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Pain, Clinical Trials, bDMARD

Pain characteristics in people with active rheumatoid arthritis receiving adalimumab and abatacept: a feasibility trial of nociceptive, neuropathic and pain sensitisation components

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Background:

There has been recent advancement of our understanding of pain in rheumatoid arthritis (RA). With the advent of biologic disease-modifying anti-rheumatic drugs (DMARDs), clinicians managing RA have a wide range of treatments to manage active disease. Many DMARDs are effective at achieving suppression of inflammation, but pain remains a key issue in RA. Despite nociceptive pain being a major feature of RA, other aspects of RA pain are associated with neuropathic and nociplastic components. Nociplastic pain is described as widespread, without evidence of proportionate tissue or nerve damage. Pain processing by the central nervous system can maintain and increase RA pain.

Objectives:

This study aimed to evaluate the causes and underlying mechanisms of pain in RA by conducting a randomised feasibility trial. Our study evaluated the pain characteristics in subjects with RA randomised to different classes of biologic therapy including TNF inhibitors (adalimumab) and T cell modulators (abatacept). In this study, we evaluated distinct aspects of pain including nociception by Visual Analog Scale (VAS), neuropathic (PainDETECT questionnaire) and nociplastic pain components using pain pressure thresholds (PPT) by quantitative sensory testing (QST).

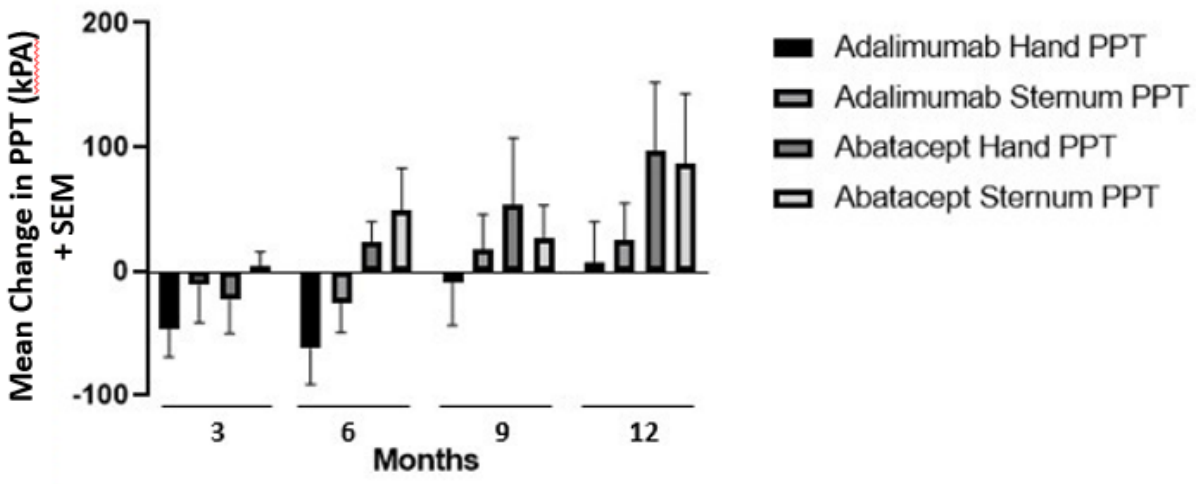
Methods:

A total of 25 participants were recruited between August 2020 and October 2022; 13 subjects were randomised to adalimumab and 12 to abatacept. All participants continued with methotrexate therapy during the study ranging between 10-25 mg weekly. The primary outcome measures included change in VAS for pain, painDETECT and PPT after 12 months' treatment in each arm. PPT were measured using a hand-held algometer (Somedic) in the wrist and finger joints, large joints, sternum and malleolus, with 3 readings taken per region and a mean value recorded (kPa) as we have previously described (1). Subjects were also stratified by CCP antibody status.

Results:

The mean age was similar in the two groups (abatacept: mean (SD) 56.5 (13.5) years versus adalimumab: 53.9 (12.4) years) . There were 12 (92%) female participants in the abatacept group and 10 (83%) in the adalimumab group. All subjects recruited to the study had a Disease Activity Score (DAS28) greater than 5.1 at baseline. There was an improvement from baseline over 12 months of follow-up in VAS pain, with a mean (SEM) of 3.7 (0.82) in the abatacept group and 2.3 (1.10) in the adalimumab group. For painDETECT measures, there was an improvement in painDETECT scores from baseline over 12 months of treatment (mean (SEM)) by 5.8 (1.93) in the abatacept group and 4.6 (2.54) in the adalimumab group. The change in PPT measures over 12 months is shown in Figure 1. Higher (positive) values for PPT indicate a higher pain threshold, Figure 1 shows a mean improvement with all subjects being able to tolerate more pain on pressure algometry.

Figure 1: Changes in PPT in the study population over time



Conclusion:

This study demonstrates that subjects with active RA demonstrate specific modalities of pain, including nociceptive, neuropathic and nociplastic elements. Furthermore, biologic therapies with different mechanisms of action may improve RA pain through distinct mechanisms. A greater improvement was observed in central (sternum) and peripheral (hand) pain sensitisation with abatacept compared with adalimumab after 12 months' treatment.

It is suggested that abatacept, a T-cell modulator, resulted in a greater improvement in pain sensitisation compared with adalimumab. Since T cells are involved in pain mediation, including by infiltrating nerves and impacting memory T cell function, further work is required to investigate the impact of T cell modulation on pain in RA. Larger future studies are required for validation of our findings.

References:

Wajed, J, Ejindu V, Heron C, Hermansson, Kiely P, Sofat N. Quantitative sensory testing in painful hand osteoarthritis demonstrates features of peripheral sensitisation. International Journal of Rheumatology 2012; 2012:703138

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