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Relationship between psychological factors and arthralgia in patients with rheumatoid arthritis

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Abstract Various factors were assessed in terms of their contribution to arthralgia in a rheumatoid arthritis patient. Eighty-two outpatients (62 women and 20 men) with rheumatoid arthritis (RA) were examined with respect to the subjective degree of arthralgia, age, disease duration, dysfunction, steroid dose, steroid period, depression, anxiety, extroversion, neurotic disorder, and number of caretakers. The results were explained on the basis of stepwise regression analysis and psychological and clinical data. We analyzed results of a correlation coefficient test on the mutual relationship between variables. Stepwise regression analysis was performed to assess factors of arthralgia in terms of "depression," "mean activity," "morning stiffness," and "steroid dose." Depression is a factor of arthralgia as shown in this study, but it is clear that other factors are also involved. Anxiety was a factor distinct from the activity of RA. The factor contributing most to arthralgia was found to be depression, whereas anxiety had no effect.

Key words Anxiety · Arthralgia · Depression · Rheumatoid arthritis (RA)

Introduction

Rheumatoid arthritis (RA) may be described as a long-term illness of repeated palliation and aggravation. Stress arising from the illness is the most significant factor in aggravating RA.

Psychological and social factors in a crisis and the course of RA have long been studied. Kawakami[1] considers that there is no premorbid nature of RA, but that psychological factors greatly affect the course of RA based on studies carried out in Europe and America over the past 50 years. The present author considers the mechanism of RA is very inadequately understood and thus should be studied in much greater detail.

Modified arthritis impact measurement scale, version 2 (AIMS2), Japanese version for quality of life (QOL) estimation of RA patients[2] was revised into the AIMS2 Japanese version for HRQL estimation, which was reported in 1994; the revised version in easier to use. However, scale 11 in the revised version has only five items that include mental strain, and scale 12 has five items that include mood. Depression and anxiety were not distributed clearly.

In this study, psychological factors that may contribute to arthralgia in RA and awareness of arthralgia are examined.

Patients and methods

Purpose of study and patient selection

Eighty-two RA outpatients (62 women and 20 men) of First Department of Internal Medicine, Showa University and Division of Internal Medicine, Yamanashi Red Cross Hospital were the subjects of this study. Diagnosis was made without reference to dementia or acute diseases, other than acute infectious disease, over a period of more than 1 month. Informed consent was obtained from all the patients. The diagnosis of RA was made in accordance with the criteria of the American Rheumatism Association (ARA)[3] published in 1988. Complications of chronic fatigue syndrome,[4] fibromyalgia,[5] and primary Sjögren's syndrome[6] were not encountered in the present study.

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Methods

Questionnaires answered by patients and doctors were used as the basis for diagnosis. Answers from patients were used to assess arthralgia, dysfunction, depression, anxiety, extroversion, and neurotic disorders. Medical records provided information on each patient's age, disease duration, stage classification, class, number of caretakers, morning stiffness, grip, joint scores, Lansbury index, steroid dose, and dose periods. Arthrosis X-rays provided data regarding sites of pain or swelling, and laboratory tests determined cell blood count including leukocyte demarcation, C-reactive protein (CRP) level, erythrocyte count, and sedimentation rates (ESR). In cases of extensive pain, arthralgia assessment was based on a visual analog scale (VAS). Pain in all the patients of this study was considered to exceed 0%. The AIMS2 Japanese version for QOL estimation of RA patients has been reported previously.[2] However, scale 11 in this version has only five items that include mental strain, and scale 12 has five items that include mood. Depression and anxiety were not distributed clearly. In addition, analysis of each patient's character was not performed.

Depression and the anxiety were evaluated using the Hospital Anxiety and Depression Scale (HAD),[7] a scale commonly used by psychiatrists; for extroversion and neurotic disorder, the Eysenck personality test (short version) was used.[8] A short questionnaire for assessing these parameters and a Modified Health Assessment Questionnaire (MHAQ)[9] were used to determine the degree of dysfunction.

Statistical analysis

Depression, anxiety, extroversion, and neurotic disorders were considered psychological factors of RA, whereas age, disease duration, Lansbury index, stage, class, dysfunction degree, steroid dose and period, and laboratory data were considered as health factors. The number of caretakers was considered as a social factor.

In this study, the F value was assigned a value of 2.0. Stepwise regression analysis was conducted to provide explanation of arthralgia in RA patients. Stress has been found to be the most significant factor in RA, and pain aggravates arthralgia.[10,11] The author also considers the psychological status of patients and their lifestyle as significant contributing factors. Furthermore, we analyzed the interrelationship between the above-mentioned variables using the correlation coefficient test.

Results

The average age of the patients was 62.1 years (range, 28–89 years). Average disease duration was 9.2 years (range, 3 months to 39 years). The mean stage was 1.8 and the class, 2.2 (Table 1) .

The average depression score was 6.46, ranging from 0 to 16 (Table 2). The highest value was 21. The average anxiety score was 7.07 (range, 0–21). The extrovert character score frequency ranged from 6 to 21; the highest value was 24, and the average value 13.77. The average neurotic character disorder score was 16.77, ranging from 9 to 24.

Patient dysfunction was due to injury. The scores for the following functions are as follows: dressing and grooming, 0–3, average, 0.67; arising, 0–3, average, 0.67; eating, 0–3, average, 0.39; walking, 0–3, average, 0.49; hygiene, 0–3, average, 0.59; reach, 0–3, average, 0.58; grip, 0–3, average, 0.52; and activity, 0–3, average, 0.51. The total average factor was 0.55 (Table 3).

The results of stepwise regression analysis for arthralgia are shown in Table 4. A P value <0.001 was considered significant. Depression was found to be a major factor of arthralgia, while the daily mean of activity and time of morning stiffness were minor factors and steroid dose was a

Table 1. Background features of patients with rheumatoid arthritis

n	82
Sex (female/male)	62/20
Age (years)	62.1 ± 13.4[a]
Disease duration (years)	9.2 ± 10.3
Stage	2.2 ± 1.2
Class	1.8 ± 0.76
Number of caretakers	0.27 ± 0.52
Morning stiffness (min)	4.4 ± 9.1
Grip (mmHg)	167 ± 179
Joint score (%)	1.22 ± 1.48
Lansbury index (%)	34.6 ± 38.1
Dose of steroid (mg)	4.3 ± 3.7
Duration of steroid (years)	4.2 ± 6.5
Arthralgia (VAS, %)	35.6 ± 26.4

VAS, visual analogue scale
[a] Mean ± SD

Table 2. Summary of the mean of various psychological factors of rheumatoid arthritis

Factor	Score[a]	Range
Depression	6.46 ± 3.96	0–16
Anxiety	7.07 ± 4.14	0–21
Extroversion	13.77 ± 3.82	6–21
Character of neurotic disorder	16.77 ± 3.49	9–24

[a] Mean ± SD

Table 3. Summary of the mean according to each factor of functional disorder in rheumatoid arthritis (MHAQ)

Factor	Score[a]	Range
Dressing and grooming	0.67 ± 0.91	0–3
Arising	0.67 ± 0.85	0–3
Eating	0.39 ± 0.82	0–3
Walking	0.49 ± 0.90	0–3
Hygiene	0.59 ± 0.90	0–3
Reach	0.58 ± 0.93	0–3
Grip	0.52 ± 0.90	0–3
Activities	0.51 ± 0.87	0–3
Average	0.55 ± 0.81	

MHAQ, modified health assessment questionaire
[a] Mean ± SD

Table 4. Regression models for various factors of rheumatoid arthritis

Dependent variable: VAS		$R^2 = 0.4203$	F value 11.02 $P < 0.001$		
Explanatory variable	Unbalanced recurrence coefficient	Standard unbalanced recurrence coefficient	F value	T value	P value
Depression	2.1027	0.3154	9.6014	3.0986	0.003
Activities	7.2585	0.2401	4.8336	2.1988	0.0310
Morning stiffness	0.5817	0.2005	4.7298	2.1748	0.033
Steroid dose	−1.2947	−0.1835	4.2850	2.0700	0.042
Platelet count	0.5497	0.1626	2.8773	1.6963	0.094

VAS, visual analogue scale

Table 5. Correlation coefficient analysis according to functional disorder

Mean activity	Factor	vs. Factor	r	P
<0.5	Depression	vs. Morning stiffness	0.3210	0.0203
		vs. VAS	0.4017	0.0031
		vs. Steroid dose	0.1124	0.4275
	Anxiety	vs. Morning stiffness	0.2463	0.0783
		vs. VAS	0.2935	0.0346
		vs. Steroid dose	0.1059	0.4548
≧0.5	Depression	vs. Morning stiffness	−0.0389	0.8382
		vs. VAS	0.3438	0.0628
		vs. Steroid dose	−0.0471	0.8046
	Anxiety	vs. Morning stiffness	−0.1464	0.4398
		vs. VAS	−0.0269	0.8876
		vs. Steroid dose	0.1528	0.4200

VAS, visual analogue scale

Table 6. Correlation coefficient analysis according to steroid dose

Steroid dose	Factor	vs. Factor	r	P
<5 mg/day	Depression	vs. Morning stiffness	0.3016	0.0738
		vs. VAS	0.6060	0.0008
		vs. Mean activity	0.5986	0.0001
	Anxiety	vs. Morning stiffness	−0.1542	0.3689
		vs. VAS	0.2764	0.1026
		vs. Mean activity	0.2186	0.2000
≧5 mg/day	Depression	vs. Morning stiffness	0.2105	0.1602
		vs. VAS	0.4395	0.0022
		vs. Mean activity	0.5155	0.0002
	Anxiety	vs. Morning stiffness	0.1544	0.3055
		vs. VAS	0.1542	0.3060
		vs. Mean activity	0.1580	0.2942

VAS, visual analogue scale

very minor factor. The stepwise regression analysis indicated that strong recurrence might be possible, as indicated by the standard unbalanced recurrence coefficient. Depression was a significant factor at $P < 1\%$, and activities, morning stiffness, and steroid dose were significant factors at $P < 5\%$. The platelet number was determined not to be a significant factor by the stepwise regression analysis.

However, when depression is intense, activity decreases, and depression worsens with steroid loading, so we considered that there was mutual influence of these factors and performed stratified sampling. The patients were classified into two groups: patients with less than 0.5 of mean activity and those with more than 0.5 of mean activity. In the group with a mean activity less than 0.5, the correlation between depression and arthralgia was the strongest ($P = 0.0031$), but correlation was also observed between depression and morning stiffness and between anxiety and arthralgia. On the other hand, in the group with a mean activity greater than 0.5, a correlation between these factors was not observed (Table 5). As regards the steroid dose, the patients were again classified into two groups: those administered with less than 5 mg/day and those receiving more than 5 mg/day. The Depression increased arthralgia and mean activity and there was a strong correlation between these two factors; however, anxiety did not increase the degree of correlation in both groups (Table 6). The patients were classified

Table 7. Correlation coefficient analysis according to depression score

Depression score	Factor	vs. Factor	*r*	*P*
0–7	Morning stiffness	vs. Steroid dose	0.1081	0.4501
		vs. VAS	0.4264	0.0018
		vs. Mean activity	0.5705	0.0001
	Dose of steroid	vs. VAS	0.0002	0.9983
		vs. Mean activity	0.1257	0.3792
	VAS	vs. Mean activity	0.5257	0.0007
8–16	Morning stiffness	vs. Steroid dose	−0.0313	0.8671
		vs. VAS	0.1724	0.3534
		vs. Mean activity	0.0072	0.9692
	Dose of steroid	vs. VAS	−0.3193	0.0799
		vs. Mean activity	0.7197	0.7004
	VAS	vs. Mean activity	−0.1159	0.5345

VAS, visual analogue scale

into two groups based on the depression score: those with 0–7 and those with 8–16. In the group of 0–7 depression score, the correlation between morning stiffness and arthralgia, morning stiffness and activity, and arthralgia and activity appreciated; however, the correlation was not significant in the other group and the depression score 8–16 did not appreciate (Table 7). In addition, a significant correlation was not found between character and arthralgia (data not shown).

Discussion

In RA patients, depression and anxiety levels are higher than in normal individuals or those with other diseases and may be rated as 14%–42%.[12,13] These levels in young patients are remarkable.[14]

Arthralgia, confinement behavior,[15] anamorphosis of joints and its symptoms, and emotional problems are the most serious causes of stress[16] in RA patients according to MacKenna[10] and Ganga.[11] Injury, hardship in daily life, feelings of despair, dependence on other people, loss of confidence, and unsatisfactory contact with society and family are factors giving rise to considerable stress. The relationship between depression and arthralgia has been reported. Parker[17] noted that helplessness and arthralgia increase nearly as do anxiety and depression.

A secondary psychological change resulting from chronic disease does not alter the condition of stress. Unsolvable stress may lead to despair in attempts to do so, which consequently will lead to depression. Depression lessens the capacity to tolerate nociception; thus, pain in the joints of patients with arthralgia limits their lifestyle, further leading to greater depression. The primary disease state is thus worsened.[18] Frequent medical treatment for RA patients enhances psychological factors of suffering and becomes an unpleasant experience.[19] Psychological factors of suffering should be managed early; effective treatment would prove economical, and good mental health would be maintained.[20]

In this study, we distinguished between anxiety and depression, and examined the correlation of the levels of anxiety and depression in patients with arthralgia. It was found that severe arthralgia results from the following conditions: strong depression, daily reduction in mean activity level, long periods of morning stiffness, and small steroid dose. However, by increasing the steroid dose depression is intensified and the mean activity level falls, so that we assumed that there is mutual interaction of these factors and performed a stratified sampling. Depression, one of the factors of arthralgia, is correlated with the mean activity level but not with the steroid dose. With slight depression, as regards the morning stiffness, arthralgia, and mean activity level, a mutual relationship was observed. Depression is a factor of arthralgia as shown in this study, but it is clear that other factors are also involved. Partial correlation was observed between arthralgia and the mean activity level and anxiety, but the correlation did not reach statistical significance. It is reported that anxiety is highly frequent in RA patients,[12,13] but anxiety is a separate factor from the mean activity level of RA patients. Character is not a factor of arthralgia, and we considered that the so-called "RA disposition" is also not a factor of arthralgia.

Judith et al.[21] found that, before the onset of RA, there is a history of depression in RA patients with arthralgia and high interleukin-6 (IL-6) levels, and those whose daily life activity level significantly decreases.[22] If the activity of such patients is improved, the feeling of personal self-sufficiency in dealing with stress may be regained.[23,24] Arthralgia is reduced effectively by coping with stress.[25] Arthralgia may also be reduced by dothiepin treatment.[26]

Intense arthralgia lessens the scope of personal activity and confidence in dealing with stress. Revenson[27] reported the frequent occurrence of stress in RA patients with consequent pain and reduced activity. The degree of pain, age, and dissatisfaction with one's dysfunction in life are better indicators of the state of affected joints and other diseases.[28] Anxiety and depression levels are less in RA patients with primary Sjögren's syndrome,[6] which thus provides some benefit. The coefficient of regression of steroid dose had a negative value in this study, and the results of multivariate analysis may have given a weak indication for steroid, even for RA, although a high dose was used in serious cases.

Yamanaka and Matsuda[29] examined psychological factors for the aggravation and remission of rheumatoid

arthritis. The aggravating factor is depression characterized by insomnia, anorexia, decreased will power, and feelings of sorrow and despair. These factors in turn may give rise to anxiety and anger. Geenen et al. states that mobility, self-care, impact on daily activity anxiety, and cheerfulness are more conspicuous than depression in RA patients.[30]

The aggravation of arthralgia has been shown to lead to anxiety and also depression.[31] Compared with patients with osteoarthritis and healthy individuals, a high state of depression cannot be easily detected and recognized in RA patients. Arthralgia differs among RA patients; hence, the extent of anxiety and depression should also differ.

Anxiety could be distinguished from depression. The correlation between anxiety and depression in arthralgia was also studied by multivariate analysis. Depression was shown to be closely related to arthralgia by stepwise regression analysis. The effect of anxiety could not be explained and was not found to be significantly involved in arthralgia. The relationship between depression and anxiety and their connection with arthralgia depend mainly on depression, but it is clear that other factors are involved in the disease. The effect of arthralgia in RA patients was explained to some extent by this study, but further study is required to determine more fully the effect of other contributing factors.[32]

Depression, activities, morning stiffness, and steroid dose were found to be the most significant factors in arthralgia in this disorder. Anxiety was not found to be significantly involved.

References

1. Kawakami N. Psychosomatic medicine and rheumatoid Arthritis. Ryumachi 1992;22:404–10.
2. Hashimoto A, Sato H, Nishibayashi Y, Shiino Y, Kutsuna T, Ishihara Y, et al. A multicenter cross-section study on the health-related quality of life of patients with rheumatoid arthritis using a revised Japanese version of the Arthritis Impact Measurement Scale version 2 (AIMS 2), focusing on physical disability and its associated factors. Rhumachi 2001;41:9–24.
3. Arnett FC, Edworthy SM, Bloch DA, Mcshane DJ, Fries JF, Cooper NS, et al. The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. Arthritis Rheum 1988;31:315–24.
4. Wood B, Wessely S. Personality and social attitudes in chronic fatigue syndrome. J Psychosom Res 1999;47:385–97.
5. Wolfe F, Hawley DJ. Evidence of disordered symptom appraisal in fibromyalgia: increased rates of reported comorbidity and comorbidity severity. Clin Exp Rheumatol 1999;17:297–303.
6. Valtysdottir ST, Gudbjornsson B, Lindqvist U, Hallgren R, Hetta J. Anxiety and depression in patients with primary Sjögren's syndrome. J Rheumatol 2000;27:165–9.
7. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatry Scand 1983;67:361–70.
8. Eysenck HJ. A short questionnaire for the measurement of two dimensions of personality. J Appl Psychol 1958;42:14–7.
9. Pincus T, Summey JA, Soraci SA, Wallston KA, Hummon NP. Assessment of patient satisfaction in activities of daily living using a modified Stanford health assessment questionnaire. Arthritis Rheum 1983;26:1346–53.
10. Mackenna W. Pain and rheumatoid arthritis. Ann Rheum 1983;26: 1346.
11. Ganga M. Perceived stressor and coping strategies among individuals with rheumatoid arthritis. J Adv Nurse 1997;25:1144–50.
12. Ahles TA, Khans S, Yunus MB, Spiegel DA, Masi AT. Psychiatric status of patients with rheumatoid arthritis, and subjects without pain: a blind comparison of DSM-III diagnoses. Am J Psychiatry 1991;148:1721–6.
13. Soderlin MK, Hakala M, Nieminen P. Anxiety and depression in a community-based rheumatoid arthritis population. Scand J Rheumatol 2000;29:177–83.
14. Abdel-Nasser AM, Abd EI-Azim S, Taal E, EI-Badawy SA, Rasker JJ, Valkenburg HA. Depression and depressive symptoms in rheumatoid arthritis patients: an analysis of their occurrence and determinants. Br J Rheumatol 1998;37:391–7.
15. Anderson KO, Bradley LA, Turner RA, Agudelo CA, Pisko EJ, Salley AN Jr, et al. Observation of pain behavior in rheumatoid arthritis patients during physical examination. Relationship to disease activity and psychological variables. Arthritis Care Res 1992;5:49–56.
16. Huyser BA, Parker JC. Negative effect and pain in arthritis. Rheum Dis Clin North Am 1999;25:105–21.
17. Parker J, Smarr K, Anderson S, Hewett J, Walker S, Bridges A, et al. Relationship of changes in helplessness and depression to disease activity in rheumatoid arthritis. J Rheumatol 1992;19:1901–5.
18. DiMatteo MR, Lepper HS, Croghan TW. Depression is a risk factor for noncompliance with medical treatment: meta-analysis of the effects of anxiety and depression on patient adherence. Arch Intern Med 2000;24:2101–7.
19. Katz PP, Yelin EH. Prevalence and correlates of depressive symptoms among persons with rheumatoid arthritis. J Rheumatol 1993;20:790–6.
20. Lambert CM, Hurst NP, Forbes JF, Lochhead A, Macleod M, Nuki G. Is day care equivalent to in-patient care for active rheumatoid arthritis? Randomized controlled clinical and economic evaluation. Br Med J 1998;28:965–9.
21. Judith F, Howard T, Susan R, Julia M. Depression and the long-term risk of pain, fatigue, and disability in patients with rheumatoid arthritis. Arthritis Rheum 1998;41:1851–7.
22. Yoshino S, Nakamura H, Hanji N, Kohda M. Effect of mirthful laughter on patients with rheumatoid arthritis. Jpn J Psychosom Med 1996;36:559–64.
23. Parker JC, Smarr KL, Buckelew SP, Stucky-Ropp RC, Hewett JE, Johnson JC. Effects of stress management on clinical outcomes in rheumatoid arthritis. Arthritis Rheum 1995;38:1807–18.
24. Smarr KL, Parker JC, Wright GW, Stucky-Ropp RC, Buckelew SP, Hoffman RW, et al. The importance of enhancing self-efficacy in rheumatoid arthritis. Arthritis Care Res 1997;10:18–26.
25. Covic T, Adamson B, Hough M. The impact of passive coping on rheumatoid arthritis pains. Rheumatology 2000;39:1027–30.
26. Ash G, Dickens CM, Creed FH, Jayson MI, Tomeson B. The effects of dothiepin on subjects with rheumatoid arthritis and depression. Rheumatology 1999;38:959–67.
27. Revenson TA. Disability and coping as predictors of psychological adjustment to rheumatoid arthritis: J Consult Clin Psychol 1989;5783:344–8.
28. Hawley DJ, Wolfe F. Anxiety and depression in patients with rheumatoid arthritis: a prospective study of 400 patients. J Rheumatol 1988;15:932–41.
29. Yamanaka T, Matsuda T. The approach to rheumatoid arthritis by behavior therapy. Rheumatology 1999;21:176–81.
30. Geenen R, Jacobs JW, Godaert G, Kraaimaat FW, Brons MR, van der Heide A, et al. Stability of health status measurement in rheumatoid arthritis. Br J Rheumatol 1995;34:1162–6.
31. Smedstad LM, Vaglum P, Kvien TK, Moum T. The relationship between self-reported pain and sociodemographic variables, anxiety, and depressive symptom in rheumatoid arthritis. J Rheumatol 1995;22:514–20.
32. Escalante A, del Rincon I. How much disability in rheumatoid arthritis is explained by rheumatoid arthritis? Arthritis Rheum 1999;42:1712–21.