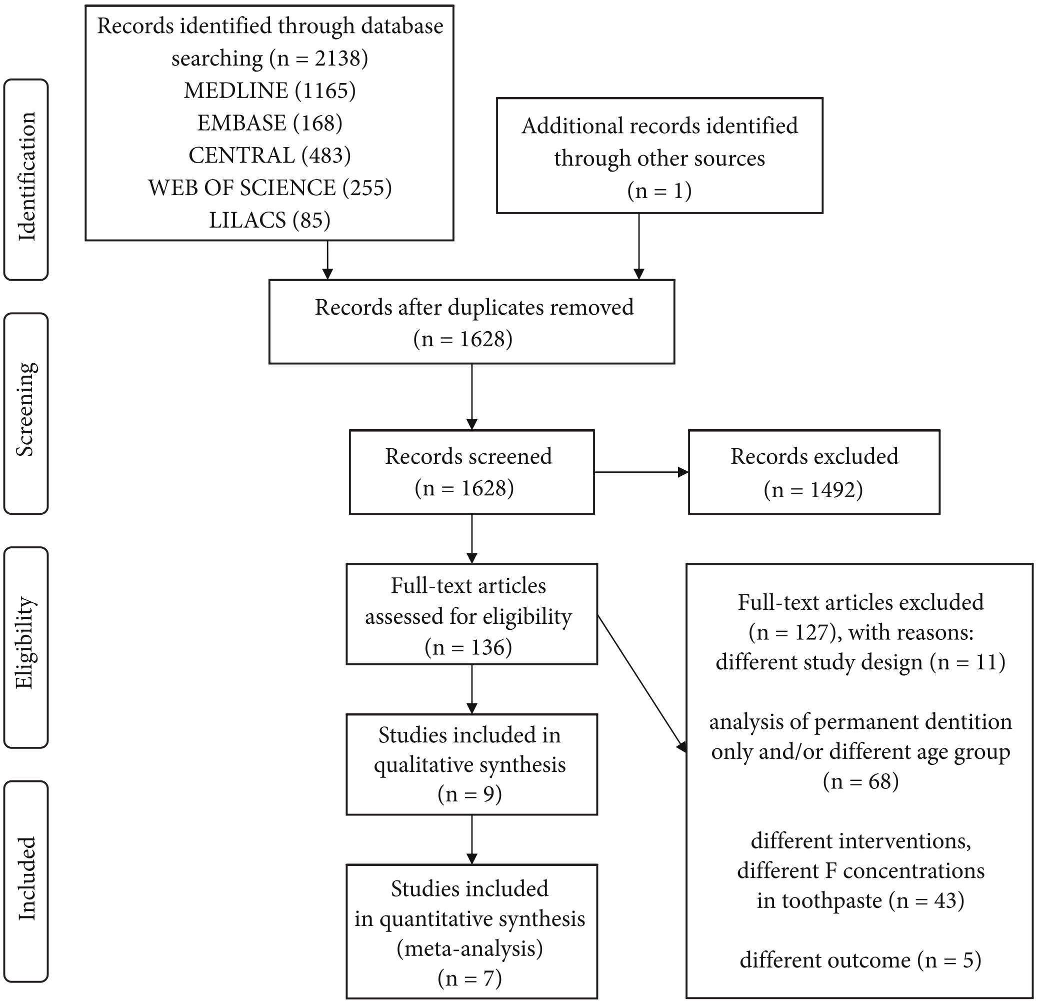

Fig. 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) flow diagram (14)

fluoride concentrations and provided caries increment data expressed as d(m)fs or d(m)ft-rate (tab. 1 and 2). Two studies did not report sufficient information necessary for inclusion in the analysis, because the fluoride concentrations of toothpastes used in control groups were not indicated (18, 23) (tab. 1 and 2). These studies retained in the review for completeness and their results were reported narratively. The analysis was conducted for the effects of low fluoride (≤ 600 ppm) toothpastes in comparison to 1000-1500 ppm of fluoride ones, as well as for dmft and dmfs – caries increment in the primary dentition of young children.

An insignificant trend of a lower prophylactic effectiveness (according to dmfs index) of toothpastes with a fluorine concentration of 1000-1500 ppm in relation to the low fluorine content (≤ 600 ppm) was demonstrated by Vilhena et al. (1100 vs 550 ppm) (tab. 1 and 2) (19).

The study of Sonju-Clasen et al. (17) as well as the study of Winter et al. (16) that compared the effectiveness of the use of toothpastes with low vs. standard fluoride concentration on both; dmft and dmfs indices showed an insignificant higher efficacy of toothpastes containing respectively 1450 ppm compared to 250 ppm of fluoride and 1550 ppm compared to 550 ppm (tab. 1 and 2).

Results of the study by Davies et al. (20) showed statistically significant difference between dmft – caries increment in 1450 ppm fluoride group and control group which did not receive any toothpaste, while the difference between the 440 ppm fluoride group and control group was not significant. Children using low fluoride toothpaste had a significant increase in the main incidence of caries at tooth level compared to standard fluoride toothpaste group. The authors' conclusion was that the toothpaste containing 1450 ppm of fluorine provides a significant clinical benefit for children in high caries risk areas with non-fluoridated drinking water (tab. 1 and 2).

Free studies that reported caries incidence at surface level showed a significant greater effectiveness of a toothpaste containing 1000-1500 ppm of fluoride in caries prophylaxis compared to a non-fluoride toothpaste (22) and to placebo (21, 24) (tab. 2).

Tab. 3. Risk of bias assessment in the included studies

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding (performance bias and detection bias)	Complete outcome data (attrition bias)	Free of selective reporting (reporting bias)	Baseline charac-teristics balanced	Free of contamination or cointervention
Winter et al. 1989	?	?	+	?	+	?	+
Sonju-Clasen et al. 1995	?	?	+	–	+	?	+
Davies et al. 2002	+	+	?	+	+	?	?
You et al. 2002	?	?	+	+	–	?	+
Rong et al. 2003	+	+	+	+	–	+	+
Jackson et al. 2005	?	?	+	+	–	–	?
Andruskevicienie et al. 2008	?	?	?	–	+	?	?
Fan et al. 2008	?	?	+	?	+	?	+
Vilhena et al. 2010	+	?	+	+	+	+	+

(+) Yes

(–) No

(?) Unclear

Additionally we reviewed study by Andruskeviciene et al. (18) confirming the prophylactic effectiveness of the 36-months program of supervised toothbrushing with 500 ppm fluoride toothpaste. The authors showed a statistically significantly smaller increase in caries in the test group participating in the program compared to the control group that did not participate in supervised brushing (and there is no other information about toothpaste used at home). The (mean ± SD) dmft increment in study and control groups were 0.77 (0.62) and 1.41 (0.92) respectively, the dmfs increment in study versus control group – 0.88 (1.11) vs 1.92 (0.92) (tab. 1).

We also reviewed study of Jackson et al. (23) that confirmed the prophylactic effectiveness of the program of supervised toothbrushing with 1450 ppm fluoride toothpaste. The study reported that 5-year-old children that used 1450 ppm fluoride toothpaste for 21 months had statistically significantly smaller increase in caries (mean dmfs-increment) in comparison to the control group (that did not participate in supervised brushing and there is no other information about toothpaste used at home), 2.43 (± 5.25) vs 2.76 (± 5.23) (tab. 2).

Discussion

The use of preventive agents containing fluorine compounds recommended by WHO and FDI is one of the main and most commonly used elements of caries disease prevention (1, 3).

Although there are recommendations suggesting alternatives to fluoride caries prophylaxis, it appears to be crucial in preventing and controlling the prevalence of this disease. There are many strategies for using fluoride compounds with well-defined safety and efficacy, depending on the dose and concentration of fluoride ions in different age groups. Fluoride prophylaxis of caries in the youngest age group (0-6 years) is reasonable if used regularly. It is realized individually at home when teethbrushing is performed by parents twice a day with fluoride toothpaste (from the appearance of the first tooth up to the age of 8), in the dental office during professional preventive procedures, as well as by fluorinating drinking water at the community level (4).

Although significant progress has been made over the past four decades in understanding the mechanism of action of fluoride in toothpastes, this is certainly an extremely complex and still open topic. It turns out that fluoride salts can react with excipients present in the toothpastes, including abrasives, detergents and other active substances, forming slightly soluble or insoluble salts. Lack of fluoride release negatively affects the clinical effectiveness of toothpastes. Therefore, the amount of fluorine present in the preparation is differentiated from the potentially (bio)available soluble (in ionic or monofluorophosphate (MFP) form) fluorine having a cariostatic effect (25). The source of this element is very important for determining its availability (sodium fluoride NaF, sodium-MFP Na_2FPO_3, tin fluoride SnF_2, aminofluoride AmF) (24). There are clinical studies that have shown statistically significant differences in the reduction of caries in children depending on the type of fluoride salt used as an active ingredient in the toothpaste (25).

Interpretation of the fluoride availability, the influence of the type of its salt and other potentially active toothpastes ingredients in terms of their prophylactic effectiveness still needs to be discussed. It is also important to consider the fact of fluoride retention in the oral cavity. Recently, new generation toothpastes have been introduced that contain chemical components precipitated in the form of fluorine reservoirs (such as MFP or calcium-fluoride-like compounds) in dental plaque and on soft or hard oral tissues, contributing to the increase of anti-caries effectiveness (25). Currently used measurements of fluorine content do not take into account these phenomena and the amount of potentially available fluorine is underestimated.

Currently, the minimum amount of potentially available fluorine in the toothpastes, which is necessary for their preventive action, is unknown (25).

Scientific evidence indicates the benefits of using 1000 ppm F toothpaste in the prevention of caries, while the amount of studies on its effectiveness in children with primary dentition is minimal. A meta-analysis by Dos Santos et al. (10), as well as systematic reviews by Wright et al. (11) and Wong et al. (12) confirm that the use of standard toothpastes containing 1000-1500 ppm of fluoride reduces the incidence of permanent caries in children, while the higher the fluoride concentration, the greater its anti-caries effect.

Brushing teeth with a toothpaste with a 1000 ppm fluoride content in children under 6 years of age is recommended for its effectiveness in the prevention of caries, however, according to some authors, is associated with an increased risk of fluorosis of permanent teeth, mainly front and first molars. This is due to the occurrence of swallowing up 60-72% of the toothpaste applied to the brush, especially by children of 15-30 months of age who have not yet mastered the ability to spit it out (26). The literature states that about 0.5 mg of fluoride can be consumed by children if a toothpaste containing 1000 ppm is used twice a day (26). This can be an important source of fluoride intake, given the aggregation of fluoride doses from various sources. There is a consistency among the data regarding the rare occurrence of moderate and severe forms of fluorosis in areas with optimal (0.5-1.0 mg/l) or lower content of fluorine in drinking water (26). It should also be emphasized that according to the meta-analysis carried out by Wong et al. (12), evidence of a relationship between tooth fluorosis and the use of fluoride toothpaste in children under 12 months of age is unreliable, and doubtful in children aged 12-24 months. The result of a study by Oliveira et al. (27) may be of great importance here as they suggest that swallowed fluoride dose should be calculated on the basis of the level of bioavailable fluoride in present in the toothpaste (totally soluble fluoride – TSF). It turns out that the use of total fluoride in the calculations causes overestimation of the swallowed dose. The dose of TSF ingested by children can be the same regardless of the used toothpaste (containing ≤ 1000 ppm total fluorine) (25, 27).

The aim of limitation of the fluoride levels in toothpastes to ≤ 600 ppm was to reduce the amount of fluoride consumed by children. Such toothpastes are sold in Europe for the use by children under 6 years old. However, the anti-caries effectiveness of such pastes remains ambiguous. Caries reduction of 21-23% in children aged 2-4 years participating in the program of supervised tooth brushing with 500 ppm F toothpaste is reported in the literature (28). Other authors showed their lower effectiveness in the prevention of caries of primary teeth than those containing 1000 ppm fluorine (29). There are also reports regarding the dependence of the effectiveness of low-fluoride toothpastes from the initial mean dmft value, or the presence of active caries changes, in relation to the toothpastes with 1000 ppm of fluoride (30). Toothpastes with low fluorine content were less effective than those with a higher fluoride content in case of high dmft values and the presence of active carious lesions.

The ambiguous results of clinical trials and their small amount in children under 6 years of age make it difficult to assess with high evidence the effectiveness of low-fluoride toothpastes. Current review of research by Walsh et al. (13), showed a similar prophylactic efficacy on primary dentition made by 1055 ppm fluoride toothpastes compared to 550 ppm and slightly higher effectiveness of 1450 ppm fluoride toothpastes compared to 440 ppm (limited evidence). The results of other comparisons are uncertain and may be questioned by further studies (13). The results of our review showed a greater effectiveness of toothpastes containing 1000-1500 ppm of fluoride in the prevention of early childhood caries compared to those with low fluorine content (≤ 600 ppm). Other reviews of published clinical trials in this area are consistent with this statement, and at the same time indicate the need for controlled use of these products (10-12). This should encourage the use of toothpastes with a fluoride content of 1000 ppm, especially among groups at particular risk, in order to maximize the preventive benefits. Those benefits are confirmed by the results of a systematic review by Wong et al. (12), and a meta-analysis by Wright et al. (11). On the other hand, a meta-analysis carried out by Santos et al. (31) did not provide evidence to support the use of low-fluorine (≤ 600 ppm) toothpastes in preschool children to prevent caries of primary tooth and fluorosis of permanent teeth. It has been shown that their use increases the risk of caries in primary dentition and does not significantly reduce the risk of aesthetically unfavorable fluorosis in the upper anterior permanent teeth in relation to the toothpastes with a 1000-1500 ppm fluorine content.

It should be emphasized that our review has some limitations resulted from the scarcity of available studies in children, especially those under 6 years of age, assessing the effectiveness of toothpastes in the prevention of caries with the results expressed as the changes in caries indicators, as well as from high overall risk of bias for studies included in the review, as a group.

Another limitation is the inability to compare the effectiveness of using toothpastes with different fluoride content depending on its content in drinking water in the study area. This is due to the fact that such an information was not provided in three trials (16-18). One study that reported an optimal level of fluoride in drinking water showed an insignificant trend of a lower prophylactic effectiveness of toothpastes with a fluorine concentration of 1000-1500 ppm in relation to the low fluorine content (≤ 600 ppm) (19).

The water resources were not fluoridated or the fluoride levels were below the optimal concentration (0.35 ppm) in five studies (20-24), four of which showed a statistically significant reduction in caries increment in groups using 1100-1500 ppm fluoride toothpastes versus placebo/non-fluorided toothpastes (21-24). The study by Davies et al. (20) showed statistically significant difference between caries increment in 1450 ppm fluoride group and control group which did not receive any toothpaste. The conclusion is that the toothpastes containing 1100-1500 ppm of fluorine provide a significant clinical benefit for children in areas with non-fluoridated drinking water.

Additionally the results of all studies included in the review may be significantly influenced by the fact that in all studies, brushing teeth twice a day by children was supervised or assisted by preschool/school staff or parents at home. This can significantly affect the correct removal of plaque and improve hygiene, and hence the indicators of caries, taking into account the relationship between dental plaque accumulation and dental caries presence (4, 32). While this supervision concerns both children from the test and control groups (16, 17, 19, 20, 24), the impact is limited to improving the results in both groups, without interfering with the comparisons. On the other hand, in the case of studies in which only the test groups (18, 21-23) were subjected to supervision, it could significantly influence the additional improvement of the results in these groups and thus the comparisons of the effectiveness of toothpastes with different fluorine content. It should be noted that a statistically significant reduction in the increment of caries in the study groups as compared to the control groups was achieved in these four studies. No significant differences were found in the remaining studies, with the exception of the studies by Davies et al. (20) and by Fan et al. (24) that showed statistically significant difference between caries increment respectively in 1450 ppm fluoride group vs. control group which did not receive any toothpaste and 1500 ppm fluoride group vs. placebo group.

Conclusions

This systematic review, despite some limitations, indicates a greater efficacy of toothpastes containing 1000-1500 ppm of fluoride in the prevention of early childhood caries compared to the toothpastes with low fluorine content (≤ 600 ppm). These results are consistent with most available literature reviews of clinical trials conducted in preschool children.

Conflict of interest
Konflikt interesów

None
Brak konfliktu interesów

Appendix
Dodatek

Excluded trials with the reasons of exclusion
Badania wyłączone z przeglądu wraz z przyczynami wykluczenia

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