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A Retrospective Study of Paresthesia of the Dental Alveolar Nerves

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Paresthesia is a rare clinical finding subsequent to surgery accompanied by the administration of local anesthetics. A small patient population was identified whose clinical problem may be explained by neurotoxicity due to a local anesthetic metabolite. Reasonable questions arise from these clinical observations that would benefit from prospective studies to explain sensory loss on a biochemical basis.

Paresthesia can be defined as an altered sensation of numbness, burning, or prickling that may reflect an alteration in the sensation of pain in the distribution of a specific sensory nerve.[1] This paper reports the results of retrospective study of 46 inferior alveolar and lingual paresthesia cases in 4987 surgical patients, 3071 of which were third molar cases. These data were evaluated to determine if any evidence exists of a neurotoxic event secondary to a drug or its metabolites.

The trigeminal nervous system consists of fibers with different degrees of myelination. The least myelinated fibers (0.5–1.0 microns) are the slowest transmitting fibers and conduct pain sensations. The more myelinated fibers conduct cold and heat (1–4 microns), touch (4–8 microns), and pressure and proprioceptive (8–13 microns) functions.[2] Taste fibers of the chorda tympani nerve which joins the lingual branch are slow conducting fibers with some degree of myelination but less than those of the fibers of touch, pressure, and proprioception.[3] Consequently clinical evaluation of sensory function is directly related to nerve fiber size as different sensory functions carried by fibers of differing sizes all present together in the nerve bundle.

It has been argued that needle trauma can cause paresthesia.[1] A 27-gauge dental needle is 510 microns in diameter, 500–1000 times greater in diameter than the 0.5–1.0 micron nerve fibers for pain, cold, or heat. This gross discrepancy in size suggests that it is not possible to selectively injure by this means the small pain fibers present in a 2–3 mm nerve and yet leave intact touch, pressure, and proprioceptive fibers of up to 13 microns.

Local anesthetics depress the conductive ability of a fiber to a greater degree as the amount of myelination decreases. Consequently, if a patient complains of lack of pain sensation in the tongue and loss of taste after an oral surgery procedure, then the surgeon should determine whether or not the loss is strictly limited to lack of function in the slowest or least myelinated nerve fibers. Evaluation and recording in the patient's records of the presence or absence of the functions of pain, cold, heat, touch, pressure, and proprioception would reflect which fiber groups have sustained changes in sensory function.[3–6]

Born,[7] administering wrist blocks using a 27-gauge needle, has implicated 0.25% or 0.5% bupivacaine (an amide) in causing a 16.3% incidence of numbness in orthopedic treatment. Clinically significant reversible nerve lesion was present in 16 of 47 cases, and one case was still numb ten weeks later. Kipp et al.[1] explained third molar paresthesia cases (60 of 1377) on radiographic evidence, but 35% of these cases "in which anatomical structures could not be clearly interpreted were classified as unknown." Barsa et al.[8] found that 2-chloroprocaine causes conduction defects in animals and the addition of epinephrine increases conduction defects and neurohistologic abnormalities. Conversely, pH and the preservative sodium bisulfite did not produce any abnormal effects.

Concern has been expressed for the neurotoxicity of local anesthetics used in dentistry. Gruber recommended against the use of procaine in 1950 because it caused more paresthesia cases than lidocaine in dental practice.[9] Prilocaine 4% (an amide), plain and with epinephrine, is accompanied by a package insert warning that "persistent paresthesia of the lips and oral tissues may occur."[10] The package insert for lidocaine warns that the "patient should be informed of the possibility of temporary loss of sensation . . . and be advised to consult the dentist if anesthesia persists."[11]

The pharmacologic classification of dental local anesthetics into esters and amides is based on the bond hydro-

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Table 1. Paresthesia Cases

Surgically Explained Group	
Excessive hemorrhage occurance	6
Infection present	1
Inferior alveolar nerve seen	21
Long buccal-surgical incision	2
Surgically unexplained	16
Total cases	46

lyzed in metabolic degradation and elimination in the human body.[5] The local anesthetic molecule is divided into three parts, the aromatic (hydrophobic) joined by an ester or amide bond to the alcoholic (hydrophilic) and tertiary amino groups. Hydrolysis of the ester or amide bond results in the formation of an alcohol product which varies in structure and activity depending on the parent molecule.[12] Increasing the length of the alcohol group leads to greater anesthetic potency. Consequently the alcoholic or hydrophilic portion of the molecule is most probably the part attributable to the clinical action of the local anesthetic on the human nerve.[5] The alcohol group is of clinical interest because alcohol is known to be neurotoxic, causing paresthesia.[13,14]

MATERIALS AND METHODS

All surgical exodontia cases (each patient is one case) performed in a private practice over a period of 60 months were retrospectively reviewed. All paresthesia cases were evaluated by reviewing the chart notes and panoramic radiographs. The study does not include any case of tumor, fracture, or cyst present near the site of surgery. Clinical notes were charted in a manner similar to Kipp's 1980 study[1] to show any presence of nerves, especially inferior alveolar, in the surgery site of excessive hemorrhage from the socket during surgery.

In the initial case series (n = 2792), 2% lidocaine with 1 : 100,000 epinephrine was used as the inferior alveolar block anesthetic agent concurrent with 0.5% bupivacaine with 1 : 200,000 epinephrine used for buccal infiltration. For the second case series (n = 2195), 3% mepivacaine was used as the inferior alveolar block anesthetic and 0.5% bupivacaine with 1 : 200,000 epinephrine for infiltration. The dental cartridges were removed from the containers and never exposed at any time to alcohol soaking or alcohol treatment before patient injection.

For the purpose of this study, an explained paresthesia case was defined as one in which surgical notes confirm presence of the nerve during surgery,[15] excessive hemorrhage occurred, infection was present, or the incision involved the long buccal nerve (Table 1). An unexplained paresthesia case had none of the preceding criteria that might account for the paresthesia.

All patients were given postoperative written instructions to report any numbness, and all patients who had any clinical suspicion of nerve involvement were asked during a postoperative visit if they had numbness. Examination of paresthesia patients postoperatively consisted of a pin-prick test and evaluation of the functions of pain, touch, pressure, and mapping of involved areas at each visit. The patient population was suburban, with no preselection of ethnic groups, age, or sex. Using a χ^2 test, the incidence of paresthesia in the lidocaine-treated groups was compared with the incidence of paresthesia in the mepivacaine-treated groups. Separate tests were performed for the explained cases, the unexplained cases, and all cases. Differences in risk to males and females also were evaluated. The paresthesia group was broken into two subgroups based on explained versus unexplained clinical findings and compared with the patients who experienced no paresthesia.

The surgical technique consisted of Stryker bur for removing bone and sectioning teeth with the bur operating under a lavage of sterile water, elevator for removing teeth and sections of teeth, root tip elevator when indicated, and use of headlight rather than overhead lighting alone to aid in close inspection of all extraction sites. Anesthesia consisted of local anesthetics, nitrous oxide and oxygen as inhalation agents, and intravenous diazepam, meperidine, and methohexital. A single surgeon performed all surgery. Paresthesia was evaluated at postsurgical intervals of 48 hours, seven days, two weeks, one month, three months, and one year. Four paresthesia cases were lost to follow-up evaluation. All other cases were followed until normal sensation returned or the patients were not inconvenienced by the paresthesia.

RESULTS

Forty-six patients with clinical paresthesia were evaluated. This represents a 1.4% incidence for third molar removal (44/3071) and 0.92% (46/4987) for all exodontia and compares favorably with the 1.3%–5.3% reported incidence.[16]

In the explained group of patients, 21 of 30 had a clinical notation of observing (but not cutting) the inferior alveolar nerve during the surgical care (Table 1).[1,15] Visualization of the nerve does not imply that this event causes paresthesia. The incidence of paresthesia in this category was significantly higher for mepivacaine-treated patients ($\chi^2 = 4.57$, $df = 1$, $P < 0.05$) than lidocaine-treated patients (Table 2). There was no difference in the incidence of paresthesia in the unexplained category. Overall the incidence of paresthetic following mepivacaine

Table 2. Incidence of Paresthesia With Mepivacaine and With Lidocaine

	Paresthesia							
	Explained		Unexplained		Both		No paresthesia	Total
	No.	%	No.	%	No.	%		
Mepivacaine	19	0.87	7	0.32	26	1.18	2169	2195
Lidocaine	11	0.39*	9	0.32	20	0.72†	2772	2792

* $P < 0.05$.
† $P = 0.09$.

showed a nonsignificant trend ($\chi^2 = 2.95$, $df = 1$, $P = 0.09$) to be less than the incidence in the lidocaine group.

The duration of paresthesia after surgery consisted of resolution to normal feeling within four weeks in 27 of the 42 cases that could be evaluated (Table 3). Two male patients, ages 56 and 60, sustained persistent paresthesias that had not resolved one and two years, respectively, postoperatively. The sensory nerves involved were two long buccal, one right lingual, 24 left inferior alveolar, and 19 right inferior alveolar. Anatomic evaluation of tooth position found vertical bony impactions involved in 17 of the 46 reported paresthesia findings. The largest group of patients with paresthesia was between the ages of 20 and 39 years old, which reflects the age group of the patient population treated.

The incidence of paresthesia was 0.84% (19/2264) in males and 0.99% (27/2723) in females (not a significant difference). The incidence of explained cases was 0.31% for males and 0.33% for females, and the incidence of unexplained cases was 0.53% for males and 0.66% for females. These data suggest a trend towards a somewhat higher incidence of paresthesia in females, but none of the differences was statistically significant.

DISCUSSION

The incidence of paresthesia following mepivacaine to that following lidocaine (1.63 : 1) for all cases of paresthesia suggests that the local anesthetic may be related to causation. The ratio in the two drug groups should be similar if the local anesthetic was unrelated to the occurence of paresthesia. This hypothesis is weakened by the similar incidence of paresthesia for both local anesthetics in the unexplained group. The distinction between unexplained and explained assumes that visualization of the nerve is related to nerve trauma which would confound the incidence of paresthesia due to the local anesthetics. If this assumption is not valid, then the overall incidence data provides evidence that the difference in the incidence of paresthesian is due to the local anesthetic used.

Table 3. Duration of Paresthesia of All Inferior Alveolar and Lingual Nerves

Mo	No. of Patients
0–1	27
2–3	6
4–6	2
7–9	3
10–12	2
>12	2
Lost to follow-up	4

Hypothetical Model of Molecular Basis of Paresthesia

It is the molecular property of local anesthetics to selectively affect the least myelinated nerve fiber first.[5] This differential sensitivity of nerve fibers to local anesthetics has been known since 1929[17] and is of great practical importance because the sensation of pain, fortunately, is eliminated first.[5,18] Many dentists are aware of the ester versus amide chemical classification of local anesthetics, but it is important to note that this is a classification of drug metabolism in humans and does not relate to the functional site of the drug.

Local metabolism occurring where the drug is acting could enzymatically hydrolyze an ester or amide bond which would result in an increased concentration of alcohol molecules on the neuron. Alcohol nerve blocks are well known to cause anesthesia and paresthesia symptoms in the human cranial V nerve.[14,15] It is not unreasonable to assume that enzymes existing in the neuron to permit normal physiologic activity could break an ester or amide bond.[19]

Another contributing clinical observation consists of the greater incidence of dental paresthesia in patients treated with local anesthetics with ester bonds than in those treated with local anesthetics with amide bonds.[9] This is explainable by the model because an ester bond requires less energy to hydrolize than an amide bond in vitro and is therefore more likely to be hydrolyzed.[12]

Thus paresthesia for an undetermined period of time can occur if the local anesthetic molecule breaks down into an alcohol product in the vicinity of a sensory nerve

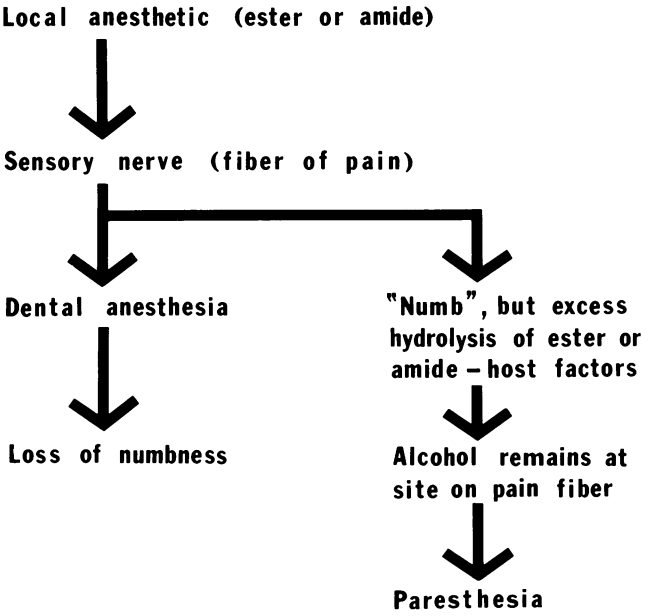

Figure 1. A molecular model for paresthesia.

(Figure 1). Previous reports have attempted to account for the similarity of the symptoms of unexplained paresthesia to those of alcohol-induced paresthesia by suggesting that local anesthetic agents may have been contaminated by alcohol, although no clinical studies support this view.[14,20] Such a contamination, however, is not necessary if an alcohol could be produced by the metabolism of the local anesthetic itself. Specific models of anesthetic blockade suggest binding of the local anesthetic occurs on the nerve's aqueous pore (hydrophilic), which could be compatible with the direct action by an alcohol (hydrophilic) on the nerve.[6] Prilocaine, an amide, is recognized by its manufacturer to cause paresthesia, and this persistant neurologic deficit "may be related to the technique employed, the total dose of local anesthetic administered, the particular drug used, the route of administration, and the physical condition of the patient."[10] Lidocaine has also been cautioned to have a persistent neurologic deficit.[11] The clinical observation of an unexplained group of paresthesia patients may in reality be explained by enzymatic hydrolysis of the local anesthetic into a drug metabolite, an alcohol.

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