Reliability and Validity Study of the Turkish Version of the Clinical Opiate Withdrawal Scale

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ABSTRACT

Introduction: The aim of the present study was to perform reliability and validity analyses of the Turkish version of the Clinical Opiate Withdrawal Scale which is used to determine the severity of opiate withdrawal.

Methods: Initially, the Clinical Opiate Withdrawal Scale (COWS) was translated into Turkish and subsequently back-translated into English. The originality of the back-translated version was approved by the author who developed the scale. After the translation was completed, the scale was used to assess the withdrawal symptoms of 100 patients with opiate withdrawal and 41 patients with alcohol withdrawal. Cronbach's alpha was used in the reliability assessment; explanatory and confirmatory factor analyses were used in structural validity assessment; and in scale validity, ROC analysis was used among diagnosis groups.

Results: The Cronbach's alpha internal consistency coefficient was calculated as 0.74 in reliability analyses. The correlation coefficient was found to be 0.975 ($p < 0.001$) for inter-rater reliability. Factor analysis was conducted for the structural validity of the scale and findings that support the unidimensional structure of the scale were observed. In the confirmatory factor analysis, CFI, GFI and RMSEA values were found to be 0.905, 0.905 and 0.079, respectively. It was detected that COWS was successful in distinguishing between opiate and alcohol withdrawal symptoms and the area under the ROC curve was 0.878.

Conclusion: This study showed that the Turkish version of COWS can be used reliably and validly for assessing opiate withdrawal.

Keywords: Clinical Opiate Withdrawal Scale, COWS, opiate withdrawal, reliability, validity

INTRODUCTION

Patients with substance dependence experience symptoms of withdrawal during detoxification. The severity of these symptoms varies depending on the severity of the dependence and the substance used. Opiate withdrawal symptoms appear within a few hours to a few days after discontinuation or reduction of heavy and/or prolonged opiate use.

Opiate withdrawal symptoms comprise of observable behavioral changes (e.g. yawning, restlessness), physiological changes (pulse rate, blood pressure, pupil diameter, and body temperature changes, etc.), and subjective experiences reported by the patient (1). Numerous clinicians ascribe greater importance to observable behavioral changes, particularly physiological findings, than to subjective experiences reported by the patient in the assessment of withdrawal symptoms (1). According to DSM IV-TR, the diagnostic criteria of opiate withdrawal are met if the patient has at least three symptoms such as dysphoric mood, nausea and/or vomiting, muscle aches, lacrimation and/or rhinorrhea, pupillary dilatation, piloerection or sweating, diarrhea, yawning, fever, or insomnia after discontinuation of opiate use for a number of weeks or more or after administration of an opiate antagonist drug following opiate use (2). Opiate withdrawal syndrome is accepted as a stereotypical medical condition because the signs and symptoms are considerably similar in all users (3). A series of scales have been developed since the 1930s to assess opiate withdrawal and its severity, such as Opiate Withdrawal Scale (OWS) (4), Subjective Opiate Withdrawal Scale (SOWS) (5), Objective Opiate Withdrawal Scale (OOWS) (5), Clinical Institute Narcotic Assessment (CINA) (6), Short Opiate Withdrawal Scale (SOWS) (7), Subjective Opiate Withdrawal Questionnaire (SOWQ) (8), and Clinical Opiate Withdrawal Scale (COWS) (1). Among these scales, COWS was developed to eliminate previous deficiencies in the older scales and was first published in the buprenorphine training guidelines (1). COWS ensures that all withdrawal signs are evaluated within approximately 2 min while interviewing the patients (1). Its use has become widespread because of its quick assessment and sensitivity to the changes that appear during withdrawal treatment (3). Currently, there is no scale in the Turkish language that can assess the opiate withdrawal syndrome quantitatively. However, quantitative measurement of opiate withdrawal is very important in the medical treatment of opiate dependence, such as buprenorphine-naloxone substitution treatment which is available in Turkey, to

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Received: 14.3.2013 **Accepted:** 14.8.2013

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determine the initial time of administration and the appropriate dosage of the medication. Administering this group of medications to patients who are still under the influence of an opiate and thus do not have withdrawal symptoms can cause severe precipitated withdrawal symptoms (9).

This study aims to assess the reliability and validity of the Turkish version of COWS and thereby to provide clinicians an assessment tool for easily scoring the severity of opiate withdrawal.

METHODS

Translation Procedure

After receiving permission from the developers of the scale to translate it into Turkish and to conduct a validity and reliability study, three psychiatrists translated it into Turkish independently from each other. After these translations were checked and agreed upon, the final translation was presented to the patients with opiate dependence to determine whether the scale represented their withdrawal experiences and whether the language was clear. The script was subsequently back translated to English by one linguist and one psychiatrist and sent to the developer of the scale who confirmed its accuracy.

Participants and Procedure

This study is a multi-centered reliability and validity study. The study was conducted in the Addiction Treatment Unit of the Department of Psychiatry at Ege University Faculty of Medicine and the Alcohol and Drug Research, Treatment and Training Centers (AMATEM) at both Bakırköy Prof. Dr. Mazhar Osman Training and Research Hospital for Psychiatry, Neurology and Neurosurgery and at Manisa Mental Hospital. The study included patients who had applied to the aforementioned addiction treatment centers because of opiate or alcohol dependence to receive treatment and who experienced withdrawal symptoms while hospitalized. The patients with alcohol dependence neither had a history of nor current opiate dependence.

Considering the fact that each addictive substance causes specific intoxication and withdrawal symptoms, no healthy control group was used for comparison. Thus, patients with alcohol withdrawal were used as the control group to reveal that COWS may differentiate opiate withdrawal from other withdrawal syndromes. Inclusion and exclusion criteria for the alcohol withdrawal control group were the same as those for the opiate withdrawal group.

The patients were interviewed by a clinician specializing in substance dependence to assess whether they fulfilled the diagnostic criteria for alcohol or opiate dependence according to the DSM IV-TR (10). The patients whose diagnoses were confirmed and who met the inclusion criteria were subsequently informed and written informed consent was obtained. The inclusion criteria for this study were an age range of 18–65 years and a history of being diagnosed with opiate dependence or alcohol dependence. The exclusion criteria were below 18 and above 65 years of age, inadequate mental capacity to fulfill research instructions, use of multiple substances, and presence of physical or neurological disorders that required ongoing treatment.

Socio-demographic information as well as the time of their latest substance use was recorded for patients who were hospitalized and participated in the study. The onset of alcohol or opiate withdrawal symptoms differs among patients and also requires medical treatment. Thus, waiting for a predetermined time and administering the scale would have posed ethical problems. Therefore, objective and subjective symptoms of the

on how to use COWS, when the patients started to describe withdrawal symptoms according to DSM-IV-TR criteria. The clinicians completed the scoring independently from each other and remained blind to each other.

Ethical consent was given to the reliability and validity study of the Turkish version of COWS by the Ege University Faculty of Medicine Clinical Trials Ethical Board.

COWS is a scale developed by Wesson & Ling (1999) in which the clinician assesses and scores all objective (pulse rate, sweating, pupil diameters, runny nose or tearing, goose-flesh skin) and subjective (restlessness, bone/joint ache, gastrointestinal upset, tremor, yawning, anxiety/irritability) symptoms which appear during opiate withdrawal. COWS assesses all symptoms which appear in opiate withdrawal and allows for a total score at the end of the scale, indicating the severity of an individual's opiate withdrawal and enabling clinicians to monitor treatment effectiveness. For example, mild abdominal pain reported by the patient is scored as a subjective symptom, whereas severe vomiting and diarrhea are scored as objective symptoms which the clinician can observe directly.

The items in the scale are weighted differentially based on the clinical experience of the developers; symptoms which progress more rapidly during withdrawal are weighted more heavily. The developers of the scale preferred to use a scoring system which can make more contribution to the total score instead of a sequential scoring system. COWS contain 11 items, one of which is subjective, six of which are objective, and four of which are both subjective and objective symptoms. COWS provide categorical assessment in pupil size and pulse with a zero point option. The total score ranges between 0 and 47, with higher scores indicating a more severe withdrawal state. Total COWS scores between 5 and 12 are regarded as mild, 13 and 24 as moderate, 25 and 36 as moderate-severe, and scores >36 are regarded as severe withdrawal symptoms. The scores of these categories are because of the author's clinical experience and were not determined by using standard statistical methods (1).

Statistical Analysis

In the statistical assessment, initially, analysis of the variance test (ANOVA) was applied to quantitative variables, and the chi-square test was applied to categorical variables in terms of socio-demographic and clinical properties among research groups. In the reliability analyses, a Cronbach's alpha internal consistency analysis was conducted for the scale. In addition, item-total score correlation coefficients were used to investigate the reliability of the scale. To control for inter-rater reliability, the correlation coefficients of the scores given by the two examiners who had passed through similar training procedures were used. In the reliability analysis, the test re-test method was not chosen because opiate withdrawal is a rapidly changing clinical manifestation. The split-half method, which is another reliability analysis, was not chosen either. However, a split half consistency is not expected because the scale does not have homogenous items.

Explanatory and confirmatory factor analyses were used in the construct validity of the scale. An explanatory factor analysis was conducted by applying a varimax rotation according to the principal components method, and factors whose eigenvalues were ≥ 1 were included in the assessment. Items with factor loads equal to ≥ 0.4 in their factor structures were evaluated. Explanatory factor structure was compared with the original one-dimensional structure of the scale. In the confirmatory factor structure, when evaluating the scale's compatibility with the one-dimensional model and stability model of the data, different types of "goodness-of-fit" indices were used with the maximum probability method. These included the following: root mean square error of approximation (RMSEA), goodness-

of-fit index (GFI), and comparative fit index (CFI). RMSEA is an absolute index of fit. RMSEA values <0.05 indicate a good fit with the data, values between 0.05 and 0.08 reflect an acceptable fit, values between 0.08 and 0.10 represent a low fit, and values >0.10 indicate an unacceptable fit. The CFI and GFI values may change between 0 and 1 and should be >0.90. Another characteristic of CFI is that it is least affected by problems in sample size and distribution. A receiver operating characteristic (ROC) analysis was performed between the opiate and alcohol withdrawal groups to detect scale validity of COWS. Moreover, the COWS total score was compared among two research groups with a t-test.

RESULTS

The research was completed with 141 participants, 100 of them diagnosed with opiate withdrawal and 41 of them diagnosed with alcohol withdrawal. Fifty-five opiate and 20 alcohol-dependent patients were recruited from Bakırköy AMATEM, 30 opiate and 15 alcohol-dependent patients from Manisa AMATEM, and 15 opiate and 6 alcohol-dependent patients from Ege University.

Socio-Demographic Characteristics

Socio-demographic and clinical characteristics of the participants are given in Table 1. The opiate withdrawal group is younger than the alcohol withdrawal group ($t=-7.80$, $p<0.001$), and there are statistically significant differences ($\chi^2=10.35$, $p<0.001$) between the two groups for being on probation (Table 1).

Reliability Analyses

For the internal consistency of COWS, the Cronbach's alpha coefficient was calculated to be 0.74. The item-total score correlation coefficients, except for the first item concerning pulse, were found to be between 0.34 and 0.75 (Table 2), while all were statistically significant ($p<0.001$). The item-total score coefficient of the first item was calculated as 0.11.

When the problem regarding the item about resting pulse rate was inspected in more detail, it was found to be a problem regarding distribution within the data collected from the alcohol withdrawal group. Therefore, an internal validity test was conducted using only the opiate withdrawal group, considering that the intended population of the scale was individuals undergoing opiate withdrawal. In the internal consistency analysis of the opiate withdrawal group, Cronbach's alpha was found to be 0.74 (Table 3).

The correlation coefficient regarding the inter-rater reliability of the COWS applications was found to be 0.97 ($p<0.001$). The results of the internal consistency analyses of each item are given in Table 4.

Validity Analyses

For the construct validity of COWS, explanatory factor analysis was conducted, and the coefficient in the Kaiser–Meier–Olkin test to investigate fit of data was found to be 0.83, and the chi-square value was calculated to be 441.83 ($p<0.001$) in the Bartlett Test. After sample adequacy was established, two factors with an eigenvalue >1 were found in the explanatory factor analysis, which explains 48.48% of the variance (Table 2). All items in the scale were represented in the structure of the factors and all items in the factors were on the positive side. The eigenvalue of the first factor was calculated to be 4.04, explaining 36.74% of the total variance. Factor loads of all items excluding the first one on the scale were detected to be >0.4, indicating the unidimensional structure of the scale. In the second factor of the scale, there is only one item regarding pulse rate. The eigenvalue of the second factor is 1.29 and has 11.74% of the variance.

Table 1. The socio-demographic and clinical characteristics of the participants

	Opioid withdrawal group n=100		Alcohol withdrawal group n=41	
Age ^a	29.4±9.0		44.8±11.2	
Gender				
Male	93	93.0%	41	100.0%
Female	7	7.0%		
Education				
Primary	71	71.0%	27	65.2%
Secondary	20	20.0%	10	24.4%
University	9	9.0%	4	9.8%
Employment status				
Employed	42	42.0%	20	48.8%
Unemployed	58	58.0%	21	51.2%
Onset of dependence (age)	13.9±3.2		15.2±5.0	
Probation ^a				
Yes	50	50.0%	4	15.4%
No	50	50.0%	22	84.6%
COWS total score	13.1±5.8		5.1±3.2	

^ap<0.001. COWS: Clinical Opiate Withdrawal Scale

Table 2. Factor structures and loads of COWS and item-total score correlation coefficients

	Factor 1	Factor 2	Item-total score coefficient
Pulse rate	0.113	0.779	0.114
Sweating	0.685	0.125	0.628
Restlessness	0.774	0.158	0.730
Pupil size	0.511	0.290	0.452
Bone/joint ache	0.816	0.151	0.754
Runny nose/tearing	0.800	0.127	0.723
Gastrointestinal upset	0.653	0.203	0.593
Tremor	0.498	0.394	0.372
Yawning	0.414	0.317	0.348
Anxiety/irritability	0.557	0.326	0.496
Gooseflesh skin	0.576	0.218	0.547
Eigenvalue	4.042	1.292	
Variance (%)	37.74	11.74	

In the confirmatory factor analysis conducted to reveal the fit of the structure of the scale, the distribution of the sample group was examined. The ratio of the chi-square value to the degrees of freedom was calculated to be 1.48, which is within the acceptable range. In the confirmatory factor analysis, the CFI value was calculated to be 0.905, the GFI value to be 0.905, and the RMSEA value to be 0.079 for the model constructed according to the unidimensional structure of COWS. Total scores of the groups were compared to examine whether COWS distinguishes between opiate 91

Table 3. Results of the internal validity analysis conducted on the opioid withdrawal group only

	Corrected item-total score correlation coefficients	Cronbach alpha coefficients of items
Pulse rate	0.232	0.739
Sweating	0.465	0.715
Restlessness	0.643	0.677
Pupil size	0.216	0.743
Bone/joint ache	0.624	0.694
Runny nose/tearing	0.585	0.706
Gastrointestinal upset	0.353	0.733
Tremor	0.517	0.706
Yawning	0.205	0.741
Anxiety/irritability	0.448	0.720
Gooseflesh skin	0.267	0.760

Table 4. Inter-rater internal consistency analysis of items

	Inter-rater correlation*
Pulse rate	0.980
Sweating	0.918
Restlessness	0.895
Pupil size	0.901
Bone/joint ache	0.872
Runny nose/tearing	0.912
Gastrointestinal upset	0.975
Tremor	0.897
Yawning	0.963
Anxiety/irritability	0.816
Gooseflesh skin	0.976
*p<0.001	

Table 5. Sensitivity and specificity values of COWS for cutoff scores

COWS cut-off score	Sensitivity	Specificity
4	92.0	51.2
5	88.0	60.9
6	86.0	73.1
7	85.0	80.4
8	82.0	90.2
9	79.0	92.6
10	72.0	92.6
COWS: Clinical Opiate Withdrawal Scale		

withdrawal and alcohol withdrawal groups. According to this, the score of the opiate withdrawal group (13.1) was found to be higher than the score of the alcohol withdrawal group (5.1) ($F=10.53$, $p<0.001$).

Figure 1. Sensitivity and specificity of the COWS

COWS: Clinical Opiate Withdrawal Scale

In the ROC analysis that was performed to assess the effectiveness of COWS to distinguish the opiate withdrawal group from the alcohol withdrawal group, the area under the ROC curve was detected to be 0.87. The cutoff score of the scale was calculated via a ROC analysis in the specificity and sensitivity analyses of COWS (Table 5). According to this in the 7/8 cutoff score, the sensitivity of the scale was 85.00% and its specificity was 80.48% (Figure 1).

DISCUSSION

This study evaluates the reliability and validity of the Turkish version of COWS, which is used for measurement and quantitative assessment of opiate withdrawal. In particular, it would make a considerable contribution to the daily practice in the field of addiction psychiatry as a scale which determines the severity of opiate withdrawal and also for the management of medication use in opiate addiction.

Reliability Analyses

The internal consistency coefficient of COWS was found to be 0.74. The internal consistency coefficient was found to be 0.78 in the comparative reliability and validity study of COWS against the single-item index of the Clinical Institute Narcotic Assessment (3). Both coefficients are acceptable and signify that the internal consistency of the scale is sufficient. With respect to correlation between item-total scores, all items showed significant correlation except for the first item which is associated with pulse rate. The pulse rate item was not problematic when the analysis was conducted using only the opiate group. The inter-rater reliability coefficient of the scale was also high. As a result, COWS may be used reliably as a scale.

Validity Analyses

Although its items are based on the older scales whose validity studies have been performed, the validity of COWS has not been studied formally (1). Tompkins et al. (3) have compared COWS to other valid scales and concluded that it is valid.

In the explanatory factor analysis, while all items except for the first one regarding pulse rate are included in the first factor supporting the unidimensional structure, the first item is in the second factor alone in the study regarding construct validity of the scale. Both the fact that the total score correlation of the first item regarding pulse is low as well as the fact that it is represented in a different factor are reasons for concern. The item that is related to pulse is one that assesses tachycardia objectively and scoring is made according to pulse rate. Because of its nature, it is not affected by subjective evaluation and interpretation. Thus, this item may not be in line with other withdrawal symptoms and may show an individual structure. Because there may be many factors affecting pulse rate, it is also possible that it shows a distinct performance from the whole scale. It would be appropriate if this item were re-evaluated in future studies.

Table 6. The Clinical Opiate Withdrawal Scale

Clinical Opiate Withdrawal Scale For each item, circle the number that best describes the patient's signs or symptoms. Rate on just the apparent relationship to opiate withdrawal. For example, if heart rate is increased because the patient was jogging just prior to assessment, the increase pulse rate would not add to the score. Patient's name: _____ Date and Time: ____/____/____ ____:____ Reason for this assessment: _____	
Resting Pulse Rate ____ beats/minute <i>Measured after patient is sitting or lying for one minute</i> 0 pulse rate 80 or under 1 pulse rate 81-100 2 pulse rate 101-120 4 pulse rate greater than 120	GI Upset: over last ½ hour 0 no GI symptoms 1 stomach cramps 2 nausea or loose stool 3 vomiting or diarrhea 5 multiple episodes of diarrhea or vomiting
Sweating: over past ½ hour not accounted for by room temperature or patient activity 0 no report of chills or flushing 1 subjective report chills or flushing 2 flushed or observable moistness on face 3 beads of sweat brow or face 4 sweat streaming off face	Tremor: observation of outstretched hands 0 no tremor 1 tremor can be felt, but not observed 2 slight tremor observable 4 gross tremor or muscle twitching
Restlessness: Observation during assessment 0 able to sit still 1 reports difficulty sitting still, but is able to do so 3 frequent shifting or extraneous movements of legs/arms 5 unable to sit still for more than a few seconds	Yawning: Observation during assessment 0 no yawning 1 yawning once or twice during assessment 2 yawning three or more time during assessment 4 yawning several times/minute
Pupil size 0 pupils pinned or normal size for room light 1 pupils possibly larger than normal for room light 2 pupils moderately dilated 5 pupils so dilated that only the rim of the iris is visible	Anxiety or Irritability 0 none 1 patient reports increasing irritability or anxiousness 2 patient obviously irritable or anxious 4 patient so irritable or anxious that participation in the assessment is difficult.
Bone or Joint aches: If patient was having pain previously, only the additional component attributed to opiates withdrawal is scored 0 not present 1 mild diffuse discomfort 2 patient reports severe diffuse aching of joints/muscles 4 patient is rubbing joints or muscles and is unable to sit still because of discomfort	Gooseflesh skin 0 skin is smooth 3 piloerection on skin can be felt or hairs standing up on arms 5 prominent piloerection
Runny nose or tearing: Not accounted for by cold symptoms or allergies 0 not present 1 nasal stuffiness or unusual moist eyes 2 nasal running or tearing 4 nose constantly running or tears streaming down cheeks	Total Score: _____ Total score is the sum of all 11 items Initial of person completing assessment: _____
Score: 5-12 = mild; 13-24 = moderate; 25-36 = moderately severe; more than 36 = severe withdrawal This version may be copied and used clinically.	

The correlation between COWS and pupil size has been found to be low ($r=0.36$) (3). These findings are in line with the nature of the scale that shows a correlation with the objective and measurement-based items, which is lower than expected. An evaluation in construct validity was tested with a confirmatory factor analysis and the unidimensional structure of the scale was confirmed. The fit of the scale to the model was deemed as acceptable in the confirmatory factor analysis.

When viewed with respect to distinctiveness supporting scale validity, COWS distinguishes the opiate withdrawal group from the alcohol withdrawal group reasonably well, both in the comparison of averages and in the ROC analysis.

When all of these characteristics are considered, COWS is a valid scale that may be used. In contrast to the findings of the study conducted by Tompkins et al. (3), the inter-rater correlation coefficient was relatively high and the explanatory and confirmatory factor analysis supported the one-dimensional structure of the scale.

The rapid and correct assessment of the severity of the opioid withdrawal syndrome is essential for monitoring patients beginning both in- and out-patient medical treatment for opioid dependence. Because patients do not always truthfully report the time and quantity of substance used and because opioid metabolism varies from patient to patient, the question regarding the optimal induction dose of buprenorphine is problematic (1). The eight cutoff scores found in this study can be considered as criteria to diagnose opioid withdrawal and time of patient monitoring prior to beginning treatment. Because precipitated withdrawal will be elicited if the initial dose is given too early, the safest approach is to wait for symptoms of withdrawal to reach moderate to severe levels. The categorical break down of COWS total scores is based on the clinical experience of the developers and not derived through statistical methods (1). According to the developers' clinical experience, the administration of the initial dose of buprenorphine at a score of ≥ 25 on the original scale does not lead to precipitated withdrawal.

There are some limitations to this study. The most significant one is that the experimenters administering and scoring the scale were not blind to the diagnoses of the patients. Although this may have led to some bias, it was not possible to achieve an absolutely blind setup for the experiment. Furthermore, a pre- and post-test design in which the scale was administered to patients before and after treatment for opioid withdrawal would have provided insight on the scale's sensitivity to change. Another

limitation is related with the aspect of pulse rate. The item assessing the resting pulse rate at first appeared to be problematic; however, when only the opioid withdrawal group's data was considered, this item proved not to be problematic.

In conclusion, this study showed that the Turkish version of COWS, which is convenient to quantify and assess the severity of opiate withdrawal, is a reliable and valid scale (Table 6). It would be very useful both in the daily practice and in scientific investigations of addiction psychiatry. The scale's sensitivity to change should be demonstrated in future studies with pre- and post-treatment evaluations.

Conflict of Interest: The authors declared no conflict of interest.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

1. Wesson DR, Ling W. The clinical opiate withdrawal scale (COWS). *J Psychoactive Drugs* 2003; 35:253-9. [\[CrossRef\]](#)
2. Mental Bozuklukların Tanısal ve Sayımsal El Kitabı, Amerikan Psikiyatri Birliği (1994) Dördüncü Baskı (DSM-IV) Çev. ed: E Köroğlu Hekimler Yayın Birliği, Ankara, 1995.
3. Tompkins AD, Bigelow GE, Harrison JA, Johnson RE, Fudala PJ, Strain EC. Concurrent validation of the Clinical Opiate Withdrawal Scale (COWS) and single-item indices against the Clinical Institute Narcotic Assessment (CINA) opiate withdrawal instrument. *Drug Alcohol Depend* 2009; 105:154-9. [\[CrossRef\]](#)
4. Bradley BP, Gossop M, Phillips GT, Legarda JJ. The development of an opiate withdrawal scale (OWS). *Br J Addict* 1987; 82:1139-42. [\[CrossRef\]](#)
5. Handelsman L, Cochrane KJ, Aronson MJ, Ness R, Rubinstein KJ, Kanof PD. Two new rating scales for opiate withdrawal. *Am J Drug Alcohol Abuse* 1987; 13:293-308. [\[CrossRef\]](#)
6. Peachey JE, Lei H. Assessment of opioid dependence with naloxone. *Br J Addict* 1988; 83:193-201. [\[CrossRef\]](#)
7. Gossop M. The development of a Short Opiate Withdrawal Scale (SOWS). *Addict Behav* 1990; 15:487-490. [\[CrossRef\]](#)
8. Loimer N, Linzmayer L, Grünberger J. Comparison between observer assessment and self-rating of withdrawal distress during opiate detoxification. *Drug Alcohol Depend* 1991; 28:265-268. [\[CrossRef\]](#)
9. Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction: A Treatment Improvement Protocol TIP 40. Center for Substance Abuse Treatment. Rockville (MD): Substance Abuse and Mental Health Services Administration (US); 2004. Report No.: (SMA) 04-3939
10. Özkürkçügil A, Aydemir Ö, Yıldız M ve ark. DSM-IV eksen I bozuklukları için yapılandırılmış klinik görüşmenin Türkçe'ye uyarlanması ve güvenilirlik çalışması. *İlaç ve Tedavi Dergisi* 1999; 12:233-236.