Retrospective Review of Voluntary Reports of Nonsurgical Paresthesia in Dentistry

Andrew S. Gaffen, *BSc, DDS;* ***Daniel A. Haas,*** *DDS, PhD, FRCD(C)*

Contact Author

Dr. Haas
Email: *daniel.haas@dentistry.utoronto.ca*

ABSTRACT

Objective: Paresthesia is an adverse event that may be associated with the administration of local anesthetics in dentistry. The purpose of this retrospective study was to analyze cases of paresthesia associated with local anesthetic injection that were voluntarily reported to Ontario's Professional Liability Program (PLP) from 1999 to 2008 inclusive, to see if the findings were consistent with those from 1973 to 1998 from this same source. **Materials and Methods:** All cases of nonsurgical paresthesia reported from 1999 to 2008 were reviewed; cases involving surgical procedures were excluded. Variables examined included patient age and gender, type and volume of local anesthetic, anatomic site of nerve injury, affected side and pain on injection or any other symptoms. **Results:** During the study period, 182 PLP reports of paresthesia following nonsurgical procedures were made; all but 2 were associated with mandibular block injection. There was no significant gender predilection, but the lingual nerve was affected more than twice as frequently as the inferior alveolar nerve. During 2006–2008 alone, 64 cases of nonsurgical paresthesia were reported to PLP, a reported incidence of 1 in 609,000 injections. For the 2 local anesthetic drugs available in dental cartridges as 4% solutions, i.e., articaine and prilocaine, the frequencies of reporting of paresthesia were significantly greater than expected (χ^2, exact binomial distribution; $p < 0.01$) based on their level of use by Ontario dentists. These data suggest that local anesthetic neurotoxicity may be at least partly involved in the development of postinjection paresthesia.

For citation purposes, the electronic version is the definitive version of this article: www.cda-adc.ca/jcda/vol-75/issue-8/579.html

Local anesthetics are the most used and most important drugs in dentistry. They are also considered the safest and most effective drugs for pain control in medicine.[1] However, given the large number of injections of local anesthetic by dentists, adverse reactions are observed. These reactions may be local or systemic in nature.

The majority of adverse reactions associated with local anesthetics are not due to the drugs themselves but to the act of drug administration.[2-4] Most often, these are psychogenic reactions related to patient anxiety. Systemic reactions include toxicity from excessive levels of the drug in the blood due to overdose or inadvertent intravascular injection and allergic reactions. Local complications include postinjection neuropathy (or paresthesia), trismus, hematoma, pain on injection, needle breakage, soft tissue injury, facial nerve paralysis, infection and mucosal lesions.[5]

Nonsurgical cases of paresthesia in dentistry are almost exclusively related to inferior alveolar nerve block injection and appear to affect the lingual nerve more frequently than the inferior alveolar nerve.[6,7] Available data indicate that 85%–94% of such cases resolve spontaneously within 8 weeks; however, about

two-thirds of those who do not recover quickly may never fully recover.[8]

One retrospective study[6] placed the incidence of nonsurgical paresthesia in dentistry in the order of 1 in 785,000 injections. The authors of another study[8] estimated the incidence of prolonged nonsurgical paresthesia to be between 1 in 160,000 and 1 in 27,000, but acknowledge that the true incidence remains unknown and could be higher.

The exact biological mechanism of injury in cases of postinjection paresthesia remains the subject of debate in the literature. The most common and most tenable hypotheses are direct trauma to the nerve from the needle, intraneural hematoma and local anesthetic neurotoxicity.[6,9,10]

Ongoing uncertainty also remains regarding the contributory roles of various etiologic factors, such as local anesthetic formulation.[1,7,9,11-13] As a result, "there is an urgent need for further studies on the problem of neurotoxicity of local anesthetics."[7] The purpose of our retrospective study was to analyze cases of nonsurgical paresthesia that were voluntarily reported to the Professional Liability Program (PLP) associated with the Royal College of Dental Surgeons of Ontario (RCDSO) over the 10-year period from 1999 to 2008 inclusive to determine whether findings were consistent with those from 1973 to 1998 based on the same source.

The PLP is a group liability insurance program that covers all licensed Ontario dentists for claims arising in the province. The plan was initiated in 1973 and is currently funded by a portion of the annual fees paid to the RCDSO by dentists. A record of all professional liability and malpractice claims reported since the plan's inception is held on file. The claims data are considered confidential, and reporting of claims by members of this plan is strictly voluntary.[6]

Materials and Methods

Records of all cases of nonsurgical paresthesia reported to the PLP from 1999 to 2008 inclusive were obtained from the PLP. Data from earlier years, 1973 to 1998 inclusive, had been reviewed previously.[6,14] As the focus of this study was nonsurgical paresthesia events, any cases involving surgical procedures were excluded from further analysis. For the remaining cases, all relevant variables available from this data source, including patient age and gender, volume and formulation of local anesthetic, injection site and technique, site of neurologic injury, presence of pain on injection and type of dental procedure, were examined.

Statistical analysis was used to test the null hypothesis that the particular local anesthetic itself had no effect on the frequency of reporting of cases. Whenever possible, the χ^2 test was used to compare expected and observed frequencies of reports of paresthesia. In cases where any expected frequency was less than 5, statistical analysis was performed using the exact binomial probability distribution. All statistical tests were 2-tailed and interpreted at the 5% level. The expected frequency of reporting of paresthesia cases from 2006 to 2008 was calculated for each anesthetic drug based on its relative use by Ontario dentists.[15] Inspection of these data revealed that reporting frequencies were higher than expected for 2 drugs; these cases were further analyzed.

A second null hypothesis was that reported paresthesia cases should show no predilection in terms of patient gender, side of injury and affected branch of the trigeminal nerve (lingual or inferior alveolar). χ^2 tests were used to determine statistically significant differences between the observed and expected number of paresthesia cases dichotomized by patient gender, side of injury and injured nerve.

Ethics approval for this study was obtained from the University of Toronto Health Sciences Research Ethics Board.

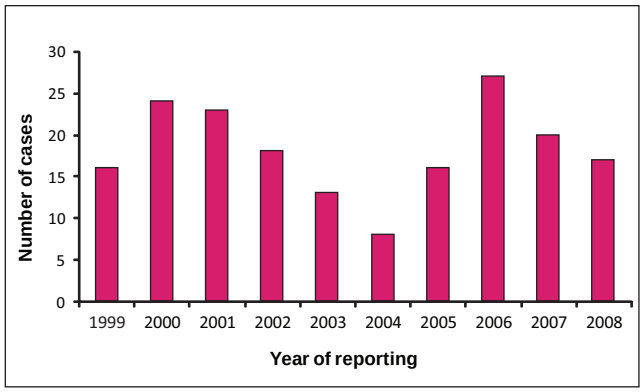

Figure 1: Distribution of cases of nonsurgical paresthesia in Ontario reported to the Professional Liability Program, 1999–2008.

Results

During the 10-year period from 1999 to 2008 inclusive, 182 reports of nonsurgical paresthesia were made to the PLP (**Fig. 1**). In general, the number of reported cases was relatively steady from 1999 to 2002, then decreased in 2003 and 2004 before increasing again from 2005 to 2007. The largest number of cases were reported in 2006 (n = 27) and 2000 (n = 24).

Roughly 13 million local anesthetic injections were administered in Ontario during 2007.[15] Given that 64 cases of nonsurgical paresthesia were reported from 2006 to 2008 inclusive, the approximate incidence of nonsurgical paresthesia in dentistry, as reported to the PLP, is 1 in 609,000 injections.

Patient Age and Gender

The distribution of nonsurgical paresthesia cases (1999–2008) by patient age is shown in **Table 1**. The mean

Table 1 Distribution of reported cases of nonsurgical paresthesia by age, 1999–2008

Age of patient (years)	No. cases
10–19	2
20–29	16
30–39	45
40–49	62
50–59	38
60–69	13
70–79	1
80–89	1
Unknown	4
Total	182

Table 3 Distribution of reported cases of nonsurgical paresthesia involving mandibular block by side of injection

Year of report	Left	Right
1999	8	7
2000	13	11
2001	12	11
2002	11	7
2003	7	6
2004	3	5
2005	8	8
2006	16	10
2007	13	7
2008	7	9
Total (n = 179)	98	81

age of affected patients was 43.8 years and the age range was 11–80 years. Most reported cases involved patients in their fourth, fifth and sixth decades of life.

In this data set, 93 reported cases of paresthesia (51.1%) occurred in females and 89 cases (48.9%) occurred in males (p = 0.77). The distribution of cases by year of reporting and patient gender can be found in **Table 2**.

Injection Technique and Side

Of the 182 reported cases of nonsurgical paresthesia, 172 (94.5%) involved mandibular block injection only. A further 8 cases (4.4%) involved mandibular block injection combined with at least one other type of anesthetic injection. A single case (0.5%) was reported to be associated with an infiltration around tooth number 35. Although not reported as such, this technique could be classified as an incisive or mental nerve block. The final case involved infiltration and intraligamentary injection in the maxillary anterior region.

Table 2 Distribution of reported cases of nonsurgical paresthesia by gender

Year of report	Female	Male
1999	6	10
2000	13	11
2001	11	12
2002	10	8
2003	9	4
2004	6	2
2005	8	8
2006	11	16
2007	8	12
2008	11	6
Total (n = 182)	93	89

Of all reported cases, in which a mandibular block injection was administered, 98 (54.7%) involved left-side injections and symptoms, while 81 (45.3%) involved right-side injections and symptoms (p = 0.20). In 1 case the side of injection was not known (**Table 3**).

Affected Area

The area most commonly reported to be affected by nonsurgical paresthesia was the tongue (n =144 or 79.1%). The lower lip and chin area was involved in 51 cases (28.0%), while paresthesia of the cheek was reported in 8 cases (4.4%). Many patients reported more than one affected area. Notably, 18 cases (9.9%) involved both the tongue and the lower lip/chin, indicating neurosensory alterations in the areas supplied by both the lingual nerve and inferior alveolar nerve. In cases involving mandibular block where only the tongue or lower lip/chin area (but not both) was reported to be affected (n =158), 126 cases (79.7%) were associated with tongue paresthesia and 32 (20.3%) were associated with lower lip/chin paresthesia. These results indicate that injury solely to the lingual nerve occurred significantly more often than injury solely to the inferior alveolar nerve ($p < 0.001$).

Other Symptoms

Altered taste sensation, suggestive of injury to the chorda tympani nerve, was reported in 26 paresthesia cases (14.3%). Eighteen patients (9.9%) reported painful or burning sensations that may indicate a dysesthesia-type injury. In 35 cases (19.2%), the reports stated that patients experienced pain or an electric shock sensation during the injection procedure.

Type of Treatment Administered

Only cases involving nonsurgical treatment were considered in this investigation. In this group, the most frequently rendered treatment was direct restoration

Table 4 Reported cases of nonsurgical paresthesia by year and local anesthetic drug

Local anesthetic drug	Cases of paresthesia (%)										
	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	Total
Articaine	7 (43.8)	17 (70.8)	11 (47.8)	9 (50.0)	9 (69.2)	7 (87.5)	7 (43.8)	20 (74.1)	12 (60.0)	10 (58.8)	109 (59.9)
Bupivacaine	0	0	0	0	0	0	0	0	0	0	0
Lidocaine	4 (25.0)	3 (12.5)	4 (17.4)	1 (5.6)	3 (23.1)	1 (12.5)	1 (6.2)	4 (14.8)	1 (5.0)	1 (5.9)	23 (12.6)
Mepivacaine	0	1 (4.2)	1 (4.3)	0	0	0	0	0	1 (5.0)	3 (17.6)	6 (3.3)
Prilocaine	4 (25.0)	2 (8.3)	5 (21.7)	5 (27.8)	0	0	5 (31.2)	1 (3.7)	5 (25.0)	2 (11.8)	29 (15.9)
Multiple	1 (6.2)	1 (4.2)	2 (8.7)	3 (16.7)	1 (7.7)	0	3 (18.8)	2 (7.4)	1 (5.0)	1 (5.9)	15 (8.2)
Total	16 (100)	24 (100)	23 (100)	18 (100)	13 (100)	8 (100)	16 (100)	27 (100)	20 (100)	17 (100)	182 (100)

Table 5 Observed and expected reports of paresthesia for all local anesthetic drugs, 2006–2008

Local anesthetic drug	No. reports[a]	Expected no. reports (total cases × proportional use of drug)
Articaine	42	26.5
Bupivacaine	0	0.4
Lidocaine	6	23.8
Mepivacaine	4	5.2
Prilocaine	8	4.1
Total	60	60

[a]*Does not include cases involving the use of more than 1 agent* (n = 4).

Table 6a Observed and expected reports of paresthesia associated with articaine compared with other local anesthetics, 2006–2008

Local anesthetic	No. reports[a]	Expected no. reports (total cases × proportional use of drug)
Articaine[b]	42	26.5
Others	18	33.5
Total	60	60

[a]*Does not include cases involving the use of more than 1 agent* (n = 4).
[b]*Significant difference between observed and expected reports* ($\chi^2 = 16.2$, $df = 1$, $p < 0.0001$).

Table 6b Observed and expected reports of paresthesia associated with prilocaine, 2006–2008

Local anesthetic	No. reports[a]	Expected no. reports (total cases × proportional use of drug)
Prilocaine[b]	8	4.1
Others	52	55.9
Total	60	60

[a]*Does not include cases involving the use of more than 1 agent* (n = 4).
[b]*Significant difference between observed and expected reports* ($\chi^2 = 4.02$, $df = 1$, $p = 0.045$), *but as the expected value was <5, an exact binomial test was applied. A significant difference could not be demonstrated by exact binomial test* ($p = 0.064$), *2-sided using the method of small p-values. However, as articaine contributes significantly to the reporting of paresthesia, a more accurate analysis of prilocaine was carried out by excluding articaine from the other drugs category* (***Table 7b***).

(120 cases, 65.9%), followed by endodontic therapy (36 cases, 19.8%), crown and bridge procedures (13 cases, 7.1%) and periodontal scaling (10 cases, 5.5%). In 2 cases (1.1%), multiple types of nonsurgical procedures were carried out. In 1 case (0.5%), local anesthetic was administered solely for pain relief without further treatment.

Local Anesthetic Drug

Over the period 1999–2008, inclusive, articaine alone was associated with 109 reported cases of paresthesia (59.9%), prilocaine with 29 cases (15.9%), lidocaine with 23 cases (12.6%) and mepivacaine with 6 cases (3.3%). No cases involved bupivacaine alone. In 15 cases (8.2%), multiple anesthetic drugs were administered (**Table 4**). In most cases ($n = 99$, 54.4%), the total amount of anesthetic injected was 1 standard dental cartridge or 1.8 mL.

The importance of the reported paresthesia frequencies for the various anesthetic drugs depends on the relative use of these agents by Ontario dentists. As drug use data for 2006–2008 are available,[15] paresthesia cases from these 3 years were subjected to further analysis. When considering the combined 2006–2008 reports, articaine and prilocaine were the only 2 drugs with a higher than expected frequency of paresthesia based on their market share (**Table 5**). As a result, these 2 drugs were analyzed separately to test for any statistically significant associations (**Table 6**).

Further, to determine more accurately whether individual significance was attached to either of these drugs prepared as 4% solutions, both articaine and prilocaine were analyzed with the other excluded.[6] This revealed that the frequency of reporting of paresthesia for both articaine and prilocaine were significantly greater than expected ($p < 0.01$) based on the distribution of local anesthetic use by Ontario dentists (**Table 7**). The PLP-

Table 7a Observed and expected reports of paresthesia associated with articaine compared with other anesthetics excluding prilocaine, 2006–2008

Local anesthetic	No. reports[a]	Expected no. reports (total cases × proportional use of drug)
Articaine[b]	42	24.7
Others (excluding prilocaine)	10	27.3
Total	52	52

[a]*Does not include cases involving the use of more than 1 agent* (n = 3).
[b]*Significant difference between observed and expected reports* ($\chi^2 = 23.1$, $df = 1$, $p < 0.0001$).

Table 7b Observed and expected reports of paresthesia associated with prilocaine compared with other anesthetics excluding articaine, 2006–2008

Local anesthetic	No. reports[a]	Expected no. reports (total cases × proportional use of drug)
Prilocaine[b]	8	2.2
Others (excluding articaine)	10	15.8
Total	18	18

[a]*Does not include cases involving the use of more than 1 agent* (n = 4).
[b]*Significant difference between observed and expected reports* (p = 0.0007 *by exact binomial test, 2-sided using method of small* p*-values).*

reported incidence of paresthesia for each anesthetic drug during 2006–2008 is found in **Table 8**.

Table 8 Reported incidence of paresthesia by anesthetic, 2006–2008

Local anesthetic	Reported incidence of paresthesia[a]
Articaine	1:410,000
Bupivacaine	0
Lidocaine	1:2,580,000
Mepivacaine	1:839,000
Prilocaine	1:332,000

[a]*Rounded to the nearest thousand.*

Discussion

Although there is an "urgent need for further studies on the problem of neurotoxicity of local anesthetics,"[7] such research may not be straightforward. Adverse effects from local anesthetics used in dentistry are generally thought to be so rare that few statistical data are available.[16] Moreover, certain (prospective) experimental designs may have difficulty getting approval from institutional review boards.[16] Even if such a prospective study did receive ethical approval, it would take an unrealistically large trial or cohort to detect statistically significant differences for an event as rare as nonsurgical paresthesia.[11] For this reason, it can be argued that "circumstantial evidence, experimental research and retrospective surveys on a great number of patients should be taken into account."[7]

The reported frequency of nonsurgical paresthesia in this study (1 in 609,000 injections) is greater than the reported incidence of paresthesia in an earlier study (1 in 785,000 injections) using data from the same source.[6] Over the 10-year period analyzed here, there was some variation in the number of reports received annually. Thus, reported incidence numbers should be viewed cautiously. That said, if one assumes that approximately half of all dental anesthetic cartridges are administered as mandibular block injections, the frequency of paresthesia estimated in this study would roughly double and would then be closer to the rate of 1 in 161,000 mandibular block injections calculated at a specialized referral centre in the United States.[8]

It must be noted that these are only estimates of incidence, and an earlier study provided evidence to suggest that the actual frequency of prolonged paresthesia might be 6 times higher or closer to 1 in 27,000 mandibular blocks.[8] Although rare, paresthesia after local anesthetic injection in dentistry should not be seen as a trivial event. The physical, social and psychological consequences endured by patients with prolonged trigeminal neuropathies can be profound.[17,18]

Both genders were represented almost equally in these voluntary reports by dentists. Other investigations into nonsurgical paresthesia based on patients consecutively referred to tertiary care centres have found a predominance of female patients with postinjection paresthesia.[7,8] This discrepancy could be explained by evidence suggesting a greater use of specific health care services by females combined with their more frequent referral to specialists.[19] However, gender differences in the physiologic response to peripheral nerve injury may also exist.[20]

As in previous research on nonsurgical paresthesia in dentistry,[6-8] in this study, the lingual nerve was affected more often than the inferior alveolar nerve. The lingual nerve might be more prone to injury because of its fascicular pattern. Around the area of mandibular block injection, the lingual nerve typically has fewer fascicles than the inferior alveolar nerve and may be unifascicular in about a third of patients.[21] Also, the lingual nerve is held taut in the tissues as patients open wide during injection and may, thus, be unable to deflect the needle.[8]

In just under 20% of cases, patients reported experiencing pain on injection; however, this study did not

investigate the relation between pain sensation on injection and subsequent paresthesia. Previous investigations indicate that the vast majority of patients experiencing pain or an electric shock sensation on injection recover with no long-term sequelae.[8,22]

Although treatment modality was included in the analysis of cases, because all treatment was nonsurgical, the type of dental procedure was not believed to be related to the development and reporting of paresthesia.

Our results indicate that articaine and prilocaine are associated with rates of reporting of nonsurgical paresthesia that are significantly higher than expected based on the rate of use of these drugs. Notably, these 2 local anesthetics are available in dental cartridges in Canada solely as 4% solutions, the highest concentration among injectable dental local anesthetics marketed in this country. The findings in this investigation are similar to those of earlier studies of nonsurgical paresthesia, which suggest that articaine alone,[7,23] prilocaine alone[8,13] or both drugs[6] may be associated with an increased risk of paresthesia. Notably, however, prilocaine is marketed as a 3% solution in Denmark, where 2 studies[7,23] have linked paresthesia to the use of articaine, but not prilocaine. Among studies linking paresthesia to the use of prilocaine, but not articaine, one was conducted in the United States before approval of articaine for use in that country,[8] while the other did not statistically analyze the association between paresthesia and the use of articaine to the exclusion of prilocaine,[13] which could have influenced its findings.

The methods used in our study are not without limitations and, as a result, the data are imperfect. Because patients were not clinically evaluated or systematically followed by the authors or PLP staff, detailed information on the precise clinical manifestations, severity and duration of paresthesia in individual cases was not always available. Also, as reporting of paresthesia events to PLP is voluntary and at the discretion of dentists, underreporting of cases almost certainly exists, and its extent is unknown. As a result, paresthesia rates calculated in this study should be seen only as a minimum estimate of incidence.[24] Furthermore, as cases associated with surgical procedures were excluded from this analysis, some reports of paresthesia that may have resulted from injection injuries before surgery as opposed to surgical nerve trauma were also not accounted for.

Of more concern is the potential for paresthesia reporting rates to differ among drugs due to a recognition or reporting bias or both.[25] This occurs when practitioners preferentially report adverse reactions associated with certain drugs because, for example, recent attention has been drawn to specific adverse events in the media or scientific literature.[24,25] Intuitively, however, if the basis for reporting to the PLP includes situations such as a threatened lawsuit, a demand for payment by a patient or lawyer or simply an unhappy patient,[26] one could reasonably assume that the magnitude and duration of the patient's neurosensory impairment would be the basis for the report as opposed to the specific content of the anesthetic cartridge. Determination of dentists' motivation for reporting paresthesia cases to PLP was beyond the scope of this project.

The true cause of nonsurgical paresthesia remains speculative. The underlying mechanism of injury may well involve a combination of mechanical injury from the needle along with neurotoxicity from the local anesthetic. Mechanical injury alone may be insufficient to result in permanent damage. The in vitro evidence for dose-dependent neurotoxicity of local anesthetics has been summarized in the literature.[11] Thus, it appears that it is not the drug per se, but the higher dose of the drug combined with mechanical insult that predisposes the nerve to permanent damage. As has been stated in reference to possible local anesthetic-induced neurotoxicity in medicine, the results of this study support the dictum of Paracelsus that "there is no safe drug, only safe doses or concentrations."[27] Results from recent in vitro and clinical investigations into the effectiveness of a 2% solution of a local anesthetic that has been traditionally used at 4% in dentistry appear promising.[28,29] Further investigation of the safety and effectiveness profiles of such lower concentration solutions appears warranted.

In conclusion, the findings of this study are consistent with and support the initial studies looking at nonsurgical paresthesia in dentistry in Ontario.[6,14] When considered along with other investigations,[7,8,13,23] the data described here strongly suggest that the 4% local anesthetic solutions used in dentistry, namely articaine and prilocaine, are associated with an increased risk of paresthesia. The routine use of these solutions for mandibular block anesthesia appears difficult to justify. As always, dentists should carefully assess the risks and benefits of all drugs they prescribe or administer.

THE AUTHORS

Dr. Gaffen *is an MSc/specialty candidate in the department of endodontics, faculty of dentistry, University of Toronto, Toronto, Ontario.*

Dr. Haas *is associate dean of clinical sciences and professor and head of dental anesthesia, faculty of dentistry, University of Toronto, Toronto, Ontario.*

Acknowledgements: *We thank the Royal College of Dental Surgeons of Ontario for its support of this study and especially Dr. Judith Heggie, Dr. Don McFarlane and staff of the Professional Liability Program for their assistance and advice, Ms. Tamara Arenovich for statistical assistance, and Dr. Howard Tenenbaum and Dr. Bettina Basrani for valuable input and suggestions.*

Correspondence to: *Dr. Daniel A. Haas, Faculty of dentistry, University of Toronto, 124 Edward St., Toronto ON M5G 1G6.*

The authors have no declared financial interests.

This article has been peer reviewed.

References

1. Malamed SF. Local anesthetics: dentistry's most important drugs, clinical update 2006. *J Calif Dent Assoc.* 2006;34(12):971-6.

2. Naguib M, Magboul MM, Samarkandi AH, Attia M. Adverse effects and drug interactions associated with local and regional anaesthesia. *Drug Saf.* 1998;18(4):221-50.

3. Aldrete JA, Johnson DA. Evaluation of intracutaneous testing for investigation of allergy to local anesthetic agents. *Anesth Analg.* 1970;49(1):173-83.

4. Malamed SF. *Handbook of local anesthesia.* 5th ed. St. Louis: Mosby; 2004.

5. Haas DA. Localized complications from local anesthesia. *J Calif Dent Assoc.* 1998;26(9):677-82.

6. Haas DA, Lennon D. A 21 year retrospective study of reports of paresthesia following local anesthetic administration. *J Can Dent Assoc.* 1995;61(4):319-20,323-6,329-30.

7. Hillerup S, Jensen R. Nerve injury caused by mandibular block analgesia. *Int J Oral Maxillofac Surg.* 2006;35(5):437-43.

8. Pogrel MA, Thamby S. Permanent nerve involvement resulting from inferior alveolar nerve blocks. *J Am Dent Assoc.* 2000;131(7):901-7.

9. Pogrel MA, Schmidt BL. Trigeminal nerve chemical neurotrauma from injectable materials. *Oral Maxillofac Surg Clin N Am.* 2001;13(2):247-53.

10. Smith MH, Lung KE. Nerve injuries after dental injection: a review of the literature. *J Can Dent Assoc.* 2006;72(6):559-64.

11. Haas DA. Articaine and paresthesia: epidemiological studies. *J Am Coll Dent.* 2006;73(3):5-10.

12. Malamed SF. Articaine versus lidocaine: the author responds. *J Calif Dent Assoc.* 2007;35(6):383-5.

13. Pogrel MA. Permanent nerve damage from inferior alveolar nerve blocks—an update to include articaine. *J Calif Dent Assoc.* 2007;35(4):271-3.

14. Miller PA, Haas DA. Incidence of local anesthetic-induced neuropathies in Ontario from 1994–1998 (abstract 3869). *J Dent Res.* 2000;79(special issue):627.

15. Gaffen AS, Haas DA. Survey of local anesthetic use by Ontario dentists. *J Can Dent Assoc.* Forthcoming 2009.

16. Peltier B, Dower JS Jr. The ethics of adopting a new drug: articaine as an example. *J Am Coll Dent.* 2006;73(3):11-20.

17. Sandstedt P, Sorensen S. Neurosensory disturbances of the trigeminal nerve: a long-term follow-up of traumatic injuries. *J Oral Maxillofac Surg.* 1995;53(5):498-505.

18. Hillerup S. Iatrogenic injury to oral branches of the trigeminal nerve: records of 449 cases. *Clin Oral Investig.* 2007;11(2):133-42.

19. Weir R, Browne G, Tunks E, Gafni A, Roberts J. Gender differences in psychosocial adjustment to chronic pain and expenditures for health care services used. *Clin J Pain.* 1996;12(4):277-90.

20. Tall JM, Stuesse SL, Cruce WL, Crisp T. Gender and the behavioral manifestations of neuropathic pain. *Pharmacol Biochem Behav.* 2001;68(1):99-104.

21. Pogrel MA, Schmidt BL, Sambajon V, Jordan RC. Lingual nerve damage due to inferior alveolar nerve blocks: a possible explanation. *J Am Dent Assoc.* 2003;134(2):195-9.

22. Harn SD, Durham TM. Incidence of lingual nerve trauma and postinjection complications in conventional mandibular block anesthesia. *J Am Dent Assoc.* 1990;121(4):519-23.

23. Legarth J. Skader på nervus lingualis opstået i forbindelse med mandibularanalgesi—anmeldt til Dansk Tandlægeforenings Patientskadeforsikring 2002–2004. *Tandlægebladet.* 2005;109:786-8. [In Danish, English summary.] Available: http://arkiv.tandlaegebladet.dk/multimedia/TB-2005-10-786.pdf (accessed 2009 Sept 11).

24. Rawlins MD. Spontaneous reporting of adverse drug reactions. I: The data. *Br J Clin Pharmacol.* 1988;26(1):1-5.

25. Stricker BH, Tijssen JG. Serum sickness-like reactions to cefaclor. *J Clin Epidemiol.* 1992;45(10):1177-84.

26. Risk management guide — a handbook for Ontario dentists. Toronto: Royal College of Dental Surgeons of Ontario. 2nd printing; October 2008. Available: www.rcdso.org/pubs/Risk_Management_Guide_Oct%202008.pdf (accessed 2009 Sept 11).

27. Eisenach JC, Yaksh TL. Safety in numbers: how do we study toxicity of spinal analgesics? *Anesthesiology.* 2002;97(5):1047-9.

28. Potocnik I, Tomsic M, Sketelj J, Bajrovic FF. Articaine is more effective than lidocaine or mepivacaine in rat sensory nerve conduction block in vitro. *J Dent Res.* 2006;85(2):162-6.

29. Hintze A, Paessler L. Comparative investigations on the efficacy of articaine 4% (epinephrine 1:200,000) and articaine 2% (epinephrine 1:200,000) in local infiltration anaesthesia in dentistry—a randomised double-blind study. *Clin Oral Investig.* 2006;10(2):145-50.