

Differences in pain and fatigue perception among a group of rheumatoid arthritis patients in the United States and in Turkey who have similar disease activity and functional status

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ABSTRACT

Objectives. *The concordance of patient reported outcomes in rheumatoid arthritis (RA) among different countries has not been studied in detail. We tried to determine the differences in pain and fatigue perception among a group of RA patients in the US and in Turkey who had similar disease activity and functional score in multidimensional health assessment questionnaire (MDHAQ FN).*

Methods. *One hundred and thirty-seven RA patients from Turkey and 129 from the US were studied. An MDHAQ was obtained and a DAS-28 was calculated for each patient. Pain and fatigue perception was compared between the two groups after adjusting for age, sex, MDHAQ FN and DAS-28.*

Results. *Turkish patients had less pain than their US counterparts when adjusted for MDHAQ FN, DAS-28, age and sex (3.56 (2.24) vs. 4.35 (2.23), $p=0.005$) whereas there was no difference in fatigue between the two groups (3.85 (2.44) vs. 4.25 (2.45), $p=0.194$). When the patients with a DAS-28 score of above 5.1 and below 2.6 were compared in both groups, Turkish patients had again less pain albeit less in the high disease activity group.*

Conclusion. *This study suggests that Turkish patients have less pain than the US patients when controlled for age, gender and MDHAQFN and DAS-28 scores. This is at odds to the conventional wisdom that pain perception is increased among the non-Western cultures.*

Introduction

Rheumatoid arthritis (RA) is a chronic inflammatory disorder that causes substantial morbidity and mortality (1). Pain is one of the major symptoms and is the usual reason for a doctor visit. However, pain is subjective and there are substantial differences in pain perception among different cultures (2). The social environment seems to be its main determinant and there are ethnic/racial differences in pain thresholds, intensity and affect (3). The conventional wisdom is that as one goes to non-Western countries pain thresholds decrease.

Egyptian women for example, report more pain than their Dutch counterparts (4). Pain control and coping and adjustment patterns differ between African Americans and Caucasians (5). A cluster analysis of the components of the Multidimensional Health Assessment Questionnaire (MDHAQ) among RA patients from Turkey and the United States (US) found that pain clustered separately between the two groups (6). Fatigue is also part of the clinical picture in most chronic diseases and is an important component of RA. It is not homogenous in different populations and is also influenced by ethnicity/race and social class (7).

We therefore aimed to determine the differences in pain and fatigue perception among a group of RA patients in the US and in Turkey who had similar disease activity and functional status.

Methods

One hundred and thirty-seven Turkish and 129 US patients were analysed. The Turkish patients were selected among those who routinely had an MDHAQ (8) evaluation during the previous three months and who were regularly attending the rheumatology outpatient clinic of Cerrahpasa Medical Faculty in Istanbul, Turkey. All patients who had completed an MDHAQ were included and there were no other selection criteria. The US patients were included from a private practice in New York where every patient seen completes an MDHAQ each visit. These were consecutive patients seen in the clinic. The demographic characteristics of the patients and their disease durations are shown in Table I.

In addition to an MDHAQ, a 28-joint count for tender and swollen joints was done, erythrocyte sedimentation rates were measured and a DAS-28 (Disease Activity Score) was calculated in each patient. The data from the US patients were obtained by a single physician (YY) whereas the information from the Turkish patients was collected by multiple physicians (SC, EK, KT, GH). DAS-28 and MDHAQ function scores (MDHAQFN), pain visual analogue scale (VAS), fatigue VAS and patient and physician global assessment of

Competing interests:

Dr Yusuf Yazici is a consultant and Speaker for BMS, Genentech, UCB, Centocor, Celgene, Roche and Merck. The other co-authors have declared no competing interests.

Table I. The demographic characteristics of the Turkish and US patients.

	Turkish patients (n=137)	American patients (n=129)	<i>p</i> -value
Female %	83%	80%	0.479*
Mean age (yr)	49.60 (12.40)	55.70 (13.60)	0.001**
Mean disease duration (yr)	10.20 (7.20)	3.29 (3.55)	0.0001**
Seropositive RA	69.4%	70.3%	0.824*

*Chi-Square test; **Mann-Whitney U-test

Table II. MDHAQFN, DAS28, pain, fatigue, tender and swollen joint counts, patient global assessment, physician global assessment and ESR levels among the Turkish and American patient groups.

	Turkish patients (n=137)	American patients (n=129)	<i>p</i> -value
MDHAQ FN	0.49 (0.46)	0.58 (0.58)	0.510
DAS-28	3.78 (1.21)	3.50 (1.42)	0.140
Pain VAS	3.53 (2.77)	4.39 (2.74)	0.009
Fatigue VAS	3.89 (2.73)	4.24 (2.82)	0.280
Tender joint count	3.52 (5.13)	3.63 (4.67)	0.580
Swollen joint count	1.23 (2.79)	1.33 (2.73)	0.860
Patient Global VAS	3.96 (2.43)	4.00 (2.56)	0.830
Physician Global VAS	2.00 (1.69)	1.59 (1.37)	0.060
ESR	33.27 (20.07)	28.95 (27.95)	0.001

Mann-Whitney U-test

disease activity VAS for the Turkish and American patients were tabulated and drug use data were obtained. Drug information was gathered from patient charts.

The groups were then compared without matching with respect to age and gender for FN, DAS-28, pain, fatigue, tender and swollen joint counts, patient global assessment, physician global assessment and ESR.

In the next stage the Turkish and US patients were compared for pain and fatigue after adjusting for age, sex, DAS-28 and MDHAQFN. The same analysis was then repeated for patients who had disease duration of 5 years or less to account for the difference in the mean duration of disease between the 2 groups. An analysis for patients who had disease duration of more than 5 years was not performed because the number of patients in the US group who met these criteria was small.

Finally the effect of high and low disease activity on pain perception and fatigue was further explored by repeat-

ing the measurements on patients with a DAS-28 >5.1 (high disease activity) and a DAS-28 <2.6 (remission).

Statistics

The numeric results were expressed as mean (standard deviation) and categorical results were expressed as percentages. Normality distribution of the numeric variables was tested by one sample Kolmogorov Smirnov test. Univariate statistical methods were used to determine statistically differences between groups. Differences in numeric variables between groups were compared using the Mann-Whitney U-test due to the non-normal distribution. Categorical variables were compared by the chi-square test. A multivariate method the ANCOVA (Analysis of Covariance) test was used to compare differences between groups in order to adjust the effect of covariates such as sex, age, DAS-28 and MDHAQ, and then the Bonferroni post-hoc test was used when a significant difference was obtained. A *p*-value <0.05 was considered as statistically

significant. Statistica 7.0 (StatSoft Inc, Tulsa, OK, USA) was used for statistical analyses.

Results

The demographic characteristics of the US and Turkish patients are shown in Table I.

Data on pain, fatigue, MDHAQFN and DAS-28 was available for all Turkish and American patients whereas drug data was obtained from 131/137 patients in the former and 126/129 in the latter.

US patients were older than their Turkish counterparts whereas Turkish patients had longer disease duration. The Turkish population were all Caucasians whereas the American population consisted of 8 (6%) patients of Asian origin, 50 (39%) African Americans, 38 (29%) Hispanic and 30 (24%) Caucasians.

An analysis of drug use among the Turkish and American patients revealed that all of the Turkish patients were using medications whereas only 53% of the American patients were on any drugs. The use of corticosteroids, methotrexate, leflunomide and sulfasalazine was significantly higher among the Turks compared to the Americans. There was no significant difference in the frequency of the use of biologics between the two groups.

MDHAQFN, DAS-28, pain, fatigue, tender and swollen joint counts, patient global assessment, physician global assessment and ESR levels among the Turkish and American patient groups are shown in Table II. Turkish patients had significantly less pain and higher ESR values.

Differences in pain and fatigue in RA patients controlled for age, sex, DAS-28 and MDHAQFN are shown in Table III. Turkish patients had less pain than US patients when adjusted for MDHAQFN, DAS-28, age and sex, whereas there was no difference in fatigue between the two groups.

When the same analysis was carried out on the patients who had disease duration of 5 years or less (39 Turkish and 120 US), Turks again had less pain (2.60(0.39) vs. 4.52(0.21) *p*=0.0001). They also had less fatigue (2.87(0.42) vs. 4.30(0.23) *p*=0.004).

American patients with different ethnic

backgrounds were also compared both within themselves and with the Turkish patients on the basis of pain and fatigue perception after adjusting for MDHAQFN, DAS-28, age and sex. There was no difference among the US patients whereas pain was less in Turks compared to the Caucasian and African Americans (3.54 (2.76) vs. 4.32 (2.66) $p=0.007$, 3.54 (2.76) vs. 3.95 (2.71) $p=0.022$). There was no difference among fatigue in these groups in any of the analyses.

The effect of high and low disease activity defined by a DAS-28 of >5.1 and <2.6 on pain and fatigue perception between the 2 groups are shown in Tables IVa and IVb. Increased disease activity as defined by DAS-28 >5.1 led to decreased difference among pain perception between the Turkish and US patients. However Turkish patients had less pain in both comparisons.

Discussion

Our study found that Turkish patients had less pain than their US counterparts when adjusted for age, gender, MDHAQFN and DAS-28. The difference in pain perception decreased among the patients with a high DAS-28 score (>5.1) although Turks had less pain irrespective of disease activity in all analyses. Fatigue was not different between the two groups when they were compared irrespective of disease duration. However, it was less in the Turkish patients among a group of patients who had disease duration of 5 years or less.

Several limitations of our study need to be discussed. The Turkish patients were younger than their American counterparts and had longer disease duration. However, when we performed an analysis among patients who had disease duration of 5 years or less, the Turks still had less pain.

Furthermore, the tender and swollen joint counts used in the DAS-28 calculations were measured by a single observer in the American group while it was performed by four physicians in the Turkish patients. This may also have influenced the results given the fact that tender and swollen joint counts are subject to variation among different observers.

Table III. Differences in pain and fatigue in Turkish and American RA patients adjusted for age, sex, DAS-28 and MDHAQFN.

	Turkish (n=137)	US (n=129)	<i>p</i> -value
Pain VAS	3.56 (2.24)	4.35 (2.23)	0.005
Fatigue VAS	3.85 (2.44)	4.25 (2.45)	0.194

Analysis of covariance.

Table IVa. The effect of high disease activity defined by a DAS-28 of >5.1 on pain and fatigue among the Turkish and US patients with RA.

	Turkish patients (n=26)	American patients (n=15)	<i>p</i> -value
Pain VAS	5.40 (2.57)	6.90 (1.74)	0.076
Fatigue VAS	6.30 (2.56)	6.20 (2.33)	0.769

Mann-Whitney U-test

Table IVb. The effect of low disease activity defined by a DAS-28 of <2.6 on pain and fatigue among the Turkish and US patients with RA.

	Turkish patients (n=26)	American patients (n=35)	<i>p</i> -value
Pain VAS	1.40 (1.87)	2.60 (2.55)	0.052
Fatigue VAS	2.60 (2.34)	2.50 (2.46)	0.870

Mann-Whitney U-test

Some centres use DAS-28 and MDHAQ during the routine follow-up of RA patients whereas others utilise them less frequently. The private practice setting in New York was an example of the former, whereas the outpatient clinic in Istanbul represented the latter. The familiarity of the patients with these indices is another factor that should be discussed in the interpretation of the data since patients who are accustomed to patient forms may respond differently from those who fill them out for the first time.

Education, depression, social status and co-morbidities are other factors that influence pain perception (9). Increased durations of formal education, disease specific education and social status have been shown to decrease pain perception (10, 11), whereas depression increases it (12). The levels of education, social status, depression and co-morbidities have not been determined in our study, and pain and fatigue perception is not controlled for these factors.

Data on drug use show that more Turkish patients were using medications com-

pared to Americans. However, most of the drug information in the US patients was obtained during the first patient visits while those of the Turkish patients were collected at the time of the study. This makes a fair analysis difficult.

The small number of patients in the different ethnic groups among the American RA patients may have prevented an accurate analysis. However the lack of difference in pain and fatigue perception among the American subgroups and the persisting decreased pain perception among the Turks and Caucasian and African Americans reinforces our results.

Most of the information for patient reported outcomes in studies on RA come from the Western world and patient management and drug development programs are guided accordingly. However, knowledge and analysis of differences in pain and fatigue perception may result in a more accurate interpretation of data and higher standards of care.

This is the first study that evaluated and compared pain and fatigue percep-

tion among a Turkish and a US patient group with RA who had similar levels of disease activity and functional status. Turkish patients reported less pain than their US counterparts: This is at odds with the common belief that the perception and reporting of pain is increased in the non-Western populations and should further be validated in other controlled studies. Meanwhile, we propose that pain should not be underrated and be given due attention especially in countries where exaggeration on the patient's part is expected.

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