Anesthetic Efficacy of the Inferior Alveolar Nerve Block in Red-haired Women

Brock Droll, DMD, MS, Melissa Drum, DDS, MS,† John Nusstein, DDS, MS,† Al Reader, DDS, MS,† and Mike Beck, DDS, MA‡*

Abstract

Introduction: The exact reasons for failure of the inferior alveolar nerve (IAN) block are not completely known, but red hair could play a role. The genetic basis for red hair involves specific mutations, red hair color (RHC) alleles, in the melanocortin-1 receptor (MC1R) gene. The purpose of this prospective randomized study was to investigate a possible link between certain variant alleles of the MC1R gene or its phenotypic expression of red hair and the anesthetic efficacy of the IAN block in women. **Materials:** One-hundred twenty-four adult female subjects (62 red haired and 62 dark haired) participated in this study. Dental anxiety was determined in each subject using the Corah Dental Anxiety Questionnaire. The subjects were given 2 cartridges of 2% lidocaine with 1:100,000 epinephrine via the IAN block. Pulpal anesthesia was measured in the posterior and anterior teeth in 4-minute cycles for 60 minutes using an electric pulp tester. The MC1R alleles were genotyped for each subject from cheek cells containing DNA collected using buccal swabs. **Results:** Women with red hair and women with 2 RHC alleles reported significantly higher levels of dental anxiety compared with women with dark hair or women with 0 RHC alleles. No significant differences in anesthetic success were found between any of the groups for any of the teeth. **Conclusions:** Red hair and the MC1R gene were significantly linked to higher levels of dental anxiety but were unrelated to success rates of the IAN block in women with healthy pulps. *(J Endod 2012;38:1564–1569)*

Key Words

Inferior alveolar nerve block, melanocortin-1 receptor, red hair

From *Private Practice, Sartell, MN; and Divisions of †Endodontics and ‡Oral Biology, The Ohio State University, Columbus, OH.

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Address requests for reprints to Dr Melissa Drum, Division of Endodontics, College of Dentistry, The Ohio State University, 305 West 12th Avenue, Columbus, OH 43210. E-mail address: drum.13@osu.edu

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The inferior alveolar nerve (IAN) block is the most frequently used injection technique for achieving local anesthesia for mandibular restorative and surgical procedures. However, the IAN block does not always result in successful pulpal anesthesia (1–6). Failure rates (ie, never achieving 2 consecutive 80 readings with the electric pulp tester) of 10% to 39% have been reported (1–6). A possible contributing reason for failure may be red hair.

The genetic basis for red hair involves specific mutations, red hair color (RHC) alleles, in the melanocortin-1 receptor (MC1R) gene, which may modulate pain pathways (7–9). An allele is an alternative form of a gene that is located at a specific position on a specific chromosome. These DNA codings determine distinct traits that can be passed on from parents to offspring. Previous research has found reduced subcutaneous efficacy of lidocaine and increased sensitivity to thermal pain in female patients with red hair (7). Others (8) have shown that the anesthetic requirement for desflurane was increased in female patients with red hair, and red hair color was also associated with a fear of dental pain and anxiety (9).

No objective study has evaluated the efficacy of lidocaine in red-haired women for anesthetizing the IAN. The purpose of this prospective, randomized study was to investigate a possible link between certain variant alleles (RHC alleles) of the MC1R gene or its phenotypic expression of red hair and the anesthetic efficacy of the IAN block in women.

Materials and Methods

One hundred twenty-four adult female subjects participated in this study. The subjects were in good health and were not taking any medications that would alter pain perception. Exclusion criteria were as follows: male, younger than 18 years of age, older than 65 years of age, allergies to local anesthetics or sulfites, pregnancy or nursing, a history of significant medical conditions (American Society of Anesthesiologists class II or higher), taking any medications (eg, over-the-counter pain-relieving medications, narcotics, sedatives, antianxiety or antidepressant medications) that may affect pain assessment, active pathosis at the site of injection, and the inability to give informed consent. The Ohio State University Human Subjects Review Committee approved the study, and written informed consent was obtained from each subject.

Sixty-two red-haired female subjects and 62 dark-haired female subjects received conventional IAN blocks. Equal numbers of mandibular right and left sides were tested, with the first and second molars, first and second premolars, and lateral and central incisors chosen as the test teeth. The mandibular contralateral canine was used as the control to ensure that the pulp tester was operating properly and that the subject was responding appropriately. Visual and clinical examinations were conducted to ensure that all teeth were free of caries, large restorations, crowns, and periodontal disease and that none had a history of trauma or sensitivity. Each subject completed the Corah Dental Anxiety Scale to rate her level of anxiety before testing (10).

Before the first injection, the experimental teeth and the contralateral canine (control) were tested 3 times with the electric pulp tester (Kerr; Analytic Technology Corp, Redmond, WA) to ensure tooth vitality and obtain baseline information. The teeth were isolated with cotton rolls and dried with an air syringe. Toothpaste was applied to the probe tip, which was placed in the middle third of the buccal or labial surface of the tooth being tested. The value at the initial sensation was recorded. The current rate was

set at 25 seconds to increase from no output (0) to the maximum output (80). Trained personnel administered all preinjection and postinjection tests.

Before the experiment, the red-haired and dark-haired female subjects were randomly assigned 6-digit numbers from a random number table. Each subject was also randomly assigned a right or left designation to determine which side of the mandible would receive the IAN block. Only the random numbers were recorded on the data collection sheets and genotype samples to further blind the experiment.

Subjects were instructed before the study on how to rate the pain for each phase of the first IAN block including needle insertion, needle placement, and deposition of anesthetic solution using a Heft-Parker visual analog scale (VAS) (11). The VAS was divided into 4 categories. No pain corresponded to 0 mm. Mild pain was defined as greater than 0 mm and less than or equal to 54 mm. Mild pain included the descriptors of faint, weak, and mild pain. Moderate pain was defined as greater than 54 mm and less than 114 mm. Severe pain was defined as equal to or greater than 114 mm. Severe pain included the descriptors of strong, intense, and maximum possible. During each phase of the first IAN block, the principal investigator informed the subject when each phase of the injection was complete. Immediately after the first IAN block, the subject rated the pain for each injection phase on the VAS. No VAS was completed after the second IAN block because the results would have been skewed by soft-tissue anesthesia from the first injection.

After wiping excess moisture off the tissue to be injected, a topical anesthetic (20% benzocaine; Patterson Dental Supply, Inc, St Paul, MN) was wiped on the mucosa using a cotton tip applicator and left to sit for 1 minute. A standard aspirating syringe was loaded with 1 cartridge of 2% lidocaine with 1:100,000 epinephrine (Xylocaine; Dentsply, Astra Zeneca LP, York, PA) under sterile conditions. All anesthetic cartridges were checked to ensure that the anesthetic solution had not expired. A standard inferior alveolar nerve block was administered with a 27-G 1½-inch needle (Monoject; Sherwood Medical, St Louis, MO) attached to the previously loaded syringe. For the conventional IAN block, the needle was inserted with landmarks described by Jorgensen and Hayden (12). The needle was then advanced to the target site (placement). After negative aspiration, the anesthetic was deposited over a 1-minute time period (deposition). All injections were given by 1 operator (BD). After the completion of the VAS, the injection was repeated with a second cartridge of 2% lidocaine with 1:100,000 epinephrine.

At 1 minute after the second IAN block injection, the second and first molars were pulp tested, and the patient was asked if her lip was numb. At 2 minutes, the second and first premolars were tested. At 3 minutes, the lateral and central incisors were tested. At 4 minutes, the contralateral canine was pulp tested, and the subject was asked if her lip was numb. This cycle of testing was repeated every 4 minutes for 60 minutes. At every fourth cycle, the control tooth (ie, the contralateral canine) was tested by a pulp tester without batteries to test the reliability of the subject. If the subject responded positively to an inactivated pulp tester, then she was not reliable and was not used in the study. If profound lip numbness was not recorded within 15 minutes, the blocks were considered unsuccessful, and the patient was reappointed. Only 1 patient failed to achieve profound lip numbness and was reappointed. All testing was stopped at 60 minutes after injection.

No response from the subject at the maximum output (80 reading) of the pulp tester was used as the criterion for pulpal anesthesia. Anesthesia was considered successful when 2 consecutive 80 readings were obtained within 15 minutes of the last IAN block injection and the 80 reading was continuously sustained through the 60th minute (ie, we would want the patient anesthetized by 15 minutes and have pulpal anesthesia for 60 minutes).

TABLE 1. Initial Values for Red-haired and Dark-haired Groups

	Red-haired group	Dark-haired group	*P* value
Total subjects (all women)	62	62	
Mean age (y)	26.3 ± 8.2	24.9 ± 3.3	.2141*
Age range (y)	18–61	19–35	
Left (%)	33 (53)	32 (52)	.8573*
Right (%)	29 (47)	30 (48)	

*There were no statistical differences between the groups.

The MC1R alleles were genotyped for each subject. Cheek cells containing DNA were collected from the subjects using a buccal swab (Boca Scientific, Boca Raton, FL). Subjects swabbed their buccal mucosa for approximately 1 minute, and 2 separate swabs were collected from each subject. The swabs were placed in the accompanying tubes and were stabilized with DNA stabilization capsules (Boca Scientific, Boca Raton, FL). The tubes were labeled with the random 6-digit numbers to keep the subjects' identity and hair trait confidential from the laboratory. The tubes were packed and shipped to the DNA Core at the Center for Genetics and Molecular Medicine at the University of Louisville, Louisville, KY, for processing. This laboratory was chosen because they had experience genotyping the MC1R gene (8, 9). Only the MC1R genes were analyzed and genotyped.

Between-group comparisons for the red-haired subjects and dark-haired subjects for age and side of the mandible were performed using the randomization test and chi-square test, respectively. Similar comparisons were performed between subjects determined not to possess MC1R gene mutations consistent with red hair (RHC alleles) and those homozygous for such mutations. Between-group comparisons for anxiety were performed using the randomization test. Between-group comparisons for needle insertion pain, needle placement pain, and solution deposition pain were done using analysis of variance and Tukey-Kramer post-tests. Between-group comparisons for anesthetic success and the incidence of anesthesia (80 readings) were analyzed using multiple chi-square tests or Fisher exact tests with P values adjusted using the step-down Bonferroni method of Holm. Comparisons were considered significant at $P < .05$. With 124 subjects (62 in each group) and a nondirectional alpha risk of .05 and assuming a success rate for the block of 53% (1), the power of the chi-square test to detect a difference of ±25 percentage points in anesthetic success was 84%.

Results

A total of 124 women, 62 with natural red hair and 62 with natural dark hair, were included in the study (Tables 1 and 2). Aside from hair color, the women were also grouped by genotype. For the purposes of this experiment, the alleles strongly linked to the RHC phenotype (D84E, R151C, R160W, D294H, I155T, and R142H) and N29insA were all considered RHC alleles. Table 2 gives the number of

TABLE 2. Initial Values for Women with 2 or 0 RHC Alleles

	2 RHC alleles	0 RHC alleles	*P* value
Total subjects (all women)	45	52	
Mean age (y)	26.0 ± 8.4	24.9 ± 3.7	.4306*
Age range (y)	19–61	18–35	
Left (%)	21 (47)	28 (54)	.4806*
Right (%)	24 (53)	24 (46)	

*There were no statistical differences between the groups.