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Treatment response and central pain processing in Anterior Cutaneous Nerve Entrapment Syndrome: An explorative study

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HIGHLIGHTS

- Chronic pain in ACNES may be more than just a localized problem.
- ACNES patients refractory to treatment show signs of generalized hyperalgesia.
- Refractory ACNES patients suffered from a longer duration of pain before treatment.
- Local treatment failure may be related to sensitized central pain processing.

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ABSTRACT

Background: 10–30% of chronic abdominal pain originates in the abdominal wall. A common cause for chronic abdominal wall pain is the Anterior Cutaneous Nerve Entrapment Syndrome (ACNES), in which an intercostal nerve branch is entrapped in the abdominal rectus sheath. Treatment consists of local anaesthetics and neurectomy, and is ineffective in 25% of cases for yet unknown reasons.

In some conditions, chronic pain is the result of altered pain processing. This so-called sensitization can manifest as segmental or even generalized hyperalgesia, and is generally difficult to treat.

Objective: The aim of this study was to assess pain processing in ACNES patients responsive and refractory to treatment by using Quantitative Sensory Testing, in order to explore whether signs of altered central pain processing are present in ACNES and are a possible explanation for poor treatment outcomes.

Methods: 50 patients treated for ACNES with locally orientated treatment were included. They were allocated to a responsive or refractory group based on their response to treatment. Patients showing an improvement of the Visual Analogue Scale (VAS) pain score combined with a current absolute VAS of <40 mm were scored as responsive.

Sensation and pain thresholds to pressure and electric skin stimulation were determined in the paravertebral bilateral ACNES dermatomes and at four control areas on the non-dominant side of the body, i.e. the musculus trapezius pars medialis, musculus rectus femoris, musculus abductor hallucis and the thenar. The ACNES dermatomes were chosen to signal segmental hyperalgesia and the sum of the control areas together as a reflection of generalized hyperalgesia. Lower thresholds were interpreted as signs of sensitized pain processing. To test for alterations in endogenous pain inhibition, a conditioned pain modulation (CPM) response to a cold pressor task was determined. Also, patients filled in three pain-related questionnaires, to evaluate possible influence of psychological characteristics on the experienced pain.

Results: Patients refractory to treatment showed significantly lower pressure pain thresholds in the ACNES dermatomes and for the sum of as well as in two individual control areas. No differences were

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found between groups for electric thresholds or CPM response. Duration of complaints before diagnosis and treatment was significantly longer in the refractory compared to the responsive group, and refractory patients scored higher on the pain-related psychological surveys.
Conclusion and Implications: In this hypothesis-generating exploratory study, ACNES patients refractory to treatment showed more signs of sensitized segmental and central pain processing. A longer duration of complaints before diagnosis and treatment may be related to these alterations in pain processing, and both findings could be associated with less effective locally orientated treatment. In order to validate these hypotheses further research is needed.
Registration number: NCT01920880 (Clinical Trials Register; http://www.clinicaltrials.gov).

1. Introduction

Chronic abdominal pain is commonly seen in medical practice, caused in 10–30% of patients by an abdominal wall problem [1,2]. Often, abdominal wall pain is caused by the entrapment of an intercostal nerve in the abdominal rectus sheath [3,4]. This so-called Anterior Cutaneous Nerve Entrapment Syndrome (ACNES) results in a localized pain that can be indicated with the tip of a finger [3]. Primary treatment consists of consecutive injections with local anaesthetics combined with corticosteroids. If such treatment is only temporarily effective, the intercostal segments of the nerve are surgically removed. Conservative local treatment is successful in one-third of patients, and surgical neurectomy is effective in 70% of the transient responders [4–6].

Why the remaining 20–25% of patients is refractory to both forms of local treatment is little understood.

As in other chronic pain syndromes, understanding the underlying mechanism of pain is of great importance for adequate treatment. From conditions such as fibromyalgia, temporomandibular disorder and osteoarthritis, it is known that the ongoing nociceptive input can lead to alterations in central pain processing [7]. This central sensitization is manifest as spreading hyperalgesia, increasing a patient's susceptibility to pain [8–10]. In some cases, pain can even become independent of peripheral nociceptive input [11]. Local treatment directed at the nociceptive source can be expected to be more ineffective in the presence of central sensitization [12]. The detection of central sensitization may thus aid in understanding and predicting the failure of locally directed treatment approaches.

Quantitative Sensory Testing (QST) is a tool for assessing alterations in pain processing at the peripheral and central levels of the nervous system. It is a validated instrument to identify neuroplasticity by evaluating responses to external stimuli of controlled intensity, such as mechanical and electrical stimuli [13,14].

The purpose of this retrospective exploratory study was to document possible changes in central pain processing in ACNES using Quantitative Sensory Testing, with the goal of better understanding treatment failure after locally directed treatment. We hypothesized that refractory patients would show lower pain thresholds as a sign of altered central pain processing.

2. Methods

This study was conducted at the Radboud university medical centre, Nijmegen. Patients were recruited from the Radboud university medical centre and from two teaching hospitals specialized in diagnosing and treating chronic abdominal wall pain: SolviMáx, subdepartment of the Máxima Medical Centre, Veldhoven and Maasziekenhuis Pantein, Boxmeer.

The study was conducted according to the principles of the Declaration of Helsinki, and in accordance with the International Conference on Harmonization guidelines of Good Clinical Practice. The regional Medical Ethics Committee approved the study protocol and all subjects provided oral and written consent before conduct of any protocol-related procedures. The study was registered in the Clinical Trials Register of the U.S. National institutes of Health (NCT01920880).

2.1. Study population

All patients of 18 years of age or older were eligible for study participation if they met the following inclusion criteria: (1) Patient (had) suffered from abdominal complaints matching ACNES with a constant superficially located site of tenderness, a small (<2 cm^2) area of maximal tenderness, and increased tenderness by abdominal muscle tensing while palpating the trigger point [1,2,4] (Carnett's test positive) [15]. (2) Patients had been treated for this condition with injection therapy or surgery at least 3 and at most 12 months before.

Exclusion criteria were: (1) a history of a chronic pain syndrome that possibly interfered with the interpretation of QST results, e.g. fibromyalgia, (2) pre-existing affected sensory input (e.g. neuropathy due to diabetes mellitus) and (3) pain localized in a surgical scar.

2.2. Allocation

The pain state before and after treatment was documented using the Visual Analogue Scale (VAS). Patients were asked to mark their pain on a 100 mm line, with the extreme left representing no pain and the extreme right the worst imaginable pain [16].

Patients were allocated to either the responsive or refractory treatment group based on their response to treatment. They were scored 'responsive' if they showed an improvement of the VAS score after treatment resulting in an absolute pain score of <40. As a VAS of 40 or higher indicates moderate to severe and clinically relevant pain, we chose this as our cut-off point [17,18]. The satisfaction of treatment result was also evaluated.

Baseline characteristics comprised age, sex, aetiology, Body Mass Index (BMI), abdominal medical history, use of analgesics, duration of pain symptoms until diagnosis and local sensory dysfunction before treatment.

2.3. Study procedures

Quantitative Sensory Testing was performed according to the Nijmegen Aalborg QST Screening protocol (NASQ) [19,20]. Mechanical, i.e. pressure, and electric stimuli were applied. All measurements were performed by the same investigator, in the same calm and climate controlled room, specifically equipped for QST measurements. The complete protocol took approximately 45 min.

After initial QST training, pressure pain detection thresholds (pPDT, stimulation just becomes painful) were obtained using a handheld pressure algometer with a 1.0 cm^2 probe (Wagner