

Is Eye Color Related to Dental Injection Pain? A Prospective, Randomized, Single-blind Study

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Abstract

Introduction: Recent studies have investigated the relationship between pain perception and specific phenotypes such as red hair color and various eye colors. Further investigations into biomarkers as they relate to pain could be useful in understanding underlying genetic components involved in these pathways. Additionally, it would be clinically useful to determine if a patient would be more likely to experience pain during dental treatment based on eye color. The purpose of this study was to investigate a link between eye color and perceived injection pain in healthy, asymptomatic white women. **Methods:** Three hundred healthy, adult, white female patients were included, 133 with dark eyes and 167 with light eyes. Dental anxiety was assessed with the Corah Dental Anxiety Scale. Subjects with their eye color masked by dark glasses received a right maxillary lateral incisor infiltration of 1 cartridge of 2% lidocaine with 1:100,000 epinephrine. Patients rated their injection pain on a 170-mm Heft-Parker visual analog scale. Photographs of the subjects' eyes were taken after the infiltrations and categorized into dark- and light-eyed groups by 3 independent observers. Comparisons for injection pain were analyzed using analysis of variance and the Tukey-Kramer test. **Results:** No significant differences were found for pain of injection between dark- or light-eyed subjects. **Conclusions:** Eye color was not shown to be a predictor for injection pain in white women. Therefore, eye color would not be clinically useful in determining if a patient would be more likely to experience pain during dental treatment. (*J Endod* 2018; ■:1–4)

Key Words

Eye color, injection pain, lidocaine with epinephrine, pain

Pain is a conscious experience, which can be modified by the interpretation of nociceptive input and influenced by memories and emotional, pathologic, genetic, and cognitive factors (1). The topics of pain and anxiety have been studied in both the medical and dental fields for many years, and the investigation of possible underlying causes as well as effective management continues today. Although the precise details that lead to pain variations among individuals are not completely known, genetics appear to play a role in these processes (2, 3). As the demands for more personalized medical treatments evolve, the identification of specific genetic elements related to pain perception promises to be a key area of focus for health care providers as they search for less painful ways to treat their patients (4).

Is it possible that certain physical traits may be indicators for how a person might respond to a painful stimulus? Previous studies have investigated the correlation of red hair color to local anesthetic failure and pain. Liem et al (5) found an increased requirement for the general anesthetic desflurane in red-haired females when compared with dark-haired females. The same group of investigators also found that female patients with red hair had increased sensitivity to thermal pain as well as a significantly reduced efficacy of subcutaneous lidocaine (6). Binkley et al (7) found that increased levels of dental anxiety and fear of dental pain were associated with patients who had the phenotype for red hair and, more specifically, those with mutations in the melanocortin-1 receptor (*MC1R*), which may have a role in pain modulation (2–4). In a study by Droll et al (8), women with red hair and mutations in the *MC1R* gene were linked with higher dental anxiety levels; however, there was no significant difference in anesthetic success after the administration of an inferior alveolar nerve block when compared with dark-haired females. Based on correlations between red hair color and perception of pain, further investigations into different biomarkers as indicators for pain have been considered.

Sutton (9) described an association between eye color and the reaction to pain resulting from tooth cavity preparation. His observations were that pain reactions and the need for local analgesia increased as iris color changed on a color scale from light (blue) to dark (brown).

Teng and Belfer (10) conducted a pilot study and found that eye color may be related to pain for pregnant females both pre- and postpartum. The coauthor, Inna Belfer, MD, PhD, an associate professor of anesthesiology at the University of Pittsburgh,

Significance

Eye color was not shown to be a predictor for injection pain in white women. Therefore, eye color would not be clinically useful in determining if a patient would be more likely to experience pain during dental treatment.

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Clinical Research

Pittsburgh, PA, and prominent pain researcher, evaluated pain during childbirth. Their results indicated that those with a light eye color had a better pain tolerance than women with dark eyes, who had a higher sensitivity to pain.

Recently, Holmgaard et al (11) found that individuals with dark hair and eyes exhibited higher pain sensitivity than those with light hair and eye color. They concluded that the dark pigmentation trait group was more sensitive to a cold-induced pain test.

Further investigations into biomarkers as they relate to pain could be useful in understanding underlying genetic components involved in these pathways. Therefore, it would be clinically useful to determine if a patient would be more likely to experience pain during dental treatment based on eye color. The purpose of this study was to investigate a link between eye color and perceived injection pain in healthy, asymptomatic white women.

Materials and Methods

Three hundred adult female subjects were included in this study. To prevent the operator (J.H.) from assessing the patients' eye color, subjects were given dark-colored safety glasses by a trained research assistant before enrollment. All subjects were in good health and were not taking any medications that could affect or alter pain perception or anxiety. Subjects completed a written health history and were verbally questioned to confirm American Society of Anesthesiologist classification I or II health status. Exclusion criteria were as follows: male; younger than 18 or older than 65 years of age; eye colors other than brown, hazel, green, or blue; patients wearing colored contact lenses; laser or surgical intervention to change or modify iris color; nonwhite; allergies to local anesthetics or sulfites; pregnant or nursing; taking any medications that may affect pain or anxiety assessment (nonsteroidal anti-inflammatory drugs, opioids, antidepressants, and alcohol); active sites of pathosis in the area of injection; or 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. After the consent and medical history forms had been completed, subjects answered the Corah Dental Anxiety Scale questionnaire to rate their level of anxiety (12).

The patient was seated in the dental chair and instructed how to rate the pain for each of the 3 stages of the injection: needle insertion, needle placement, and deposition of anesthetic solution. The Heft-Parker visual analog scale (VAS) (13) was used in this study and was explained to the patient before injection. Each subject rated the pain for initial needle insertion, needle placement to the target site, and deposition of the anesthetic solution at the target site. Each phase of the injection was stated verbally to the patient as it was being performed. The VAS was a 170-mm line with various descriptive terms. The subjects placed a mark on the scale where it best described their pain level. To interpret the data, the VAS was divided into 4 categories with corresponding descriptive terms. No pain corresponded to 0 mm on the scale. 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 and included the descriptor moderate. Severe pain was defined as equal to or greater than 114 mm. Severe pain included the descriptors of strong, intense, and maximum possible. Patients recorded their pain immediately after the injection.

After the appropriate instructions were specified, the dental chair was placed in the supine position with the patient's head parallel to the floor. A visual and clinical examination of the oral cavity was done, ensuring that the site of injection was free from signs of inflammation, infection, or pathosis. The dental syringe had been previously prepared

and covered with a patient napkin on a dental tray next to the chair. A timer was set and positioned in direct sight of the operator before the injection. All subjects received a standard maxillary infiltration. A 27-gauge 1½-inch needle (Sherwood Medical Co, St Louis, MO) was used with a standard aspirating syringe (Hu-Friedy, Chicago, IL) and 1 cartridge of 2% lidocaine with 1:100,000 epinephrine (Xylocaine; AstraZeneca LP, Dentsply, York, PA). The first author (J.H.) administered all of the injections.

The target site was centered over the root apex of the maxillary right lateral incisor. No topical anesthetic, distraction techniques, or verbalization (other than stating the injection phase currently being performed) were used during the injection procedure to reduce any confounding factors that might affect the patient's measurable pain. The upper lip was lifted and the tissue pulled taught with the index finger and thumb. The needle was gently placed into the alveolar mucosa at the height of the mucobuccal fold (needle insertion). The needle was advanced into the tissue until it was estimated to be at the apex of the tooth and oriented parallel to the tooth's long axis (needle placement phase). No anesthetic solution was administered during this phase. After aspiration, solution deposition was accomplished by giving 1 cartridge of anesthetic over a 60-second time period. Care was taken to ensure that the deposition was constant and steady with a rate of ¼ cartridge per 15 seconds using the timer.

In order to categorize subjects by their eye color, a photograph of the patients' eyes was taken after the infiltration. An iPhone 6 (Apple Inc, Cupertino, CA) was used to capture the images. Flash settings and filter settings were disabled during image capturing. Subjects were seated in a designated location with sufficient indoor lighting to aid in appropriate lighting conditions. An up-close photograph (approximately 6 inches away) was taken of the subjects' eyes. Once the image was taken, a subjective observation was made to ensure that the photograph and eye color corresponded well to the actual eye color of the patient. Subjects were asked to state their self-reported eye color. Their observation was only noted when a discrepancy between the observer and patient response was apparent or when iris color appeared to have varying amounts of color shades, which was often described by patients as hazel or greenish-brown. Images were then uploaded into a secure folder where they would later be categorized into either light-eyed or dark-eyed groups.

Three independent observers (a female assistant endodontic professor and 2 male endodontic residents) categorized the subjects' eye color. Images were digitally visualized on a Dell HD P2214H computer monitor (Dell Inc, Round Rock, TX) and then placed into the appropriate category based on their independent observation. After the initial categorization, if all 3 observers agreed on the subject's eye color, the category for that particular subject was finalized. If there was disagreement among any of the observers, then the eye color for those particular individuals was reviewed again by the 3 observers to make a final determination of either a light- or dark-eyed categorization. If iris color could not be unanimously agreed on, the subject was excluded from the study. For standardization, subjects who displayed either a complete color in blue or green or a majority of blue/green colors were considered light eyes, whereas a complete color in brown or a majority of brown tones in iris color were categorized as dark eyes (Fig. 1).

A between-group comparison for the light-eyed subjects and dark-eyed subjects for age was performed using the randomization test. A between-group comparison for anxiety was analyzed using the Mann-Whitney-Wilcoxon test. Comparisons for needle insertion, placement, and deposition pain were performed using analysis of variance. Post hoc analysis was done using the Tukey-Kramer test. With a nondirectional alpha risk of 0.05 and assuming a standard deviation of 38 mm (14), a sample size of 300 subjects was required to demonstrate a difference of ± 15 mm on the VAS with a power of 0.93.

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