

Are teething gels safe, or even necessary for our children? A review of the safety, efficacy and use of topical lidocaine teething gels.

Title:

Are teething gels safe, or even necessary for our children? A review of the safety, efficacy and use of topical lidocaine teething gels.

Short informative title:

Safety of topical lidocaine teething gels

Type of manuscript:

Review article

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This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: [10.1111/jpc.14769](https://doi.org/10.1111/jpc.14769)

Acknowledgements:

This work was supported by the Australian Government Research Training Program Scholarship (no. 241616)

Conflict of interest statement:

The authors have no conflict of interest.

Abstract

Lidocaine-based teething gels have been widely available in Australia for decades in both commercial preparations and those compounded by pharmacies. However, many case reports have highlighted potential risks and toxicity associated with lidocaine-based teething gels when used in infants and young children including seizures, respiratory arrest and death. The Australian and New Zealand Society of Paediatric Dentistry and the American Academy of Paediatrics do not recommend topical agents for teething and the US Food and Drug Administration do not recommend topical lidocaine for this purpose due to concerns of toxicity. Literature supporting the efficacy of lidocaine for teething is scant and difficult to interpret due to the flawed design of the trials conducted and varied formulations used. This opinion article aims to summarise the available literature showing the limited effectiveness and associated risks of topical lidocaine gels for use in teething. In light of these findings, the authors recommend that regulatory bodies such as the Australian Therapeutic Goods

Administration review the efficacy and safety of this type of medicine and consider removing the indication for teething or limiting the age of use to older children.

Introduction

Teething is a natural and expected part of child development which refers to the eruption of the primary teeth, usually occurring between the ages of 6 months to 3 years. It involves intra-osseous movement of the unerupted tooth in the alveolar jaw bone until it emerges into its final functional position in the oral cavity.^{1, 2} The emergence of the tooth through the gum takes place over an eight day period comprising four days prior, the day of eruption, then three of final eruption days.^{1, 3} The tooth is encompassed in a dental follicle which is a rich source of eicosanoids, cytokines and growth factors,⁴ and it is thought these inflammatory mediators are responsible for the local symptoms which often alarm parents.³

Teething gels containing the local anaesthetic lidocaine are widely available both as ready-made commercial products and compounded preparations made on a case-by-case basis by pharmacies. Despite this, professional organisations do not currently recommend topical agents to treat teething as there is growing concern regarding the safety and efficacy of topical lidocaine when used in babies and young children. This opinion article aims to summarise the evidence for both efficacy and safety of the use of lidocaine in teething gels.

Symptoms of teething

While a wide variety of concerns have been historically ascribed to the teething process, it is accepted now in modern literature that tooth eruption is an expected, natural and part of child development associated with minor self-limiting signs and symptoms.³ A meta-analysis published in 2016 showed that the most common signs and symptoms of teething included gingival irritation, irritability and drooling, and while the eruption of the primary teeth was possibly associated with a slight increase in body temperature, it was not classified as fever.⁵ Other reviews have documented disturbed sleep, facial flushing, gum rubbing/biting/sucking

and ear tugging with teething,³ but a cohort study refutes any strong association between tooth eruption and major physiological symptoms.² While pain is a common feature reported by parents, the aetiology of pain, fever or any serious illness should not be automatically attributed to tooth eruption,² as children of this age are susceptible to a multitude of childhood infections which are a much more likely explanation.³

Current recommended treatment

The Australian and New Zealand Society of Paediatric Dentistry,⁶ the Australian Dental Association,⁷ the American Academy of Paediatrics⁸ and the UK National Institute for Health and Care Excellence⁹ all recommend local measures only for treatment of teething, such as chilled teething rings, or other cool objects such as washcloths or pacifiers, and massaging the gum with a clean finger. Topical agents, including topical lidocaine, are not recommended.

Topical lidocaine products available for teething

Currently in Australia, products with lidocaine in concentrations between 0.5-0.66% are commercially available and is indicated for infant teething, as stated their product information.^{10, 11} Many pharmacies also compound lidocaine-based products for teething in young children and infants with concentrations up to 2% lidocaine. Topical lidocaine products can only be sold in pharmacies in both New Zealand and Australia as they are classified as Pharmacy Medicine.¹² Accurate dosing of teething gels is difficult to achieve, and overenthusiastic application can lead to toxicity. Application of the gel in the oral cavity makes it hard to determine the actual dose administered to the child as it quickly gets mixed with saliva and increases the child's risk of swallowing and ingestion. This risk is further increased if the child is crying, drooling or salivating more when teething. Swallowing also anaesthetises the child's mucous membranes, increasing their risk of aspiration.

Pharmacology and toxicology of Lidocaine

Lidocaine is an amide-type local anaesthetic currently marketed for topical use on oral mucous membranes for various conditions, including mouth ulcers and teething in children over six months old. Reversible loss of sensation in localised areas of the body is achieved by blockade of voltage-gated sodium channels therefore preventing propagation of action potentials down the neuron, inhibiting the transmission of the pain signal.¹³ Orally ingested lidocaine has a bioavailability between 30-35%, although aspirated lidocaine will be absorbed directly through the respiratory tract and circulate to the central nervous system (CNS), without undergoing liver metabolism.¹³ The most common signs of lidocaine toxicity are CNS effects, postulated to be due to the selective blocking of inhibitory cortical synapses, including agitation, coma, confusion, hearing loss, respiratory depression, seizures and visual disturbances.¹³⁻¹⁵ Severe adverse cardiovascular effects such as rhythm disturbances, conduction abnormalities and cardiac arrest are also possible¹⁴ but are less frequent and tend to arise after the patient has already manifested signs of CNS toxicity.¹³

Efficacy of topical lidocaine for teething

In 2018, the UK Medicine and Healthcare Products Regulatory Agency (MHRA) extensively searched and reviewed the literature to determine whether studies demonstrated the efficacy of lidocaine for teething, which will be summarised here⁹. They commented that all studies considered relevant for inclusion had design flaws which limited the ability to draw conclusions from the data. In addition, children with a variety of oral conditions beyond teething were often included and the outcome criteria were not limited to the effectiveness of treating teething only.

A blinded, placebo-controlled, randomised trial conducted by Hopper et al¹⁶ compared 2% lidocaine versus placebo in 100 children aged between 6 months to 8 years with painful, infectious mouth ulcers. They concluded that one hour after the gel was applied, there was no difference in improving oral intake in these children between those who had been treated with viscous lidocaine and versus placebo. However, this study had a very significant placebo

effect, they focused only on short-term oral intake and pain scores were not collected. In contrast, Wolf and Otto¹⁷ conducted a double-blinded, comparative study assessing the effectiveness of 2% lidocaine gel in teething children from 6 months to 8 years old and found that lidocaine gel produced a statistically significant difference in pain reduction on the oral mucosa or gingivae in the age group from 4-8 years. However, children younger than 4 years were only treated with the lidocaine gel, and patients who presented with a wide range of oral conditions were involved, inclusive of bites, aphthous ulcers, mouth blisters, labial herpes simplex infections, gingivitis and hand-foot-mouth disease. Lastly, the MHRA reported another small exploratory study with 2% lidocaine paste showing a trend in efficacy reported by parents in teething children, but there was not enough data for statistical analysis.⁹

The MHRA concluded that “there are no robust data providing convincing evidence of efficacy for oral lidocaine products in the treatment of teething in children”.⁹

It should also be noted that the concentrations and formulations of products containing lidocaine gel vary widely, including those commercially available and those which are compounded. These products may therefore be different to those used in the published literature, thereby making it difficult to draw definitive conclusions on how they compare.⁹

Review of safety and case reports

There is a growing plethora of case reports identifying adverse reactions of varying severity and accidental ingestions associated with the use of lidocaine gels in young children and babies for treating teething and other oral conditions.

Curtis et al¹³ conducted a review of case reports to evaluate the toxic exposures and safety of orally applied local anaesthetic gels from PubMed as well as the American Association of Poison Control Centre reports from 1983 to 2003. They identified four cases of lidocaine exposures from children aged 5 months-22 months that had led to serious adverse reactions including seizures, respiratory arrest¹⁸⁻²⁰ and one death.²¹ Mofenson et al¹⁵ reported a case of an 11-month old baby boy whose parents applied lidocaine 2% viscous gel for a week which was prescribed for teething and the baby consequently developed seizures. Hess and

Walson²⁰ reported a 1-year old girl who also developed seizures after being administered lidocaine viscous 2% gel over a 12 hour period. Another case of a 5-month old boy was reported who developed seizures secondary to the use of topical lidocaine 2% gel.²²

A review of literature²³ identified a further 4 cases of severe adverse effects including respiratory arrest and seizures due to topical lidocaine ingestion in children under 3.5 years.²⁴⁻

²⁶ The MHRA identified a total of 197 paediatric adverse events reported in both EU countries and the UK up to November 2017 relating to the use of oral lidocaine products in patients younger than 18 years old, with the majority of reports involving infants under 1 year.⁹ While most reports were not thought to result in harm, serious but rare adverse effects included seizures and Stevens-Johnson syndrome were reported.

Furthermore, in 2014 the Food and Drug Administration (FDA) in the USA reviewed 22 case reports of serious adverse reactions, including deaths, in infants and young children aged between 5 months to 3.5 years who were administered 2% oral viscous lidocaine for the treatment of various oral conditions, including teething and stomatitis, or who had accidental ingestions.⁸ As a result, oral viscous lidocaine in the USA is no longer approved for treating teething pain due to the serious harms associated with its use. These harms are now highlighted with a Boxed Warning (FDA's strongest warning) in the product information to alert the prescribers and the public to this issue.⁸

Lastly, the Women's and Children's Hospital (WCH) in Adelaide, Australia used to compound a mouth paint containing lidocaine 2% and chlorhexidine 0.5% for treatment of teething in young children.²⁷ As of 2019, this product has now been discontinued as South Australia Health no longer recommends the use of any teething gels for infant teething.²⁷ In addition, personal communication has identified that there were over 10 presentations to the WCH emergency department over the last 4 years due to accidental overconsumption of lidocaine from infant teething gels. The majority of these cases reported receiving the WCH teething gel. However, the WCH were aware that community pharmacies also compound similar products that claim to be based on the WCH teething gel formula.²⁷

Conclusion and recommendations

In light of the lack of high quality clinical data to support the efficacy of topical lidocaine gel in teething, and the high number of global case reports documenting severe adverse reactions to topical lidocaine gel when used in young children and infants, the benefit and safety of this medicine for use in teething is questioned. Orally applied lidocaine products were originally marketed prior to the modern practice of evidence-based medicine at a time when they were generally considered as safe.⁹ Given that teething is an expected, physiologic process associated with self-limiting discomfort, the documented risk of lidocaine gel, and the fact that global dental organisations do not recommend the use of topical agents for teething, the authors call on regulatory authorities such as the Therapeutic Goods Administration to consider a change of indication and/or scheduling for these products in all formulations, including compounded preparations. A safety alert should also be issued for compounded preparations which have increased concentrations of lidocaine and are recommended for teething by pharmacists as an off-label indication. In addition, all healthcare workers, including those directly working with parents and caregivers such as lactation consultants and midwives, should also be informed of the risks of this medicine to ensure that all caregivers receive consistent advice.

Key points:

1. Teething is a natural, self-limiting process where authorities such as the Australian and New Zealand Society of Paediatric Dentistry recommend management with local measures such as chilled teething rings. Topical agents including lidocaine gels are not recommended.
2. There is no substantial evidence supporting the efficacy of lidocaine gel for teething. In addition, many case reports of varying severity exist including respiratory arrest, seizures and death, when lidocaine gel has been used in babies and young children for teething and other oral conditions.
3. Regulatory authorities such as the TGA should consider a change in indication and/or scheduling of topical lidocaine products.

References

1. Memarpour M, Soltanimehr E, Eskandarian T. Signs and symptoms associated with primary tooth eruption: a clinical trial of nonpharmacological remedies. *BMC Oral Health*. 2015;15:88.
2. Wake M, Hesketh K, Lucas J. Teething and tooth eruption in infants: A cohort study. *Pediatrics*. 2000;106(6):1374-9.
3. McIntyre GT, McIntyre GM. Teething troubles? *Br Dent J*. 2002;192(5):251-5.
4. Sandy JR. Tooth eruption and orthodontic movement. *Br Dent J*. 1992;172(4):141-9.
5. Massignan C, Cardoso M, Porporatti AL, Aydinov S, Canto Gde L, Mezzomo LA, et al. Signs and Symptoms of Primary Tooth Eruption: A Meta-analysis. *Pediatrics*. 2016;137(3):e20153501.
6. Australian and New Zealand Society of Paediatric Dentistry. The Dental Home URL: "<https://www.anzspd.org.au/viewStory/dental-home>". Accessed 12 August 2019.
7. Australian Dental Association. Children 0-11, Babies URL: "<https://www.ada.org.au/Your-Dental-Health/Children-0-11/Babies>". Accessed 12 August 2019.
8. FDA Drug Safety Communications . FDA recommends not to use lidocaine to treat teething pain and requires new Boxed Warning 2014 [updated 24/06/2014. URL: "<https://www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-fda-recommends-not-using-lidocaine-treat-teething-pain-and-requires>". " Accessed 12 August 2019.
9. Medicines and Healthcare Products Regulatory Agency. Oral lidocaine products: risk minimisation measures for use in teething. MHRA UK Public Assessment Report December 2018.
10. AusDi. Medijel Oral Gel Lignocaine hydrochloride 0.66%, Aminacrine hydrochloride 0.05% Key Pharmaceuticals PtyLtd [
11. AusDi. SM-33 Lidocaine 0.5%, Salicylic Acid 0.25%, Sodium salicylate 2.03%, Tannic acid 0.5%, Menthol 0.05%, Thymol 0.05%, Glycerol 20%, Ethanol (95%) 40%: Bayer Australia Limited; [
12. Australian Government. Federal Register of Legislation 2019 The Poisons Standard. URL: "<https://www.legislation.gov.au/Details/F2019L01197>" Accessed 20 November 2019.
13. Curtis LA, Dolan TS, Seibert HE. Are one or two dangerous? Lidocaine and topical anesthetic exposures in children. *J Emerg Med*. 2009;37(1):32-9.
14. Brown DL, Skiendzielewski JJ. Lidocaine toxicity. *Ann Emerg Med*. 1980;9(12):627-9.
15. Mofenson HC, Caraccio TR, Miller H, Greensher J. Lidocaine toxicity from topical mucosal application. With a review of the clinical pharmacology of lidocaine. *Clin Pediatr (Phila)*. 1983;22(3):190-2.
16. Hopper SM, McCarthy M, Tancharoen C, Lee KJ, Davidson A, Babl FE. Topical lidocaine to improve oral intake in children with painful infectious mouth ulcers: a blinded, randomized, placebo-controlled trial. *Ann Emerg Med*. 2014;63(3):292-9.
17. Wolf D, Otto J. Efficacy and Safety of a Lidocaine Gel in Patients from 6 Months up to 8 Years with Acute Painful Sites in the Oral Cavity: A Randomized, Placebo-Controlled, Double-Blind, Comparative Study. *Int J Pediatr*. 2015;2015:141767.
18. Sakai RI, Lattin JE. Lidocaine ingestion. *Am J Dis Child*. 1980;134(3):323.
19. Garrettson LK, McGee EB. Rapid onset of seizures following aspiration of viscous lidocaine. *J Toxicol Clin Toxicol*. 1992;30(3):413-22.

20. Hess GP, Walson PD. Seizures secondary to oral viscous lidocaine. *Ann Emerg Med*. 1988;17(7):725-7.
21. Amitai Y, Whitesell L, Lovejoy FH, Jr. Death following accidental lidocaine overdose in a child. *N Engl J Med*. 1986;314(3):182-3.
22. Smith M, Wolfram W, Rose R. Toxicity--seizures in an infant caused by (or related to) oral viscous lidocaine use. *J Emerg Med*. 1992;10(5):587-90.
23. Balit CR, Lynch AM, Gilmore SP, Murray L, Isbister GK. Lignocaine and chlorhexidine toxicity in children resulting from mouth paint ingestion: a bottling problem. *J Paediatr Child Health*. 2006;42(6):350-3.
24. Giard MJ, Uden DL, Whitlock DJ, Watson DM. Seizures induced by oral viscous lidocaine. *Clin Pharm*. 1983;2(2):110.
25. Gonzalez del Rey J, Wason S, Druckenbrod RW. Lidocaine overdose: another preventable case? *Pediatr Emerg Care*. 1994;10(6):344-6.
26. Rothstein P, Dornbusch J, Shaywitz BA. Prolonged seizures associated with the use of viscous lidocaine. *J Pediatr*. 1982;101(3):461-3.
27. Teething gel safety advice - Personal Communication. LT. Received 12 August 2019.

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Acknowledgements:

This work was supported by the Australian Government Research Training Program Scholarship (no. 241616)

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