Fatigue is related to poor pain outcomes in women with established rheumatoid arthritis

Sirs,

We report a study that supports the inclusion of fatigue in rheumatoid arthritis (RA) as a core outcome measure in clinical practice and clinical trials. The importance of pain as a core outcome measure in RA is widely recognised by patients and clinicians (1, 2). While fatigue is an acknow-ledged symptom of RA (3), unlike pain, it is not included in the American College of Rheumatology (ACR) core set of outcome measurements and improvement criteria (4). Fatigue has been proposed for further evaluation as a patient-derived outcome measure (5).

To test the hypothesis that higher fatigue levels at follow-up are associated with worse pain outcomes, women who participated in a quality of life study in 2000 were re-evaluated after 4 years. The Arthritis Impact Measurement Scales 2 was used to measure 12 health status dimensions (6). The evaluation of fatigue as a health status dimension, not included at baseline, was added and measured using a visual analogue scale (0-10cm, 0, no fatigue, 10, worst possible fatigue) (7). Prioritisation for improvement of the 12 health status dimensions, as well as fatigue, was also explored.

The original cohort of 58 women returned 48 (83%) sets of completed questionnaires; the mean respondent age at follow-up was 54 years; the mean disease duration was 18 years. High fatigue and pain levels were reported. The mean score for the 12 health status dimensions at the two time-points were not statistically different (8). Arthritis pain and social activity were allocated the highest scores both at baseline and at follow-up (5.4±2.3, 5.0±3.0, and 4.8±1.9, 5.0±2.1 respectively). Of interest, fatigue was allocated the highest mean score, 6.42±2.6, of all the 13 health status outcomes evaluated at 4 years and was prioritised for improvement over pain, by 65% of women.

At 4 years, 3 pain subgroups were identified based on arbitrary cut-off points (9) (Fig. 1a). Group A represented patients with minimal pain levels, (defined as pain scores \leq 3 on a 10 point scale), at both baseline and 4-year follow-up. Group B represented patients with pain levels at 4 years that were either the same as, or worse than, those reported at baseline. In this group, either the baseline or the 4-year pain scores, or both, were \geq 3, and any reduction in pain scores was <2. Group C represented patients with a baseline score of >3, who reported improved pain levels defined as a decrease of ≥ 2 at 4-year follow-up. Fatigue levels were examined to determine whether a difference between fatigue levels could be demonstrated across the 3 pain-outcome subgroups (Fig. 1b). The highest fatigue



Fig. 1. Outcomes in women with rheumatoid arthritis. (a) Pain outcomes. Three pain subgroups were identified at 4 years. Group A, who described minimal pain score levels, ≤ 3 (0-10), at baseline and 4-year follow-up. Group B who described pain levels at 4 years that were either the same as, or worse than, those reported at baseline. In this group, either the baseline or the 4-year pain scores, or both, were ≥ 3 , and any reduction in pain scores was <2. Group C who described improved pain levels defined by a baseline pain score of >3, which decreased by ≥ 2 at follow-up. (b) Fatigue levels and pain outcomes. Statistically significant differences were found between the mean fatigue values across the three pain subgroups, (p=0.001; α =0.05). Significant differences were found between group B and group A (p=0.001; α =0.05). No difference was observed between group A and group C (p=0.61; α =0.05).

levels were observed in group B. A wide range of fatigue levels was seen across all 3 pain subgroups. Group A, demonstrated fatigue levels of 3-6 (mean 4.0); group B, demonstrated fatigue levels of 4-10 (mean 7.4); and group C, reported fatigue levels of 0-9 (mean 5.0). Statistically significant differences were found between the three group means (*p*=0.001;α=0.05) (ANOVA). Significant differences were found between group B and group A ($p=0.001; \alpha=0.05$), and between group B and group C $(p=0.01;\alpha=0.05)$. No significant difference was observed between group A and group C ($p=0.61; \alpha=0.05$) using Scheffe's post hoc test. These results support the hypothesis that women who demonstrated higher fatigue levels at follow-up reported worse pain outcomes.

As the physiological basis of fatigue is not yet understood, exploration of factors that may contribute to the experience of fatigue in RA is worthwhile. Moreover, the exact nature of the relationship between pain and fatigue in RA warrants further elucidation. The inclusion of fatigue as a core outcome measure in clinical studies of patients with RA merits further study (10).

P. MINNOCK¹, RGN, MSc

B. BRESNIHAN^{1, 2}, MD, Professor

¹Rheumatology Rehabilitation, Our Lady's Hospice and St Vincent's University Hospital, Dublin; ²University College Dublin, Dublin, Ireland.

Address correspondence to: Patricia Minnock, RGN, MSc, Rheumatology Rehabilitation, Our Lady's Hospice, Harold's Cross, Dublin 6, Ireland.

E-mail: pminnock@olh.ie

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