

Is Povidone Iodine an Effective Means of Preventing Dental Caries in High Risk Pre-Operative Children

Bridget Lamberts, B.Sc., Jeong Hwa Lee, B.Sc., Jinah Lee, B.Sc., M.A., Allen Leko B.Sc.,
Michael Ling HB.Sc., Melissa Miller, B.A., B.Sc., M.Sc., Farah Minhas HB.Sc. and
George Nassar B.A., B.Sc., B.Ed

All authors are second year DDS students at the Faculty of Dentistry, University of Toronto, Toronto.

Faculty of Dentistry, University of Toronto
124 Edward St.
Toronto, Ontario
M5G 1G6
Phone: (416) 979-4900 ext. 3441
Fax: (416) 979-4944
E-mail: bridget.lamberts@utoronto.ca

Word count of text alone: 1,488
Word count of manuscript: 2,609

Is Povidone-Iodine an Effective Means of Preventing Dental Caries in High Risk Pre-Cooperative Children: An Evidence-Based Study of the Literature

Abstract

This evidence-based review of the literature was performed on published data regarding the use of the antimicrobial agent povidone-iodine in the prevention of caries in high risk, pre-cooperative children. Three search strategies were employed to find relevant studies of strong design; a search of electronic bibliographic databases, a review of the references from accepted studies, and an investigation into a number of pediatric dentistry textbooks. A total of 628 articles were identified. Based on the inclusion criteria, four studies deemed relevant for review were critically appraised according to an “efficacy” checklist with 17 items. Of these, three were kept based on checklist score and strength of study design. The three studies were inconsistent in terms of definitions of caries, outcome criteria, povidone-iodine dose, application method, duration and frequency of treatment, definition of high risk, standardization of examiners, and stages of dental development of the subjects. Scores for all three investigations were greater than 10, and presented fair evidence for the use of povidone-iodine as a preventive agent in this population. MeSH key words: child, preschool, dental caries, antimicrobial, povidone-iodine

Introduction

This literature review was based on a broad question posed by Canadian dental professionals regarding what techniques/materials are most efficacious in treating pre-cooperative children at high risk of caries. Pre-cooperative children, defined as children below the age of 4.5 years, pose a treatment challenge to dentists because they lack the cognitive ability

to cooperate¹. Traditional methods for managing pre-cooperative children include distraction, behavior modification, physical restraint, and pharmacologic management such as sedation and general anesthesia². The above methods are usually employed to facilitate restorative treatment using various measures such as stainless steel crowns, composite resins, glass ionomer cements and the atraumatic restorative technique (ART). Invasive treatment is not only costly and potentially dangerous, but is also known to have a high relapse rate². In addition, during the preliminary stages of research for this question, we were unable to find consistent, high quality evidence on invasive treatments, behavioral techniques, or pharmacological management with children under 4.5 years of age. For these reasons, we decided to concentrate on the efficacy of preventive measures to pre-exclude invasive treatment with this population.

According to the literature, the evidence on preventive measures for treating pre-cooperative children at high risk of caries is limited. Although the association of *Streptococcus mutans* with early childhood caries as one of the causative agents has been known for some time², preventive methods of targeting this bacterial pathology through the application of antimicrobial agents is a relatively unexplored approach to treating caries-risk in young children. Anti-microbial therapies include fluoride dentifrice, fluoride varnish, fluoride gels, chlorhexidine, and povidone-iodine treatment. Studies for the pre-cooperative age group focus on topical anti-microbial therapies, including in-office povidone iodine and chlorhexidine application. In terms of primary evidence investigating the use of anti-microbial agents for caries prevention in high-risk pre-cooperative children, three studies on povidone-iodine and one discussing chlorhexidine met our inclusion criteria.

Methods

The search for relevant evidence on preventive measures for high-risk pre-cooperative children included the identification, selection and critical appraisal of articles found through three main strategies.

Search Strategy

The search avenues employed incorporated electronic bibliographic databases, textbooks and reference lists from articles accepted for this review. Antimicrobials, chlorhexidine, povidone-iodine, children, and preschool were the search terms used.

All electronic database searches were limited to articles written in English, published in dental journals and studying human subjects. The following databases were utilized: Pubmed (1966 to present), EMBASE (1980 to 2005 Week 08), MEDLINE (1996 to 2005 Week 3) and Healthstar (1975 to November 2004). They yielded 256, 31, 151, and 104 articles deemed potentially relevant for this review.

A subsequent search was undertaken in which the reference lists of all articles accepted and scored were examined and used as an additional source of studies. Of 86 studies examined, no relevant information was retrieved.

Lastly, six pediatric dentistry textbooks published between 1975 and 2002 and their references lists were reviewed. This process yielded no relevant information for this review.

Determination of Relevance

After eliminating duplicate articles resulting from overlap among scientific databases, a total of four articles were retrieved and reviewed. An article was considered relevant if it met the following inclusion criteria:

- 1) The article reported primary research. Articles pertaining to the restoration of childhood caries, bacterial count reduction, or treatment of the mother was excluded.
- 2) The studies examined anti-bacterial treatment of children.
- 3) The study was conducted on pre-cooperative children up to 4.5 years of age at the start of the study.
- 4) Children must be considered at high risk of caries by socio-economic status or previous caries experience.
- 5) Study design must be a RCT, cohort, cross-sectional, or case-control study.
- 6) Study with odds ratios of finding from which odds ratios could be calculated.

Validity Instrument

Out of 4 articles, 3 were deemed relevant^{3,4,5} and were scored according to a “checklist to assess evidence of efficacy of therapy or prevention⁶ (Table 1). The highest possible score was 17.

Results

Three relevant articles were critically appraised for this review (Table 2). The studies presented fairly strong evidence, receiving scores between 10-14 out of a maximum of 17. All studies were randomized controlled trials and were either single or double blinded (Table 2).

Two studies by Lopez *et al.*^{3,4} presented the strongest evidence supporting the use of antimicrobials to reduce the risk of caries in high-risk children. While both studies were well designed, neither study controlled for outside care, such as unreported dental visits or other preventive treatment. The pilot study³ did not mention whether ethical approval was received. A specific treatment protocol for the application of povidone-iodine including doses was given in the 2001 study; this was not reported in the 1999 study. Both studies had a high rate of loss to follow-up. In the 2001 study, the authors note that the loss was balanced between the control and experimental groups.

Amin *et al.*⁵ presented weaker evidence in support of the use of antimicrobials to prevent caries in high-risk children. As with Lopez *et al.* studies,^{3,4} the researchers did not control for outside care. There was a significantly different distribution of males and females between the treatment and control groups. However, this was the only study to examine potential negative side effects of the povidone-iodine treatment through parent interviews and height and weight measurements of the treatment group. The authors did observe that povidone-iodine treatment was well received by patients, was quick and simple to apply, did not cause any staining of composite restorations, and had no negative side effects. However, the lower score achieved by this article weakens its conclusion that povidone-iodine solution had no effect in the prevention of caries.

Discussion

The evidence for the use of povidone-iodine as a topical anti-microbial agent reducing caries in pre-cooperative children at high risk is fair overall, due to inconsistencies in study

methods. The definition of caries as an outcome measure varied among the studies as well as the criteria used to identify carious lesions. Povidone-iodine treatment was not described in a coherent manner between studies, in that dose, application method, duration, and frequency of treatment was not consistent or was not completely described. In addition, the age of children varied among studies, as did the definition of high risk. Lopez *et al.*^{3,4} investigated early childhood caries, where Amin *et al.*⁵ considered all carious surfaces, including posterior teeth, increasing the number of potentially carious surfaces in his study. Based on the different types of decay studied, inclusion criteria for the investigations varied. This makes it difficult to compare results between studies since caries differed in etiology and the children varied in their dental development.

The studies were inconsistent or incomplete in their description of the quality and consistency of their examiners, as well as the calibration of their instruments. In all three investigations, the researchers failed to control for outside dental care including dental visits, external antimicrobial applications, diet or oral hygiene practices, which may be related to caries progression. Amin *et al.*⁵ was the only investigator to study any potential negative effects of the treatment, and to comment on the costs and benefits of povidone-iodine from a patient and operator perspective. As a result of these inconsistencies, it is difficult to effectively compare the results of all three studies.

Future research investigating the use of topical anti-microbial agent, such as povidone-iodine, as a preventive measure for pre-cooperative children at high risk of caries should employ

stronger study designs. Some of the drawbacks of the present studies can be avoided by implementing the following recommendations:

- Employ consistent definitions for “ pre-cooperative” and “high risk for caries”
- Ensure studies are ethically reviewed
- Implement a placebo treatment in all interventions to prevent any treatment biases
- Use comparable inclusion and caries outcome criteria between studies
- Calibrate trained examiners to a known standard
- Increase the sample size and minimize subject loss
- Determine the effects of povidone-iodine for different time durations and the length of its effects after removal
- Consistently control for outside care for the duration of the studies
- Further explore the costs and benefits of povidone-iodine treatment and other preventive measures
- Perform studies to compare between different antimicrobial agents

In summary, anti-microbial therapy, specifically povidone-iodine is currently the most notable preventive technique for pre-cooperative high caries risk children within the literature. The current evidence is beginning to suggest it is an effective means of preventing carious lesion formation in this population. Further investigation through larger, well-designed randomized controlled trials that employ clear and consistent definitions of pre-cooperative, high risk and caries outcome will serve to substantiate this claim.

Acknowledgements: The authors would like to thank Ms. Sabrina Peressini for her guidance with this review.

References:

1. Malamed SF, Morris SC. Nitrous oxide-oxygen: a new look at a very old technique. *J Calif Dent Assoc* 2003; 31(5):397-403.
2. Nathan JE. Managing behaviour of precooperative children. 1995; 39 (4): 789-816.
3. Lopez L., Berkowitz R, Zlotnik H, Moss M, Weinstein P. Topical antimicrobial therapy in the prevention of early childhood caries. *Pediatr Dent* 1999; 21 (1): 9-11.
4. Lopez L, Berkowitz R, Spiekerman C, Weinstein P. Topical antimicrobial therapy in the prevention of early childhood caries: a follow-up report. *Pediatr Dent* 2002; 24 (2): 204-6.
5. Amin MS, Harrison RL, Benton TS, Roberts M. Effect of povidone-iodine on *Streptococcus mutans* in children with extensive dental caries. *Pediatr Dent* 2004; 26 (1): 5-10
6. Leake JL, Department of Biological and Diagnostic Sciences, Faculty of Dentistry, University of Toronto. Unpublished document. Course notes DENT 300Y 2005. The checklist was adapted from Fletcher RH, Fletcher SW, Wagner EH. *Clinical epidemiology. The essentials*. 3rd ed. Baltimore: Williams and Wilkins, 1996; and Sackett DL, Richardson WS, Rosenberg W, Haynes RB. *Evidence-based medicine: how to practice and teach*. EBM.

Table 1. Checklist to Assess Evidence of Efficacy of Therapy or Prevention

General Question

1. Was the study ethical?
2. Was a strong design used to assess efficacy?
3. Were outcomes (benefits and harms) validly and reliably measured?
4. Were interventions validly and reliably measured?

What Were the Results?

5. Was the treatment effect large enough to be clinically important?
6. Was the estimate of the treatment effect beyond chance and relatively precise?
7. If the findings were “no difference” was the power of the study 80% or better?

Are the Results of the Study Valid?

8. Was the assignment of patients to treatments randomized?
9. Was loss to follow-up less than 20% and balanced between test and controls?
10. Were patients analyzed in the groups to which they were randomized?
11. Was the study of sufficient duration?
12. Were patients, health care workers, and study personnel “blind” to the treatment?
13. Were the groups similar at the start of the trial?
14. Aside from the experimental intervention, were the groups treated equally?
15. Was care received outside the study identified and controlled for?

Will the Results Help in Caring For Your Patients?

16. Were all clinically important outcomes considered?
17. Are the likely benefits of treatment worth the potential harms and costs?

Table 2. Studies presenting evidence for the effectiveness of povidone-iodine in the prevention of dental caries in high-risk pre-cooperative children

Authors (and study design)	Population	Intervention	Control treatment	Outcome	Critical appraisal comments	Conclusion, strength of evidence, and classification
Lopez et al, 1999 (randomized control trial)	-31 children, 18 females and 13 males, aged 12 to 19 months, who were clients of a Women, Infants, and Children clinic in Puerto Rico -Inclusion criteria: 1. unremarkable medical history 2. presence of 4 PMI with no visible defects 3. clinically caries free 4. use of nursing bottle at naptime and/or bedtime which contained liquid other than water 5. two consecutive positive MS cultures (8 weeks apart) from pooled PMI plaque	Application of 10% povidone iodine solution every 2 months (n=15, examined for a mean of 192 days)	Application of placebo solution (commercial instant tea without lemon or sweetener in deionized water) every 2 months (n=16, examined for a mean of 224 days)	Treatment failure was defined as the appearance of a white spot lesion on any of the PMI	-Study was not reviewed by an ethics committee -Loss to follow-up was 48% -Examiners did not identify and control for outside care, such as dental visits or antimicrobial applications outside of the study -Authors did not specify who examined and treated subjects and whether or not they were qualified and calibrated	-5 of the 16 control subjects (31%) and none of the 15 experimental subjects (0%) experienced treatment failure (p=0.04) -Evidence level 1-A
Lopez et al, 2001 (randomized control trial)	-83 children, 40 females and 43 males, aged 12 to 19 months, who were clients of a Women, Infants, and Children	Application of 10% povidone iodine solution every 2 months for 12 months (n=39)	Application of placebo solution (commercial instant tea without lemon or sweetener in deionized water)	Treatment failure was defined as the appearance of a white spot lesion on any of the PMI	-Loss to follow up was 34% in the control group and 48% in the treatment group	-14 of the 44 control subjects (32%) and 3 of the 39 experimental subjects (8%) experience

	<p>clinic in Puerto Rico</p> <p>-Inclusion criteria were the same as above (Lopez et al, 1999)</p>		<p>every 2 months for 12 months (n=44)</p>		<p>-Examiners did not identify and control for outside care, such as dental visits or antimicrobial applications outside of the study</p> <p>-Authors did not specify who examined and treated subjects and whether or not they were qualified and calibrated</p>	<p>treatment failure (p=0.0013)</p> <p>-Evidence level 1-A</p>
<p>Amin et al, 2004 (randomized control trial)</p>	<p>-25 children, 13 female and 12 male, aged 2 to 7 years, who presented for treatment at a pediatric dental practice in Burnaby, British Columbia</p> <p>-Inclusion criteria: 1. residents of non-fluoridated communities 2. required treatment for caries under general anesthetic 3. unremarkable medical history 4. at least 15 teeth remaining after completion of treatment</p>	<p>-Application of 10% povidone iodine solution every 2 months for 6 months</p> <p>-Recall examination at 6 (n=13) and 12 months (n=11)</p>	<p>-No treatment</p> <p>-Recall examination at 6 (n=12) and 12 months (n=8)</p>	<p>-<i>Streptococcus mutans</i> counts (at 6 months only)</p> <p>-Presence of newly decalcified or carious surfaces</p>	<p>-Single blind study</p> <p>-No treatment placebo</p> <p>-Significantly different distribution of males and females between the treatment and control groups</p> <p>-Examiners did not identify and control for outside care, such as dental visits or antimicrobial applications outside of the study</p> <p>-Study was underpowered</p>	<p>-<i>S. mutans</i> counts decreased significantly in all children at 6 months (p=0.03); there was no significant difference between the treatment and control groups (p=0.58)</p> <p>-At 12 months, 5 of 8 children in the control group (63%) and 2 of 11 children in the experimental group (18%) had new decay (not statistically significant)</p> <p>-Evidence Level 1-B</p>

PMI – primary maxillary incisor; MS – mutans streptococci