Topical Iodine and Fluoride Varnish Effectiveness in the Primary Dentition: A Quasi-experimental Study

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ABSTRACT

Purpose: Combining fluorides with antimicrobials may be of value because fluorides alone do not provide complete protection. The purpose of this quasi-experimental study was to compare the effectiveness of combined topical treatment with 10% polyvinyl-pyrollidone iodine (PVP-I) and 5% sodium fluoride varnish (FV) with FV alone.
Methods: One hundred seventy-two 12- to 30-month-old children received either combined or single therapy in Majuro, Republic of the Marshall Islands, between June 2008 and March 2009. The children received a mean of 2.5 treatments in the PVP-I combined group (range=2-3) and 2.8 treatments in the FV group (range=2-4) and were then examined.
Results: The percentage of children with any new decayed primary teeth was 41% (n=81) in the PVP-I combined group and 54% (n=90) in the FV group. Multivariate log-binomial regression was used to compare the rate of any new decay between groups, controlling for the number of teeth at baseline and the number of treatment visits. The risk ratio for treatment is 0.69 (95% confidence interval [CI]=0.51-0.94). No adverse effects were observed.
Conclusion: Combined treatment with 10% polyvinylpyrollidone iodine and 5% sodium fluoride varnish reduced the rate of new tooth decay by 31% over fluoride varnish alone.

(J Dent Child 2011;78(3):143-7)

Received February 25, 2010; Last Revision June 27, 2010; Revision Accepted September 9, 2010.

KEYWORDS: ORAL HEALTH, FLUORIDE, FLUORIDE VARNISH, PVP-IODINE, PRESCHOOL CHILDREN, DENTAL CARIES

The twice-yearly regimen of topical fluoride prescribed by nearly all dentists reduces new tooth decay by only approximately 30%, even allowing for the fact that most of these studies were not done in young children at high risk for caries.[1] Fluoride varnish (**FV**) is marginally better than other forms of topical fluoride, but the extra benefit of topical fluoride beyond the use of fluoridated toothpaste is not substantial.[2]

Three recently published studies further raise questions about the effectiveness of FV in the primary dentition in children at high risk for caries. The first study[3] used a community-randomized, no treatment (no varnish) controlled design in 20 First Nation communities in Northwest Ontario, Canada, and in non-Aboriginal childcare or preschool organizations in a neighboring city. Communities were assigned to 1 of 2 groups: (1) FV applied in the community setting once every 4 months (treatment); or (2) no treatment (control). Children were 6-months to 5-years-old at enrollment (14%=<1-year-old; 25%=1-year-old). The study reported an 18% reduction when Aboriginal communities with and without treatment were compared and a 24% reduction when all children were included. The study reported a relative risk of new decayed and filled surfaces in primary teeth of 1.96 (95% confidence interval [**CI**]=1.08-3.56) for the control group vs treatment group. Thus, both groups continued to develop new tooth decay in spite of the fluoride treatments.

The second study[4] was a 1-group observational investigation in which American Indian preschoolers received fluoride applications at the 9-, 12-, 15-, 18-, 24-, and 30-month well-child visits; the results were compared to a "historical control" of nonstudy preschool children

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from the same community who had dental assessments at an age comparable to the study children (mean=52.8 months). The author reported that children who received 4 or more FV treatments during the study period had 15.4 decayed, missing, and filled surfaces in primary teeth (dmfs; 95% CI=10.8-20.4) vs 23.6 dmfs (95% CI=19.5-25.8) for the control group children—a 35% reduction in decayed surfaces. Children who received 1, 2, or 3 treatments during the 21-month study period showed no significant difference in dmfs from the control group children.

The third study[5] was a 2-arm randomized clinical trial that tested whether an intensive FV regimen (3 applications/2 weeks) applied annually had an equivalent effect on caries progression in the primary dentition compared to single applications applied semi-annually. All participants(N=600; mean age= 55.3±4.6 SD months) received 3 varnish applications (active varnish or placebo) at semiannual visits over 3 years. The standard group received one active and 2 placebo treatments each six months. Children were assessed clinically at baseline and 12, 24, and 36 months after the study initiation. The mean numbers of new decayed primary tooth surfaces observed over 3 years were 9.8 (±8.6 SD) and 7.4 (±7.7 SD) in the intensive and standard groups, respectively. The adjusted rate ratio was 1.13 (95% CI=0.94-1.37, *P*=.20). Thus, intensive treatment with FV was not equivalent to biannual treatment, and tooth decay continued to develop in both conditions.

Increasing the frequency of application has not resulted in major reductions in tooth decay progression in children at high risk for decay.[6] Biologically, the mechanism of remineralization has limits regarding repeated exposure of teeth to acid degradation because of a carbohydrate-laden diet.[7-9] This is true whether or not there is fluoride in the drinking water.

There are several studies of the utility of antiseptic agents to inhibit caries in older individuals.[10,11] The rationale is based on findings that show that children with a lot of tooth decay are much more heavily infected with cariogenic organisms than previously thought.[12-14] PVP-iodine (**PVP-I**) interferes with the ability of *Streptococcus mutans* to bind to tooth surfaces by disrupting the expression and production of glucosyltransferase.[15] Thus, PVP-iodine makes it more difficult for the organism to maintain its place in the biofilm next to the tooth, which is required for the bacterial acids to damage the tooth surface.

The in vitro and in vivo iodine antiseptic literature on dental caries from 3 decades ago was promising, but most human studies were very small.[16,17] There has been a recent series of pilot and small-scale clinical studies examining the efficacy of PVP-I in young children, some with established active early childhood caries, with strongly encouraging data.[18-22] One quasi-experimental study compared 3 applications of either FV alone or FV plus PVP-I in children 60-to 83-months-old and found the proportion of caries-free permanent molars was greater in the combined treatment group; however, decay continued to develop in the primary teeth in both groups.[22]

The purpose of this study was to compare the effectiveness of combined treatment with polyvinyl-pyrollidone iodine followed by fluoride varnish vs treatment with fluoride varnish alone. The hypothesis tested was that combination treatment was more effective in preventing new decayed teeth than fluoride varnish alone.

METHODS

This study employed a quasi-experimental design with 2 groups of children. This study was conducted on Majuro atoll in the Republic of the Marshall Islands (**RMI**). The Ministry of Health was a participant in the Pacific Islands Early Childhood Caries Prevention Project conducted by the University of Washington, Seattle, Wash. RMI is also a grantee of the Targeted State Maternal and Child Oral Health Service Systems program. The Institutional Review Board of the University of Washington approved the evaluation.

The children (N=172) were part of an ongoing public health intervention program conducted by the Ministry of Health and were 12-to 30-months-old (average age= 20-months-old) at the start of the study. In this isolated population, nearly 50% of children have tooth decay by 36-months-old and there are few dental resources.[23] Parents gave their permission for the children to be part of the program. Special educational materials designed for populations with low health literacy were used to inform parents.

Children in one isolated community received the combination treatment, and children seen at the main hospital dental clinic in Majuro received FV alone. Every child within the particular setting received the same treatment. The goal was to provide 3 treatments per year. Children received a mean of 2.5 treatments in the PVP-I combined group (range=2-3) and 2.8 treatments in the FV group (range=2-4). The differences were due to attendance.

PVP-I (1% active iodine, Allegiance Health Corporation, McGaw Park, Ill), approved by the FDA for topical use in the mouth, was applied at the well-child visits along with FV. The children were seated in a portable dental chair or on the clinician's lap in the knee-to-knee position. Clinically, the teeth were dried with gauze and then painted with approximately 0.2 ml PVP-I. The exact amount applied clinically was not standardized. Figure 1 shows the clinical application. After application, the excess iodine was wiped from the teeth and then the teeth were coated with FV at the same visit.

FV (Cavity Shield, Omnii Oral Pharmaceuticals, West Palm Beach, Fla) was applied at approximately the

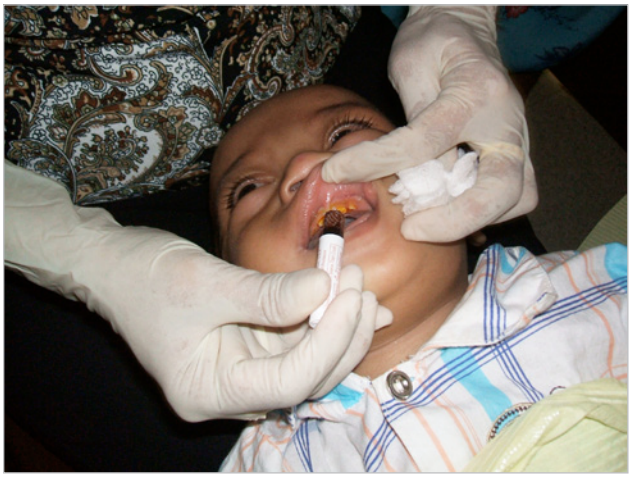

Figure 1. Clinical photograph showing application of topical polyvinylpyrollidone iodine in a preschool child.

Table 1. Log-binomial Regression Results Comparing Combined Treatment with Polyvinylpyrollidone Iodine and Fluoride Varnish vs. Fluoride Varnish Alone in Preschoolers

Variables	Risk ratio	95% confidence interval	*P*-value
Bivariate			
Treatment (1 vs 2)	0.75	0.54-1.30	<.08
Multivariate			
Treatment (1 vs 2)	0.69	0.51-0.94	.02
No. of teeth at start	1.08	1.02-1.04	<.001
No. of treatments	1.02	0.76-1.37	.90

same intervals as the combined treatment. The teeth were wiped with cotton gauze, and the varnish was applied with a disposable brush. Parents were asked not to allow their children to eat or brush their teeth for 1 hour.

Children in both groups were given toothbrushes (Looney Tunes 3-8 years, Colgate-Palmolive, New York, NY) and fluoridated toothpaste (My First Colgate, 0.34% sodium monofluorophosphate, Sydney, Australia) as part of the RMI dental public health program.

A single trained examiner clinically evaluated the children in June 2008 and March 2009. The examiner knew that one group was receiving the new treatment but was not aware which groups had received either the combined treatment or FV only. Caries prevalence is very high in this population and progresses rapidly.[23] The primary clinical evaluation outcome of the study was the number of decayed primary teeth, defined as a cavitated tooth. The examiner, who was trained according to World Health Organization (**WHO**) diagnostic protocol, examined the teeth visually using a disposable dental mirror and artificial light. Compared to a gold standard examiner, this study's examiner previously demonstrated excellent reliability for caries diagnosis (intraclass correlation coefficient=.96-1.00).

Deidentified data were provided for the analysis. The data were cleaned and entered into SPSS 16 for the Mac (SPSS Inc, Chicago, Ill). To assess the outcome, the d component of the WHO assessment scheme at the first examination was subtracted from the decayed component at the second examination and dichotomized as either with or without new decay. Multivariate log-binomial regression with robust standard error estimates was used to compare the rate of any new decay between groups, controlling for the number of teeth at baseline and the number of treatment visits.[24]

RESULTS

All children were examined at both time points in both cohorts. One child was lost to follow-up. Boys and girls were equally distributed in both groups. The socioeconomic characteristics of the 2 groups of children were quite similar (per capita income average=$2,500).

The mean (±SD) number of decayed teeth at the initial examination was 2.4 (±3.3 SD) in the PVP-I combined treatment group and 2.7 (±4.1 SD) in the FV alone group. (Wilcoxon rank sum test, *P*=.61). The mean (±SD) number of teeth at baseline was 17.1 (±4.4 SD) in the PVP-I combined treatment group and 15.1 (±5.3 SD) in the FV alone group (Wilcoxon rank sum test, *P*<.01).

The proportion of children with any new decayed primary teeth was approximately 41% (N=81) in the PVP-I combined group and approximately 54% (N=90) in the FV group. The risk ratio for treatment was 0.69 (95% CI=0.51-0.94). Combined treatment with PVP-I and FV reduced the rate of new tooth decay by 31% over FV. Table 1 gives the results of the regression analysis, controlling for both the number of teeth at baseline and the number of treatments. Adjusting for baseline decay did not change the results (data not shown).

None of the children experienced any side effects secondary to PVP-I treatment. No teeth were stained in the PVP-I plus fluoride cohort. There were also no adverse effects unrelated to the treatments.

DISCUSSION

This study's results are generally consistent with earlier pilot studies, suggesting that a combination treatment with antiseptics and FV is more effective than fluoride treatment alone. The results contrast those of our earlier retrospective cohort study of children in transitional dentition, however, where the combined treatment benefitted erupting permanent molars but did not appear to protect the already infected and extensively damaged primary dentition.[22] Application of PVP-I topically before FV is clinically simple, quick, and inexpensive. None of the previous studies, nor this one, reported any side effects. The results of this study are important because rates of tooth decay are so high in many at-risk populations.

The study used a quasi-experimental design in which children were not randomly assigned to treatments. Two locations arbitrarily chosen by the dental program were the test area and other control area, based on staff and resource availability. Nevertheless, these results improve on our previous work[22] on older children because time effects are controlled. The earlier study had compared results from 2 different school years widely separated, while in this study both groups were examined during the same period. In this study, the examiner was also blind to the treatments the children received whereas the examiner in the earlier study was aware of the treatments. The follow-up period was only 1 school year. The examinations were a routine part of an ongoing dental public health program conducted by the RMI government. In this case, however, the examiner was unaware of which area had been assigned to particular treatments. The follow-up period was short, but new lesions develop quickly in this high risk population. Nevertheless, these limitations impact the generalizability of the results.

While these findings should be interpreted with caution, the results, taken along with earlier studies, are significant and argue persuasively for randomized clinical trials of combination treatment in children at high risk for tooth decay. Such studies need to follow the children for a longer time and should be focused on children with erupting teeth where the antimicrobial effect is maximized. Similar studies are needed to prevent a relapse in children with severe Early Childhood Caries who are treated. Xylitol, with specific activity against *S mutans*, is also a candidate for combination treatment in addition to PVP-I.[25,26] A recent review of prevention technology, published since the Surgeon General's report was issued, made the same recommendation.[27]

CONCLUSIONS

1. Combined topical treatment with 10% polyvinylpyrollidone iodine followed with 5% sodium fluoride varnish is more effective than treatment with varnish alone.
2. PVP-Iodine is non-staining and acceptable to children.
3. Combined treatment is inexpensive and clinically simple and quick.

ACKNOWLEDGMENTS

This project was supported, in part, by: Head Start Innovation and Improvement Project grant no. 90YD0188 from the Office of Head Start, Agency for Children and Families; grant no. U54DE019346 from the National Institute of Dental and Craniofacial Research, National Institutes of Health NIH; and grant no. H47MC08647, Targeted State Maternal and Child Oral Health Service Systems, from the Health Resources and Services Administration.

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