Original Article

Development of Anti-TNF-A Treatment Adherence Scale: Patients with Rheumatic Disease

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Abstract

Background: In recent years, there has been an increase in the use of anti-TNF-α therapies in the treatment of rheumatological diseases.
Aim: The aim of this study was to develop a subcutaneous anti-TNF-α treatment adherence scale and investigate and confirm the reliability and validity of this new instrument.
This methodological study was performed in an university hospitals between April 2018 and March 2019. The sample of the study (n:165) consisted of individuals who were completed the first month of SC anti TNF-α treatment. The research data were collected by using an individual introduction form and the newly developed *Anti TNF-α Treatment Adherence Scale*. In the analysis of the data, the test-retest reliability analysis, validity analysis, factor analysis, structural equation model and internal consistency analysis were used.
Results: The item-total test correlation values were determined to be between 0.33 and 0.71. In the fit index calculations, it was found that the Root Mean Square Error of Approximation was 0.10, Goodness of Fit Index was 0.999, Adjusted Goodness of Fit Index was 0.998, Comparative Fit Index was 0.926; and $\chi 2$ was 2.670 ($p<0.001$). Cronbach α coefficient was calculated as 0.690 for factor 1, 0.765 for factor 2, 0.628 for factor 3 and 0.671 for the overall scale.
Conclusion: In this study, Anti TNF-α Treatment Adherence Scale was determined that it is a valid and reliable scale. It is the first assessment tool that can be used in the evaluation of drug adherence in SC Anti-TNF-α treatment performed by patients / their relatives due to rheumatologic and all inflammatory diseases.

Keywords: Anti-TNF drug, reliability, rheumatological diseases, treatment adherence, validity

Introduction

Anti-TNF-α treatment in rheumatological diseases: Rheumatic diseases are progressive, autoimmune, and inflammatory diseases which often affect the musculoskeletal system (Kaya, 2012; WHO, 2018). Salicylates, non-steroidal anti-inflammatory drugs (NSAID), steroid medication, modifying drugs and biological agents are used in their treatment.

Biological agents are agents which are obtained from living organisms or products of these organisms via biotechnological methods and are used in the treatment of the disease aimed at the therapeutic goal when traditional treatments like NSAID and disease modifying medication remain incapable (Fajit & Wenzel, 2014; Furst & Louie, 2019; NASS, 2018; NICE, 2016). Anti-tumor necrosis factor-alpha (TNF-α), which is from the biological agent group, regresses the inflammatory process, signs and symptoms of the disease by suppressing the pro-inflammatory cytokines and TNF-α synthesis (Aydin &Akici, 2018; Bruner et al., 2014; Fajit & Wenzel, 2014; NASS, 2018). Drugs from this group have a different molecular structure attaining a substantial success in the management of chronic autoimmune diseases like rheumatoid arthritis, ankylosing spondylitis, and psoriatic arthritis (Aydin & Akici, 2018; NASS, 2018; Hamilton et al., 2017). Today adalimumab, etanercept, certolizumab pegol, golimumab, and infliximab are certified as anti-TNF agents (Bruner et al., 2014; Landewé et al., 2014; NICE, 2016) and out of these drugs, infliximab is administered intravenously (IV) and the others are administered subcutaneously (SC) (Elbey, 2015; Maxwell et al., 2015).

Conscious use of anti-TNF-α drugs is crucial for effectiveness of the therapy and prevention of complications. Besides positive impacts, these drugs may have undesirable consequences such as hypersensitivity, tuberculosis, congestive heart failure, malignancy condition, unresponsiveness to induction treatment, decreased response in maintenance and expensive continuation of treatment agents (Bruner et al., 2014; Hamilton et al., 2017; NICE, 2016) Patients need to be careful about infectious diseases, injection site reactions, hematologic, neurologic and autoimmune reactions and seek medical advice in case of these diseases (Bruner et al., 2014; NICE, 2016). They should discontinue the drugs without consulting the doctor when the disease regresses (Sayarlioglu, 2013). It should not be forgotten that in the subcutaneous treatment, patients face difficulties during the preparation of injection procedure and face difficulties due to reasons like drug cost and thus they skip the doses of their drugs and have a difficulty adherence to the therapy (Osborn & Gonzalez, 2016; Farsaei et al., 2014).

Anti-TNF-α drugs adherence: Drug adherence is a major determinant of the effectiveness of drugs against rheumatologic diseases. Nonadherence to treatment leads to failure in the management of rheumatic disease, negative health outcomes and increased costs. It is possible to assess drug adherence using direct or indirect methods. Direct methods measuring drug adherence comprise results obtained from laboratory findings and observations. However, sometimes there may not be a laboratory analysis to assess the Adherence specific to every drug and these analyses may not be practical or cost-effective. Direct observations are made during IV and SC injection of the drug when the patient receives treatment in the hospital or in the day treatment unit. This prevents assessing the adherence of drugs administered subcutaneously by the patient at home (Marengo & Suarez-Almazor, 2015).

The anti-TNF-α treatment used in the management of rheumatic diseases comprises drugs that are administered in parenteral route, require cost and alter the disease outcomes positively. The studies have revealed that both direct and indirect methods are used in assessing the adherence of patients to these drugs (Anghel, Farcas & Oprean, 2018; Marengo & Suarez-Almazor, 2015). Indirect methods are mostly preferred in the evaluation of adherence with the medication taken by the patient at home. The indirect method is given limited information about the prescription of the drug and the follow-up of the number of drugs used and remaining. In addition to, the drug adherence scales are aimed at oral drugs.

Nurses, who are in constant interaction with patients during the treatment process, have an important role in improving treatment adherence (Greenley et al., 2013). It is important that patients who administer subcutaneous anti-TNF- α drugs are informed by nurses about drug use, possible side effects, drug administration and storage conditions, and followed up at intervals. Since this drugs are effective with regular long-term

use in an appropriate way, monitoring the administration of drugs and identifying and treating developing side effects will positively affect drug adherence (ACR, 2022). Nurses use direct and indirect methods to assess patients' medication adherence. However, in the presence of signs of infection, etc. there are options such as skipping the treatment by informing the doctor or nurse, as well as evaluating the difficulties experienced by the patient due to subcutaneous administration. In addition to no self-report-based measurement tool directly developed for the SC anti-TNF-α drug adherence has been encountered.

Objective:The study was conducted to develop a measurement tool for doctors and nurses to assess patient Adherence in every phase of the SC anti-TNF-α treatment.

Hypothesis of the Study: H1:The scale developed to evaluate SC anti-TNF-α treatment adherence is valid. H2: The scale developed to evaluate SC anti-TNF-α treatment adherence is reliable.

Methods

Study Design and Sample: This methodological study was planned to develop a scale for assessing the adherence to SC anti-TNF-α treatment in individuals with rheumatic disease and to conduct a validity and reliability study of this scale. The study was carried out with 165 patients followed and treated in the rheumatology outpatient clinic in a hospital between April 2018 and March 2019. The population of the study comprised patients who received and administered themselves the SC anti-TNF-α treatment due to rheumatic disease. The inclusion criteria of the study were being over 18 years, having completed the first month of the SC anti-TNF-α treatment, agreeing to participate in the study, and having no obstacle to communication. The patients applying the first dose of the SC anti-TNF-α treatment were not included in the study.

Determining the sample size: In scale development studies it is recommended that the sample size be 5-10 times greater than the item number in order to test the total item correlation (Sonmez & Alcapınar, 2016; Tezbasaran, 2008). Within the scope of the study, the sample size was calculated to be at least 28x5=140 for the trial scale comprising 28 items. However, the study was completed with 165 patients who met the inclusion criteria during the time of the study and could be reached.

Data Collection Tools: Data were collected using a individual information form and the adherence to Anti-TNF-α Treatment Scale. Individual information form was prepared by the researchers to seek an answer to questions related to socio-demographic characteristics of patients such as age, sex, education and income status, as well as disease and treatment.

The Adherence to Anti-TNF-α Treatment Scale Development Process

Preparation of scale items: Researcher conducted in-depth interviews patients (n=10) about SC anti TNF treatment in 45-60 minutes in a room in the rheumatology outpatient clinic. The information obtained from the in-depth interviews was recorded in the semi-structured interview form. These patients (n=10) were not included in the sample. In the in-depth interviews, four semi-structured questions were prepared about Anti-TNF-α knowledge, storage conditions, SC administration, difficulties faced when administering the drug and side effects. These questions were asked to the patient by the researcher. According to the theoretical basis of the research and the data obtained from the semi-structured forms, an item pool containing 30 questions was created.

For content validity, the adherence of each statement in the question pool was asessed by 9 experts (the experts had to possess at least 10 years' experience in management of rheumatic diseases) from 1 (not convenient) to 4 (very convenient) points and they were asked to write down their recommendations for each item. After receiving the expert opinion, the number of items in the question pool was decreased to 28. It was determined that content validity index of the 28-item draft scale at the item level was high and it reflected subjects related to the SC Anti-TNF-α Treatment (Kendall's W=0.154; p=0.086) (Table 1). The scale items were tested by being applied to 5 patients who had the same characteristics as the sample group in terms of comprehensibility and were not included in the study. In the study, the item-total test correlation values of the patients' answers to the scale questions were examined and 17

items were excluded from the scale because their item correlation values remained under 0.20. Other remaining items were determined to be correlated. The final 5-point likert scale with 11 items which was created after the exploratory factor analysis, validity and reliability analyses is divided into 3 subscales as "Preparation", "Application" and "Post-application follow-up". Positive items in the scale (item 1 to 6) are scored as: "Always" 5 points; "Usually" 4 points; "Sometimes" 3 points; "Seldom" 2 points; and "Never" 1 point. Items containing a negative statement (item 7 to 11) are calculated reversely. The highest score calculated in the scale is 35 and higher scores signify that medication adherence increases.

Application of Data Collection Forms: In the study, the individual information form and the Adherence to Anti-TNF-α Treatment Scale forms were applied in a
quiet room in the rheumatology outpatient clinic by conducting face-to-face interview with the patient in approximately 10-15 minutes. Six weeks after the first application of the questionnaires, the Anti-TNF-α treatment Adherence scale was administered to the same patients for the second time, and the post-test was completed.

Data Analysis: In evaluation of the data, descriptive statistical methods (number, percentage, mean, standard deviation) were used. The test-retest reliability analyses of the items of the scale were performed using the Wilcoxon test and reliability of the scale items was analyzed using the "Reliability Analysis". The total score correlation analysis and 27% upper-lower distinctiveness of the items were also checked. The item total score analysis was examined via the Pearson Product-moment Correlation analysis. The factor structure was tested via the "Exploratory Factor Analysis (EFA)" and the construct validity was tested via the "Confirmatory Factor Analysis (CFA)". For reliability, the internal consistency of the scale was examined via the Cronbach's alpha coefficient.

Ethics approval and written informed consents statements: Prior to starting the study, written permission dated 27.02.2018 and numbered 41 was obtained from the institution where the study was conducted and from the relevant ethics committee. In study, adhering to the Helsinki Declaration, written informed consent was obtained from all patients who wanted to participate in the study.

Results

Distribution of the Socio-demographic and Medical Characteristics of the Patients: It was determined that mean age of the participants was 43.50±13.38 years. Of the patients, 55.8% were male, 80.6% were married and 33.3% were high school graduate. A great majority of the patients suffered from ankylosing spondylitis (60.6%), 66.7% received antirheumatic therapy, and 34.5% administered adalimumab. 47.3% of the patients administered SC . Anti-TNF drugs every two weeks (Table 2).

Validity Analyses of the Scale: Prior to the exploratory factor analysis which was conducted to reveal the factor pattern of the scale aiming to measure the adherence of patients to the SC Anti-TNF-α treatment, the KMO value was found to be 0.595 in the Kaiser-Meyer-Olkin (KMO) test which was conducted to test the convenience of the sample size for factorization. In the Bartlett's Test for Sphericity, it was determined that the chi-square value was statistically significant ($\chi 2(55) = 531.538$; $p<0.01$) (Table 3).
When examining the factor structure of the scale, it was determined that there were three components with an eigenvalue above 1 for 11 items.

The contribution made by these components to the total variance was 50.101%. In the analysis repeated for three factors, the contribution made by the factors to the total variance was determined to be 24.886% for "Post-application Follow-up" the first factor; 17.600% for "Application" the second factor; and 15.615% for "Preparation" the third factor (Table 3).

In the exploratory factor analysis which was carried out to reveal the factor pattern of the scale aiming to measure the adherence to SC Anti-TNF-α t treatment, the acceptance level for factor load values was found to be 0.400. When examining the diagram demonstrating factor number in the horizontal axis and eigenvalues in the vertical axis, it was determined that the high-acceleration downfall decreased after the fourth point. It

was determined that the contribution made by each factor forming after the fourth point to the variance decreased and the contributions of the variances to be added were very close to each other.

Three factors were specified in line with the eigenvalues and variance percentages, data acquired from the diagram and the exploratory factor analysis (Figure 1). Figure 2 shows the first-level multi-factor confirmatory factor analysis results of the Adherence to SC Anti-TNF-α Treatment Scale. Accordingly, it was determined that the lowest factor load value of the 11-item scale was 0.46 and the highest factor load value was 0.99 (Figure 2).

In the study, as a result of the structural equation model it was determined that the scale was significant at the level of $p<0.001$ and 11 items and three subscales comprising the scale were associated with the scale structure.

In the fit index calculations, it was found that the Root Mean Square Error of Approximation (RMSEA) was 0.10, Goodness of Fit Index (GFI) was 0.999, Adjusted Goodness of Fit Index (AGFI) was 0.998, Comparative Fit Index (CFI) was 0.926; and $\chi 2$ was 2.670 ($p<0.001$) (Table 4).

In the internal consistency analysis of the scale, the Cronbach's α coefficient was calculated to be 0.690 for factor 1, 0.765 for factor 2, 0.628 for factor 3 and 0.671 for the overall scale (Table 3).

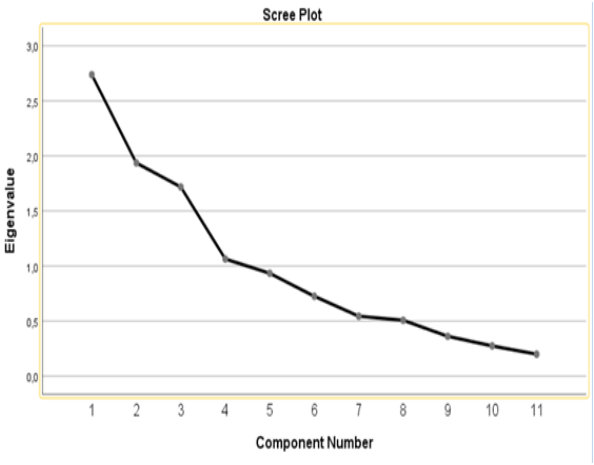

Figure 1. Factor analysis graph of eigenvalues and factor number of Anti-TNF-α Treatment Adherence Scale

Table 1. Distribution of expert opinion scores and content validity rates of the Anti TNF-α Treatment Adherence Scale

Items of scale	1 not convenient	2 The item needs to be brought into proper shape	3 Convenient but needs minor modifications	4 very convenient
Item 1	0	1	0	8
Item 2	0	0	0	9
Item 3	0	0	0	9
Item 4	0	0	1	8
Item 5	0	0	0	9
Item 6	0	0	0	9
Item 7	0	0	0	9
Item 8	0	0	0	9
Item 9	0	0	0	9
Item 10	0	0	0	9
Item 11	0	0	0	9
Item 12	0	0	1	8
Item 13	0	0	0	9
Item 14	0	0	0	9
Item 15	0	0	0	9
Item 16	0	0	1	8
Item 17	1	0	1	7

Item 18	1	0	1	7
Item 19	1	0	1	7
Item 20	0	1	0	8
Item 21	0	0	0	9
Item 22	0	0	0	9
Item 23	0	0	0	9
Item 24	0	0	0	9
Item 25	0	0	0	9
Item 26	0	0	0	9
Item 27	0	0	0	9
Item 28	0	0	0	9
	Kendall's W = 0.154	p=0.086		

Table 2. Distribution of patients' socio-demographic and medical characteristics

Characteristic		**n**	**%**
Sex	Male	92	55.8
	Female	73	44.2
Age (years)	$\bar{X} \pm SD$	43,50±13,38	
Marital Status	Married	133	80.6
	Single	32	19.4
Educational Status	Literate	6	3.6
	Primary school	36	21.8
	Middle School	17	10.3
	High school	55	33.3
	University	51	30.9
Social Security	SGK	158	95.8
	Private health insurance	4	2.4
	Green card	2	1.2
	No social security	1	0.6
Working status	Yes	90	54.5
	No	75	45.5
Diagnosis	Ankylosing spondylitis	100	60.6
	Rheumatoid arthritis	56	33.9
	Psoriatic arthritis	9	5.5
Disease Duration(years))	$\bar{X} \pm SD$	45.00±13.76	
Treatment- NSAİİ	Yes	112	67.9
	No	53	32.1
Treatment - Antirheumatic	Yes	110	66.7
	No	55	33.3
Treatment- Steroid	Yes	48	29.1
	No	117	70.9
Chronic Diseases[a]	Yes	52	31.5

	No	113	68.5
Number of Drugs Used Daily (piece)	$\bar{X} \pm SD$	1.68±2.27	
Anti TNF-α Treatment	Adalimumab	57	34.5
	Etanercept	39	23.6
	Golimumab	43	26.1
	Certolizumab pegol	26	15.8
Frequency of Use	Once a week	35	21.2
	Twice a week	2	1.2
	Every 10 days	3	1.8
	Biweekly	78	47.3
	Every three weeks	2	1.2
	Once in a month	45	27.3
Total		165	100.0

Table 3. Explanatory factor analysis and reliability results of the Anti-TNF-α Treatment Adherence Scale

Factors and items	Explained Variance (%)	Eigen Value (Λ)	Factor Load
F1: Post-application follow-up (α=0.690)			
18.After applying the drug, there is swelling and a lump at the injection site.	24.88	2.738	0.825
19. Bleeding occurs at the injection site after applying the drug.			
17. There is pain at the injection site after the drug is administered.			
25. There are times when I don't take the drug when I feel good.			
26. There are times when I don't take the drug when I feel bad.			
F2:Application (α=0.765)			
13. I give all the drug in the auto-injector/injector under the skin	17.60	1.936	0.880
12. I apply the auto injector/needle at the appropriate angle			
11. I use the automatic injector/injector comfortably			
F3: Preparation (α=0.628)			
7. Before I take my drug, I keep it at room temperature for 15-30 minutes.	15.615	1.718	0.891

6. Before I take my drug, I check the drug in the syringe for particles and discoloration. 5. I always wash my hands before taking my drug. **Total(α=0.671)**	
KMO =0.595; χ2(55) =531.538; Bartlett Test of Sphericity (p) = 0.000	

Table 4. Results of multi-factor confirmatory factor Adherence indices related to the Anti-TNF-α Treatment Adherence Scale

RMSEA	NFI	CFI	IFI	GFI	TLI	AGFI	CMIN	CMIN/df
0,10	0,888	0,926	0,927	0,999	0,900	0,998	109,475	2,670

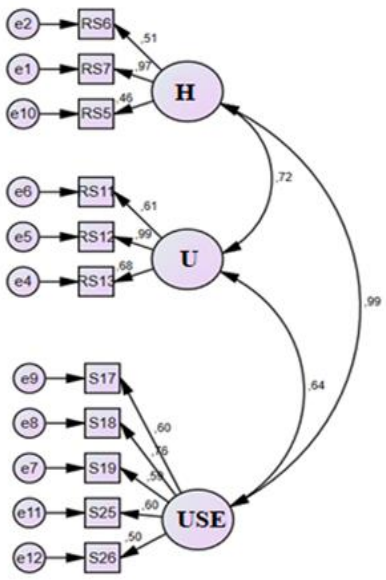

Figure 2. Model of Anti-TNF-α Treatment Adherence Scale First Level Multifactor Confirmatory Factor Analysis

Discussion

New developments in science and technology contribute to the emergence of new methods in the management of rheumatic diseases every passing day. This necessitates bringing forward new concepts in disease, treatment and care management and developing appropriate measurement tools to assess these concepts. As in the past, today the approach followed in measuring the attitudes usually contains preparing and implementing a scale for the relevant attitude (Tezbasaran, 2008). In the study, detailed information was obtained concerning what attitudes to measure in the SC anti-TNF-α treatment as a result of experiences, observations and literature review regarding the SC anti-TNF-α treatment in line with the study's theory and validity and reliability studies were conducted for the scale developed (Bozkirli & Yucel, 2012; Elbey, 2015; Maxwell et al., 2015; Osborn & Gonzalez, 2016; Sayarlioglu, 2013; Tezel, 2010).

Two basic properties (validity and reliability) are sought in a measurement tool. While validity is the ability of the measurement tool to properly and accurately measure the property to be measured, reliability is the ability of the measurement tool to always measure the property measured exactly the same and consistently (Erefe, 2004; Tezbasaran, 2008). In order to reveal "what" the measurement tool measures and "how accurately" it measures it, different validity methods (content validity, criterion-referenced validity, construct validity) should be used (Esin, 2014). Content validity which is among these validity methods is used for assessing whether the overall scale and each

item in the scale measure every concept to be measured and whether they contain different concepts outside the concept to be measured or not (Erefe, 2004; Esin, 2014; Tezbasaran, 2008).

In order to do this, language, cultural equivalence and content validity of items are assessed using the Content Validity Index (CVI), Lawshe and Davis techniques (Erefe, 2004; Esin, 2014). In the present study, the fit between the Kendall's W test and measurement values of the data was examined and as the value in the W test approached 1, the fit between the experts was interpreted to be high (Aksoy, Mert & Cetin, 2020). According to these results, the experts in the present study had a consensus on the scale items.

In order to assess the construct validity of the scale, the factor analysis was used for confirming the correlations between the factors. In the factor analysis, factor loads of items in the scale are assessed. Prior to using the exploratory factor analysis, it is necessary to test the convenience of the sample size for factorization and thus provide two conditions; the Kaiser-Meyer-Olkin (KMO) test and the Bartlett's Test for Sphericity(Buyukozturk, 2007; Esin, 2014). The KMO test was used for the first condition and the KMO value was found to be 0.595. The KMO test is a type of test used for measuring the adequacy of the sample size. As the value obtained at the end of this test approaches 1, the adequacy of the sample size increases and as it diverges from 1, the adequacy decreases. While some thinkers believe that the KMO value for the sample size should be at least 0.60, some believe that this value should be 0.80 and even 0.90 (Sonmez &Alcapınar, 2016; Cokluk, Sekercioglu & Buyukozturk, 2012). Esin (2014) suggests that a KMO value below 0.50 indicates that the sample size is not adequate for validity analyses. In line with the literature knowledge (Esin, 2014; Buyukozturk, 2007), the sample size was on margin to conduct a factor analysis and fact that the chi-square value determined in the Bartlett's Test for Sphericity was statistically significant made us think that the data had a multivariate normal distribution.

In the study, it was determined that the three components in the factor analysis accounted for 50% of the total variance. According to this result, it can be asserted that the scale has a good level of fit. In the confirmatory factor analysis, it is recommended that the factor item loads be above 30% (Esin, 2014; Buyukozturk, 2002). Cakir (2014) stated that high load values of items in factors indicate that they measure a construct-concept-factor together and factor load values of 0.40 or above are a good criterion for choice. In this study, the lowest factor load value related to the 11 items was 0.46 and the highest value was 0.99. According to the literature (Buyukozturk, 2002; Cakir 2014; Eksi Uymaz &Nahcivan, 2013), it can be asserted that the scale has a construct validity.

In the studies, it is recommended to calculate fit index values in the confirmatory factor analysis in order to prove the construct validity of the scale and it is stated that the GFI, AGFI, NFI and CFI indices of > 0.90 and the RMSEA value of <0.05 indicate a good fit (Capik, 2014). The RMSEA value between 0.05 and 0.08 indicates an adequate fit and the value between 0.08 and 1 indicates an acceptable fit. The RMSEA value above 1 indicates an unacceptable fit (Schermelleh-Engel, Moosbrugger & And Muller, 2003). In the present study, according to the first-level multi-factor analysis results, it can be asserted that the goodness of fit index values concerning the Adherence to SC Anti-TNF-α Treatment Scale were at an acceptable level.

The Cronbach's α coefficient is used in testing the internal consistency of the scale (Erefe, 2004). In the present study, the Cronbach's α value was found to be 0.690 for factor 1, 0.765 for factor 2, 0.628 for factor 3 and 0.671 for the overall scale (11 items). There are different classifications for the interpretation of the Cronbach's alpha coefficient in the literature. In the assessment criterion of the Cronbach α coefficient; if $0.00 \leq \alpha < 0.40$, "the scale is not reliable", if $0.40 \leq \alpha < 0.60$, "the scale has a low reliability", if $0.60 \leq \alpha < 0.80$, "the scale is very reliable" and if $0.80 \leq \alpha < 1.00$, "the scale is highly reliable" (Alpar, 2010). In another classification, if $0.90 \leq \alpha$, "it is excellent", if $0.70 \leq \alpha < 0.90$, "it is good", if $0.60 \leq \alpha < 0.70$, "it is acceptable", if $0.50 \leq \alpha < 0.60$, "it is low", if $0\ \alpha < 0.50$, "it is unacceptable" (Kılıc, 2016). In the scale development study, Polat and Avdal found that the internal consistency

of the sub-dimensions was 0.56-0.80, overall Cronbach alpha value of the scale was 0.654 and was a reliable scale (Polat & Avdal, 2020). Accordingly, it can be asserted that the scale developed within the scope of the study is reliable.

The low number and/or absence of nurses working in rheumatology outpatient clinics in our country and the doctors' inability to spare enough time for patient education due to workload prevent patients from receiving routine training on SC anti-TNF drugs. After determining the treatment adherence level of the patients with this scale we developed, in order to increase the adherence of the patients, nurses can intermittent evaluation and provide counseling to patients with low adherence to treatment about route of administration, storage conditions, side effects.

Limitations: This is the first scale development study to evaluate treatment adherence in patients using SC anti-TNF-α treatment for rheumatological disease. This situation limited the discussion part of the research. In addition, the fact that 165 patients were reached at the time of data collection is another limitation of this study.

Conclusion: This scale, whose structural validity and reliability has been ensured, can be used by the rheumatology team in the evaluation of SC anti-TNF-α treatment adherence. It is recommended to conduct relevant studies with larger sample size and use anti-Tnf-α Treatment Adherence Scale in all inflammatory diseases using SC anti-TNF-α.

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