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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 hypoesthesia. Pressure pain thresholds (PPTs) were assessed bilaterally in 15 healthy females at the bony part of the epicondylus lateralis humeri, at the belly of m. extensor carpi ulnaris and at m. brachioradialis where the superficial radial nerve branches pass underneath ("muscle/nerve" site). Following a double blind design, a local anaesthetic cream (EMLA®) or a control cream was applied to the skin and PPTs were reassessed. The PPT was significantly ($p < 0.001$) lower at the "muscle/nerve" site than at the bony 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/tendalgia); 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 semiobjective 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 hypoesthesia 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 anaesthetic 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 36.8 years (range 20–54 years) and ten female volunteers with an average age of 50.6 years (range 28–63 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.

Algometry

The pressure algometer (Somedic Sales 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 50–60 kPa/second was chosen. 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, prone position. The subjects were carefully informed that the investigation aimed at determining the individual pain threshold, not pain tolerance. Use of the algometer was demonstrated, and the subjects were instructed to push the button as soon as the 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.

First session. 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 nerve branches pass underneath was palpated, and the site where light pressure evoked local pain and radiating paresthesia in the dorso-radial 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. Impaired sensitivity was noted in the protocol. The PPT for each site was determined with the pressure algometer. The sites were assessed in a balanced, sequential order. Five PPTs were assessed for each site. The skin was anaesthetised by applying a eutectic mixture of a local anaesthetic (EMLA®, Astra AB, Sweden) to an area of 16 cm^2 surrounding each spot to be examined (0.2g/cm^2). A control cream (ACO Fuktkräm®, ACO, Sweden) with identical appearance but without anaesthetic components was applied on the other side. Although we attempted to follow a double-blind design, most subjects exhibited a vasoconstrictive response to the EMLA cream. The creams were kept under occlusive cover (Coverderm®) for 60 minutes before being removed. Skin sensitivity was then systematically reassessed using the sensory examination techniques described above. Unaltered sensitivity (no difference between the sides) was recorded as 2, partial loss of sensitivity as 1, and complete anaesthesia as 0. PPTs were reassessed as described previously.

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 in 5 subjects). ACO Fuktkräm® 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 to the other side. After removing the cream, PPTs were reassessed bilaterally.

Statistics

To estimate the difference in PPTs between tissues, the mean pairwise differences between the PPTs at different sites were computed, both before and after cream treatment. Before cream application, the two sides were pooled. Similarly, to check differences between the sides treated with EMLA® or control cream, and the effect of the cream treatment, mean pairwise differences between the corresponding sites, and the same site, respectively, were calculated. Significance levels were computed using Student's paired two-tailed *t*-test. The confidence interval for the relative frequency of a positive anaesthetic effect for warmth and touch was computed using the binomial distribution. Spearman's rank order correlation coefficient was calculated.

RESULTS

Skin sensitivity testing

After application of EMLA® cream, the average score for temperature sensitivity decreased from 2.00 to 0.73, while after control cream it remained at 2.00. The average score for light touch decreased from 2.00 to 0.93 after EMLA® cream, but remained at 2.00 after control cream. The relative frequency of a positive anaesthetic effect (graded 0 or 1) was 91.1 ± 8.3% for temperature and touch, respectively.

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

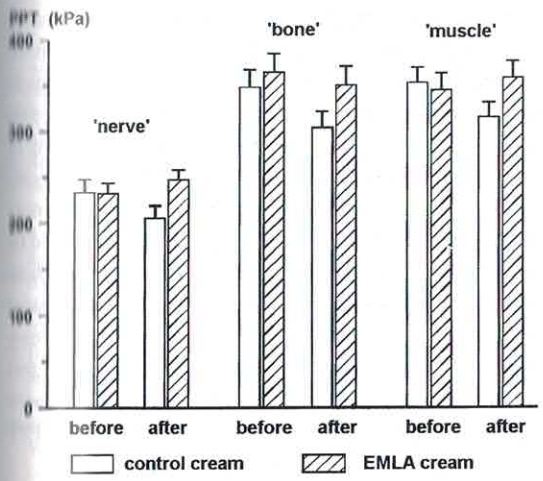

Fig. 1. Mean pressure pain thresholds (PPTs) (± SEM) in three different sites in the lower arm before and after application of local anaesthetic cream (EMLA®) and control cream in 15 healthy individuals. The PPT was significantly ($p < 0.001$) lower at the "muscle/nerve" site than at the bony and the "pure" muscle sites. The PPTs over the bony and the "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 ($p < 0.001$).

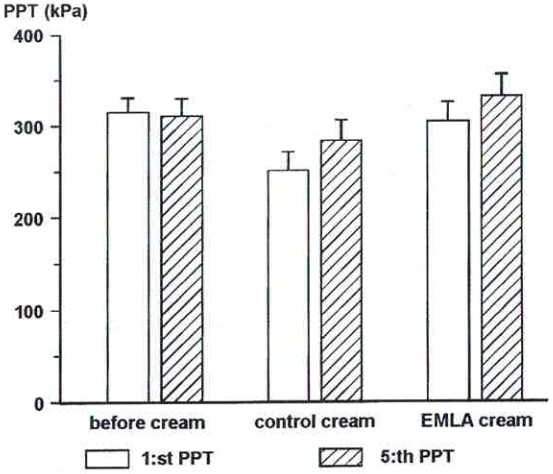

Fig. 2. Mean values (± SEM) of the first and fifth pressure pain thresholds (PPTs) over the three examined areas in 15 healthy subjects. Before cream application, there was no difference between the fifth and first assessments. However, PPT on the fifth assessment was significantly higher than on the first assessment after control and EMLA® cream application.

sites did not differ. These relations were not changed by EMLA® cream.

Figure 1 illustrates PPTs before and after cream application. Initial assessments showed no differences in PPTs between the sites intended to receive EMLA® (right arm in 8 subjects and left arm in 7) and sites that were intended to receive control cream. There was no significant difference in any area when PPTs were compared before and after application of EMLA® cream. However, PPTs after control cream were lower ($p < 0.001$) over all examined sites than those obtained prior to cream application. The PPT decrease was 11.9% over the "muscle/nerve" site, 12.7% over the bony site and 10.6% over the "pure" muscle site. Thus, EMLA® cream increased PPTs compared with control cream in all examined areas ($p < 0.001$), i.e. by 20.0% over the "muscle/nerve" site, by 15.5% over the bony site and by 13.6% over the "pure" muscle site.

To find out whether repeated assessments influenced PPTs, we compared the first and the fifth PPT at each site. Prior to cream application, there was no difference in PPT between the fifth and the first assessments (Fig. 2). The PPT on the fifth assessment was higher than that on the first after EMLA® cream ($p < 0.05$) and after control cream ($p < 0.01$), the increases amounting to 9.0% and 13.1%, respectively. All areas tested revealed the same results (not shown). There was no statistically significant correlation between the absolute PPT values before cream application and the increase in PPT following EMLA® cream (compared to control cream) ($r = 0.5$, NS).

The possible effect of the control cream (ACO Fuktkräm®) *per se* on PPTs was assessed in the second session. There was no statistically significant difference in PPTs between the sites intended to receive the control cream (right arm in 5 subjects, left in 5) and the contralateral side. When reassessing PPTs, again there was no significant difference between the sites treated with the control cream and the contralateral side. However, PPTs were lower when reassessed 60 minutes after control cream application ($p < 0.05$), and on the contralateral side ($p < 0.05$), compared to the initial values.

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 hypoesthesia, 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/nerve" 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/nerve" site: myotomes C5-6, dermatome Th1, "pure" muscle site: myotomes C7-8, dermatome Th1 and bony site: sclerotome C7, dermatome 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.

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 sensibility 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 mean difference in PPTs between EMLA® cream and control cream sites was 16.4%, thus supporting the conclusion that skin sensitivity does influence PPTs. The increas sensitivity in the control cream group probably depend on sensitization of skin mechanosensitive nocicept caused by the initial PPT assessments. Supporting t suggestion, although not conclusively, was the finding unaltered PPTs after EMLA® cream application co pared to baseline values. However, sensitization of mo deeply located mechanosensitive nociceptors, masked the effect of EMLA® cream, cannot be excluded. The was no statistically significant correlation between initi PPT values and the increase following EMLA® crea application (compared to control cream), signifying th the contribution of cutaneous sensitivity was not se preferentially in the range of low or high absolute PP values.

To find out whether repeated probe pressing infl enced the PPT, we compared the first and the fifth PPT each site. Prior to cream application, there was n difference between them. After EMLA® and contro cream application, the fifth PPT was significantly high than the first. Since this effect was present with bot creams, it does not seem to depend on skin sensitivity The PPT increase could be explained by centra habituating mechanisms to a familiar stimulus, or b the activation of intrasegmental pain inhibitory mecha isms (6, 7, 11, 21).

In conclusion, we found no difference in PPT between the "pure" muscle site and the bony site, bu the "muscle/nerve" site had a lower PPT. These relation were not influenced by skin hypoesthesia, and thu reflect the relative pressure pain sensitivity in deeper tissues. Skin hypoesthesia 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 hypoesthesia in patients with different chronic pain syndromes may increase our understanding of their underlying pathophysiological mechanisms, and possibly provide an aid in differential diagnosis, treatment evaluation and patient follow-up.

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