Pressure Pain Threshold With and Without Iontophoretic Anesthesia of the Masseter Muscle in Asymptomatic Males

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Aims: *The pressure pain threshold (PPT) in the superficial masseter muscle was measured with and without cutaneous anesthesia to determine whether there would be a difference in PPT scores.* **Methods:** *In 14 healthy male subjects, cutaneous tissues in the target areas were anesthetized with lidocaine with the help of an iontophoretic device. As a control, physiologic saline solution was applied iontophoretically to the contralateral masseter site. The subject and the PPT examiner did not know which side contained anesthesia, and the selection of which side to anesthetize was done in a random fashion. Multiple PPT measurements were made in the target sites before and immediately after the iontophoretic anesthesia.* **Results:** *The PPT level on the lidocaine side was not statistically different from the PPT level recorded on the control side (339.0 ± 87.6 kPa and 337.5 ± 77.7 kPa, respectively).* **Conclusion:** *Pressure pain sensation in the human masseter is not derived predominantly from the cutaneous tissues, but from the muscle itself.*

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Key words: lidocaine, physiologic saline, cutaneous tissues, pressure increment rate, fluid volume change

Palpation findings, whether gathered with a fingertip or with the aid of a pressure-measuring device, are used to confirm whether a patient's pain is musculoskeletal in nature.[1] Several studies have used pressure algometric devices to determine the pressure pain threshold (PPT) levels at various muscle sites in normal and painful human subjects.[2–13] When direct injection (local anesthetic and/or saline solution) to the muscle was used, the pressure pain level shifted significantly from the baseline.[14,15] From the evidence noted above, it would be reasonable to conclude that palpation pain is elicited predominantly from the muscle or fascial tissues.

Recently, several researchers have questioned this assumption by proposing that the pain elicited during palpation might be coming from both the myofascial tissues and from the cutaneous and subcutaneous tissues.[16–18] These researchers have tested this assumption by measuring PPT levels in muscle sites before and after anesthetizing the overlying cutaneous tissues. For example, Jensen et al[16] demonstrated a 70% increase in PPT levels in anesthetized muscles versus a 22% increase in saline-injected sites.

Kosek and Ekholm[17] demonstrated a much smaller change from baseline (only 16%) in resting muscle PPT levels in anesthetized sites, versus a negative 12% change in control sites. In their study, a eutectic mixture of a local anesthesia cream was applied to the cutaneous tissues overlying the quadriceps muscle in 14 asymptomatic female subjects. Finally, Reid et al[18] demonstrated much smaller increases (6.0% in males and 6.4% in females) in PPT levels on the anesthetized side for the masseter muscle in asymptomatic subjects (23 male and 16 female).

It is interesting to note that the magnitude of the anesthetic effect on PPT levels reported by Jensen et al[16] was not replicated by either Kosek and Ekholm[17] or Reid et al.[18] In fact, both subsequent studies reported a much smaller effect. Of course, these different findings might be a result of the fact that different muscle sites were being compared or that clearly different PPT testing methodologies were used (eg, size of tip, rate of pressure being applied). It seems likely that the injection of fluid into the cutaneous tissues might in itself induce tissue trauma, which could initially make the site less reactive than normal. This would clearly appear to be the case in the Jensen et al study,[16] since a 22% increase in PPT levels on the control site was reported. In agreement with this observation is that the control sites in other studies,[17,18] in which no fluid was injected, showed decreased PPT levels when tested.

There are 2 nonneedle, noninjection methods of producing a cutaneous anesthesia. These methods are: *(1)* application of dermal penetrating creams and gels that contain local anesthetic, and *(2)* the use of iontophoresis to induce local anesthetic into the cutaneous tissues. The advantage of iontophoresis is that it allows a uniform, nontraumatic induction of local anesthetic. Iontophoretic anesthesia has been shown to reduce the burning surface pain reported in patients with oral herpes[19] and dermatologic diseases.[20,21] In an attempt to avoid the confounding effect of needle-induced fluids on PPT levels and to produce a uniform cutaneous anesthesia, our study involved the use of an iontophoretic technique to induce cutaneous tissue anesthesia. The purpose of our study was to measure PPT in the masseter muscle with and without anesthesia of the cutaneous tissues. The null hypothesis being tested was that there would be no difference in the pre- versus postiontophoresis PPT scores between the control side and the anesthetized side.

Materials and Methods

Subjects

Fourteen healthy male subjects (aged from 23 to 30 years; mean: 26.2 years old) were recruited from graduate students and staff of the School of Dentistry, Iwate Medical University. Inclusion criteria were a jaw-opening range of more than 40 mm between the incisal edges of the maxilla and the mandible and no reports of jaw joint sounds, spontaneous masticatory muscle pain, or cervical region pain. None of the subjects could have a past history of a temporomandibular disorder, a cervical disorder, or a dermatologic problem in the facial region. All subjects were prohibited from eating, smoking, and drinking coffee or tea for at least 3 hours before the experiment.

Iontophoresis

An iontophoretic device was used to induce cutaneous and subcutaneous tissue anesthesia in all subjects. Based on prior research,[22] 1 mL of non–epinephrine-containing lidocaine (4%) was soaked in cotton and then placed in the anode (2.0 cm in diameter) of the device. In addition to the lidocaine iontophoresis, an equal volume of physiologic saline (0.9%) was placed in the electrode reservoir on the opposite side. The site of electrode placement and subsequent palpation was a point on the superficial masseter 20 mm along a line drawn from the angle of the mandible to the alar of the nose. The selection of the side to receive lidocaine versus saline was made randomly, and neither the subject nor the PPT device operator was aware of the selection. Based on prior research,[22] the electric current utilized during the iontophoresis was 1.5 mA.

Anesthetic Efficacy Testing

On a separate day, to determine that complete cutaneous anesthesia was being achieved, a test of skin anesthesia depth was performed. This testing was performed on 7 of the 14 subjects in the study and it involved the iontophoretic application of lidocaine anesthetic to the target region of the masseter for a total time period of 9 minutes. During this period, after 3, 6, and 9 minutes had elapsed, the device was removed for less than 30 seconds and a 30-gauge sterile injection needle was inserted into the skin. The subjects were asked to indicate when they first felt any pain sensation elicited by insertion of the needle perpendicular to

the skin. The depth of the needle penetration was measured by the use of a sterile sliding rubber disk that moved along the needle shaft. After the needle was removed, the length from the tip of the needle to the rubber disk was measured with a caliper.

Cutaneous Tissue Depth Testing

To know how deep the cutaneous tissues overlying the masseter at the target site were in the study sample, ultrasonic measurement of these tissues was performed. This testing involved the use of a real-time ultrasound scanner (U-Sonic RT2000, Yokokawa) on the right side. The subjects were asked to sit upright with natural head posture. The anterior border of the masseter was palpated to orient the transducer perpendicular to the target area, and then ultrasound images were obtained. Contrast among tissues was confirmed by the subjects alternately clenching and relaxing the jaw muscles.[23] Scanning was performed by the examiner applying very light pressure with the transducer against the skin while the subjects were relaxed. The thickness was measured to the nearest millimeter between the 2 cursors set on the surface of the skin and the surface layer of the masseter muscle on the monitor screen.

Pressure Pain Threshold Measurements

At a separate visit from the first 2 experiments, PPT testing was performed in the cutaneous tissues over the masseter with and without local anesthesia. This involved the examiner applying an algometric device against the target site and slowly increasing the pressure until the patient indicated the first occurrence of pain. The rate of pressure application was kept steady, and the device used was a custom-made, computer-controlled, automatic PPT measuring system.[24] The device allowed the examiner to set the precise rate of pressure to be applied, and the point of contact with the muscle site was a circular, spongy, rubber-covered tip with a diameter of 1.0 cm. In this study, the pressure increment rate was set at 62.4 kPa/s (0.5 kg/s). The subjects were instructed to press a button to indicate the precise moment they detected change from "being pressed" to "initial pain recognition." The time point from onset of the trial to the point when the button was pushed and the rate of pressure change during the trial were stored on a computer disk for further analysis (Fig 1). A load-time regression line was calculated to evaluate the pressure increment rate applied. If the pressure increment rate was not steady (usually due to movement of the patient's head), the trial was repeated. The variability accepted as steady was a pressure inside the 56.2 to 68.6 kPa/s range. Fortunately, no data was excluded for this reason. Before and after the iontophoretic conditioning of the muscle, PPT measurements were performed 3 times, with a 60-second interval between measurements.

Bias Control Procedures

All the pressure trials were performed by a well-trained examiner who was blinded to which side received anesthesia. Finally, as a method of checking the effectiveness of the blinding, subjects were asked at the end of the experiment which side they thought to be the anesthetized side.

Statistical Analysis

Differences in PPT before and after iontophoresis were analyzed with the nonpaired t test. The paired t test was applied for normalized data between the lidocaine side and the saline side. Power analysis was also applied.[25]

Results

Efficacy of Iontophoresis

The needle insertion depth before pain was experienced by the subjects and the distance between the skin surface and the fascia of the masseter (measured with ultrasonography) are shown in Table 1. These data indicate that the mean needle insertion depths without pain were: 3.5 ± 1.9 mm, 6.0 ± 2.3 mm, and 7.2 ± 1.3 mm with respect to iontophoretic anesthesia applied for 3, 6, and 9 minutes, respectively. The mean thickness of the tissues overlying muscle was 5.7 ± 1.3 mm as measured by ultrasonography. These data were interpreted to indicate that the use of an iontophoretic current for 9 minutes should have easily produced excellent anesthesia of all of the cutaneous tissues.

Pressure Pain Threshold Level Data

Mean PPT values before iontophoresis with the muscle at rest were 334.4 ± 68.2 kPa on the anesthetized side and 335.4 ± 62.3 kPa on the control side (Table 2). After iontophoresis these levels were 339.0 ± 87.6 kPa on the anesthetized side and 337.5 ± 77.7 kPa on the saline side. The

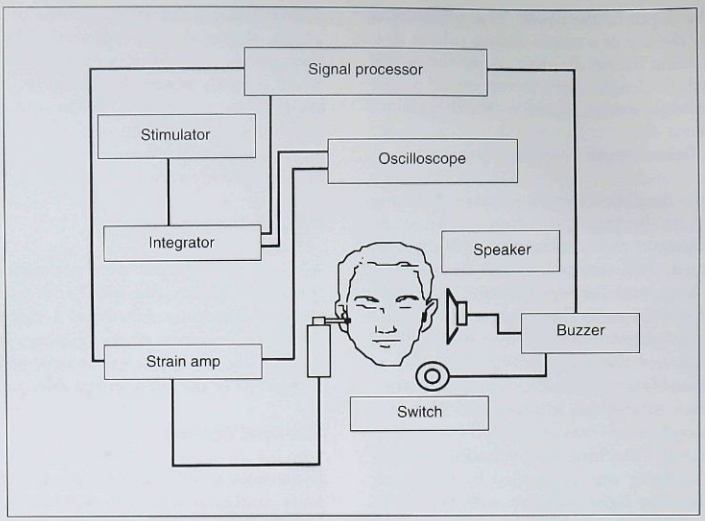

Fig 1 Block diagram of PPT measuring system. The system works as follows: *(1)* a target signal (desired force rate per second) is generated by being integrated with a signal from a stimulator; *(2)* the output from the strain amplifier on the PPT measuring device is recorded; and *(3)* these 2 signals are displayed on an oscilloscope. The operator's task is to keep the actual signal (strain gauge) in sync with the target signals as it is being applied.

posttreatment data were converted to a percentage of baseline, and the anesthetized side showed a 102.3 ± 19.8% change, while the control side showed a 101.4 ± 17.0% change. These differences were shown not to be statistically significant when tested with a nonpaired t test for the anesthetized side (t = 0.245, P = 0.811, df = 13) and the control side (t = 0.135, P = 0.894, df = 13). Finally, the researchers calculated the power for detecting a 20% mean difference in PPT levels for the sample size (n = 14) with an alpha of 0.05 and a 2-tailed t test. The data showed a power of 94%.

With regard to the bias control measures, the authors were confident that the blinding procedures remained intact throughout the experiment. When asked to guess which side had been anesthetized, the correct guess rate was 7 out of 14 subjects, or a 50:50 response rate. Six subjects selected the wrong side and 1 subject was unable to judge which side had been anesthetized.

Discussion

Our data allow us to accept the null hypothesis that there is no difference in PPT values on the control versus the anesthetized side from before to after the iontophoresis procedure. These data also imply that the pain occurring in a careful PPT examination of the masseter in healthy male subjects comes predominantly from the muscle and fascial tissues, not from the cutaneous tissues as suggested by prior researchers.[16–18] Actually, our data are similar to that of Reid et al,[18] in that they found a change of 6.0% in male subjects, while our data showed a 2.2% change. The major difference between these 2 studies is the procedure used for anesthetic infusion. With the iontophoretic method, the anesthetic was induced uniformly, starting at the skin surface and penetrating down to the muscle, and we were able to confirm the efficacy of this method in a separate experiment. Another difference is that Reid et al[18] reported lower baseline (before anesthesia) levels of PPT.

Table 1 Needle Insertion Depth by Time of Iontophoresis and Thickness of Cutaneous Tissues, Based on Echo Images

Subject	Needle insertion depth (mm)			Tissue thickness (mm)
	3 min	6 min	9 min	
1	7.2	6.1	6.4	6.0
2	4.9	7.4	7.4	4.0
3	2.0	2.0	6.1	5.0
4	2.5	6.3	7.7	6.0
5	2.5	4.2	5.3	6.0
6	2.6	8.4	8.3	8.0
7	2.5	7.9	8.9	5.0
Mean	3.46	6.04	7.16	5.71
SD	1.90	2.26	1.28	1.25

Table 2 Pressure Pain Threshold Values

Subject	Anesthetized side			Saline side		
	Before (kPa)	After (kPa)	Ratio*	Before (kPa)	After (kPa)	Ratio*
1	263.3	257.1	97.6	295.8	289.5	97.9
2	220.9	242.1	109.6	249.6	350.7	140.5
3	368.2	339.5	92.2	338.2	297.0	87.8
4	385.6	318.2	82.5	325.7	313.2	96.2
5	224.6	278.3	123.9	327.0	371.9	113.7
6	356.9	344.4	96.5	319.5	388.1	121.5
7	381.9	495.5	129.7	499.2	572.8	114.8
8	342.0	366.9	107.3	285.8	278.3	97.4
9	287.0	327.0	113.9	348.2	335.7	96.4
10	353.2	365.7	103.5	322.0	333.2	103.5
11	285.8	197.2	69.0	265.8	248.4	93.4
12	369.4	359.4	97.3	338.2	320.7	94.8
13	458.0	334.5	73.0	406.8	284.5	69.9
14	384.4	520.4	135.4	374.4	340.7	91.0
Mean	334.37	339.01	102.25	335.44	337.49	101.35
SD	68.24	87.63	19.75	62.31	77.66	16.95

* Ratio = after PPT values/before PPT values × 100.

This difference is very likely due to the faster rate of pressure applications being applied in our study versus their study (62.4 kPa/s versus 30 kPa/s, respectively). The rate of pressure being applied in our study was based on data reported in prior research,[26] which determined through repeated tests that the low variability between examiners was achieved when a rate of 62.4 kPa/s was used for pressure application. This rate was also preferred by the examiners in terms of optimum operator control of the device. Our data are clearly different in several ways with the findings of some previous reports.[16,17] Unfortunately, we cannot directly contrast our data to these, since they used different muscle sites.

Two subjects in our study showed a relative insensitivity to the 30-gauge needle (penetration to a depth of 5 mm and 7 mm was seen, even with only 3 minutes of iontophoresis). In other words, these 2 subjects allowed the penetration of the needle to a depth well beyond that at which all other subjects stated they felt pain. Such variability is not uncommon in human pain experiments, and these data could be explained by the fact that

a 30-gauge needle is not always perceived as a painful stimulus in all subjects. In general, the mean value of needle insertion depth after 6 minutes of iontophoresis matched the average thickness of the cutaneous tissues. Because of the possibility that the ultrasound transducer could compress the cutaneous tissues and thereby reduce the distance from the skin surface to the muscle during the image scanning,[23] 6 minutes was not considered enough time to anesthetize all the cutaneous tissues. Besides, 1 subject (#3) revealed that at 6 minutes the cutaneous anesthesia depth was slightly less than the thickness of these tissues as determined by ultrasonography. For these various reasons, we selected an iontophoresis protocol of 9 minutes duration at 1.5 mA for the actual experiment.

A concern in any PPT study is whether the examiners are following the prescribed protocol. We looked at our data closely to be sure that the actual pressure rate was within the established limits. This was done by checking its mean velocity, the regression line of the pressure level, its residual variance, and the residual maxima of the PPT forces being applied on a subject-by-subject basis. This was considered important, since it is well known that the PPT score is affected by a change in pressure increment rate.[16,27] After checking, it was determined that all pressure increment rate data showed a value higher than 0.99 in residual variance, and their actual velocities were between 56.2 and 68.6 kPa/s.

Pressure pain in the masseter muscle region in asymptomatic male subjects is not substantially determined by afferent input from the cutaneous tissues. The cutaneous tissues undoubtedly contribute to sensations of pain on palpation, but the magnitude of this contribution appears to be small for this subject group at this muscle site. At this time, we cannot determine whether this observation is true for other muscle sites. Obviously, future research in this area needs to be directed at different muscle sites and at female subjects, since these subjects might react differently than males. Our data also does not rule out the possibility that cutaneous anesthesia might not produce a statistical and clinically important increase in PPT levels in myofascial pain patients, and careful testing of this population is also needed.

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