Effect of acupuncture on hand pain in patients with Rheumatoid Arthritis - Clinical research protocol

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Abstract
Rheumatoid Arthritis (RA) is a systemic inflammatory disease characterized by functional disability and pain. Although acupuncture is widely used, western acupuncture studies on RA have shown no conclusive positive results. Acupuncture is regarded as a reflex therapy and Traditional Chinese Medicine (TCM) diagnosis has been shown to be a neurovegetative state allowing choose acupoints dependently of the individual neurovegetative state.

The foregoing, there is a need to answer the following question: Can the classic criteria for selection of acupuncture points, according to the Shang Han Lun influence the effects of acupuncture on pain in patients with RA with hand impairment?

Thus, in the experimental case (1 patient) acupuncture treatment will be done according to the diagnosis TCM, using the following points TK5: Clusa Externa (Wai guan), C3: Mare Minus (Shao Hai), R7: Amnis Recurrens (Fuli), F39: Campana Suspensa (Xuán zhong), while control case (1 patient) without acupuncture technique.

In the experimental case, there was a significant improvement in the amount of force tolerated, considering Hand Grip, reflecting a decrease in pain. This improvement was also verified by the Visual Analogue Scale (VAS), compared with the control case.

The results of this study will be an important acupuncture method to be considered for reducing pain in patients with RA. The data can come to bear a clinical trial in a larger scale and with additional parameters.

In the future extensive work, if their clinical efficacy is proven, acupuncture could be an adjunctive strategy for a complementary treatment of RA.

Key words: rheumatoid arthritis, acupuncture, clinical case

Introduction
Rheumatoid arthritis (RA) is an inflammatory, multisystem, and chronic autoimmune disease. Manifested by symmetrical persistent inflammatory synovitis involving destructive polyarthritis of the synovium. Over 90% of patients with RA have involvement of hands and around 30% exhibit limitations in daily life activities (1). According to data from the World Health Organization, about 1-2% of the world population suffers from RA and its prevalence is about 0.2 to 0.5% of the Portuguese population (2). The socio-economic impact is high (3).

Treatment of RA is dominated by the use of anti-inflammatory non-steroids, including Cox-2 inhibitors, modifying anti-rheumatic drugs disease and analgesics. Recently started using biological agents (4). However, this type of drugs is associated with unwanted side effects, toxicity and limited efficacy (5) (6). Biological agents have higher costs and side effects, such as life threatening infections and increased risk of malignancy, limit their use (3).

These and other limitations have led about 60 to 90% of patients with RA dissatisfied with conventional treatments, resort to Complementary and Alternative Medicines treatment, including acupuncture (3) (4) (5).

It is known that the acupuncture stimulates the nervous system releasing neurochemical and induce biochemical changes that influence the homeostatic mechanisms of the body. It can also positively affect brain areas that reduce the sensitivity to pain, inflammation and stress, by promoting the release
of vascular factors and immunomodulators and improve the biomechanical functions (7). Acupuncture in RA may decrease pro-inflammatory cytokines IL-1 and IL-6, and increased cytokine inhibitors IL-4 and IL-10 (8); induce the expression of vasoactive intestinal peptide, an anti-inflammatory neuropeptides (9); inhibit the function of synovial mast cells (which are substantially involved in the initiation of inflammatory arthritis) and restore the hypothalamic-pituitary-adrenal axis (10). It is also known that the acupuncture stimulates the nervous system, what leads to the release of endorphins and other neurohumoral factors, changes in the treatment of pain in the brain and spinal cord (11) and an increase in local microcirculation (12) that helps the reduction of edema.

In planning, we conducted this study using validated outcome measures to assess the feasibility of the protocol, and to obtain preliminary data on efficacy of acupuncture treatment as an adjunct for the treatment of chronic pain in two patients with RA.

Materials and Methods

Sample Recruitment: This was a convenience sample of a total of 2 patients meeting the selection criteria for the study. Patients were selected from a national rheumatology center in the period from July to September 2015. The proposal of this study was to identify the effects of adjuvant treatment of acupuncture in the treatment of pain of the hand of patients (PMH) with Rheumatoid Arthritis.

Inclusion criteria:
- the patients included who have signed an informed consent
- present active RA fulfilling the ACR criteria of RA
- show impairment of hand strength with or without pain in the hands during the grip procedure
- chronic pain: either persistent or intermittent over a minimum period of three months prior to recruitment
- current pain: greater than 30/100 mm on a pain visual analogue scale (VAS) within the last 24 hours
- patients under the age of 18 years
- the patients included who have signed an informed consent
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Exclusion Criteria:
- patients who are under the age of 18 years
- previously had acupuncture
- have localized skin infections
- have severe chronic or uncontrolled co-morbid disease

Acupuncture Treatment: Will be held the treatment with acupuncture points selected for the study, namely: TK5: Wai guan (Clusa External), C3: Shao Hai (Mare Minus), R7: Fuliu (Amnis Recurrens) F39: xuan zhong (Campana Suspension) according to the Chinese classic diagnosis as defined by the Chinese Medicine Heidelberg Model. We decided to use the technique Leopard Spot Technique (LST), an acupuncture technique that through the puncture causes bleeding using sterile needles subcutaneous (0,30mmx8mm). This technique is known to increase the local microcirculation and vegetative induce a response (13).

Research Variables - Hand Pain (Hand average pain - left and right):

- VAS (quantitative measure score, between 0 to 10).
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Measuring instruments:

Sample characterization questionnaire - It was created for the purposes of the study, allows collection of information about the social, demographic and clinical conditions of participants.

Visual Analogue Scale (VAS) - In this study we resorted to the VAS as a way to measure the intensity of pain in the patient.

Algometry - As the pain is a central theme of our work, we develop equipment that would allow us to quantify the pain. So in partnership with the Faculty of Engineering of Porto, we created an algometry that I will describe:

According to the specifications provided, it developed a prototype (Figure 1) for the acquisition of the force applied in different situations: Measure the force applied at two points, considering the hand grip. With this equipment, we try to measure the Kg / cm2 tolerated by each patient before the onset of pain in the hand. This is a quantitative variable, measured in Kg / cm2. It is expected that the higher the strength tolerated, reduced the intensity of pain.

The prototype comprises: - an Arduino Uno R3 for acquisition and control (n°1); two adapters FlexiForce Adapter (n° 2) for signal conditioning from the sensors; two FlexiForce piezoresistive sensors 25
lb / SQI (weight pounds / square inch), or 1,757 kgf/cm² Tekscan company (nº 3).
The sensors were characterized tested in order to obtain the individual characteristic of each sensor (Figure 2) required for transforming the voltage signal applied force. For the control interface, an application was developed in LabVIEW 2013 to establish communication with the Arduino Uno R3. To this end, it was implemented LIFA library (LabVIEW Interface for Arduino) on Arduino and used analog inputs A0 and A1 of the same. The connection between Arduino and the laptop computer where the application was installed was done by USB cable.

Table 1 - Sample characterization according to age and gender

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Experimental Case (EC)</th>
<th>Control Case (CC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>47</td>
<td>53</td>
</tr>
<tr>
<td>Sex</td>
<td>Female</td>
<td>Female</td>
</tr>
</tbody>
</table>

Table 2 - Hand pain measures and VAS, evaluated six times. The first moment (T0) performed before the first session, the second (T1), five minutes after completing treatment (T2) 24 hours after the first session (T3) five minutes after the second treatment (T4) 72h and the first session (T5) 5 minutes after the third treatment.

With this equipment, we try to measure the Kg/cm² tolerated by each patient before the onset of pain in the hand. The participants were guided and informed clearly to identify the moment when the stimulus causes painful sensation. At this time, the pressure ceases to be applied and the device records its value.

Results

Two female patients were evaluated for hand pain. They were divided into two cases one of which was treated with acupuncture technique (experimental case) and the other not (control case). The characteristics of the two groups are presented in Table 1 and hand pain measures and VAS, evaluated six times, in the Table 2.

Comparing the clinical cases (EC vs CC) there were no significant differences at T0 (baseline) measurement performed by algometry and VAS parameters (Table 2 and Figure 2).

However, EC 5 minutes after (T1) completion of acupuncture, there was an increase in the pressure of algometer tolerance in both hands, translated by an increased tolerance to pain. Such improvement in EC, comparatively to the CC, it was also found in measurements T3 (in both hands) and T5 mainly in the left hand.

In percentage terms, there was an improvement when it is measured the tolerance to pain with algometry after performing acupuncture session. Thus, from T0 to T1 improved 46.65% to the left and 146.91% on the right. T2 to T3 improved 9.20% on the left, and 15.60% on the right. T4 to T5 improved 25.38% to the left, and 12.51% on the right.

In general, there was a significant improvement from baseline to end of study. From T0 to T5 was an improvement of 45.28% on the left, and 32.92% on the right.

In the CC, there were no significant changes during...
ing the various measurements. There was a slight decrease in pain threshold measured by T0 to T5 algometry. In measuring the VAS there was an increased perception of pain, passing the value 5 to the value 6.

Discussion
RA disease, the most common inflammatory arthritis is a chronic inflammatory disease and multi-system, which is characterized by symmetric poly-arthritis, especially of the hands. The failure and consequent socio-economic costs for patients, families and society requires early recognition of the diagnosis and the implementation of the last advances in the treatment of RA. Acupuncture besides being recommended by the World Health Organization has been a feature sought by rheumatoid arthritis patients, however, its efficacy has not been established. This preliminary study may provide guidance for the clinical trial of larger scale and considering other parameters and more adequate conditions. From this study were only evaluated the acute effects of acupuncture treatment. In an attempt to answer the research question, the results show that acupuncture considering the mentioned points, can improve the hand pain and VAS parameters. In the present research work it was observed that the pain improved after the first treatment, as well as for the second treatment and the third treatment, with a significant values. Both assessments take place 5 min after treatment. The instrument was used to evaluate the hand pain was purposely created for this study, although not yet tested for a larger population. The mechanism concerning it involves the compression of the bone structures. The technique chosen to assess the hand pain may lead to a worsening of pain given that we are evaluating patients with an associated inflammatory factor.

Although in this study, the VAS reflected higher improvement based on changes values, the algometry values can express more realistic meanings since these measurements are more objective than those of VAS. But both suggest a clear meliorated tendency than the control situation where worse tendency is shown. From these results it is also interesting to note that the hand pain got worse for patients who didn’t treatment, both in algometry as the VAS.

Apart from the above, the study also noted some limitations that would like to correct a later study: We have present a few limitations on the work methodology. In fact, there is a possibility that the results could have occasionally occurred, considering the small sample size; do not place blind patients and acupuncturists; the evaluation of the results was carried out by the researcher, which may be an evaluation bias. In the future, these limitations should be overcome taking larger experimental and control groups, each with different treatment points.

Conclusion
In this protocol study we conclude that, in respect of hand pain variables, the adequate acupuncture seems to effectively decreased the pain. The realization of a longitudinal study will assess the findings. Thus, studies with higher sample, as well as the achievement of a greater number of treatments according to an individual diagnosed, as envisaged by traditional Chinese medicine, will support best understanding of the effects by acupuncture on the relieve hand pain in these RA patients.

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References
1. Horsten, NCA; Ursum, J; Roorda, LD; Schaardenburg, D; Dekker, J; Hoeksma, AF. Prevalence of hand symptoms, impairments and activity limitations in rheumatoid arthritis in relation to disease duration. J. Rehabil. Med. 2010; 42: 916-921
4. Wang, C; Pablo, P; Chen, X; Schmid, C; Mclendon, T; Acupuncture for pain relief in patients with Rheumatoid Arthritis: a systematic review. Arthritis Care & Research. 2008; 59: 1249-1256
5. Wang, J; Cui, M; Jiao, YT; Xu, J; Zhao, Y; Han, M; Liu, J. Content Analysis of systematic reviews of effectiveness of Traditional Chinese Medicine. Journal of Traditional Chinese Medicine. 2013; 33(2):156-63
7. Hui, KK; Marina, O; Liu, J; Rosen, BR; Kwong, KK. Acupuncture, the limbic system, and the anti-correlated networks of the brain. Autonomic Neuroscience. 2010; 157: 81-90
9. He, TF; Yang, WJ; Zhang, SH; Zhang, CY; Li, LB; Chen, YF. Electroacupuncture Inhibits Inflammation Reaction by Upregulating Vasoactive Intestinal Peptide in Rats with Adjuvant-Induced Arthritis. Evidence-Based Complementary and Alternative Medicine, 2011; Article ID 290489
10. Gao, J; Liu, XG; Huang, DJ; Tang, Y; Zhou, HY; Yin, HY; Chen, T. Involvement of the hypothalamus-pituitary-adrenal axis in moxibustion-induced changes of NF-kappaB signaling in the synovial tissue in rheumatic arthritic rats. Zhen Ci Yan Jiu 2010; 35: 198-203
11. Cheng, KJ. Neuroanatomical basis of acupunc-
ture treatment for some common illnesses. Acupunct Med 2009; 27: 61-4
12 Doenitz, C; Anjos, A; Efferth, T; Greten, T; Greten, H. Can Heat and cold be parameterizes? Clinical data of a preliminar study. Journal of Chinese Integrative Medicine, Vol. 10, Nº5, May 2012: 532 – 537