Scientific Article

The Incidence of Adverse Reactions Following 4% Septocaine (Articaine) in Children

A. Adewumi, BDS, MPed Dent RCS[1] • M. Hall, DMD[2] • M. Guelmann, DDS[3] • J. Riley, PhD[4]

Abstract: ***Purpose:*** *The purpose of this study was to report the incidence of adverse events following the use of 4% Septocaine in children.* ***Methods:*** *A prospective study was carried out on children attending university-based pediatric dental clinics for restorative care under local anesthesia. Data collection included patient demographics, medical history, amount and site of injection, and treatment complexity. Follow-up telephone interviews were conducted with the parents at 3, 5, 24, and 48 hours regarding prolonged paresthesia, soft tissue injury, and pain.* ***Results:*** *Two hundred sixty-four 2 to 14 year-olds were recruited for the study. Complete interview information was obtained from 204 patients. Prolonged paresthesia at 3 hours post-injection was reported for 40% of the population and at 5 hours for 11%. Soft tissue injury occurred in 14% of the patients at 3 hours and was found to be highest among children younger than 7 years old. The lip was the most commonly affected site for accidental injury and it was not related to injection site. Twenty percent reported postprocedural pain at 3 and 5 hours post-treatment.* ***Conclusions:*** *Since prolonged numbness appears to be the most frequent adverse event and occurred primarily in children younger than 7 years old, parents need to be informed and reassured accordingly.*
(Pediatr Dent 2008;30:424-8) Received September 25, 2007 / Last Revision December 1, 2007 / Revision Accepted December 6, 2007

KEYWORDS: LOCAL ANESTHETICS, CHILD, ARTICAINE

Articaine hydrochloride is a local anesthetic (LA) that originated in 1976 in Germany and has been used widely in other European countries and Canada.[1] In April 2000, the US Food and Drug Administration approved it for use in the United States under the name of Septocaine (Septodont, New Castle, Del). Articaine belongs to the amide group of local anesthetics and is unique in that it contains a thiophene ring and an ester group.[2] The thiophene ring increases the lipid solubility of the anesthetic, giving it a faster onset of action. The ester group enables the drug's biotransformation in the plasma and the liver. Other members of the amide group include lidocaine, mepivacaine, and prilocaine. They also have a fast onset of action, profound anesthesia, and low allergenicity.

Articaine reversibly blocks the conduction of nerve impulses by blocking the sodium and potassium channels during the propagation of action potential.[3] The elimination half-time of articaine is about 20 minutes. Its rapid breakdown to the inactive metabolite articainic acid accounts for a very low systemic toxicity and, consequently, the possibility of repeated injections.[4] The primary metabolite, articainic acid is excreted via the kidneys. Equal analgesic efficacy along with lower systemic toxicity (ie, wide therapeutic range) allows articaine to be used in concentrations higher than other amide local anesthetics. It is also able to diffuse more easily through soft tissue and bone than other local anesthetics.[2] Cowan found that the duration of soft tissue anesthesia produced by 4% Septocaine varies considerably, with the mean being 3 hours and 54 minutes±1 hour and 36 minutes.[5] He suggested that this is slightly longer than lidocaine, mepivacaine, and prilocaine. Other studies have discussed the safety and efficacy of Septocaine in adults and children. Malamed et al reported a 2% incidence of accidental lip injury in 50 children between 4 to 13 years of age.[6] Wright et al retrospectively reported on the use of articaine in 211 children younger than 4 years old and found no adverse systemic reactions.[7] Dudkiewicz et al also found 4% articaine to be safe and efficient in 4 to 18 year-old children with no adverse effects.[8]

In spite of these published studies, some authors expressed concern about the use of Septocaine due to reports of prolonged paresthesia[9,10] They recommended a widespread survey of the relationship of prolonged dysesthesia (impairment of sensation) to the anesthetic drug of choice.

Haas and Lennon's retrospective report of paresthesia over a 21-year period showed that the 2 most commonly reported local anesthetics when paresthesia occurred were articaine and prilocaine.[11] Of the 143 records they studied, 4 (all males) were under the age of 20 years. Despite the widespread use of

[1]*Dr. Adewumi is assistant professor,* [2]*Dr. Hall is resident, and* [3]*Dr. Guelmann is associate professor and chair, all in the Department of Pediatric Dentistry, and* [4]*Dr. Riley is associate professor, Department of Community Dentistry & Behavioral Science, all at the College of Dentistry, University of Florida, Gainesville, Fla.*
Correspond with Dr. Adewumi at aadewumi@dental.ufl.edu

Septocaine in children, its use in children younger than 4 years of age is not recommended by the manufacturer. [3]

Since no studies have exclusively studied adverse events of Septocaine in children, it was the purpose of this study to prospectively document the adverse events associated with the use of 4% Septocaine with 1:100,000 epinephrine as a local anesthetic agent in children of all ages receiving regular dental treatment. We also tested for associations between each specific adverse event

Methods

Following approval from the Institutional Review Board of the University of Florida, a prospective clinical study was conducted at the Pediatric Dental Clinics of the College of Dentistry in Gainesville, Fla. A LA data sheet and questionnaire (Figure 1) in the form of a structured telephone interview were developed. Research assistants were recruited for the study and trained in data collection and interview technique for standardization purposes. Recruited for the study were children with a negative history of atopic or allergic reactions to LA who presented for regular restorative treatment with or without sedation requiring LA. Subjects whose parents did not speak English were excluded from the study. The treatment complexity was defined as simple (Class I, Class II) restorations, complex (stainless steel crowns, pulp therapy, dental extractions), and combination (ie, simple and complex dental treatment). Prior to implementing the study, a pilot questionnaire was conducted on 20 patients. The Septocaine monograph stipulated that complete anesthesia should last approximately 1 hour for infiltrations and up to approximately 2 hours for nerve blocks.[3] The determination of the interview times was, therefore, based on that recommendation. We also based subsequent evaluation times of adverse effects on a combination of methodology of other studies[6,12] and our estimation of the effects of the sedatives.

At the time of treatment, parents were approached by the research assistant. Explanation of the study was given, informed consent was obtained, and, where appropriate, assent was given by the patient. During the restorative session, provided by faculty and residents at 2 dental clinics, LA information was collected. Upon completion of dental procedures, parents were reminded of the follow-up telephone interviews. The structured interviews consisted of 4 short telephone calls at 3, 5, 24, and 48 hours postinjection. The same research assistant who collected the initial data conducted all 4 consecutive phone calls. The information collected from each interview was recorded on the questionnaire form.

Prolonged paresthesia was defined as numbness ≥ 3 hours post administration of LA injection. Soft tissue injury (STI) was defined as injury to the lips, tongue, or cheek since the dental appointment. Postprocedural pain was defined as noninjection site pain occurring ≥ 3 hours after dental treatment. Confusion was defined as disorientation or aggressive behavior of the child since dental treatment was performed. Chest pain was localized pain along the front of the body between the neck and abdomen. Headaches were recorded if there was a positive history (excluding those with a baseline history). The completed LA information sheets and questionnaires were then coded and entered into the Statistical Package for the Social Sciences 15.0 (SPSS Inc, Chicago, IL) for data analysis. Descriptive statistics were obtained and cross-tabulation analysis was performed using Pearson's chi-squared test, and significance was set at $P<.05$.

Figure 1. Questionnaire for follow-up phone calls

Date: _____ _____ _____ _____
Time: _____ _____ _____ _____

		3 hs	5 hs	24 hs	48 hs
Does your child have any pain? If so, please ask child to touch where it hurts. _____ Does it hurt a little, a lot, the most pain ever? _____	Y/N				
Has your child bitten his/her cheek, lip or tongue? If so, where? _____	Y/N				
Has your child had any headaches since the dental appointment?	Y/N				
Is your child still numb? Please touch the numbed area with your finger to see if it's still numb.	Y/N				
Does your child seem to be confused? If so, how much, a little or a lot?	Y/N				
Has your child complained of chest pain since the dental appt? If so, how much, a little or a lot?	Y/N				

Results

A total of 264 2 to 14 year-olds (mean=6.8±2.9) were recruited for the study. Complete questionnaires were obtained on 204 participants. Fifty-two percent

were girls (N=137), 56% were Caucasians, 35% African Americans, 8% Hispanics, 1% Asians, and less than 1% fell under the category of "other ethnicities." The age distribution is shown in Table 1. Two hundred ten patients (80%) were treated without sedation (Table 2), 234 (89%) received 68 mg (1 carpule) or less of Septocaine, and 25 (10%) received between 90 and 136 mg. One hundred twenty-five children (47%) received simple restorations, 81 (31%) had complex treatments, 50 (19%) had a combination of simple and complex procedures and missing data accounted for 8 (3%) of the patients. The incidence of headache, chest pain, and confusion was between less than 1% and 2%. Overall, although more girls complained of numbness (*P*=.06) and sustained soft tissue injuries (*P*=.08) than boys, the differences were not statistically significant. Twenty-one boys (16%) and 21 girls (15%) complained of pain. Patients ages 3-7 years were more likely to report numbness and soft tissue injuries than those ages 8-14. There were no racial differences observed on any of the measures of adverse events. No association between the amount of LA and reports of adverse events was found. The LA site was not found to be related to soft tissue injuries (STIs). The overall incidence of numbness, pain, and accidental STI was 33%.

Forty percent of the sample had prolonged paresthesia at 3 hours postinjection. This was reduced to 11% at 5 hours (Table 3). Approximately 25% of the data on paresthesia at 24 and 48 hours were missing due to parental unavailability during the phone calls. Of the remaining data recorded, however, no reports of paresthesia were observed at 24 and 48 hours. For the complete responders, the overall incidence of paresthesia was 42% and there was no association between paresthesia and amount of LA or injection site.

Table 1. AGE DISTRIBUTION OF THE SAMPLE POPULATION

Yrs of age	No. (%) of patients
2-≤7	132 (50)
8-14	132 (50)
Total	**264 (100)**

Table 2. DISTRIBUTION OF PATIENTS TREATED WITH 4% SEPTOCAINE

Sedations	No. (%) of patients
None	210 (80)
Midazolam	26 (10)
Midazolam and hydroxyzine	19 (7)
Midazolam and demerol	4 (1)
Other combinations	5 (2)
Total	**264 (100)**

Table 3. INCIDENCE OF REPORTED NUMBNESS, PAIN AND SOFT TISSUE INJURY FROM 4% SEPTOCAINE*

	3 hs N (%)	5 hs N (%)	24 hs N (%)	48 hs N (%)
Numbness				
Yes	82 (40)	22 (11)	0 (0)	0 (0)
Total	**203 (100)**	**206 (100)**	**192 (100)**	**178 (100)**
Pain				
Yes	40 (20)	42 (21)	11 (6)	6 (3)
Total	**200 (100)**	**203 (100)**	**190 (100)**	**184 (100)**
Soft tissue injury				
Yes	29 (14)	5 (2)	2 (1)	1 (1)
Total	**203 (100)**	**206 (100)**	**193 (100)**	**179 (100)**

* Missing data were excluded.

Twenty percent and 21% reported pain at 3 hours and 5 hours post treatment, respectively (Table 3). At 24 hours, 6% reported pain and at 48 hours, 3%. The overall incidence of procedural pain reported by the parents was 31%.

Fourteen percent had STIs at 3 hours and this was reduced to 2% at 5 hours (Table 3). Of the complete responders, 20% reported sustaining an STI. The highest STI incidence was reported in 3 to 7 year-olds, with the lip being the most commonly affected site (Figure 2).

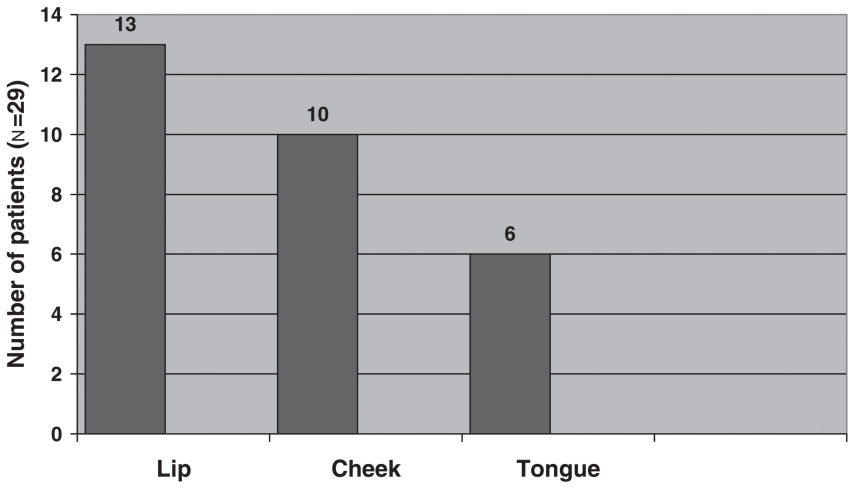
Cross tabulations were performed using Pearson's chi-square test to check for associations between adverse events. There was a positive association between pain and injury for children who reported pain at 5 hours or more (*P*=.002). Furthermore, children who had pain at any time in the 48 hours were likely to have sustained a soft tissue injury (*P*=.03). The observed relationship between paresthesia and STI among those who reported numbness at 3 hours was not statistically significant (*P*=.06). This association reached statistical significance at 5 hours or more (*P*<.001)

Discussion

The use of Septocaine has been a concern for many clinicians due to a potential for neurotoxicity.[9-11] We believe that these events can be more significant in children who may find them particularly distressing. Though several studies have evaluated the safety and efficacy of 4% articaine in children, only one study by Haas and Lennon reported on the adverse events. It was not possible to determine if their study involved children.[11]

Ram and Amir compared articaine with lidocaine in children.[12] In their study, parents were instructed to ask the child and to record the time the feeling of numbness

Figure 2. Distribution of reported soft tissue injuries



disappeared. Parents were asked by phone after 1, 2, or more hours to report it and were also asked about the occurrence of adverse effects. The authors found the duration of numbness of soft tissues to be longer for articaine (3.43±0.70 hours) than lidocaine (3.00±0.80 hours), and this reached statistical significance. Our study found the reported incidence of numbness to be 40% after 3 hours and 11% after 5 hours.

Overall, more girls complained of numbness and sustained soft tissue injuries than boys. Pain reports, however, were more evenly distributed among both sexes. Gender distribution was also similar to previous studies, and we did not find any racial differences in the reports of adverse events.[11-13] The incidence of lip injury was higher (Figure 3) compared to the cheek and tongue. Using our methodology of data entry, however, it was not possible to establish an association with injection site. This study confirmed the suspicions of clinicians regarding the relationship between numbness and soft tissue injuries, especially in children. Most patients received approximately 1 carpule of Septocaine (68mg) and we were not unduly concerned about overdosage. Wright et al reported on the use of articaine in children younger than 4 years, however they still expressed caution with LA doses when using sedation.[7] We explicitly agree with their recommendation that dentists should seriously consider prescribing doses ≤ 5mg/kg when treating children 4 to 12-years-old. Despite the limited evidence available on the use of septocaine in children under the age of 4 years, the protocol in use at the University of Florida is based on the study by previous authors.[7]

In designing this prospective data collection study, we felt it pertinent to report on other adverse events that could be attributable to either the local anesthetic solution or the sedative used in facilitating dental treatment. Some of these adverse events (headache, confusion, and chest pain) were also reported in the Septodont monograph.[3] Our results showed that 5 (2%) children reported having a headache at 3 hours and this was reduced to 2 (<1%) at 5 hours and beyond. Further examination of the data showed that, of the 5 patients who complained of headaches at 3 hours, only 1 received sedation. It is, therefore, probable that the headaches were not unrelated to the local anesthetic. These results are consistent with studies published by Malamed.[6,13]

Three children (1%) reported "a little" confusion at 3 hours. There was a statistically significant association with the 3 sedation patients (2 had midazolam with hydroxyzine, 1 had midazolam only) that also reported "a little" confusion at 3 hours (P=.008). There were no further reports of confusion beyond 3 hours. In contrast to headaches, these episodes of confusion are more likely related to the sedation than the LA solution. Chest pain was not reported in any of the patients studied in this population.

There were some limitations of this study. In general, 25-30% of data were missing, particularly in the 24 to 48-hour period, due to unavailability of the parent and in spite of prior participation in earlier interviews. Considering patient demographics and socioeconomic status, this study was designed so that follow-up calls reduced the need for additional patient visits within the observation period. In addition, the results of the outcome variables were based in part on the subjective evaluation of the parents. Nonetheless, clinicians often rely on subjective evaluations of parents and guardians, when making clinical judgments or decisions regarding treatment outcomes in pediatric patients. Furthermore, the methodology of parental questioning used in this study mirrored that used by other investigators in this line of research.[6,12-14]

Conclusions

Based on this study's results, when using 4% Septocaine in children ages 2-14 years old, the following conclusions can be drawn:

1. Some children may experience anxiety due to prolonged numbness (one third of children);
2. Post-operative soft tissue injuries are likely to occur in 3 to 7 year-olds;
3. Parents should be prepared for postprocedural adverse events, especially for young patients;
4. A similar study using 2% lidocaine within a shorter observational period is recommended.

References

1. Ferger P, Marxkors R. Ein Neues Anasthetikum in der zahnarztlichen Prosthetik. (A new anesthetic in dental prosthetics) Dtsch Zahnarztl Z 1973;28:87-9.
2. Malamed SF. Handbook of Local Anesthesia. 4th ed. St. Louis, Mo: CV Mosby; 1997.
3. Septodont USA. Pain control. Anesthetics. Available at: "http://www.septodontusa.com/home/Portals/_septodontUS/documents/Septocaine2.ppt". Accessed March 31, 2007.
4. Oertel R, Rahn R, Kirch W. Clinical pharmacokinetics of articane. Clin Pharmokinet 1997;33:417-25.
5. Cowan A. Clinical assessment of a new local anesthetic agent-carticaine. Oral Surg 1977;43:174-80.
6. Malamed SF, Gagnon S, Leblanc D. A comparison between articaine HCL and lidocaine HCL in pediatric dental patients. Pediatr Dent 2000;22:307-11.
7. Wright GZ, Weinberger SJ, Friedman CS, Plotzke O. The use of articaine local anesthesia in children under 4 years of age: A retrospective report. Anesth Prog 1989;36: 268-71.
8. Dudkiewicz A, Schwartz S, Laliberté R. Effectiveness of mandibular infiltration anesthesia in children using the local anesthetic Ultracaine (articaine hydrochloride). J Can Dent Assoc 1987;1:29-31.
9. van Eeden SP, Patel MF. Prolonged paresthesia following inferior nerve block using articaine. Br J Oral Maxillofac Surg 2002;40:519-20.
10. Pedlar J. Letter to the editor. Br Dent J 2003;194:181.
11. Haas DA, Lennon D. A 21-year retrospective study of reports of paresthesia following local anesthetic administration. J Can Dent Assoc 1995;61:319-30.
12. Ram D, Amir E. Comparison of articaine 4% and lidocaine 2% in pediatric dental patients. Int J Paediatr Dent 2006;16:252-6.
13. Malamed SF, Gagnon S, Leblanc D. Efficacy of articaine: A new amide local anesthetic. J Am Dent Assoc 2000;131:635-42.
14. Wright GZ, Weinberger SJ, Marti R, Plotzke O. The effectiveness of infiltration anesthesia in the mandibular primary molar region. Pediatr Dent 1991;13:278-83.

Abstract of the Scientific Literature

Predicting the number of root canals detected in permanent maxillary molars

The aim of this study was to evaluate the association of several factors on the number of root canals detected in permanent maxillary molars undergoing non-surgical root canal therapy (NSRCT). Data were derived from the University of Pennsylvania Graduate Endondontic electronic database (PennEndo). This database contains different characteristics of each individual and tooth undergoing NSRCT in their clinical program including patient age, tooth type, the number of canals detected in each tooth, the presence of caries, periapical and pulpal diagnoses, source of clinic referral, and the presence or absence of a dental restoration. Clinic protocol included access preparation, examination of the floor of the pulp chamber with a surgical operating microscope. Multiple logistic regression analysis was used to determine those variables associated with the number of root canals detected in maxillary molars. Data from 1328 individuals served as the sample, with participants ranging in age from 6 to 82 years. Overall, 59.7% of maxillary molars had three canals while another 34.9% had four canals. Independent analysis revealed that as age increased, the chance of locating fewer canals decreased (OR=0.97), and those whose tooth had caries were found to have more canals. However, final regression modeling revealed that only the age of the individual was an accurate predictor of the number of canals found in permanent maxillary molars.

Comments: *Large clinical databases like the one used in this study are amenable to identifying factors related to oral health status and outcomes through regression modeling. This study provides initial evidence of the influence age may have in identifying canals in permanent maxillary molars. Clinicians are likely to identify more canals when performing NSRCT among the pediatric population.* ***PJL***

Address correspondence to Dr. M. Iqbal, Department of Endodontics, University of Pennsylvania, School of Dental Medicine, Robert Schattner Center, 240 S 40th St., Philadelphia, Pa 19104-6030; email: miqal@pobox.upenn.edu

Iqbal M, Fillmore E. Preoperative predictors of number of root canals clinically detected in maxillary molars: a PennEndo Database study. J Endod 2008;34(4):413-6.

31 references