The Effect of Topical Anesthesia on Pain Perception in Patients with Local Myalgia

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ABSTRACT

Temporomandibular disorders (TMD) is a term used to embrace pain and dysfunction in the jaw-, face- and temple region. Myofascial pain is considered the most common condition included in TMD. The diagnostic criteria for myalgia are based on the patient’s symptoms and clinical signs, where pain to palpation of the jaw muscles is vital. The aim of this experimental trial was to examine whether pain perception is influenced by topical anesthesia in patients with local myalgia of the jaw muscles. Our hypothesis was that the pressure pain thresholds (PPT) at jaw muscle sites are affected after topical application of anesthesia in patients with local myalgia.

Ten women (median age 36 years) with TMD related to myalgia participated in the study. The PPT at masseter muscle and temporal muscle sites bilaterally and the first dorsal intraossei on the dominant hand were measured using an electronic algometer. After a baseline registration, EMLA or placebo cream was applied on the chosen sites in a randomized order. A new registration was carried out five minutes after the application. The values for each participant before and after the application were compared using Wilcoxon rank sum test. A P-value < 0.05 was considered statistically significant.

The PPT increased significantly after application of topical anesthesia, but not placebo cream. The results indicate that the superficial nociceptors were sensitized and sensitive to topical anesthesia in patients with TMD related to myalgia. The interpretation of a pain response to pressure thus seems to be complex and warrant further studies.
INTRODUCTION

Myofascial pain and TMD
Temporomandibular disorder (TMD) is a term used to embrace pain and dysfunction in the jaw-, face-, and temple region (Okeson, 2008). The condition affects about ten percent of adults and is more common in women. The incidence of TMD seems to be almost similar in men and women, but men recover faster. Women are thus at a higher risk for suffering from long-standing pain in the jaw-face region, and frequent and severe symptoms of TMD are almost three times more common among females. The onset of signs and symptoms of TMD seems to coincide with the beginning of adolescence and the prevalence peaks in the middle-age whereas the condition is less common among older people (Yekkalam and Wänman, 2014). The etiology of TMD is multifactorial and major contributing factors can be highly individual for each patient. Injuries following macro or micro trauma are considered possible initiating factors for developing TMD. Other contributing factors appear to be lack of load resistance in the tissues involved and other unfavorable biomechanical factors (Marklund, 2009).

Myofascial pain is considered the most common condition included in TMD (Al-Ani et al., 2005). The first time myofascial pain was described was more than a century ago, by William Gowers (1904). He described the condition as fibrositis, a local idiopathic muscular rheumatism (Inanici and Yunus, 2004).

Palpation and Diagnostic Criteria
In 1992 the Research Diagnostic Criteria for TMD (RDC/TMD) was launched (Dworkin and LeResche, 1992) aiming at improved structure and unity in measurements and interpretation of the examination. The RDC/TMD has since been used worldwide and validated in several studies. The criteria was recently modified and updated to Diagnostic Criteria (DC/TMD) in order to improve sensitivity and specificity (Schiffman et al., 2014). The construct of DC/TMD criteria is based on the patient’s symptoms and registered clinical signs with pain to palpation as one important clinical sign. Thus, the criteria are based on pain in the masticatory muscles (masseter or temporalis), and whether this pain is modified by jaw movement. The provoked pain during palpation also has to be confirmed by the patient as “familiar pain”.
Palpation is a method where the clinician uses finger pressure to provoke the tissue in order to identify possible painful areas, classify the severity of the pain and set a diagnosis. Traditionally, in diagnosing subgroups of TMD, the elicited pain was graded by assessing the patient’s response to the stimuli. A palpation that is expressed as somewhat painful or noticed as a difference between sides the pain was classified as grade I. The response was classified as grade II if the patient shows visible pain reaction, i.e. palpebral reflex in the eye, and grade III if a protective or withdrawal reflex was elicited. In the revised criteria, the pain to palpation is noted, regardless of grading but a new criteria – familiar pain - has been introduced (Schiffman et al., 2014).

The diagnostic criteria for any condition, such as myofascial pain/myalgia, are optimal if no one truly affected is undiagnosed and nobody not truly affected is incorrectly diagnosed. In a relatively healthy population the criteria should ideally be more specific than sensitive. The revised DC/TMD criteria has been presented to have both high sensitivity and specificity (Schiffman et al., 2014).

The outcome of palpation of muscles is thus of great importance. The palpation is recommended to be a consistent force of 1 kg and to last for two seconds (Schiffman et al., 2014), but the technique may still vary between clinicians (force, the speed of increasing force and finding the right location). The present study will try to evaluate the validity of palpation i.e. whether it measures what it is supposed to measure. If topical anesthesia affects the pressure pain thresholds (PPT) we may question if the elicited pain during palpation of muscles is caused in part by nociceptors in the skin.

**Pressure pain thresholds**

Pain is a complex mechanism. Painful stimuli are not synonymous with pain perception and pain can be perceived in absence of painful stimuli. Pain is defined as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage” (Bonica, 1979). Perception is a psychological term for the process of interpreting sensory input by transforming it into meaningful information.
Painful stimuli, or noxious stimuli, are registered by peripheral nociceptors and the nervous signal is then transmitted via afferent A-delta and C-fibers to various parts of the brain. Pain can be experienced because of tissue damage, in presence of threatening tissue damage or in absence of abovementioned states. Pain therefore serves as a functional protective mechanism for avoiding tissue damage and can because of various pain modulatory systems such as central and peripheral sensitization, damage to nerves and various psychological states be enhanced or inhibited. Pain can thus be perceived even though no painful stimulus is present (Cortelli et al., 2013). It is highly individual how a person perceives and manages pain.

The mechanisms of pain inhibition and sensitization are generally unknown, but several studies indicate that both peripheral and central actions are involved and that the latter have major impact in chronic pain, as in myofascial pain. It is believed that muscular overload can lead to ischemia and peripheral release of pain- and inflammatory substances that may sensitize peripheral nociceptive receptors. A peripheral sensitization during a long period of time is suggested to be enough for developing a central sensitization. As mentioned before, various mechanisms can inhibit or intensify the perception of pain. One possible mechanism for myofascial pain can be lack of inhibitory functions (Ernberg, 2002).

**Aim**

The aim of this double blind randomized trial was to test the hypothesis that topical application of anesthetic cream would affect PPT values over masseter and temporal muscle sites in patients with TMD related to myalgia.

**MATERIALS AND METHOD**

**Participants**

Ten women with TMD related to myalgia (median age 36 years, range 19 to 63 years) were recruited among patients referred to the Department of Clinical Oral Physiology, Norrlands University Hospital Umeå, Sweden.

The inclusion criteria were:
- Females ≥ 18 years old
- pain in the jaw or temple region associated with familiar pain to palpation, fulfilling criteria of local myalgia,
- no signs of widespread pain and general hyperalgesia,
- able to understand Swedish, oral and written language.

Exclusion criteria were:
- general joint- or muscle disease,
- general pain,
- elite athletes.

The selection of patients in this experimental trial fulfilled the criteria for myalgia pain according to the DC/TMD (Schiffman et al., 2014).

The patients were examined by TMD specialists to confirm the TMD diagnosis according to the DC/TMD criteria before inclusion in the study. The participants were informed about the study procedure but not the specific aim. Participants were instructed to not consume pain killers or alcohol 24 hours before the experiment.

**Experimental design**

The trial was designed to evaluate PPT before and after application of topical anesthesia. The measure sites were the anterior part of the temporal muscles, the belly of the masseter muscles, and the thumb muscle on the back of the dominant hand (first dorsal intraossei) as a reference site (Fig. 1).

The experiment was carried out by two investigators (Investigator 1 and 2). Investigator 1 carried out all measurements, and was blinded to the randomized applications of the topical anesthetic cream vs the placebo cream. Investigator 2 marked the measurement points, carried out the randomization of the application of the cream and the randomized order of measurement points for each participant, and was also responsible for the registration of the measurement data.

PPT was measured with an electronic algometer (Somedic) with a handheld probe with an area of 1 cm² to apply the pressure. The probe was set at an increase in pressure by 20 kPa/sec and applied on the chosen sites with a constant increase of pressure. The
increase of pressure was assisted with the aid of colored lights indicating the pace at which the pressure was applied. The algometer had a connected handheld button which the subjects were instructed to press when the pain was perceived, which also stopped the registration. The value was registered as the patient’s PPT at that particular site and measurement. For each site, three repeated registrations were carried out and mean values calculated. The data was registered on software connected to the algometer (SenseAPP), together with a backup Excel copy as the experiment proceeded.

The algometer used in this experimental study is an instrument designed to apply and measure pain pressure thresholds in both clinical and experimental settings. The algometer is designed to resemble palpation of the muscles and is therefore a useful tool to investigate the question formulations in this particular study. The algometer is a reliable way to investigate PPTs given the investigator is familiar with the procedure (Chesterton et al., 2007).

**Test procedure**

The participants were informed about the general study design, that participating in the study was voluntary and that they had the right to discontinue at any time without further explanation. A trial measurement was performed on the thumb (first dorsal intraossei) on the non-dominant hand to ensure that the participant understood the instructions. This value was not used in further analysis. The five different test sites were marked with an ink pen (Fig. 1). After the baseline-measurement with three registrations for each site Investigator 1 left the room.

Topical anesthetic (EMLA 25 mg/g lidokain + 25 mg/g prilocain) and placebo creams (LIV, Lahega) were applied by Investigator 2 on the left or the right side, in random order. The creams were applied using a two cm diameter circle template, which was positioned with the previously marked point in the center.

The EMLA and placebo creams were left on the skin for five minutes and then wiped off with cotton swabs. Investigator 1 returned to the room and performed the second registration, three measurements per site, in the same order as in the baseline test and the data was recorded in the same manner. When all measurements were completed the marked points were cleaned off with gauze compress and alcohol.
Data analysis
The order of measurements and the random order of EMLA or placebo cream were determined using the statistical software SPSS prior to the experiment. The data was recorded by the software SENSapp and a backup copy was simultaneously recorded in an Excel document.

Statistical methods
The data was analyzed using SPSS (version 22.0). The mean PPT-values for each site and for each participant were calculated. The PPT-values for the right and left sites were pooled for the masseter and temporalis muscles, respectively. The mean values before and after application of EMLA/placebo for each site (masseter muscle bilaterally, temporal muscle bilaterally and the thumb muscle) were then compared for significant differences in pressure pain threshold means using a non-parametric test (Related-Samples Wilcoxon Signed Rank test). A P-value < 0.05 was considered statistically significant.

Literature search
A literature search was carried out for articles relevant for our study. Articles about algometry were found using the terms “algometry”, “reliability” and “pressure pain threshold”. This search resulted in 22 articles filtered on humans and reviews. Furthermore, for articles about EMLA the MeSH-term “cutaneous administration” and “EMLA” were used and the results filtered on humans and reviews generated 15 articles. Background on pain in general MeSH-term “nociception” and “pain” resulted in 53 articles filtered on reviews and humans and changes in pain perception due to hormonal changes were found searching the MeSH-terms “temporomandibular disorder” and “menstrual cycle”, which resulted in 13 articles. To compare our results to others the MeSH-terms “anesthetice, local”, “pain threshold” and “pressure” were used and generated 12 articles filtered on humans.

We chose the articles we have referred to after screening titles, abstracts and assessing the level of relevance and significance to our study and that we assessed had the highest scientific quality (large number of participants, reviews etc.). Several additional articles were provided by our tutors.
Ethical reflection
If PPT is affected, conventional muscle palpation as a tool for diagnosing TMD myalgia may be questioned due to low validity. After the planning of the study a review of the ethical concerns in relation to the experiment was carried out and sent to The ethical committee at Umeå University for evaluation EPN Dnr 2013/328-31. The ethical aspects of concern were how to anonymize the patients participating in the study, guidelines regarding confidentiality, the need for a signed consent from all participants and that the experiment inevitably will cause the patients short temporary pain. This pain exposure is controlled by the patients themselves as they, by pressing the button connected to the algometer, can terminate the pressure application i.e. the pain exposure. The study design and methods used does not have any side effects nor will it have any negative consequences for the patients participating. The patient does not personally benefit from participating in the study but can by participating contribute to an increased understanding and better diagnostic tools for the condition they have been diagnosed with. The results of this study will not be reported for each patient individually but on a group level. The Ethics Forum at the Department of Odontology finds that appropriate ethics considerations have been integrated into this degree project.

RESULTS
The mean values and standard deviation (SD) is presented in Table 1. Compared to the baseline registration, the PPT increased at the sites where EMLA was added for both the temporal (P = 0.007) and masseter muscle sites (P = 0.017) (Fig. 2). There were no statistically significant differences between baseline and after application with placebo cream neither for the temporal (P = 0.9) nor the masseter muscle sites (P = 0.3) (Fig. 2). There were no significant differences in PPT of the thumb muscle before and after application of EMLA (P = 0.7) or placebo cream (P = 0.7), (Fig. 2). There was a large inter-individual variation in PPT (Fig. 3).
DISCUSSION

The main finding of this study was that application of topical anesthesia for five minutes increased PPT significantly at jaw muscle sites in patients with TMD related to myalgia.

During palpation, the perceived pain may not only originate from deep structures but also from superficial structures in the skin, connective tissue as well as from the periost (Kosek et al., 1999). The results indicate that a significant part of the elicited pain originates from nociceptors in the skin and sub mucosa near to the muscles since the PPTs increased significantly after the application of EMLA. This may be because the chronic muscle pain affects nociceptors in the skin surrounding the affected muscles due peripheral sensitization (Kosek et al., 1999). Contrary to the tender muscles (masseter and temporalis), the non-symptom muscle (thumb) did not show signs of hyperalgesia and the PPT did not change significantly after EMLA was added.

Serotonin levels in serum are believed to correlate to hyperalgesia/allodynia in muscles affected by chronic pain, such as myofascial pain. Patients with low serotonin serum levels seem to have more muscle tenderness than patients with higher levels of serotonin. One explanation for this may be that in patients with chronic pain have more serotonin fixed to pain receptors (Ernberg et al., 1999b). Serotonin is believed to sensitize peripheral nociceptive nerves and it has been shown that injection of serotonin into masseter muscle in healthy females can cause a decreased PPT (Ernberg et al., 2000). An increased amount of serotonin has been found in jaw-muscles directly after trauma (puncture). The serotonin is believed to be released from either blood platelets in the area or peripheral nerve ends (Ernberg et al., 1999a). This peripheral release of serotonin may partially be the explanation of the sensitization of tissues surrounding muscles affected by chronic pain, in this case myofascial pain.

The literature suggests that EMLA is an effective topical anesthetic agent (Barcohana et al., 2003), when a sufficient amount of cream is left on the skin for an adequate amount of time, ideally for at least one hour. Some of these previous studies have investigated the anesthetic effect before various superficial surgical procedures and venipuncture. i.e.
more invasive and painful procedures when deeper anesthesia is needed (Lycka, 1992) compared to palpation. In the present study the cream was only left on the skin for five minutes, which has not been proven effective for anesthetizing the skin. However, since our results showed significant differences between the EMLA and placebo creams our interpretation is that the anesthetic effect was sufficient for superficial anesthesia and inhibition of the pain response during pressure even though the cream was only left on for five minutes. Our aim in the present study was to achieve only a topical anesthesia and we therefore assessed that leaving the cream on for five minutes was sufficient.

The pain pressure threshold was defined as the lowest pressure needed for experiencing pain. This is an individual cognitive decision by the patient to press the button and thereby specify the pain pressure threshold.

Myofascial pain is more common among females and one explanation for this can be hormonal differences between the sexes. There seem to be a relationship between pain intensity and changes in estrogen levels. The pain intensity in women seems to be higher when the levels of estrogen are low. Quick changes in estrogen blood levels are also believed to result in higher levels of pain intensity (LeResche et al., 2003). It has been showed that the pain perception varies in different states of the menstrual cycle, probably due to different levels of hormones (L Riley III et al., 1999). We did not take into consideration where the participants were in their menstrual cycle in this study. The participants served as their own controls and comparisons between participants are therefore not relevant.

**Conclusion**

In conclusion this study shows that the PPT increased significantly in patients with myofascial pain in jaw muscles after application of topical anesthesia. This finding indicates that the nociceptors adjacent to the affected muscles may have been sensitized (hyperalgesia). The interpretation of a pain response to pressure thus seems to be complex and warrant further studies.
ACKNOWLEDGMENTS

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REFERENCES


### Table 1. Mean values and standard deviations (SD) of PPTs for the different muscle sites at baseline and after application of placebo and EMLA cream (n=10).

<table>
<thead>
<tr>
<th></th>
<th>Baseline Mean (SD)</th>
<th>Placebo Mean (SD)</th>
<th>EMLA Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Masseter</strong></td>
<td>116.7 (56.8)</td>
<td>132.2 (53.6)</td>
<td>138.3 (75.4) *</td>
</tr>
<tr>
<td><strong>Temporalsis</strong></td>
<td>131.1 (63.8)</td>
<td>132.8 (72.9)</td>
<td>150.0 (77.5) *</td>
</tr>
<tr>
<td><strong>Thumb</strong></td>
<td>236.7 (105.2)</td>
<td>193.0 (83.5)</td>
<td>280.5 (134.1)</td>
</tr>
</tbody>
</table>
Figure 1. The different measurement sites (temporalis (a), masseter (b), thumb (c)) marked with white circles.
Figure 2. Boxplots illustrating the mean values of PPTs (kPa) before (baseline) and after (medepos) application of placebo/EMLA cream on the masseter muscle (A), temporal (B) and thumb muscle (first dorsal interossei) (C).
Figure 3: Mean PPT (kPa) at baseline and after application of EMLA and placebo cream for the masseter (A) and temporalis (B) muscles.