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A new self-rating scale for detecting atypical or second-generation antipsychotic side effects

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Abstract

We aimed to construct and assess a new self rating scale to detect the side effects of second generation antipsychotics. This scale was designed to allow a timely, sensitive and reliable method of gathering information on the number and severity of side effects an individual suffers from. The Glasgow Antipsychotic Side-effect Scale (GASS) was developed after literature review, discussion with members of the mental health team and with service user feedback. Fifty individuals taking second generation antipsychotics completed the GASS along with the Liverpool University Neuroleptic Side Effect Rating Scale, and one week later completed the

GASS for a second time. Fifty comparison subjects also completed the GASS. The GASS was shown to have good discriminatory power and construct validity, along with good re-test reliability, and is put forward as a short, helpful and valid clinical tool.

Key words

neuroleptic drugs; atypical antipsychotics; antipsychotic agents/adverse effects; drug monitoring; questionnaires

Introduction

Adherence with antipsychotic medication is perhaps the main determinant of relapse in schizophrenia (Robinson, *et al.*, 2002). The tolerability or experience of side effects of a particular antipsychotic medication has been regarded as both one of the key factors predicting continued adherence (Tacchi and Scott, 2005; Lambert, *et al.*, 2004) and crucially the experience of adverse antipsychotic side effects is commonly stated by patients as an important reason for non-adherence (Patel and David, 2007). This highlights the importance of an open and systematic discussion regarding medication-related side effects, as an acknowledgement of the risks as well as benefits of a particular treatment help to establish a collaborative approach between clinicians and service users and contribute to a therapeutic rapport.

Antipsychotic side-effect rating scales have been used over the years to help identify and quantify the various side effects that can occur on these medications. A literature review was undertaken to identify all currently available antipsychotic side-effect rating scales using Medline and other Internet search engines with various keywords including *neuroleptic*, *side effects*, *antipsychotic*, *rating scale* and *schizophrenia*. Also, medical, pharmacy and nursing staff were questioned about their experience of identifying antipsychotic side effects. All nine

currently widely available antipsychotic side-effect rating scales were identified and reviewed to identify their strengths and weaknesses (see Table 1).

Antipsychotic side effect rating scales have been around for a long time. They include traditional observer rated side-effect scales such as the Simpson-Angus (Simpson and Angus, 1970) or the Barnes Akathisia scale (Barnes, 1989). These more often were found in research settings than routine clinical practice, and arguably side-effect scales, focusing only on movement disorder or extra-pyramidal symptoms, have now become less relevant as the widely used atypical or second-generation antipsychotics (SGAs) have a lower incidence of extra-pyramidal side effects (Geddes, *et al.*, 2000).

Additionally, although observer rated scales may avoid over-reporting bias, they can be more time consuming than self-report scales, and less likely to identify potentially embarrassing concerns such as sexual dysfunction. The Liverpool University Neuroleptic Side-Effect Rating Scale (LUNSERS) (Day, *et al.*, 1995) is a commonly used self-report scale, which concentrates on one-word symptoms but again is over a decade old. The LUNSERS also takes time to complete as it is three pages long, and a recent audit (Negi, 2007) found that use of the LUNSERS did not improve case-record documentation of side effects. Finally, experience with the LUNSERS found that patients commonly have to ask for help in understanding terms

such as 'chilblains', emphasising that the use of simple plain English is vital in self-report scales.

We aimed to devise an easy to understand self-report side-effect scale that was brief, valid, practical and informative. It was envisaged that a short self-report scale would facilitate further discussion in the clinic regarding the tolerability of antipsychotic medication.

Method

Ethical approval for the study was granted by the local Research and Ethics Committee.

Constructing the scale

After referring to existing scales, important antipsychotic side effects were listed using information from the British National Formulary (BNF 51, Joint Formulary Committee, 2005) and the pharmaceutical industry. Consistent with the NICE guidelines (NICE, 2002), these side effects were then ranked in importance by both authors in terms of medical consequences. In addition, a focus group of patients already taking antipsychotic medication ranked the list of side effects in terms of acceptability. Twenty-two questions were arrived at, which summarised the prioritised side effects with priority given to

long-term adverse medical consequences. These were then grouped into medical systems (see Table 2).

The majority of side effects addressed by the new scale are contained in LUNSERS, but the 22 questions were converted into unambiguous plain English. The new scale, termed the Glasgow Antipsychotic Side-effect Scale or GASS was scored 0,1,2,3 for questions 1–20, with higher scores reflecting more frequent experience of side effects. Questions 21 and 22 scored 0 for 'no' and 3 for 'yes'. Total GASS scores were arbitrarily divided into suggested ranges for categorical severity, that is, 0–21 = absent/mild side effects; 22–42 = moderate side effects and 43–63 = severe side effects. A separate (unscored) column was added to allow people completing the GASS to note if the side effect experienced was distressing.

Participants

Fifty outpatients aged 18–65 who were currently prescribed and taking a SGA (regardless of diagnosis or other medication prescribed) consented to participate. These individuals were recruited from outpatient and clozapine clinics in the three North Glasgow resource centres. Adherence with prescribed medication was confirmed at interview. Fifty comparison subjects within the same age range also agreed to participate after excluding individuals on prescribed medication and those working in mental health care. These individuals were recruited by

Table 1 Existing side-effect rating scales

Scale	Number questions	Completion	Advantages	Disadvantages
Simpson Angus Scale (SAS) (Simpson and Angus, 1970)	10	Clinician rated	Objective rating of EPSE, quick and easy to perform	Focus on extrapyramidal side effects (EPSE) only
Abnormal Involuntary Movement Scale (AIMS)(Guy, 1976)	12	Clinician rated	Objectively records presence and severity of involuntary movements; quick to perform	Focus on abnormal movements only
Extrapyramidal Side Effect Rating Scale (ESRS) (Chouinard, <i>et al.</i> , 1980)	12	Clinician rated	Quick to perform, objective documenting of EPSE	EPSE only. No differentiation between dyskinesia and dystonia
Drug Attitude Inventory (Hogan, <i>et al.</i> , 1983)	30	Self rated	Simple to understand questions and true/false answers. Assesses attitude	Not specifically aimed at detecting antipsychotic side-effects
Side Effects Rating Scale for the Registration of Unwanted Effects of Psychotropics (Lingjaerde, <i>et al.</i> , 1987)	47	Clinician rated	Covers an extensive range of side effects from antipsychotic medication	Requires a lengthy semi structured interview and clinical observation
Barnes Akathisia Rating Scale (Barnes, 1989)	4	Clinician and self rated components	Both subjective and objective rating of akathisia; quick	Focuses on akathisia only
Hillside Akathisia Scale (HAS) (Fleischhaker, <i>et al.</i> , 1989)	5	Clinician and self rated components	Both subjective and objective rating of akathisia; quick	Focuses on akathisia only
Liverpool University Neuroleptic Side Effect Rating Scale (LUNSERS) (Day, <i>et al.</i> , 1995)	51	Self rated	Assesses wide range of side effects; red herring questions for over-reporting of side-effects	One-word symptoms that can be difficult to understand
Antipsychotic Non-Neurological Side Effect Rating Scale (ANNSERS) (Yusufi, <i>et al.</i> , 2005)	35	Clinician and self rated components	Covers wide range of side effects for 1st and 2nd generation antipsychotics	Lengthy and time consuming

Table 2 Glasgow Antipsychotic Side-effect Scale (GASS)**Glasgow Antipsychotic Side-effect Scale (GASS)**

Name: _____ **Age:** _____ **Sex: M / F** _____

Please list current medication and total daily doses below:

This questionnaire is about how you have been recently. It is being used to determine if you are suffering from excessive side effects from your antipsychotic medication.

Please place a tick in the column which best indicates the degree to which you have experienced the following side effects. Tick the **end** box if you found that the side effect distressed you.

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Over the <u>past week</u>:	<i>Never</i>	<i>Once</i>	<i>A few times</i>	<i>Everyday</i>	<i>Tick this box if distressing</i>
1. I felt sleepy during the day					
2. I felt drugged or like a zombie					
3. I felt dizzy when I stood up and/or have fainted					
4. I have felt my heart beating irregularly or unusually fast					
5. My muscles have been tense or jerky					
6. My hands or arms have been shaky					
7. My legs have felt restless and/or I couldn't sit still					
8. I have been drooling					
9. My movements or walking have been slower than usual					
10. I have had, or people have noticed uncontrollable movements of my face or body					
11. My vision has been blurry					
12. My mouth has been dry					
13. I have had difficulty passing urine					
14. I have felt like I am going to be sick or have vomited					
15. I have wet the bed					
16. I have been very thirsty and/or passing urine frequently					
17. The areas around my nipples have been sore and swollen					
18. I have noticed fluid coming from my nipples					
19. I have had problems enjoying sex					
20. <u>Men only</u> : I have had problems getting an erection					
Tick yes or no for the following questions about the <u>last three months</u>	<i>No</i>	<i>Yes</i>	<i>Tick this box if distressing</i>		
21. <u>Women only</u> : I have noticed a change in my periods					
22. <u>Men and women</u> : I have been gaining weight					

Staff Information

1. Allow the patient to fill in the questionnaire themselves. Questions 1-20 relate to the previous week and questions 21-22 to the last three months.

2. Scoring

For questions 1-20 award 1 point for the answer "once", 2 points for the answer "a few times" and 3 points for the answer "everyday". Please note zero points are awarded for an answer of "never".

For questions 21 and 22 award 3 points for a "yes" answer and 0 points for a "no".

Total for all questions=

3. For male and female patients a *total score* of:

0-21 = absent/mild side effects

22-42 = moderate side effects

43 and over = severe side effects

4. Side effects covered by questions
1-2 sedation and CNS side effects
3-4 cardiovascular side effects
5-10 extra-pyramidal side effects
11-13 anticholinergic side effects
14 gastro-intestinal side effects
15 genitourinary side effects
16 screening for diabetes mellitus
17-21 prolactinaemic side effects
22 weight gain

The column relating to the distress experienced with a particular side effect is not scored, but is intended to inform the clinician of the service user's views and condition.

directly approaching members of public in the streets of central Glasgow. Individuals unable to read English were also excluded.

Assessment of the new scale

Outpatients completed both the LUNTERS and the GASS at the same time, with the choice of which scale was completed

first being randomly assigned via coin tossing. The outpatients were also asked to complete a copy of the GASS again a week later to assess test-retest reliability. Comparison subjects completed the GASS to report that the GASS could differentiate between those taking and those not taking SGAs.

Statistical analyses were performed using MedCalc for Windows, version 9.2.0.1 (*MedCalc Software*). Categorical

differences were determined using the Mann–Whitney test, with significance set at $P < 0.05$. Level of agreement between the scales was assessed using the weighted κ and Spearman correlation coefficient.

Results

The GASS is illustrated above (see Table 2).

Table 3 shows the mean ages and the mean GASS score for the two groups.

There was no significant difference in age between the two groups ($U = 1410$, $P = 0.27$). The GASS scores for the two groups differed significantly (Mann–Whitney U -test, $U = 2336$, $P < 0.0001$) with a mean of 14.3 for those on antipsychotic medication, and 3.6 for those not on medication. This confirms the construct validity of the GASS.

Figure 1 shows the spread of the GASS scores within each of the proposed categorical cut-off points, for both cases and normal comparisons. Cases prescribed polypharmacy or monotherapy are also shown separately. As expected, all controls scored within the absent to mild category.

Twenty-nine of the outpatient group were prescribed clozapine, nine risperidone (seven oral, two depot), eight olanzapine and four amisulpride. All doses were prescribed within BNF limits. Thirty-six outpatients were prescribed only a SGAs, whereas the remaining 14 were on other regular medications (eight on antidepressants, five on mood stabilisers, one procyclidine, one methadone and one oral hypoglycaemics).

Repeating the analysis of GASS scores excluding the results of the 14 polypharmacy outpatients still showed that outpatients had a significantly higher mean GASS score of 11.5 ($SD = 7.9$) and they differed significantly from the normal comparisons (U score 1681, $P < 0.0001$).

When the GASS was compared to the LUNRSERS in the 50 outpatients, the κ score = 0.73, with Spearman rank correlation coefficient = 0.93 (sum of squared differences = 1548). This indicates a strong level of agreement between the GASS and LUNRSERS.

Only 17 of the 50 outpatients returned (by post) the second GASS questionnaire adequately filled out a week later. Test–retest reliability was good, with $\kappa = 0.72$. The Mann–Whitney U -test failed to identify any significant difference in the GASS score of those who returned the second GASS questionnaire and those who did not ($U = 308$, $P = 0.57$) or in their age

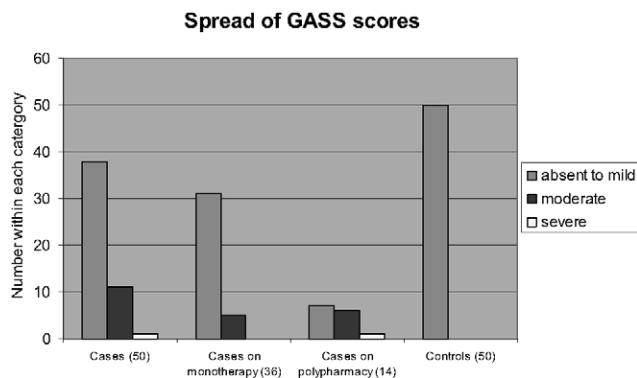


Figure 1 Spread of Glasgow Antipsychotic Side-effect Scale scores.

($U = 284$, $P = 0.94$). There were 10 men and seven women in the group that returned the second GASS compared with 16 men and 17 women in the group that did not.

Discussion

We have constructed a new self-report rating scale assessing SGA side effects that is easy to use. The GASS takes 5 min to complete and contains self-explanatory questions in everyday plain English while providing a structured systematic method of reviewing antipsychotic side effects. In the waiting room of a busy community mental health team or on the inpatient unit, the use of simple and jargon-free language will surely enhance understanding and accurate completion of a self-report scale, particularly if that scale is seen as brief. Furthermore, recognising that the experience of a side effect may not necessarily be adverse even if it is common or may not cause distress or functional impairment when present, following our data collection we added a column to the GASS allowing the subject to rate whether the experienced side effect was in fact distressing (or not). This was left as a simple global 'yes/no' response in view of the complexity of this judgement. Thus, the GASS allows a grading not only of the frequency of an experienced side effect but also a subjective judgement of the distress associated with a particular side effect.

The widespread use of SGAs along with their recommendation by influential guidelines (NICE, 2002) is in large part because of a perception of increased tolerability, although recent independent studies (e.g., Lieberman, *et al.*, 2005) have confirmed SGAs have important adverse side effects with associated long-term health implications. Many studies have reported that adherence with prescribed medication is a key determinant of relapse prevention (see Tacchi and Scott, 2005), and medication side effects are commonly cited by patients as a main reason for non-adherence (Patel and David, 2007), perhaps because clinicians consistently underestimate the severity and frequency of side effects. The routine use of rating scales or systematised evaluation in psychiatry is not

Table 3 Mean ages and GASS scores of participants

Statistic	Cases ($n = 50$)	Comparisons ($n = 50$)
Mean age (years) [SD]	41.4 [9.1]	39.9 [14.1]
Age range (years)	24–65	19–65
No. males	26	21
Mean GASS [SD]	14.3 [10.5]	3.6 [4.1]

GASS, Glasgow Antipsychotic Side-effect Scale; SD, standard deviation.

widespread, but arguably will increase and can be used to enhance the clinician–patient interaction. Self-report scales generally are less onerous for the busy clinician but also allow more complete and considered responses as well as minimising potential embarrassment on subjects such as sexual dysfunction.

Older side-effect rating scales (see Table 1) such as AIMS, Simpson Angus and Barnes Akathisia tended to focus exclusively on movement disorder and extrapyramidal symptoms and were usually observer rated. The more recent scales such as LUNSERS and ANNSERS are more comprehensive and suitable for SGAs but are lengthy and time consuming. The LUNSERS is regularly used in the United Kingdom, despite its size, age and occasionally confusing language, illustrating that a systematic appraisal of medication side effects is considered important. Both the weighted κ score and Spearman's rank correlation score reported a very good level of agreement between the LUNSERS and the GASS in a representative psychiatric outpatient population. This is not surprising given that the majority of the questions in the GASS are also covered by the LUNSERS. The test–retest results also indicate that the GASS is reliable and stable over time. We reported that individuals taking SGAs had significantly higher GASS scores than matched normal comparison subjects, as hypothesised, and this was not confounded by polypharmacy.

We believe our use of medical and consumer opinion as well as the literature review enhances the face validity of the GASS, and as the GASS combines brevity with validity, it is suitable for busy clinical environments and as part of routine clinical monitoring, for example, during ward round or outpatient review. The GASS can also be completed outside the actual clinical interview, and can thus open up discussion between clinician and service user on medication tolerability in a systematic and structured manner, rather than relying on an *ad hoc* approach.

Given these results, we suggest the GASS is a valid reliable tool, which could aid systematic clinical assessment, particularly in view of its brevity and user-friendly language.

Study limitations

The GASS was only assessed in outpatients taking SGAs; hence, the results may not be applicable to those on typical or first-generation antipsychotics or acute inpatients. It may not be possible to generalise the results of this study beyond a white middle-aged population in view of the age range and ethnicity of the two study groups. The subjective rating of distress caused by each side effect requires further study.

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