PRESSURE PAIN THRESHOLDS IN DIFFERENT TISSUES IN ONE BODY REGION

THE INFLUENCE OF SKIN SENSITIVITY IN PRESSURE ALGOMETRY

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ABSTRACT. This study aimed at determining whether there are differences in pressure pain sensitivity in different tissues in the same body region when systematically assessed, before and after skin hyposthenia. Pressure pain thresholds (PPTs) were measured bilaterally in 15 healthy females at the bony part of the epicondyles lateralis humeri, at the belly of m. extensor carpi ulnaris and at m. brachioradialis where the superficial radial nerve branches pass underneath ("muscle/skewer" site). Following a double blind design, a local anaesthetic cream (EMLA®) or a control cream was applied to the skin and PPTs were measured. The PPT was significantly (p < 0.001) lower at the "skewer/muscle" site than at the belly and "pure" muscle sites. The PPTs over the bony and "pure" muscle sites did not differ. There was no significant difference when PPTs were compared before and after application of EMLA® cream. However, PPTs after control cream were lower (p < 0.001) over all examined areas than those obtained prior to cream application. Thus, EMLA® cream increased PPTs compared to control sites in all examined areas (p < 0.001). Under the given circumstances, skin pressure pain sensitivity was demonstrated to influence the PPT.

Key words: pain threshold; pressure algometry; sensitivity; sensitivity testing.

INTRODUCTION

Tenderness is not only a symptom of localized musculoskeletal pain (e.g. myalgia/myositis); it is also a diagnostic finding in certain chronic pain syndromes (e.g. fibromyalgia). Assessment of tenderness by palpation is subjective and liable to error. Pressure algometry is a semiquantitative method for assessment of tenderness. The short-term reliability of this method is good (13, 16, 19, 20) and it is easy to use in clinical practice. However, when trying to analyse tenderness in patients, a good knowledge of the normal variations in tenderness in healthy individuals is necessary. The establishment of normal reference values has been hampered by the large number of factors influencing pressure pain threshold (PPT) assessment (14). Also, great interindividual variability in PPTs has been found in healthy individuals, and the long-term reliability is questionable (16). However, since relative PPT-values in different locations remain fairly constant for each individual (16), it may be possible to design a system with reference sites to bypass the general drifts in PPT values over time. The knowledge of a normal tenderness profile in different tissues located in the same body region would permit analysis of different pain syndromes in order to determine whether tenderness is localized to a specific tissue (e.g. muscle) or is more generalized. Pressure algometry is often used on the assumption that it reflects pressure pain sensitivity in deep tissues. However, Jensen et al. (13) found a 70% increase in PPT following a subcutaneous injection of local anaesthetic in the human temporal region. Even if the spread of some local anaesthetics to deeper tissues cannot be ruled out, this result suggests that skin sensitivity influences the PPT. This was further supported by our finding that skin hyposthenia induced by local anaesthetic cream (EMLA®) over m. quadriceps femoris in healthy subjects increased PPT by 28.8% compared to control cream (17). Therefore, it is possible that skin sensitivity to pressure pain might influence PPTs.

In previous studies of healthy volunteers (12, 16) the finding that PPTs in the trunk normally increased in a cranio-caudal direction stressed the importance of comparing sites in the same body region. To determine the relative tenderness in different tissues, we set out to assess the PPTs in muscle, bone and a muscle site with
underlying nerve tissue, in the same body region. Assessments were made before and after skin hypoesthesia induced by a local anesthetic cream.

The study addressed the following questions:

1. Do PPTs in different tissues in the same body region differ?
2. Does induced skin hypoesthesia influence PPTs in muscle, bone and muscle with underlying nerve?
3. Do repeated PPT assessments in the same site influence subsequent PPTs?

MATERIALS AND METHODS

Subjects
Fifteen female volunteers with an average age of 56.8 years (range 20-54 years) and ten female volunteers with an average age of 50.6 years (range 25-63 years) participated in the first and second sessions (see below), respectively. None suffered from any musculoskeletal or dermatological problems. The study was approved by the regional ethical committee, and all subjects gave their informed consent.

Allogery
The pressure algometer (Scoidal Sensical AB, Pivken, Sweden) consisted of a vertical grip and a 10 mm-diameter rod with a pressure-sensitive strain gauge at the tip, connected to a power supply, an amplifier, and a display. The rod tip was flat and covered with 2.5 cm of rubber to avoid painful skin stimuli due to sharp metal edges. The display showed pressure (in kPa) and a scale indicating the rate of pressure force increase. The scale enabled the examiner to maintain a fairly constant rate of pressure increase. In this study, a rate of 50 kPa/s was used. The subject indicated the pain threshold by pressing a push-button, which froze the current pressure value on the digital display. The algometer was calibrated before examining each subject.

Procedure
All the measurements in both sessions were made by the same investigator (EK) with the subjects in a relaxed, seated position. The subjects were carefully instructed to flex both the butts as soon as a sensation of pressure became painful. Two assessments were performed on sites not included in the study, in order to familiarize the subjects with the pressure algometry technique. Five sites were assessed in each session: the right and left internal malleoli, the right and left olecranon fossa, and the right and left proximal tibial region. The investigator marked the skin at the bony part of the epicondylus lateralis humeri and the belly of m. extensor carpi ulnaris. The site over the m. brachioradialis where the superficial radial artery brachioradialis passes underneath was palpated, and the site where light pressure evoked local pain and radiating paraesthesia in the dorsoradial part of the hand was marked ("muscle/nerve" site). Skin sensitivity was systematically assessed by gently brushing the skin with a brush, and by rolling a warm metalic roller (40°C) over the points to be examined. The subjects were asked to compare the sensations between the two sides and adjacent skin. Impaired sensitivity was noted in the protocol. The PPT for each site was determined with the pressure algometer. The sites were assessed balanced, sequential order. Five PPTs were assessed for each site. The skin was anesthetized by applying a cotton tip soaked with 1% lignocaine (EMLA® 5% cream) surrounding each spot to be examined (0.2g/cm² of Novotro® counter cream (ACO Fuklurmin®) ACO, Sweden) with slight appearance but without anesthetic components was applied to the other side. Although we attempted to follow a double-blind design, most subjects exhibited a vasomotoric response to the EMLA cream. The cream was kept under occlusive cover (Coverden®) for 60 minutes before being removed. Sensitivity was then systematically re-assessed using the same examination techniques described above. Unpaired t-test (difference between the sides) was recorded as paired t-test of sensitivity as 1, and complete anesthesia as 0. PPTs were measured as described previously.

Statistical analysis
To estimate the difference in PPTs between tissues, the two-way ANOVA was performed on the PPTs at different sites and p<0.05 considered a significant difference. The between-group comparisons were performed using the Student-Newman-Keuls test, and after adjustment for multiple comparisons, the significance level was 0.05 for all tests. The pressure of pain was assessed by determining the pressure at which the subjects perceived pain. The pressure values were obtained from the pressure algometer (Scoidal Sensical AB, Pivken, Sweden).

RESULTS

Skin sensitivity testing

After application of EMLA cream, the average score for temperature sensitivity decreased from 2.00 to 0.63 while after control cream it remained at 2.00. The average score for light touch decreased from 2.00 to 1.00 after application of EMLA cream, but remained at 2.00 after control cream. The mean pressure of pain after application of EMLA cream was 1.91 ± 8.8% for the pressure pain thresholds.

Pressure pain thresholds

The PPT was lower over the "muscle/nerve" site than over the bony site (p = 0.001) and the "pure" muscle site (p < 0.001). The PPTs over the bony and "pure" muscle sites showed no significant difference.

DISCUSSION

Confirming our previous results (16), we found lower PPTs over the "muscle/nerve" site, but no difference between the bony and "pure" muscle sites. These results are in agreement with our previous findings, suggesting that the effect of EMLA cream on skin sensitivity is more pronounced over the "muscle/nerve" site, possibly due to altered nerve conduction in this region. The lower pressure pain thresholds over the "muscle/nerve" site may be attributed to the presence of sensory nerves in this region, which are sensitive to mechanical stimuli, and the effect of EMLA cream on these nerves may result in a decreased pain threshold.
underlying nerve tissue, in the same body region. Assessments were made before and after skin hypothermia induced by a local anesthetic cream.

The study addressed the following questions:

1. Do PPTs in different tissues in the same body region differ?
2. Does induced skin hypothermia influence PPTs in muscle, bone and muscle with underlying nerve?
3. Do repeated PPT assessments in the same site influence subsequent PPTs?

MATERIALS AND METHODS

Subjects
Fifteen female volunteers with an average age of 36.8 years (range 20-54 years) and ten female volunteers with an average age of 56.2 years (range 25-65 years) participated in the first and second sessions (see below), respectively. None suffered from any musculoskeletal or dermatological problems. The study was approved by the regional ethical committee, and all subjects gave their informed consent.

Allography
The pressure allography (Sensical Scales AB, Farsta, Sweden) consisted of a pistol grip and a 10 mm-diameter rod with a pressure-sensitive strain gauge at the tip, connected to a power supply, an amplifier, and a display. The rod tip was flat and covered with 2 mm of rubber to avoid painful skin stimuli due to sharp metal edges. The display showed pressure in (kPa) and a scale indicating the rate of pressure force increase. The scale enabled the examiner to maintain a fairly constant rate of pressure increase. In this study, a rate of 50 kPa/sec/record was chosen. The subject indicated the pain threshold by pressing a push-button, which froze the current pressure value on the display.

Procedure
All measurements in both sessions were made by the same investigator (EK) with the subjects in a relaxed, prone position. The subjects were carefully instructed to breathe as deeply as possible to avoid sensations of pressure became painful. Two assessments were performed on sites not included in the study. In order to familiarize the subjects with the pressure allography technique. First of all, the investigator marked the skin at the bony part of the epicondylus lateralis humeri and the bony part of the epicondylus lateralis humeri, and the belly of m. extensor carpi ulnaris. The sites were marked with an ink marker. The superficial radial nerve branch innervated was palpated, and the site where light pressure evoked local pain and radiating paresthesia in the dorsoradial part of the hand was marked ("muscle/nerve" site). Skin sensitivity was systematically assessed by gently brushing the skin with a hairbrush and by rolling a warm metallic roller (40°C) over the points to be examined. The subjects were asked to compare the sensations between the two sides and adjacent skin. Unpaired t-test was used in the analysis. The PPT for each site was determined with the pressure allography. The sites were assessed and compared, sequential order. Five PPTs were assessed for each site. The skin was anaesthetized by applying a cotton tip soaked on a local anesthetic (EMLA™, Astracare AB, Sweden) to the area surrounding each spot to be examined (0.2% lidocaine and 2.5% prilocaine) with cotton swabs (ACO Fuklidan™, ACO, Sweden) with some appearance but without anaesthetic components were applied to the other side. Although we attempted to follow a double-blind design, most subjects exhibited a visionary response releasing the EMLA cream. The cream was kept under occlusive ointment (Covadon®) for 60 minutes before being removed. Sensitivity was then systematically measured using the same examination technique described above. Unpaired t-test (difference between the sides) was recorded as a partial loss of sensitivity as 1, and complete anaesthesia as 0. PPTs were measured as described previously.

In the second session, the investigator marked the skin over the belly of m. extensor carpi ulnaris bilaterally. Five PPTs were assessed on each side in a counterbalanced order (right side first for 5 subjects, left side first for 5 subjects). ACO Fuklidan™ was applied to one side (right arm in 5 subjects, left in 5) and kept under occlusive cover for 60 minutes. No cream was applied on the other side. After removing the cream, PPTs were reassessed bilaterally.

Statistics
To estimate the difference in PPTs between tissues, the non-parametric differences between the PPTs as different sites were compared, both before and after cream treatment. Before cream application, the two sides were pooled. Similarly, in the differences between the sides treated with EMLA cream and control, and the effect of the cream treatment, mean pairwise differences between the corresponding sites, and the same sites, respectively, were calculated. Significance levels were subjected using Student's paired t-test. The confidence interval for the relative frequency of a positive anesthesic effect for warmth and touch was computed using the binomial distribution. Spearman's rank correlation coefficients were calculated.

RESULTS
Skin sensitivity testing
After application of EMLA™ cream, the average score for temperature sensitivity decreased from 2.00 to 0.37 while after control cream it remained at 2.00. The average score for light touch decreased from 2.00 to 0.09 after EMLA™ cream, but remained at 2.00 after control cream. The relative frequency of a positive anesthesic effect (grade 0.65) was 99.1 ± 8.3% for temperature and touch, respectively.

Pressure pain thresholds
The PPT was lower over the "muscle/nerve" site that over the bony site (p < 0.001) and the "pure" muscle site (p < 0.001). The PPTs over the bony and "pure" muscle sites did not differ. These relations were not changed by EMLA™ cream.

Discussion
Confirming our previous results (16), we found lower PPTs over the "muscle/nerve" site, but no difference between the bony and "pure" muscle sites. These
relations remained unaltered by skin hypoxia, and thus reflected the sensitivity of deeper structures. Sensory fibres innervating nerve trunk connective tissue (nervi nervorum) have been proposed to contribute to nerve trunk pain (3,22). In fact, a subset of nervi nervorum, distinct from nerve fibres that innervate the blood vessels of nerve sheaths, with presumably nociceptive functions and positioned to respond to mechanical pressure and tension, have been found in animals (5). The lower PPT over the "muscle/tendon" site found in the present study could hypothetically be explained by coactivation of nervi nervorum during PPT assessment. The sites in our study were located in the same body region, although they were not segmentally equivalent ("muscle/tendon" site: stylohyoid CS-6, dermato- my Th1, "pure" muscle site: stylohyoid C7-S, dermatomy Th1 and bony site: sternocleidomastoide C7, dermato- my Th1). Lower PPT (10) and pressure pain tolerance (9) have been reported over bony sites than over muscular sites, while others (18) found lower PPT over muscle than bone. However, the muscle sites and the bony sites in those studies were not located within the same body region, which disguises further comparisons and might explain the contradictory results.

We chose to apply the local anaesthetic as a cream instead of injecting it, since this approach minimizes spread of the compound to subcutaneous tissues. The effects of the EMLA® cream have been well documented (1, 2, 4, 8, 15). An application time of 60 minutes was chosen, since this is the minimal duration needed to obtain an analgesic effect, but also the upper time limit after which there is a potential risk of spread to subcutaneous tissues (4). The sensitivity testing revealed that there was a decrease in perception of warmth after 60 minutes, implying an anaesthetic effect on thin unmyelinated fibres. The decrease in sensitivity to brush indicated that large-diameter myelinated fibres were also partially affected. We refrained from quantifying the analgesic effect in order to avoid tissue damage possibly influencing the subsequent PPT assessments.

When studying the possible effect of control cream on PPTs, we found that PPTs decreased significantly and similarly following the initial PPT determinations in untreated sites and sites treated with control cream. Thus, no effect on PPTs by the control cream per se was found. Although PPTs decreased significantly after control cream application, they remained unaltered following EMLA® cream application. The difference in PPTs between EMLA® cream and control cream sites was 16.4%, thus supporting the conclusion that skin sensitivity does influence PPTs. The increase in sensitivity in the control cream group probably depends on sensitization of skin mechanosensitive nociceptors caused by the initial PPT assessments. Supporting this suggestion, although not conclusively, was the finding of unaltered PPTs after EMLA® cream application compared to baseline values. However, sensitization of more deeply located mechanosensitive nociceptors, masked by the effect of EMLA® cream, cannot be excluded. There was a statistically significant correlation between initial PPT values and the increase following EMLA® cream application (compared to control cream), signifying that the contribution of cutaneous sensitivity was not seen preferentially in the range of low or high absolute PPT values.

To find out whether repeated probe pressing influenced the PPT, we compared the first and the fifth PPT at each site. Prior to cream application, there was no difference between them. After EMLA® cream and control cream application, the fifth PPT was significantly higher than the first. Since this effect was present with both creams, it does not seem to depend on skin sensitivity. The PPT increase could be explained by central habituating mechanisms to a familiar stimulus, or by the activation of intrasegmental pain inhibitory mechanisms (6, 7, 11, 21).

In conclusion, we found no difference in PPT between the "pure" muscle site and the bony site, but the "muscle/tendon" site had a lower PPT. These relations were not influenced by skin hypoxia, and they reflect the relative pressure pain sensitivity in deeper tissues. Skin hypoxia by EMLA® increased PPT compared to control sites. Therefore, under the given circumstances, we conclude that skin pressure pain sensitivity influenced the PPT. The sensitivity of pressure pain sensitivity over different tissues and after skin hypoxia in patients with different chronic pain syndromes may increase our understanding of the underlying pathophysiological mechanisms, and possibly provide an aid in differential diagnosis, treatment evaluation and patient follow-up.

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REFERENCES
15. Acute Care 27, 1999
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tome Th1). Lower PPT (10) and pressure pain tolerance (9) have been reported over bony sites than over muscle sites, while others (18) found lower PPT over muscle than bone. However, the muscle sites and the bony sites in those studies were not located within the same body region, which disqualifies further comparisons and might explain the contradictory results.

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In conclusion, we found no difference in PPTs between the "pure" muscle site and the bony site, but the "muscle/scene" site had a lower PPT. These relations were not influenced by skin hypoxia, and the reflect the relative pressure pain sensitivity in deeper tissues. Skin hypoxia by EMLA® increased PPT compared to control sites. Therefore, under the given circumstances, we conclude that skin pressure pain sensitivity influenced the PPTs. Assessment of pressure pain sensitivity over different tissues and after skin hypoxia in patients with different chronic pain syndromes may increase our understanding of their underlying pathophysiological mechanisms, and possibly provide an aid in different diagnostic, treatment evaluation and patient follow-up.

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REFERENCES


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