

A Bibliometric Study of Cariology to Identify Methodologies and Therapeutics to Cross the Blood-Brain Barrier

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Abstract

Background

The management of dental caries has to evolve in tandem with drug delivery systems and new evidence on the blood-brain barrier phenomenon. While the conventional local anesthesia administration approach for management of dental caries is a syringe approach, that approach may not be appropriate for the millions of people with dental caries worldwide across the lifespan and for that reasons, dentists look to novel drug delivery approaches to bypass the blood-brain barrier to make caries management more palatable.

Types of Studies Reviewed

Various literature studies as well as a search of the Pubmed, Google Scholar, MESH, and [Clinicialtrials.gov](https://clinicaltrials.gov) website and databases were conducted to gauge the current and future state of research on local anesthetics usage in cariology and the blood-brain barrier.

Results

A lack of clinical studies and existing journal articles specifically addressing local anesthetics and cariology leaves the general dentist with no guidance on what the current state of thinking is on local anesthetics used to safely cross the blood brain barrier in the management of dental caries.

Practical Implications

Hopefully this bibliometric study introduces the practicing dentist to ways to bypass the blood-brain barrier while serving as a springboard for additional studies and advocacy both within and outside of the dental profession on cariology and drug delivery approaches.

Keywords: Cariology, Blood-Brain Barrier, Drug Delivery, Local Anesthetics, Dentistry

1. Introduction

Dental caries is a worldwide phenomenon with Wong and colleagues reporting that dental caries and other oral diseases affect over 3.5 billion people [1]. This first question is what are dental caries? Noted by Rathee and colleagues, caries are an infectious disease resulting from tooth-adherent cariogenic bacteria metabolizing sugars to produce acid, which over time demineralizes the tooth [2]. A secondary first question is what is the blood brain barrier? Noted by Daneman and colleagues, the blood-brain barrier (BBB) describes the unique properties of the

microvasculature of the central nervous system [3]. As caries affect people across the lifespan, are often correlated with high-sugar diets, and may be prevalent in military communities and in the general population and may be treated in both pediatric and adult patients through the usage of general and local anesthesia according to Table 1, it is prudent for general dentists to be mindful that new anesthesia administration techniques' impact on the blood brain barrier [4,5]. Noted by Rodrigues and colleagues, Lidocaine hydrochloride, Prilocaine hydrochloride, Mepivacaine hydrochloride, Bupivacaine hydrochloride, and Articaine

hydrochloride are anesthetic salts used in local anesthesia [6]. In cariology, practitioners must be aware these local anesthetics may penetrate the blood brain barrier due to advances in local anesthesia delivery techniques.

Year	Author(s)	Title	Institution	DOI/OCLC Number
2016	Antonia Caroline Johanna Steuber, Dirk Ziebolz, Knut Brockmann	Mundgesundheitszustand und zahnärztlicher Behandlungsbedarf von Kindern unter ambulanter zahnärztlicher Narkosesanierung eine retrospektive Untersuchung anhand der Behandlungsdokumentation aus den Jahren 2002-2011 der Universitätsmedizin Göttingen	Georg-August-Universität Göttingen	961190758
2008	Anita Alm	On dental caries and caries-related factors in children and teenagers	Department of cariology, Institute of Odontology, Sahlgrenska Academy, University of Gothenburg, Västra Götalandsregionen, Folkhälsan, Hälsohögskolan, Högskolan	472929919
2006	Kerstin Magnusson	Effect of varnish and toothpaste with fluoride- and antimicrobial agents on approximal caries and mutans streptococci in high caries risk adolescents	Dept. of Cariology, Institute of Odontology, The Sahlgrenska Academy at Göteborg University Göteborg	938287193
2006	Christer Eriksson	Glycoforms of the scavenger receptor cysteine-rich protein gp-340 with differential bacterial adhesion and relationship to dental caries	Department of Odontology/Cariology, Umeå University, Umeå	185334558
2003	Rikka Ihälin	Horseradish Peroxidase-Iodide system: a potential antibacterial agent against periodontal pathogens in human saliva	Department of cariology, Institute of Dentistry, Turku Immunology Centre, Turku Graduate School of Biomedical Sciences, Turku, Finland	474025410
2002	Sofia Tranaeus	Clinical application of QLF and DIAGNOdent: two new methods for quantification of dental caries	Karolinska Institutet, Huddinge	463096123
2002	Sara Elena Marchi	Effects of B vitamin supplementation on homocysteine levels in cardiac patients at Rush Preventative Cariology Center	Rush University	60829353
1995	Lill-Kari Wendt	On oral health in infants and toddlers	Dept. of Cariology, Faculty of Odontology, Göteborg University, Göteborg	32796919
1994	Birgitta Sundin	Dental Carrier and sugar-containing products: analytical studies in teenagers	Dept. of Pedodontics, Faculty of Odontology, Lund University, Malmö, Sweden	1483183095
1993	Tuomo Nuuja	Use and Effect of an experimental antiplaque preparation in military medicine	Dept. of Cariology and Dental Public Health, University of Helsinki, Helsinki	29650721
1991	Elisabeth Camling	Studies of naturally-occurring antibodies to mutans streptococci in humans	University of Göteborg	478782308
1991	Birgitta Lindquist	Mutans streptococci in human dentition: some factors influencing colonization and distribution	Department of Cariology, Faculty of Odontology, University of Göteborg, Göteborg	478782221
1997	Irina Kuzmina	A caries prevention program among children in a district of Moscow: planning, implementation and outcome	Department of Cariology and Endodontics, School of Dentistry, Faculty of Health Sciences, Cph	487131189
1998	Anne Beate Sonju Clasen	Aspects of caries development in deciduous enamel	University of Oslo	487428667
1987	Britta Mansson-Rahemtulla	Human salivary peroxidase: characterization of some of the system components and their activity	University of Umeå	485289443
1987	Marita Luomanen	Effect of CO2 laser surgery of rat mouth mucosa	University of Finland	18593066
1987	Kaisu Pienihakkinen	Screening for high caries increment in children	University of Turku	29157227
1986	Ingegerd Johansson	The effect of malnutrition on saliva composition and caries development	Dept. of Cariology, University of Umeå, Umeå	483665556
1985	Risto Tuominen	Endentulousness and its treatment in Finland	University of Helsinki	12279039

Table 1: Selected World Cat Dissertations3, 1985-2008

Prior to discussing which of these local anesthetics may penetrate the blood-brain barrier and their corresponding effects, if known, it is best to provide a general overview of some of the novel local anesthetic administration techniques searched for using

the National Library of Medicine Medical Subject Headings or MESH, [ClinicalTrials.gov](https://clinicaltrials.gov), PubMed, and Google Scholar using the strategy detailed in Table 2 [7-10].

Items	Specification
Date of Search	March 26, 2026
Database and other sources searched	MESH, ClinicalTrials.gov, PubMed, Scopus, Google Scholar
Timeframe	March 26, 2026-March 26, 2026
Inclusion and Exclusion Criteria	Inclusion Criteria: - Studies investigating the effect of local anesthetics on the blood brain barrier with or without dental applications - Publications in English Exclusion Criteria: - Publications in languages not specified in the inclusion criteria - Studies that do not address the objective of the review
Selection Process	Selection performed by the Author using the search terms “local anesthesia and blood brain barrier”
Additional Considerations	Articles identified through titles and abstracts in the initially retrieved papers

Table 2: Summary of Search

- Nanoparticle Transport allows therapeutic molecules of Lidocaine hydrochloride, or other local anesthetics into carriers to be administered intravenously (IV), oral, transdermal, and intranasal routes [11,12]. Jimenz and colleagues goes on to explain that therapeutic models, such as Lidocaine hydrochloride, or other local anesthetics can be bound to various carriers, such as: polymer nanoparticles (PLGA), Liposome Nanoparticles, Polymer Micelles [13]. Nanoparticle Transport administration has the advantage for general dentists in that it can be administered using existing technology that both the patient and the dentist is familiar with, in that IV is used for sedation dentistry and dentists can write prescriptions to compounding pharmacies initially for local anesthetics, such as Lidocaine hydrochloride, and eventually to chain and other pharmacies as oral, IV, transdermal, and intrasanel administrations become mass manufactured [14].
- To customize the administration of local anesthetics, Jeong and colleagues recommend stimuli-responsive hydrogels, modulation of drug release in response to physiological conditions [15]. In cariology, hydrogels can be used prior to treating caries to target specific sites of pain within the operative area (e.g. specific tooth) from sites within the brain. Noted by Cuk and colleagues, injectable hydrogels may be utilized by dentists to administer local anesthetics via hydrogels in addition to topical, dermal, and mucosal systems noted by Kim and colleagues [16,17]. The various hydrogel administration techniques may also be familiar to dentists versed in cariology and thus may be easy to incorporate into clinical practice for both patients and dentists,
- Noted by Kwak and colleagues and Altuhafy and colleagues,

computer controlled local anesthesia delivery systems can be used to administer local anesthetics in a pain-free manner which has implications for cariology in that computer assisted anesthesia administration helps to mitigate the fear which is holding back some of the population with caries, especially children, from completing treatment or actually visiting the dentist initially [18]. Even though a few of the various local anesthetic administration techniques were briefly overviewed, it still remains an open question among dentists as to what local anesthetic(s) are best to be used for penetrating the blood brain barrier.

2. Methods

This bibliometric study was divided into a couple of arms: PubMed, Google Scholar, ClinicalTrials.gov, and Medical Subject Headings or MESH.

- For the PubMed arm, whose sample results are displayed in Table 3, PubMed was accessed on the NLM (National Library of Medicine National Center for Biotechnology Information) website and the terms “local anesthesia and blood brain barrier” were typed into the PubMed search bar and on the “customer filer” sidebar, the option “Free full text” was selected under the heading “Text Availability”. This procedure was followed as PubMed is a collection of reputable scientific literature across disciplines and many researchers do not want to pay to access full text of articles. This PubMed search resulted in 22 results and all results were deemed to be relevant because the articles discussed the blood-brain barrier either in the title or abstract of the article.

Year	Author(s)	Title
2023	Qui Y, Mo C, Xu S, Chen L, Ye W, Kang Y, Chen G, Zhu T.	Research progress on perioperative blood-brain barrier damage and its potential mechanism
2023	Sun Y, Zabihi M, Li Q, Li X, Ubogu EE, Raja SN, Wesselmann U, Zhao C.	Drug Permeability: From the Blood-Brain Barrier to the Peripheral Nerve Barriers
2023	Zhang S, Wang Y, Zhang S, Huang C, Ding Q, Xia J, Wu D, Gao W.	Emerging Anesthetic Nanomedicines: Current States and Challenges
2022	Epelbaum S, Burgos N, Canny M, Matthews D, Shoutout M, Santin MD, Desseaux C, Bouchoux G.	Pilot Study of repeated blood-brain barrier disruption in patients with mild Alzheimer’s disease with an implantable ultrasound device

Table 3: PubMed (2026) Search

- For the Google Scholar arm, whose sample results are displayed in Table 4, Google Scholar was accessed by typing in “Google Scholar” into the Google search bar on the Google homepage. With the radio button, “Articles”, clicked, the search terms, “local anesthesia and blood brain barrier” were typed into the Google Scholar search bar. Google Scholar was used because it is a reputable search engine for retrieving scientific literature. The “Any Type–Review articles” button was clicked to narrow the search results from approximately 216,000 results to 24,000 results to make the search results more manageable to pursue. Additionally under the “Any time” heading, a “Custom range” was selected from 2016 to 2026 to further narrow the results to 689.

Year	Author(s)	Title
2026	S Andersson, R Anandampillai	Systemic toxic effects of local anaesthetics
2026	BF Gruenbaum, A Zlotnik, M Dubilet, et. al.	Role of Blood-Brain Barrier Permeability in Delirium Pathophysiology and Treatment
2026	X Wang, Y Tang, Z Jin, Q Li.	Molecularly engineered controlled release systems for local anesthetics in precise pain management
2026	H Le, GTT Vu, A Abioye, A Adejare.	Recent Advances in Nanoparticle-Based Drug Delivery Strategies to Cross the Blood-Brain Barrier in Targeted Treatment of Alzheimer’s Disease

Table 4: Google Scholar (2026) Search

- For the ClinicalTrials.gov arm, whose sample results are displayed in Table 5, the “Condition/disease” dropdown box included the terms “dental caries” and resulted in 1,312 studies. However, the ClinicalTrials.gov studies failed to specifically address how to use local anesthesia in the management of dental caries in dental practice, which makes this a topic that needs a lot of investigation and it could also be possible that cariology has not been studied as extensively in the United States of America as it has been studied in Sweden since many doctoral dissertations from WorldCat came from Swedish institutions.

Year	Author(s)	Title
2026	Cairo University	Detection of Proximal Caries in Bitewing Radiography Using Artificial Intelligence
2025	Karolinska Institute	Evaluation of Selective and Stepwise Excavation in Young Permanent Teeth with Deep Caries Lesions.
2022	Cairo University	Clinical Evaluation of SDF Combined with KI Versus SDF Management in Class I Carious Lesions
2012	CES University	Effect of Therapeutic Measures in Dental Caries Reduction in Children With Primary Dentition From Medellin City

Table 5: ClinicalTrials.gov6 Trials on Cariology, 2026

- For the Medical Subject Headings or MESH arm, whose results are displayed in Table 6f, entering in the search terms, “local anesthesia and blood brain barrier” did not yield any results in the Medical Subject Headings. This is disheartening as the public and dentists have no way to inform themselves on the effects of local anesthesia and the blood brain barrier to lessen dental anxiety and to contribute to dental professional knowledge.

Term(s)	In MESH5? (Y/N)
• local anesthesia and blood brain barrier	• local anesthesia and blood brain barrier(N)

Table 6: Local located in MESH4 (2026)

3. Results

From the PubMed search, it was learned from Sun and colleagues that there is a working hypothesis that CNS drug delivery strategies can be used for peripheral nerve drug delivery. This has direct implications for cariology in that local anesthetics crossing the blood-brain barrier can easily travel via peripheral nerves, by also being able to cross the blood-spinal cord barrier, to the affected teeth or tooth, at least in theory, to anesthetize for treatment of caries. Also, it was learned from Epelbaum and colleagues that the blood-brain barrier can also be penetrated using an implantable ultrasound device which may be outside the scope of practice of dentists for cariology, but does reaffirm hope of delivering local anesthetics that can penetrate the blood brain barrier.

From the MESH and clinicaltrials.gov arms, it was discovered that there is a lack of current knowledge about how to cross the blood-brain barrier in cariology and that is why this bibliometric study was undertaken. Granted that confirmation bias, small sample sizes within all arms of the study are inherent in a study that is conducted by one person with no funding, the certainty of the evidence was tried to be upheld by referring to reputable databases, e.g. PubMed, in the study, and based on the author's knowledge of source selection validity.

4. Discussion

However, all the arms of this bibliometric study does not truly address what local anesthetic the dentist should choose for use when penetrating the blood-brain barrier. Albalawi and colleagues notes no difference between systemic or local toxicity of Lidocaine and Articaine which gives rise to the hope that dentists can use Lidocaine or Articaine in combination with various delivery systems, e.g. IV, to successfully penetrate the blood brain barrier in a way that is less fearful and more convenient to the patient than a traditional syringe approach used in cariology.

5. Conclusion

As dental caries are a worldwide phenomenon across the lifespan, it is incumbent upon dentists to understand how local anesthesia, e.g. lidocaine, can be administered to make dental caries treatment more palatable to patients. While there are many approaches to penetrating the blood brain barrier using existing drug delivery mechanisms familiar to dentists and patients alike, such as oral or IV formulations, it is difficult to ascertain if other local anesthetics besides Lidocaine or Articaine will have increased toxicity or adverse side effects when they cross the blood brain barrier as opposed to syringe local administration approach loathed by patients by currently used in cariology today. Also, a lack of studies and regulatory approvals for these local anesthetics crossing the blood-brain barrier makes it difficult for dentists to use this right now in their practices but greater awareness of the capability of local anesthetics, such as Lidocaine, to penetrate

the blood brain barrier is one step in the right direction towards increasing awareness in the dental professional and beyond.

References

1. S, Jiarui J, et. al. (2025). The global, regional, and national burden of oral disorders in 204 countries and territories, 1990-2021, and projections to 2050: A Systematic analysis for the Global Burden of Disease Study 2021. *Regenesi Repair Rehabilitation*. 1(3); 56-63.
2. Rathee M, Sapra A. Dental Caries. (2023). Accessed March 25, 2026.
3. Daneman, R., & Prat, A. (2015). The blood-brain barrier. Cold Spring Harbor perspectives in biology, 7(1), a020412.
4. OCLC. WorldCat: Find items in libraries near you. Updated March 25, 2026. Accessed March 25, 2026.
5. National Library of Medicine. Medical Subject Headings (2025). Updated March 25, 2026. Accessed March 25, 2026.
6. Rodrigues, G. A., & Bronzato, J. D. (2025). A narrative review on local anesthetics in dentistry: mechanism of action, characteristics, and clinical considerations. *Journal of Oral and Maxillofacial Anesthesia*, 4, 8.
7. National Library of Medicine. Medical Subject Headings (2025). Updated March 25, 2026. Accessed March 25, 2026.
8. National Library of Medicine National Center for Biotechnology Information. Focus Your Search (all filters optional). Updated March 25, (2026). Accessed March 25, 2026.
9. Jiménez, A., Estudillo, E., Guzmán-Ruiz, M. A., Herrera-Mundo, N., Victoria-Acosta, G., Cortés-Malagón, E. M., & López-Ornelas, A. (2025). Nanotechnology to overcome blood-brain barrier permeability and damage in neurodegenerative diseases. *Pharmaceutics*, 17(3), 281.
10. Jiménez, A., Estudillo, E., Guzmán-Ruiz, M. A., Herrera-Mundo, N., Victoria-Acosta, G., Cortés-Malagón, E. M., & López-Ornelas, A. (2025). Nanotechnology to overcome blood-brain barrier permeability and damage in neurodegenerative diseases. *Pharmaceutics*, 17(3), 281.
11. Jiménez, A., Estudillo, E., Guzmán-Ruiz, M. A., Herrera-Mundo, N., Victoria-Acosta, G., Cortés-Malagón, E. M., & López-Ornelas, A. (2025). Nanotechnology to overcome blood-brain barrier permeability and damage in neurodegenerative diseases. *Pharmaceutics*, 17(3), 281.
12. Jeong, J. O., Kim, M., Kim, S., Lee, K. K., & Choi, H. (2025). Advanced hydrogel systems for local anesthetic delivery: Toward prolonged and targeted pain relief. *Gels*, 11(2), 131.
13. Čuk, A., Sande, S. A., & Hiorth, M. (2025). Development of an injectable, in situ formed hydrogel for controlled release of local anesthetics. *Journal of Drug Delivery Science and Technology*, 112, 107242.
14. Jeong, J. O., Kim, M., Kim, S., Lee, K. K., & Choi, H. (2025). Advanced hydrogel systems for local anesthetic delivery:

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- Toward prolonged and targeted pain relief. *Gels*, 11(2), 131.
15. Kwak, E. J., Pang, N. S., Cho, J. H., Jung, B. Y., Kim, K. D., & Park, W. (2016). Computer-controlled local anesthetic delivery for painless anesthesia: a literature review. *Journal of dental anesthesia and pain medicine*, 16(2), 81.
16. Altuhafy, M., Sodhi, G. S., & Khan, J. (2024). Efficacy of computer-controlled local anesthesia delivery system on pain in dental anesthesia: a systematic review of randomized clinical trials. *Journal of dental anesthesia and pain medicine*, 24(4), 245.
17. Sun, Y., Zabihi, M., Li, Q., Li, X., Kim, B. J., Ubogu, E. E., ... & Zhao, C. (2023). Drug permeability: from the blood–brain barrier to the peripheral nerve barriers. *Advanced therapeutics*, 6(4), 2200150.
18. Albalawi, F., Lim, J. C., DiRenzo, K. V., Hersh, E. V., & Mitchell, C. H. (2018). Effects of lidocaine and articaine on neuronal survival and recovery. *Anesthesia progress*, 65(2), 82-88.

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