

Editorial

Effective rheumatoid arthritis treatment requires comprehensive management strategies

Chad S Boomershine

Division of Rheumatology and Immunology, Vanderbilt Center for Molecular Neuroscience, Vanderbilt Center for Integrative Health, Vanderbilt University, 1161 21st Ave S, T3219 MCN Nashville, TN 37232-2681, USA

Corresponding author: Chad S Boomershine, chad.boomershine@vanderbilt.edu

Published: 21 December 2009

This article is online at <http://arthritis-research.com/content/11/6/138>

© 2009 BioMed Central Ltd

Arthritis Research & Therapy 2009, **11**:138 (doi:10.1186/ar2872)

See related research by Lee *et al.*, <http://arthritis-research.com/content/11/5/R160>

Abstract

Work by Lee and colleagues has shown that decreased sleep quality and increased psychiatric distress increase pain sensitivity at both articular and nonarticular sites in rheumatoid arthritis (RA) patients. This work is consistent with prior studies showing that factors independent of RA disease activity can influence RA outcome measures. Owing to increasing pressure on rheumatologists to use outcome measures to inform treatment decisions, the work by Lee and colleagues highlights the need for comprehensive RA management strategies to understand and address the human factors that influence outcomes measures. Such strategies will ensure appropriate use of increasingly expensive therapies while maximizing patient satisfaction and reimbursement.

Newly published work has important implications for the care of rheumatoid arthritis (RA) patients [1]. In their study, Lee and colleagues correlated pain sensitivity at articular, periarticular and muscle sites with measures of RA disease activity as well as with measures of sleep quality and psychiatric distress. Interestingly, the authors found pain sensitivity was not influenced by the C-reactive protein (CRP) level. While correlations between pain sensitivity and other disease activity measures existed, the associations varied by site. As would be expected, pain sensitivity correlated with the swollen joint count only at articular sites. The 28-joint disease activity score (DAS28)-CRP, however, correlated with pain sensitivity at both articular and periarticular sites – probably due to the fact that the tender joint count (TJC) was associated with pain sensitivity at all sites. Decreased sleep quality was also associated with pain sensitivity at all sites, but the psychiatric distress level correlated with pain sensitivity only at articular and periarticular sites. While the authors found that patients with concomitant RA and

fibromyalgia syndrome (RA-FMS patients) had increased pain sensitivity at all sites associated with increased TJC and decreased sleep quality, the inverse relationship between sleep quality and pain sensitivity at all sites remained when the data were reanalyzed after excluding RA-FMS patients. The psychiatric distress levels were also similar between RA patients with and without FMS, indicating that the increase in pain sensitivity associated with psychiatric distress was independent of the presence of FMS.

The tendency for the TJC to be elevated by conditions independent of RA disease activity presents a challenge for RA disease management. The DAS28-CRP is calculated by a weighted combination of CRP, swollen joint count and TJC [2]. The relative weighting of each component was designated to coincide with clinical decision-making by rheumatologists, specifically making a treatment change. The weighting of the TJC is twice that of the swollen joint count in the DAS28-CRP formula, indicating treatment decisions are biased more by the number of tender joints than by the number of swollen joints. This bias can lead to overaggressive treatment of RA patients with joint tenderness arising from factors independent of RA disease activity. The tendency for DAS28 scores to overestimate RA disease activity in RA-FMS patients has been demonstrated previously [3]. FMS independently increases DAS28 scores by almost a full point, resulting in the overestimation of RA disease activity in 63% of RA-FMS patients. Consistent with the findings of Lee and colleagues, the overestimation of disease severity in RA-FMS patients was due to higher TJC and perceived disease activity scores. RA-FMS patients also had significantly worse scores on other outcome measures used to assess disease severity, including the health assessment questionnaire and the Medical Outcomes Study Short Form 36.

CRP = C-reactive protein; DAS28 = 28-joint disease activity score; FIBRO = Fatigue, Insomnia, Blues, Rigidity, Owl; FMS = fibromyalgia syndrome; RA = rheumatoid arthritis; TJC = tender joint count.

Given the increasing pressure on physicians from regulatory agencies and insurance companies to base treatment decisions on outcome measures [4], the work by Lee and colleagues highlights the importance of an individualized, comprehensive approach to RA management [1]. Experience has shown that many RA patients present with joint tenderness and synovitis accompanied by a variety of symptoms I have previously characterized in FMS with the FIBRO mnemonic – Fatigue, Insomnia, Blues (depression and/or anxiety), Rigidity (muscle and joint stiffness), Ow! (pain and work disability) [5]. While FIBRO symptoms resolve along with synovitis in response to antirheumatic therapies in some cases, many patients remain symptomatic despite the lack of objective evidence for synovitis resulting in persistently poor outcome measure scores. Outcome measure scores in these patients only improve when the underlying cause(s) of their FIBRO symptoms are understood and addressed, requiring the use of nonrheumatic therapies as in FMS [5]. Corroboration for these observations comes from work showing that RA-FMS patients have increased RA disease severity and are resistant to standard therapy [6]. The presence of FMS is not required, however, for associated symptoms to impact RA disease severity. Many RA patients without FMS report pain at nonarticular sites and suffer from persistent pain even when inflammation appears well controlled [7], and sleep disturbance has been shown to worsen pain severity in RA patients independent of the coexistence of FMS [8].

As physicians, we have access to increasingly powerful therapies to combat disease. With great power, however, must also come great responsibility. We must be prudent in our use of new therapies as they can have enormous costs, both financial and human, to our patients and society. All too often we assume patients who fail to respond to therapy merely require more or stronger treatments. The work by Lee and colleagues reminds us that it is important to consider human factors existing outside the primary disease that can influence treatment outcomes [1]. In the past, some physicians have avoided consideration of these factors due to the assumption that such considerations were not necessary for disease management. However, use of patient satisfaction surveys in determining physician reimbursement and societal pressures for improved utilization of healthcare dollars make identification and management of FIBRO symptoms increasingly important [9]. While existing questionnaires such as the modified VAS Fibromyalgia Impact Questionnaire [5] and the Symptom Impact Questionnaire (SIQR) [10] can be used to rapidly identify FIBRO symptoms, physicians must acknowledge the necessity of treating these symptoms in order for the implementation of comprehensive treatment strategies that improve patient care to occur.

Competing interests

CB has received funding from Pfizer Inc., Eli Lilly Inc. and Forest Laboratories, Inc.

References

1. Lee YC, Chibnik LB, Lu B, Wasan AD, Edwards RR, Fossel AH, Helfgott SM, Solomon DH, Clauw DJ, Karlson EW: **The relationship between disease activity, sleep, psychiatric distress and pain sensitivity in rheumatoid arthritis: a cross-sectional study.** *Arthritis Res Ther* 2009, **11**:R160.
2. Prevoo MLL, Van't Hof MA, Kuper HH, Van Leeuwen MA, Van De Putte LBA, Van Riel PLCM: **Modified disease activity scores that include twenty-eight-joint counts. Development and validation in a prospective longitudinal study of patients with rheumatoid arthritis.** *Arthritis Rheum* 1995; **38**:44-48.
3. Ranzolin A, Tavares Brenol JC, Bredemeier M, Guarienti J, Rizzatti M, Feldman D, Xavier RM: **Association of concomitant fibromyalgia with worse disease activity score in 28 joints, health assessment questionnaire, and short form 36 scores in patients with rheumatoid arthritis.** *Arthritis Rheum* 2009, **61**: 794-800.
4. Wolfe F, Michaud K, Pincus T, Furst D, Keystone E: **The disease activity score is not suitable as the sole criterion for initiation and evaluation of anti-tumor necrosis factor therapy in the clinic: discordance between assessment measures and limitations in questionnaire use for regulatory purposes.** *Arthritis Rheum* 2005, **52**:3873-3879.
5. Boomershine CS, Crofford LJ: **A symptom-based approach to pharmacologic management of fibromyalgia.** *Nat Rev Rheumatol* 2009, **5**:191-199.
6. Wolfe F, Michaud K: **Severe rheumatoid arthritis, worse outcomes, comorbid illness, and sociodemographic disadvantage characterize RA patients with fibromyalgia.** *J Rheumatol* 2004, **31**:695-700.
7. Buskila D, Sarzi-Puttini P: **Fibromyalgia and autoimmune diseases: the pain behind autoimmunity.** *Isr Med Assoc J* 2008, **10**:77-78.
8. Wolfe F, Michaud K, Li T: **Sleep disturbance in patients with rheumatoid arthritis: evaluation by medical outcomes study and visual analog sleep scales.** *J Rheumatol* 2006, **33**:1942-1951.
9. Teisberg EO, Wallace S: **Creating a high-value delivery system for health care.** *Semin Thorac Cardiovasc Surg* 2009, **21**:35-42.
10. Bennett RM, Friend R, Jones KD, Ward R, Han BK, Ross RL: **The Revised Fibromyalgia Impact Questionnaire (FIQR): validation and psychometric properties.** *Arthritis Res Ther* 2009, **11**: R120.