Impact of rheumatoid arthritis in Turkey: a questionnaire study

H. Direskeneli[1], N. Akkoç[2], C. Bes[3], N. Çakir[4], A. Çefle[5], V. Çobankara[6], E. Dalkiliç[7], A. Dinç[8], İ. Ertenli[9], A. Gül[10], V. Hamuryudan[11], M. İnanç[10], U. Kalyoncu[12], Y. Karaaslan[13], T. Kaşifoğlu[14], G. Keser[15], G. Keskin[16], B. Kisacik[17], S. Kiraz[9], S. Masatlioğlu[18], A.M. Onat[17], S. Özbek[19], M.A. Öztürk[20], Ö.N. Pamuk[21], S. Pay[22], T. Pirildar[23], M. Sayarlioğlu[24], S. Şenel[25], T. Şentürk[26], D. Taşan[27], E. Terzioğlu[28], A. Yazici[29], E. Yücel[30]

[1]Division of Rheumatology, School of Medicine, Marmara University; [2]Division of Rheumatology, School of Medicine, Dokuz Eylül University; [3]Division of Rheumatology, School of Medicine, Izzet Baysal University; [4]Rheumatology Clinic, Fatih Sultan Mehmet Research and Education Hospital; [5]Division of Rheumatology, School of Medicine, Kocaeli University; [6]Division of Rheumatology, School of Medicine, Pamukkale University; [7]Division of Rheumatology, School of Medicine, Uludağ University; [8]Private Office; [9]Division of Rheumatology, School of Medicine, Hacettepe University; [10]Division of Rheumatology, Istanbul School of Medicine, Istanbul University; [11]Division of Rheumatology, Cerrahpaşa School of Medicine, Istanbul University; [12]Rheumatology Clinic, Antakya State Hospital; [13]Rheumatology Clinic, Hitit University, School of Medicine, Numune Research and Education Hospital; [14]Division of Rheumatology, School of Medicine, Eskişehir Osmangazi University; [15]Division of Rheumatology, School of Medicine, Ege University; [16]Rheumatology Clininc, Dışkapı Research and Education Hospital; [17]Division of Rheumatology, School of Medicine, Gaziantep University; [18]Division of Rheumatology, School of Medicine, Medeniyet University; [19]Division of Rheumatology, School of Medicine, Çukurova University; [20]Division of Rheumatology, School of Medicine, Gazi University; [21]Division of Rheumatology, School of Medicine, Trakya University; [22]Division of Rheumatology, Gulhane Military Medical Academy School of Medicine; [23]Division of Rheumatology, School of Medicine, Celal Bayar University; [24]Division of Rheumatology, School of Medicine, Sütçü İmam University; [25]Division of Rheumatology, School of Medicine, Cumhuriyet University; [26]Division of Rheumatology, School of Medicine, Adnan Menderes University; [27]Rheumatology Clinic, Kartal Education and Research Hospital; [28]Division of Rheumatology, School of Medicine, Akdeniz University; [29]Rheumatology Clinic, Sakarya Research and Education Hospital; [30]Division of Rheumatology, Başkent University, Turkey.

Abstract

Objective

Unmet needs of rheumatoid arthritis (RA) patients regarding physician/patient communication, treatment preferences and quality of life issues were investigated in a Turkish survey study.

Methods

The study was conducted with the contribution of 33 rheumatologists, and included 519 RA patients. The study population included patients who had been on biologic therapy for >6 months and were still receiving biologic therapy (BT group), and those who were biologic naive, but found eligible for biologic treatment (NBT group). Of the RA patients, 35.5% initially had a visit to an internal disease specialist, 25.5% to a physical therapy and rehabilitation specialist, and 12.2% to a rheumatology specialist for their RA complaints. The diagnosis of RA was made by a rheumatologist in 48.2% of patients.

Results

The majority of RA patients (86.3%) visit their doctor within 15-week intervals. Most of the physician-patient communication focused on disease symptoms (99.0%) and impact of the disease on quality of life (61.8%). The proportion of RA patients who perceived their health status as good/very good/excellent was higher in the BT group than in the NBT group (74.3% vs. 51.5%, p<0.001). However, of those RA patients in the NBT group, only 24.8% have been recommended to start a biologic treatment by their doctors. With respect to dose frequency options, once-monthly injections were preferred (80%) to a bi-weekly injection schedule (8%).

Conclusion

In conclusion, RA patients receiving biologic therapy reported higher rates of improved symptoms and better quality of life and seemed to be more satisfied with their treatment in our study.

Key words

rheumatoid arthritis, quality of life, patient survey

Haner Direskeneli, MD, Professor
Nurullah Akkoç, MD, Professor
Cemal Bes, MD, Assoc. Professor
Necati Çakir, MD, Professor
Ayşe Çefle, MD, Professor
Veli Çobankara, MD, Professor
Ediz Dalkiliç, MD
Ayhan Dinç, MD, Professor
İhsan Ertenli, MD, Professor
Ahmet Gül, MD, Professor
Vedat Hamuryudan, MD, Professor
Murat İnanç, MD, Professor
Umut Kalyoncu, MD, Assoc. Professor
Yaşar Karaaslan, MD, Professor
Timuçin Kaşifoğlu, MD, Assoc. Professor
Gökhan Keser, MD, Professor
Göksal Keskin, MD, Assoc. Professor
Bünyamin Kisacik, MD, Assoc. Professor
Sedat Kiraz, MD, Professor
Seval Masatlioğlu, MD, Assoc. Professor
Ahmet M. Onat, MD, Assoc. Professor
Süleyman Özbek, MD, Professor
Mehmet A. Öztürk, MD, Professor
Ömer N. Pamuk, MD, Professor
Salih Pay, MD, Professor
Timur Pirildar, MD, Professor
Mehmet Sayarlioğlu, MD, Professor
Soner Şenel, MD
Taşkin Şentürk, MD, Professor
Demet Taşan, MD
Ender Terzioğlu, MD, Professor
Ayten Yazici, MD
Eftal Yücel, MD, Professor

Please address correspondence and reprint requests to:
Prof. H. Direskeneli,
Division of Rheumatology,
School of Medicine,
University of Marmara,
Istanbul, Turkey.
E-mail: hanerdireskeneli@gmail.com

Received on August 18, 2013; accepted in revised form on December 5, 2013.

Competing interests:
The survey and manuscript was sponsored by Merck Sharpe-Dohme Turkey, a subsidiary of Merck & Co., Inc., Whitehouse Station, NJ, USA.
The Investigators of the survey have received honoraria from MSD Turkey.
No payments were made to authors for the writing of this manuscript.

Introduction

Rheumatoid arthritis (RA) is a chronic inflammatory disease with a prevalence of 0.36% in Turkey (1). Studies, especially performed in routine patient care, has shown that RA has a significant impact on quality of life and can result in functional impairment and disability, leading to loss of work, high medical and social costs, and substantial morbidity and mortality (2-4).

Traditional pharmacologic approaches in the treatment of RA have relied on combinations of non-steroidal anti-inflammatory drugs (NSAIDs), analgesics, glucocorticoids, and disease-modifying anti-rheumatic drugs (DMARDs). Conventional DMARDs have long been the mainstay of treatment and recent studies also demonstrated the efficacy of combinational approaches such as triple therapy (5, 6).

Although treatment strategies have moved toward early initiation of DMARDs to prevent structural joint damage and disability (7), some patients fail to respond adequately to DMARDs and many do not maintain a stable response, with up to one third of RA patients discontinuing DMARDs due to the lack of efficacy. Thus, newer biologic treatments provide important clinical alternatives (7).

Progress in understanding cellular and molecular mechanisms underlying the disease, as well as the availability of new drugs have changed the management of RA. The goal in management has become controlling the disease process with the aim of complete abrogation of inflammation, rather than only controlling the symptoms. Therefore, the current treatment goal in RA is to achieve persistent, total disease suppression resulting in remission, if not cure (3).

Although many US and European guidelines are available for treating patients with RA, it is recommended that clinics should focus on individualised treatments using standard algorithms and their own experience in order to provide a more rational and cost-effective treatment of RA (8-10).

Biologic agents aimed at cellular and molecular targets have further transformed the management of the disease. As of 2013, four TNF-alpha inhibitors were approved for use in Turkey: infliximab, etanercept, adalimumab and golimumab (11). Recently, rituximab, tocilizumab and abatacept were also introduced as biologic agents (12). However, there is a paucity of data in Turkey about the use of biological agents.

In the present RAHAT (*understanding RA patients with surveys - in Turkish*) study, we aimed to shed light on the unmet needs of RA patients regarding physician/patient consultation and support, treatment preferences and quality of life issues in order to provide a valuable perspective to rheumatologists and help shape management and treatment strategies in RA. Within this context, we performed a multicentre questionnaire study, translated from a previously validated questionnaire (RAISE), investigated mostly in Caucasian populations in European countries and Canada (13), to assess therapeutic approaches in RA patients as well as to compare the unmet needs of RA patients who were on biologic treatment with those who were biologic naïve but eligible for biologic treatment.

Materials and methods

The study was conducted with the contribution of 33 rheumatologists from 29 pre-determined rheumatology clinics, and included RA patients older than 18 years of age. The study population included RA patients who had been on biologic therapy for at least 6 months and were still receiving biologic therapy (BT group), and those who were biologic naive, but eligible for biologic treatment (NBT group). Eligibility criteria for biologic treatment were as follows: erosive disease, a DAS28 (disease activity score in 28 joints) score >3.2 and moderate-to-severe disease based on clinical assessment by the attending physician. Patients who had obvious cognitive impairment resulting in an inability to understand or give clear answers to the questions in the questionnaire were excluded from the study.

As an observational questionnaire study, no intervention or treatment recommendation in addition to current daily practice was made to the patients. After obtaining informed consents, pa-

Table I. Demographic characteristics of the patients.

	Total	Treatment Groups		*p*-value
		BT	NBT	
Age, years	49.7 ± 12.7	49.4 ± 12.9	49.9 ± 12.5	0.573
Gender				
Male	75 (14.5)	44 (15.7)	31 (13.0)	0.386
Female	443 (85.5)	236 (84.3)	207 (87.0)	
Weight, kg	71.6 ± 14.7	72.1 ± 15.1	71.0 ± 14.3	0.389
Height, cm	161.9 ± 7.5	161.8 ± 8.0	161.9 ± 6.9	0.806
Education level				
Illiterate	66 (13.1)	34 (12.5)	32 (13.8)	0.594
Drop out from primary school	25 (5.0)	10 (3.7)	15 (6.5)	
Primary school	255 (50.7)	135 (49.8)	120 (51.7)	
High school	100 (19.9)	58 (21.4)	42 (18.1)	
University	48 (9.5)	29 (10.7)	19 (8.2)	
Postgraduate	(1.8)	5 (1.8)	4 (1.7)	
Living alone	21 (4.1)	12 (4.3)	9 (3.8)	0.772

Data are expressed as mean±standard deviation or number (%).

Table II. Disease-related characteristics of the RA patients.

	Total	Treatment Groups		*p*-value
		BT	NBT	
Age at the onset of symptoms, years	35.4 ± 14.1	32.8 ± 13.8	38.5 ± 13.9	**<0.001**
Age at diagnosis, years	40.1 ± 13.5	38.2 ± 13.1	42.2 ± 13.6	**0.003**
Time elapsed between the onset of symptoms and diagnosis, years	4.7 ± 8.2	5.4 ± 9.1	3.8 ± 6.9	**0.049**
Perceived health status				
Good/very good/excellent	330 (63.8)	208 (74.3)	122 (51.5)	**<0.001**
Poor/very poor	187 (36.2)	72 (25.7)	115 (48.5)	

Data are expressed as mean±standard deviation or number (%).

tients were asked to complete a study questionnaire that was administered by a single trained healthcare staff to all participants. The study questionnaire included questions about demographic characteristics, information about their disease, daily living parameters of RA patients, their current and previous treatments, their unmet needs and their attitudes towards new treatment options. The study conducted in compliance with EN ISO 14155, final version (2008) of the Declaration of Helsinki, Good Clinical Practice and the ethical regulations set by the Legal Regulations for the Clinical Studies in Turkey. Considering a confidence level of 95%, an accuracy of ± 4.5%, and an estimated RA prevalence of 0.36% in Turkey, we calculated that at least 472 patients would be needed. Allowing a 10% drop-out rate, we included 519 RA patients. Special attention was paid to achieve a ratio of 1:1 between patients in the BT and NBT groups. Additionally, as prespecified in study protocol, of patients in the BT group, 40% were selected from those who had been receiving intravenous treatment (infliximab) and 60% from those who have been receiving subcutaneous treatments (adalimumab and etanercept, 1:1 ratio). Data were analysed using the Statistical Package for the Social Sciences for Windows (version 15.0; SPSS Inc., Chicago, IL, USA). Descriptive statistics were given as frequency and cross tables for categorical variables; as mean ± standard deviation for numerical variables. A chi-square test was used to compare categorical variables between independent groups. The Monte Carlo simulation was used for comparison when chi-square assumptions were not met. The Mann Whitney-U test was used to compare numerical variables between groups when normal distribution assumptions were not met. A p-value <0.05 was considered as statistically significant.

Results

Clinical characteristics, diagnosis and follow-up

A total of 519 patients were interviewed. Of these, 281 (54.1%) were in the BT group and 238 (45.9%) were in the NBT group. The two groups were comparable with respect to demographic characteristics (Table I). The mean treatment periods were 26.3±19.8, 27.7±24.4, and 29.9±24.4 months for patients receiving adalimumab, etanercept and infliximab, respectively.

The mean age at the onset of symptoms was lower in the BT group (32.8±13.8 *vs*. 38.5±13.9 years p<0.001). Similarly, patients in the BT group were diagnosed with RA at a significantly younger age than the patients in the NBT group. However, time to diagnosis after the onset of symptoms was significantly shorter for the patients in the NBT group (Table II).

Among all of the patients, 35.5% initially had a visit to an internal disease specialist, 25.5% to a physical therapy and rehabilitation specialist, and 12.2% to a rheumatology specialist for their RA complaints. A majority of the patients (54.5%) were referred to the rheumatology specialist within 1 week after their initial presentation. The time elapsed until referral to the rheumatology specialist was >48 weeks in only 9.0% of the patients. Of the patients, 48.2% were diagnosed with RA by a rheumatology specialist.

The majority of the RA patients (86.3%) visited their doctor every <15 weeks. Most of the physician-patient communication centred on symptoms (99.0%), effects of the disease on quality of life (61.8%), effects of the disease on daily activities (51.1%), treatment (79.2%), current dose of medication (62.6%), route of administration of current treatment (52.4%), short-term side effects (55.5%) and blood tests and other analysis (86.5%).

Therapy choices

Non-prescription therapies that the RA patients have already used were as follows: physical therapy (20.0%), exercise (19.5%), rest (16.2%), complementary/alternative/herbal/homeopathic /OTC medication (14.8%), and

acupuncture 0.8%. Fifty-seven percent of the patients were not utilising any non-prescription therapy. Prescription medications that the patients have been currently using are shown in Table III.
The proportions of the patients who cannot perform the injection themselves were 60.8% for the patients receiving adalimumab and 38.7% for the patients receiving etanercept. The proportions of the patients reporting that it is difficult/very difficult to administer the drug injections were 14.3% for adalimumab and 8.2% for etanercept.

Patients' perceptions of their clinical status

The proportion of RA patients who perceived their health status as good/very good/excellent was higher in the BT group than the NBT group (51.5% *vs*. 74.3%, $p<0.001$). However, the survey revealed that the majority of the patients in both groups still suffer from some RA symptoms despite treatment. The majority of the patients (71.5%) had pain scores <4. The proportion of RA patients reporting a pain score <4 was significantly higher in the BT group than in the NBT group (64.3% *vs*. 77.6%, $p=0.001$). More than half of the patients still suffer from fatigue/malaise (67.6%), pain in hand and/or foot (74.0%), pain in other joints (52.8%), tender/swollen joints (61.7%), difficulty in walking (55.3%), and weakness (60.1%) on a regular basis despite treatment. Almost all RA symptoms were more common in the NBT group than the BT group (Table IV).
More than half of the patients reported that RA has affected quality of life-related conditions. The proportion of patients who reported that RA has affected their ability to get adequate sleep and rest was significantly higher in the BT group than in the NBT group (64.8% *vs*. 52.8%, $p=0.006$). There were no significant differences between the two groups with respect to the other parameters (Table V).

Patients' approach to their disease status

The majority of the patients believe that their current treatment prevents or slows down the progression of joint deformity, prevents or slows down the progression of the disease, provides short-term relief and that their current medication is the newest, most advanced treatment and it works consistently from dose to dose. Most patients are of the opinion that their current medication is a convenient treatment regimen. The proportions of patients who agreed with the above-mentioned parameters were higher in the BT group than the NBT group (Table VI).
The proportion of RA patients who believe that their current treatment pro-

Table III. Prescription medications that the RA patients are currently using.

	Total	Treatment Groups		*p*-value
		BT	NBT	
NSAID	311 (59.9)	166 (59.1)	145 (60.9)	0.668
Oral corticosteroids	347 (66.9)	168 (59.8)	179 (75.2)	**<0.001**
Methotrexate	346 (66.7)	182 (64.8)	164 (68.9)	0.319
Leflunomide	164 (31.6)	78 (27.8)	86 (36.1)	**0.041**
Adalimumab	97 (18.7)	97 (34.5)	-	-
Etanercept	101 (19.5)	101 (35.9)	-	-
Infliximab	82 (15.8)	82 (29.2)	-	-

Data are expressed as number (%).

Table IV. Symptoms on a regular basis in RA patients.

	Total	Treatment Groups		*p*-value
		BT	NBT	
Fatigue/tiredness	351 (67.6)	173 (61.6)	178 (74.8)	**0.001**
Pain in hand and/or foot	384 (74.0)	182 (64.8)	202 (84.9)	**<0.001**
Pain in other joints	274 (52.8)	128 (45.6)	146 (61.3)	**<0.001**
Decreased joint movement	197 (38.0)	93 (33.1)	104 (43.7)	**0.013**
Joint tenderness/swelling	320 (61.7)	148 (52.7)	172 (72.3)	**<0.001**
Early morning joint stiffness	241 (46.4)	106 (37.7)	135 (56.7)	**<0.001**
Fever	165 (31.8)	84 (29.9)	81 (34.0)	0.313
Difficulty walking	287 (55.3)	139 (49.5)	148 (62.2)	**0.004**
Difficulty with dexterity	232 (44.7)	104 (37.0)	128 (53.8)	**<0.001**
Difficulty sleeping	175 (33.7)	80 (28.5)	95 (39.9)	**0.006**
Limited ability to perform daily activities	204 (39.3)	95 (33.8)	109 (45.8)	**0.005**
Decreased ability to participate in leisure activities	77 (14.8)	40 (14.2)	37 (15.5)	0.675
General malaise	243 (46.8)	107 (38.1)	136 (57.1)	**<0.001**
Overall weakness	312 (60.1)	151 (53.7)	161 (67.6)	**0.001**

Data are expressed as number (%).

Table V. Quality of life-related conditions affected by the disease.

	Total	Treatment Groups		*p*-value
		BT	NBT	
Relationships with friends and family	203 (39.3)	110 (39.3)	93 (39.2)	0.992
Anxiety level	324 (62.5)	176 (62.6)	148 (62.4)	0.965
Level of anger	355 (68.5)	199 (70.8)	156 (65.8)	0.223
Level of discouragement	267 (51.7)	151 (53.9)	116 (49.2)	0.279
Depression level	278 (53.9)	149 (53.0)	129 (54.9)	0.672
Ability to do household chores	353 (72.0)	195 (73.0)	158 (70.9)	0.592
Ability to care for family members/ take care of family's needs	322 (66.1)	183 (68.8)	139 (62.9)	0.171
Ability to dress myself	266 (51.5)	146 (52.0)	120 (50.8)	0.801
Ability to participate in sports activities	141 (53.2)	83 (56.5)	58 (49.2)	0.236
Ability to pursue hobbies	187 (55.7)	114 (59.4)	73 (50.7)	0.113
Ability to get adequate rest/sleep	306 (59.3)	182 (64.8)	124 (52.8)	**0.006**
Ability to participate in sexual activity	200 (51.3)	115 (53.7)	85 (48.3)	0.285

Data are expressed as number (%).

Table VI. Opinions of RA patients about their current medication.

Agreement with the following statements	Total	Treatment Groups BT	Treatment Groups NBT	*p*-value
Prevents or slows down the progression of joint deformity	361 (70.0)	215 (77.1)	146 (61.6)	**<0.001**
Prevents or slows down the progression of the disease	385 (74.6)	227 (81.7)	158 (66.4)	**<0.001**
Provides short-term relief of symptoms	336 (65.0)	180 (64.5)	156 (65.5)	0.807
Provides long-lasting relief of my RA symptoms	231 (44.7)	149 (53.4)	82 (34.5)	**<0.001**
My current medication is the newest, most advanced treatment	300 (60.6)	200 (74.6)	100 (44.1)	**<0.001**
My medication works consistently from dose to dose	315 (61.5)	216 (76.9)	99 (42.9)	**<0.001**
My current medication is a convenient treatment regimen	335 (66.2)	230 (81.9)	105 (46.7)	**<0.001**

Data are expressed as number (%).

Table VII. Issues that treatment provides substantial benefit.

	Total	Treatment Groups BT	Treatment Groups NBT	*p*-value*
Less pain/swelling/stiffness	442 (85.2)	258 (91.8)	184 (77.3)	**<0.001**
Less fatigue	156 (30.1)	93 (33.1)	63 (26.5)	0.101
Lasts between doses/fewer or no breakthrough pain or flares	109 (21.0)	73 (26.0)	36 (15.1)	**0.002**

Data are expressed as number (%).

Table VIII. Number of good/bad days per month prior to/after being put on current treatment medication.

	Total	Treatment Groups BT	Treatment Groups NBT	*p*-value
Number of good days per month				
Before	6.7 ± 7.3	6.2 ± 7.3	7.3 ± 7.3	0.056
After	21.1 ± 7.2	23.4 ± 6.5	18.5 ± 7.2	<0.001
Number of bad days per month				
Before	23.3 ± 7.3	23.8 ± 7.3	22.7 ± 7.2	0.057
After	8.9 ± 7.2	6.6 ± 6.5	11.5 ± 7.2	<0.001

Data are expressed as mean±standard deviation.

vided substantial benefit in decreasing pain/swelling/stiffness was significantly higher in the BT group than in the NBT group (Table VII).

The majority of the patients reported that the switching from their previous therapy to their current therapy has affected their ability to do household chores (71.6%), to care for family members/take care of family needs (68.7%), to dress themselves (74.0%), and their ability to get adequate rest/sleep (61.4%), relationships with friends and family (58.0%), anxiety level (55.9%) and anger level (54.8%) in a positive manner.

The RA patients reported that the number of good days per month was increased while the number of bad days per month was decreased after being put on their current treatment medication. When compared to the NBT group, the BT group had significantly more good days and fewer bad days per month after being put on their current treatment medication (Table VIII).

Among the patients, 61.9% have never worked, and 24.0% were not currently working. Twenty patients reported RA as the main reason for not working. Patients reported a mean of 28.5±31.6 working days lost due to RA in the past 90 days and a mean percentage reduction in earned income of 39.4±25.0. In the BT group, 22.4% and 44.9% of the patients reported increased working days and increased productivity at work, respectively, after the initiation of biologic therapy.

Of biologic users, 72.9% reported that their current therapy was much more effective than their previous non-biologic regimen in alleviating/controlling the disease symptoms and 75.1% reported that their current therapy was much more effective than their previous non-biologic regimen in improving their overall quality of life.

Approach to biologics in NBT group

Among patients in the NBT group, only 24.8% have been recommended a biologic product by their doctors. Of those patients who were recommended a biologic, 51.0% were informed about what they could expect from the drug; 51.0% were informed about how the drug works, 82.4% were informed about how the drug is administered, 72.5% were informed about frequency of dosing, 56.9% were informed about its short-term side effects, 35.3% were informed about its safety over the long-term, and only 25.5% were informed about how to apply the injection.

Of the RA patients who were not recommended a biologic, 2.9% did not get a prescription for a biologic because of safety concerns and needle/infusion anxiety. On the other hand, 11.7% did not get a prescription for a biologic, because they feel good enough on their current treatment regimen; 40.4% did not get a prescription for a biologic because their doctor did not think it was the right choice for them; 2.9% did not get a prescription for a biologic because their symptoms were not severe enough to warrant something so potent, and 5.3% did not get a prescription for a biologic because they were happy with their current treatment regimen. Of biologic naive patients who were not recommended biologic treatment, 67.9% were not aware of biologics. When considering those patients who were aware of biologic treatment, 78.5% reported that their source of information was medical staff, while 7.9% reported that they had only heard the names of biologics without any relevant information about these agents, and only 3.9%

of these patients had learned that biologics were injectable products.

Approach to mode of administration

The majority of biologic naive patients reported that they would be willing to use a medication requiring a subcutaneous injection if their doctor recommended it (95.3%), if it had a less frequency of administration (78.2%), if it was easy to use personally (69.3%) and if it was able to be self injected at home (66.5%). Among dose frequencies, once-monthly injection was preferred more frequently (80%) compared to bi-weekly injection (8%). Among biologic users, a prefilled, single-use auto-injector device was preferred by 58.6% with easy-to-understand instructions (89%) and less injection-site reaction (55.3%).

Discussion

In the present study, we evaluated RA patients receiving (n=281) and not receiving (n=238) biologic therapy. We assessed, via a questionnaire, the unmet needs and perceptions regarding treatment of RA in these two groups, which were comparable with respect to demographic characteristics.

In recent years, querying patients' perspective has gained importance in assessing patient outcomes (14). It is known that RA has unfavourable effects on quality of life. In a cross-sectional non-interventional study, Inotai *et al*. (15) compared quality of life of RA patients receiving biological (n=85) and non-biological (n=168) therapies, and concluded that patients on biological treatment have lower disease activity and higher utility. In the present study also, more than half of the patients reported that RA had affected their quality of life-related conditions. However, the proportion of RA patients who perceived their health status as good/very or good/excellent was higher in the BT group than the NBT group. Of biologic users, 75.1% reported that their current therapy was much more effective than their previous non-biologic regimen in improving their overall quality of life.

The majority of the patients believe that their current therapy slows down the progression of the disease and provides relief of RA symptoms. When compared to the NBT group, the BT group had significantly more good days and fewer bad days per month after being put on their current treatment medication. However, the survey revealed that the majority of the patients still suffered from some RA symptoms despite treatment. Almost all RA symptoms were more common in the NBT group than the BT group. The proportion of patients reporting a pain score <4 was higher in the BT group.

Recent studies have evaluated disease activity-reducing effects of biologic therapy and compared biologic and non-biologic therapies or one biologic agent with another. The Dutch Rheumatoid Arthritis Monitoring (DREAM) registry found that after 6 months of treatment with anti-TNF agents, the prevalence of DAS-28 <2.6 was 27% and the prevalence of minimal disease activity (MDA) was 34%, while ACR/European League Against Rheumatism (EULAR) remission criteria was reached by only 6% of RA patients (16). Studies have reported satisfactory outcomes in terms of residual disease activity at 1 year in Switzerland, where the prescription of biologic agents is not limited and biologic therapy is initiated earlier in patients with low disease activity levels (17). However, similar results are also reported with conventional DMARD combinations in early RA, and 70 to 90% DAS28-remissions are observed at 12 months (5). Whether extensive use of biologics resulted in better outcomes in the real world setting is also controversial (18).

It is known that RA causes work productivity loss (19). In the present study, 61.9% of the surveyed patients had never worked and 24.0% were not working currently. Twenty patients reported RA as the main reason for not working. With regard to patients working, 22.4% reported increased working days and 44.9% reported increased productivity at work after the initiation of biologic therapy.

In the present study, RA patients reported their doctors (54.3%), television/radio (31.2%), the Internet (26.6%) and family/friends/neighbours (15.8%) as their sources of information about the disease. The majority of the patients (72.8%) reported that most of the time their doctors explained their disease in a way that they could understand. Similarly, Garneau *et al*. (20) reported that 98% of the participants used rheumatologists as a source for information and 87% rated the source as extremely useful. The Internet was the most frequently used non-provider source (63%) and 40% found it very useful in this study. However, the Internet as the source of information seems still very limited in Turkey. Besides, sometimes information from the Internet may be rather confusing, especially for the non-oriented patients.

Most of the surveyed patients in this study (86.3%) visited their doctors every <15 weeks. At these visits, physician-patient communication primarily focused on symptoms and treatment. Since it allows early switching or adjustment of therapies that fail to adequately control disease activity, regular monitoring of RA patients through tight control is recommended (21, 22).

Finally, a less frequent dosing (once-monthly) with an easy-to-use, pre-filled auto-injector is preferred by most RA patients for drug administration.

Our results are in accordance with the previously published RAISE study. Similar to our observations, patient-physician interaction is found to be limited about the impact of RA on QoL issues in this study. Although most RA patients believe that their current treatment provided substantial benefit for their symptoms and patients on BT are observed to have more "good" days, RA significantly limit the daily life of patients. Information about BT is also observed to be limited in patients using non-BT therapies in RAISE (13).

In conclusion, RA patients receiving biologic therapy reported higher rates of improved symptoms and quality of life-related conditions, and seemed more satisfied with their treatment in our study. It is important for rheumatologists to have sufficient knowledge about the indications and effects of biologic treatments since it will enable appropriate patient selection and early initiation of treatment. The results of this survey provided information for rheumatologists about the perceptions, expectations and preferences of RA patients with regard to RA treatment.

References

1. AKKOC N, AKAR S: Epidemiology of rheumatoid arthritis in Turkey. *Clin Rheumatol* 2006; 25: 560-1.
2. SCOTT DL: Biologics-based therapy for the treatment of rheumatoid arthritis. *Clin Pharmacol Ther* 2012; 91: 30-43.
3. COLMEGNA I, OHATA BR, MENARD HA: Current understanding of rheumatoid arthritis therapy. *Clin Pharmacol Ther* 2012; 91: 607-20.
4. PINCUS T, CALLAHAN LF, SALE WG: Severe functional declines, work disability, and increased mortality in studied over nine years seventy-five Rheumatoid Artritis Patients. *Arthritis and Rheum* 1984; 27: 864-72.
5. LEIRISALO-REPO M, KAUTIAINEN H, LAASONEN L: Infliximab for 6 months added on combination therapy in early rheumatoid arthritis: 2-year results from an investigator-initiated, randomised, double-blind, placebo-controlled study (the NEO-RACo Study). *Ann Rheum Dis* 2013; 72: 851-7.
6. HARRIS JA, BYKERK VP, HITCHON CA: Determining best practices in early rheumatoid arthritis by comparing differences in treatment at sites in the Canadian early arthritis cohort. *J Rheumatol* 2013; 40; 1823-30.
7. CURTIS JR, SINGH JA: Use of biologics in rheumatoid arthritis: current and emerging paradigms of care. *Clin Ther* 2011; 33: 679-707.
8. KEYSTONE EC, SMOLEN J, VAN RIEL P: Developing an effective treatment algorithm for rheumatoid arthritis. *Rheumatology* (Oxford) 2012; 51 (Suppl. 5): v48-v54.
9. TAK PP: A personalized medicine approach to biologic treatment of rheumatoid arthritis: a preliminary treatment algorithm. *Rheumatology* (Oxford) 2012; 51: 600-9.
10. DUDLER J, MÖLLER B, MICHEL BA, VILLIGER PM: Biologics in rheumatoid arthritis--recommendations for Swiss practice. *Swiss Med Wkly* 2011; 141: w13189.
11. AGARWAL SK: Biologic agents in rheumatoid arthritis: an update for managed care professionals. *J Manag Care Pharm* 2011; 179 (Suppl. B): S14-8.
12. CHIU Y, OSTOR AJ, HAMMOND A *et al*.: Access to the next wave of biologic therapies (Abatacept and Tocilizumab) for the treatment of rheumatoid arthritis in England and Wales : Addressing treatment outside the current NICE guidance. *Clin Rheumatol* 2012; 31: 1005-12.
13. MCINNES IB, COMBE B, BURMESTER G: Understanding the patient perspective – results of the Rheumatoid Arthritis: Insights, Strategies & Expectations (RAISE) patient needs survey *Clin Exp Rheumatol* 2013; 31: 350-7.
14. HER M, KAVANAUGH A: Patient-reported outcomes in rheumatoid arthritis. *Curr Opin Rheumatol* 2012; 24(3: 327-34.
15. INOTAI A, ROJKOVICH B, FÜLÖP A, JÁSZAY E, AGH T, MÉSZÁROS A: Health-related quality of life and utility in patients receiving biological and non-biological treatments in rheumatoid arthritis. *Rheumatol Int* 2012; 32: 963-9.
16. DE PUNDER YM, FRANSEN J, KIEVIT W *et al*.: The prevalence of clinical remission in RA patients treated with anti-TNF: results from the Dutch Rheumatoid Arthritis Monitoring (DREAM) registry. *Rheumatology* (Oxford) 2012; 51: 1610-7.
17. ZUFFEREY P, DUDLER J, SCHERER A, FINCKH A: Disease activity in rheumatoid arthritis patients at initiation of biologic agents and 1 year of treatment: Results from the Swiss SCQM registry. *Joint Bone Spine* 2013 Mar; 80: 160-4.
18. SOKKA T, HAUGEBERG G, ASIK AINEN J: Similar clinical outcomes in rheumatoid arthritis with more versus less expensive treatment strategies. Observational data from two rheumatology clinics. *Clin Exp Rheumatol* 2013; 31: 409-14.
19. FILIPOVIC I, WALKER D, FORSTER F, CURRY AS: Quantifying the economic burden of productivity loss in rheumatoid arthritis. *Rheumatology* (Oxford) 2011; 50: 1083-90.
20. GARNEAU K, IVERSEN M, JAN S, PARMAR K, TSAO P, SOLOMON DH: Rheumatoid arthritis decision making: many information sources but not all rated as useful. *J Clin Rheumatol* 2011; 17: 231-5.
21. MEASE PJ: Improving the routine management of rheumatoid arthritis: the value of tight control. *J Rheumatol* 2010; 37: 1570-8.
22. FRAENKEL L, PETERS E, CHARPENTIER P *et al*.: Decision tool to improve the quality of care in rheumatoid arthritis. *Arthritis Care Res* (Hoboken) 2012; 64: 977-85.