Research Article

Validation of the glasgow antipsychotic side-effect scale (gass) in greece

Abstract

The aim of the present study was to evaluate the linguistic adaptation and psychometric validation into the Greek language of the GASS scale for the assessment of side effects in patients treated with second generation antipsychotic medication. The GASS scale takes 5minutes to complete (21 items for men and women) and contains self-explanatory questions in everyday plain English while providing a structured systematic method of reviewing antipsychotic side effects. The translation and cultural adaptation of the questionnaire was performed according to international standards. Internal consistency using the Cronbach α coefficient and test-retest reliability using the intraclass correlation coefficient (ICC) was used to assess the reliability of the instrument. Patient's sample consisted of 80 participants with a mean age of 42.6years. Internal consistency and intraclass correlation coefficient were adequate (Cronbach $\alpha = 0.79$ and ICC = 0.96). The test-retest percent agreement for the aforementioned categories was 95.9. Agreement was satisfactory according to Kappa coefficient which was equal to 0.78 (p<0.001).The Greek validation of the GASS scale shows appropriate feasibility, reliability, and discriminative performance as a patient-reported outcome to be used for the assessment of the impact of side effects on patients with schizophrenia.

Keywords: second generation antipsychotics, gass scale, validation

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Abbreviations: SGAs, second generation antipsychotics; FGA, first-generation antipsychotics; GASS, glasgow antipsychotic side-effect scale; DDDs, defined daily doses; LUNSERS, liverpool university neuroleptic side effect rating scale; UKUSERS, udvalg for kliniske undersogelser side-effect rating scale; SMARTS, systematic monitoring of adverse events related to treatments; ANNSERS, non-neurological side effect rating scale

Introduction

Schizophrenia is a chronic mental illness that requires long-term antipsychotic treatment to both manage disease symptoms and delay relapses.[1] The discovery of antipsychotic medications has improved outcomes in persons with schizophrenia through control of symptoms.[2] Newer antipsychotic treatments have proven useful in reducing both relapses and the severity of symptoms.[3]

The past years the prescription of SGAs has increased.[4]The Service Division of Scotland reported that all NHS Boards except NHS Shetland show increased prescribing of antipsychotic drugs since 2008/2009. The use of antipsychotic drugs has increased from 7.0 to 8.0 DDDs per 1,000 populations per day between 2008/2009 and 2012/2013. From 2006 to 2011 there has been a dramatic 59% increase in the use of SGAs medication.[5] In Greece the last 5years there has been a documented 18.6% increase in the use of antipsychotic drugs.[6]

Second generation antipsychotics (SGAs) are generally preferred over typical antipsychotics for schizophrenia treatment as they are associated with fewer extra pyramidal symptoms, lower risk of tardive dyskinesia, and possibly greater improvement in negative symptoms.[7] Schizophrenia and bipolar disorder are examples of chronic illnesses a high risk of relapse associated with major functional consequences.[8] One of the contributing factors to relapse in schizophrenia is poor or partial adherence to medication.[9] Use of the second-generation antipsychotics, which have a different adverse event profile than the first-generation antipsychotics, was hoped to improve adherence[10]

and, consequently, treatment outcomes compared with first-generation antipsychotics[11,12] However, treatment adherence remains low.[11] Nonadherence significantly increases the risk of relapse and is associated with impaired functional outcomes in schizophrenia.[13,14] In a systematic review Olivares J[15] found that non- adherence to antipsychotic medication was the most frequent reported factor that may drive to relapse, he also reported that treatment related factors such as side-effects were associated with increased relapse rates.[15]

The majority of patients with schizophrenia (84%) discontinue their index antipsychotic during the follow-up period and in the long-term 40 to 50% seem to be non-compliant with no real difference in terms of adherence between first-generation antipsychotics (FGA) and second-generation antipsychotics (SGA).[16,17] The most striking result of the CATIE study, which enrolled almost 1,500 individuals with chronic schizophrenia, was the high rate of treatment discontinuation (up to 74%) over the 18-month period of the trial and the short median time to discontinuation of treatment (about 6 months) in all phases of the trial.[18]

Antipsychotic drugs potentially cause a wide range of adverse effects including extra pyramidal symptoms, sedation, weight gain, metabolic disturbance, sexual dysfunction, urinary symptoms, gastrointestinal symptoms, and symptoms that reflect raised prolactin, for example, menstrual irregularities and galactorrhoea. Adverse effects are clinically important as they add to the suffering of patients, impair quality of life, can be stigmatizing and often lead to poor or lack of adherence with antipsychotic medication, which in turn usually leads to relapse of the underlying psychiatric disorder.[19]

Guidelines recommend that side effects should be monitored regularly.[20–23] Many efforts have been made to develop or validate specific instruments to assess side effects of medication used in schizophrenia. Antipsychotic side effect rating scales were first introduced in the 1970s. Since then a number of side effect and adverse effect scales have been developed.[24,25]

Each and every developed side effect scale, currently in use, has its own specific features. Some assess only specific side effects[24] whereas some assess a range of side effects.[25–29] Some are completed by clinicians, whereas others can be completed by patients.[25,26,29,30]

A number of scales focus primary on EPS such as the Abnormal Involuntary Movement Scale (AIMS),[28] extra pyramidal Symptom Rating Scale (ESRS),[25] the Simpson-Angus Scale (SAS)[24] and the Udvalg for Kliniske Undersogelser Side-Effect Rating Scale (UKUSERS).[26]

Newer side effect rating scales have been developed to asses a range of side effects such as the Antipsychotic Non-Neurological Side Effect Rating Scale (ANNSERS),[27] a physician- or self- rated scale addressing a wide range of FGA and SGA side effects.

The Liverpool University Neuroleptic Side-Effect Rating Scale (LUNSERS)[29] is one of the most popular self-completed side effect rating scales in Britain assessing a wide range of side effects includes 41 items, plus 10 'red herring' items but is time consuming and one word symptoms can be difficult for patients to understand.

Other newer self-completed side effect scales include the Systematic Monitoring of Adverse events Related to Treatments (SMARTS)[30] and the Glasgow Antipsychotic Side-effect Scale (GASS).[25]

The SMARTS checklist assesses whether patients are currently 'troubled' by 11 well-established potential antipsychotic side effects. Patients provide their responses to these questions by circling relevant side effects. An additional open question enquires about any other possible side effects.[31]

Among currently used scales, the GASS is one of the most practical for clinical use. It is a self-report rating scale assessing SGA side effects includes ratings of both neuromuscular and metabolic side effects. The scale was calibrated against the Liverpool University Neuroleptic Side-Effect Rating Scale (LUNSERS)[29] in 50 outpatients on SGAs, compared to 50 healthy individuals not on antipsychotics, and was found to have good discriminatory power; construct validity; and test–retest reliability.

The GASS takes 5minutes to complete (21 items for men and women) and contains self-explanatory questions in everyday plain English while providing a structured systematic method of reviewing antipsychotic side effects.[31]

The aim of the present study was to evaluate the linguistic adaptation and psychometric validation into the Greek language of the GASS for the assessment of side effects in patients treated with second generation antipsychotic medication.

Materials and methods

Participants

The study was carried out at 2 Psychiatric Clinics in Greece. In particular at the Depot and Clozapine Clinic of Agioi Anargyroi Hospital Department of Psychiatry and at the Depot of "Aghios Charalambos" Mental Health Clinic. Inclusion criteria included participants' age being at least 18 years, having a diagnosis of schizophrenia or schizoaffective disorder as established by the Structured Clinical Interview for DSM-IV, being adherent to treatment and currently prescribed and taking SGA (regardless of other concomitant medication). All participants were above the 8 grade level status.

After complete description of the study to the participants, written informed consent was obtained. Permission to conduct the Validation of the GASS Scale was obtained by the author of the original instrument. Ethical approval for the study was granted by the Research and Ethics Committee of Agioi Anargyroi Hospital.

Translating the scale

The GASS scale was translated into Greek from the original questionnaire as recommended in the literature review.[32] Upon agreement, two professional translators, native speakers of the Greek (i.e. target) language and fluent in the English (i.e. source) language undertook independent forward translations into the target language. A reconciled version of the instrument was developed and a backward translation of this reconciled version back into the original language was performed by a professional translator. The back-translation and the original one were compared and any discrepancies between them led to changes in the reconciled translation in the Greek language. An expert committee reviewed this latest version and gave their feedback. At the next stage, the questionnaire was administered to a small group of patients who volunteered to take part at the cognitive debriefing phase in order to assess clarity and comprehension of the questionnaire items. After this final feedback, the final Greek version was produced.

Statistical analysis

Internal consistency and reliability was determined by calculation of the Cronbach α coefficient. Cronbach α equal to or greater than 0.70 was considered acceptable.[33] Student's t-tests were used to compare mean values. To conceptualize the overlap, between patient and controls, effect size was also reported. According to the literature, effect sizes of 0.2-0.5 are considered small, between 0.51 and 0.80 moderate and over 0.8 effect- sizes are considered large.[34] To assess the consistency of the scores, test-retest stability was determined by administering the GASS questionnaire to 80 patients on two separate occasions one week apart. Intra-class correlation coefficients (ICCs) were computed to determine the level of agreement. ICCs equal or lower to 0.40 indicate poor to fair agreement, 0.41-0.60 moderate agreement, 0.61-0.80 good agreement and over 0.80 excellent agreements.[35] Paired t -tests were also used to investigate the differences after one week re-administration. Kappa values were calculated to assess the agreement for the categorization of patients into three groups (Absent/mild, moderate and severe side effects) between first and second administration. The maximum Kappa value is 1, corresponding to perfect agreement, values greater or equal to 0.75 are considered as excellent agreement and values greater than 0.4 indicate acceptable reliability.[36] P values reported are two-tailed. Statistical significance level was set at .05 and analysis was conducted using SPSS 19.0.
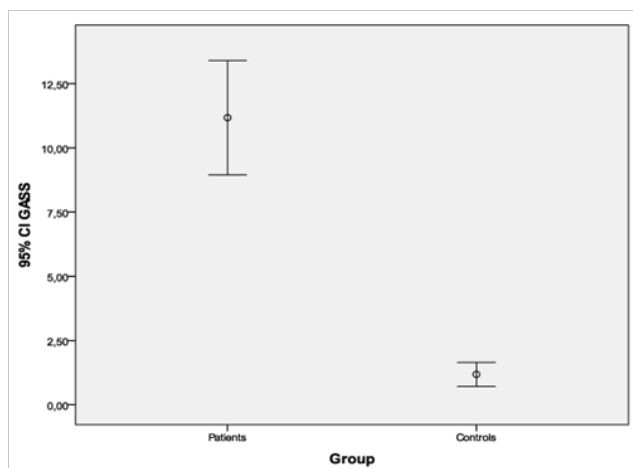
Results and discussion

Patient's sample consisted of 80 participants (68.8% men and 31.3% women) with a mean age of 42.6years (SD= 14.5years). All patients were on second generation antipsychotic medication either on long acting formulations or clozapine, as follows: 5 patients were on clozapine, 40 olanzapine long acting, 25 risperidone long acting and 10 paliperidone long acting respectively. All dosing regimens were within BNF limits. Approximately a third of the patients, 31.3%, were on monotherapy, whereas the remaining 68.7% was on combination with antidepressants (11.3%) or mood stabilizers (67.5%). The control group consisted of 50 participants (70% men and 30% women) with a mean age of 43.4 years (SD=13.9 years). The sample's characteristics are shown in (Table 1).

Table 1 Samples characteristics

	Patients N (%)	Controls N (%)	P
Age(years), mean (SD)	42.6(14.5)	43.4(13.9)	0.756*
Sex			
Men	55(68.8)	35 (70.0)	0.881**
Women	25(31.3)	15(30.0)	
SGA			
No	0(0.0)		
Yes	80(100)		
Antidepressants			
No	71(88.8)		
Yes	9(11.3)		
Polypharmacy			
No	71(88.8)		
Yes	9(11.3)		
Moodstabilizer			
No	26(32.5)		
Yes	54(67.5)		
Monotherapy			
No	55(68.8)		
Yes	25(31.3)		

*Student's t-test; **chi-square test
Second generation antipsychotics (SGAs)

Figure 1 Mean GASS values for patient and control groups.

Cronbach's α for the GASS scale was 0.79 and exceeded the minimum reliability standard of 0.70 indicating acceptable internal consistency reliability.[33] Mean scores of the GASS scale was 11.2 (SD=10.0) for the patient's group and 1.2 (SD=1.6) for the control group (Figure 1). The difference between patients and controls was statistically significant (p<0.001) with a large effect size equal to 1.39 showing the discriminative validity of the questionnaire.[34] 10% of patients were categorized as having moderate side effects and 90% were categorized as having absent/mild side effects. All controls were categorized as having absent or mild side effects. After excluding patients on polypharmacy, the difference between patients and controls still remained statistically significant (p<0.001).

Test retest stability analysis showed excellent agreement with ICC equal to 0.96 (95% CI: 0.93-0.98, p<0.001). The mean GASS was 9.9 (SD=7.9) at the first administration and 10.1 (SD=8.1) at the second administration after one week from the first (p=0.608). Subjects at the first and second administration were categorized in three groups (Absent/mild, moderate and severe side effects). The test-retest percent agreement for the aforementioned categories was 95.9. Agreement was satisfactory according to Kappa coefficient which was equal to 0.78 (p<0.001).

GASS scores according to patient's characteristics are shown in (Table 2). There were no statistically significant difference amongst monotherapy and polypharmacy. The concomitant use of antipsychotics and mood stabilizers had no significant effect on GASS scores. However, women and patients receiving antidepressants reported statistically significant higher scores in GASS, p≤ 0.008 and p≤ 0.038 respectively. Our findings are similar to other studies. Women are more susceptible to side effects due to antipsychotic medication. Women's bodies, on average, contain 25% more adipose tissue than those of men.[37] Since most antipsychotic drugs are highly lipophilic molecules they might be accumulated in lipid stores resulting the development of noticeable side effects.[37] Furthermore the use of antidepressants in patients who suffer from schizophrenia might represent a progressive stage of the illness with chronicity and negative symptoms, inadequate response to the antipsychotic medication, or failure of multiple challenges with antipsychotic medications with accumulated side effects. The use of antidepressants in patients suffering from schizophrenia is rather controversial, except the decreased risk for suicidal behaviour.[38]

Table 2 Mean GASS scores according to patient's characteristics

	GASS		P
	Mean	SD	
Sex			
Men	9.8	9.6	0.008
Women	14.2	10.3	
Antidepressants			
No	10.3	9.5	0.038
Yes	17.7	12.1	
Polypharmacy			
No	11.44	10.5	0.495
Yes	9	5.1	
Moodstabilizer			
No	13.2	9.9	0.219
Yes	10.2	9.9	
Monotherapy			
No	10.2	9.9	0.179
Yes	13.4	10.1	

Glasgow Antipsychotic Rating Scale (GASS)

The GASS scale was developed by Waddell L and Taylor M in 2008 and is currently amongst the most popular and easy to use antipsychotic side- effect rating scales in the UK.[31,39] The scale has not been previously translated or validated in Greek population. It is the first time a self rating scale related to adverse events of antipsychotic drugs is being validated in the Greek language. Our results show that the GASS scale presents adequate characteristics for use in patients with schizophrenia and schizoaffective disorder in Greece. The Cronbach's alpha value for the scale was 0.79; indicating acceptable internal consistency reliability and the differences in mean scores of the GASS scale between patients and controls show the discriminative validity of the questionnaire. Regarding reliability, coefficient alpha estimates of the GASS were generally acceptable against the background observations. There are multiple factors for considering a reliability coefficient such as the construct being measured, time available for testing, how the scores are to be used, amongst others, so that reliability coefficients as low as 0.79 are acceptable. Therefore, in

general the reliability estimates reported here were within acceptable range. GASS might be a simplistic instrument. However, is gathering information that only needs to be used in a practical way rather than inferential way, the reliability and validity requirements are more basic. It is actually measuring the real-world events, such as troubling side-effects, that they are intended to measure. This type of internal validity could be assessed by comparing the questionnaire responses with objective measures of the side effects; for example comparing the self-reported shaking of the hands or arms with some objective measure. Other alternative measures such as Cohen's kappa statistic or the Fleiss kappa, were not performed since they are more complicated and are rather suitable for objective than subjective rating.[40,41]

Since GASS is a simple and easy to administer self-rating scale. The completion time is low (<10min) compared with longer questionnaires such as the LUNCERs scale (approx. 20 min).[25] Simple checklists are promoted as more effective clinical intervention for improving service.[42]

Conclusion

Antipsychotic drugs can cause a wide range of potential adverse effects.[19] Adverse effects of antipsychotics are often neither diagnosed nor treated.[43] In his audit, Cleary A[43] investigated current practice within a rural mental health service area on the monitoring and documentation of side effects of antipsychotic depot medication. According to the audit, side effects were not recorded in 72% of cases. Locally developed checklists scales were used in 25% of the case notes examined, this percentage is low when considering the popularity of using an evidenced-based tool in practice, for example, the Liverpool University Neuroleptic Side Effect Rating Scale (LUNSERS).[25] He concluded that Collaborative practice with feedback from service users is essential in service improvement and care delivery.[43]

The GASS scale is a valid reliable tool, which could aid systematic clinical assessment. The GASS includes ratings of both neuromuscular and metabolic side effects. It is quick to complete, either for the clinician or patient. The use of a plain language helps comprehension. It is independent of any commercial interest and can be used without cost.[31,39]

Despite the above results, this study presents some limitations that should be considered. The GASS questionnaire is a simple, self-reported screening tool. It is argued to be inadequate to understand some forms of information - i.e. "I felt dizzy when I stood up and/or have fainted" (question n. 3) or "I have been drooling" (question n.8) etc. Furthermore, it is asking only a limited amount of information without explanation and there is no way to tell how truthful a respondent is being. Therefore there is a level of subjectivity that is not acknowledged. The scale was only assessed in outpatients on long acting antipsychotic medication and clozapine, excluding a range of SGAs that do not have a depot formulation and FGAs. The differences in the side-effect profile of the medications, we did not assessed, might influence the screening accuracy of the questionnaire.

Overall the Greek validation of the GASS scale shows appropriate feasibility, reliability, and discriminative performance as a patient-reported outcome to be used for the assessment of the impact of side effects on patients with schizophrenia. This information could be very important to improve therapeutic alliances and treatment adherence among patients with schizophrenia. Since drug induced side-effects are pivotal in medication non-adherence for all patients, the current validation of GASS can be a useful study for further assessment of antipsychotic medications in different population samples, such as first episode and bipolar sufferers on antipsychotic drug regimes.

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