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SMARTS (Systematic Monitoring of Adverse events Related to TreatmentS): The development of a pragmatic patient-completed checklist to assess antipsychotic drug side effects

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Abstract

Objectives: Antipsychotic drug side effects are common and can cause stigmatisation, decreased quality of life, poor adherence, and secondary morbidity and mortality. Systematic assessment of anticipated side effects is recommended as part of good clinical care, but is uncommon in practice and patients may not spontaneously report side effects. We aimed to develop a simple patient-completed checklist to screen systematically for potential antipsychotic side effects.

Methods: The SMARTS checklist was developed over a series of group meetings by an international faculty of 12 experts (including psychiatrists, a general physician and a psychopharmacologist) based on their clinical experience and knowledge of the literature. The emphasis is on tolerability (i.e. assessment of side effects that 'trouble' the patient) as subjective impact of side effects is most relevant to medication adherence. The development took account of feedback from practising psychiatrists in Europe, the Middle East and Africa, a process that contributed to face validity.

Results: 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. The checklist has been translated into Italian and Turkish.

Conclusions: The SMARTS checklist aims to strike a balance between brevity and capturing the most common and important antipsychotic side effects. It is appropriate for completion by patients prior to a clinical consultation, for example, in the waiting room. It can then form the focus for a more detailed clinical discussion about side effects. It can be used alone or form part of a more comprehensive assessment of antipsychotic side effects including blood tests and a physical examination when appropriate. The checklist assesses current problems and can be used longitudinally to assess change.

Keywords: antipsychotics, checklist, rating scale, side effects, tolerability

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Introduction

The side effect profiles of different antipsychotics vary greatly and individual patients also show considerable variation in their susceptibility to develop specific side effects [Haddad and Sharma, 2007]. Antipsychotic drugs can cause a wide range of potential side effects including extrapyramidal symptoms, sedation, weight gain,

metabolic disturbance, sexual dysfunction, urinary symptoms, gastrointestinal symptoms, and symptoms that reflect raised prolactin, for example, menstrual irregularities and galactorrhoea. Side effects are clinically important as they can cause suffering, impair quality of life, be stigmatising and can lead to nonadherence with antipsychotic medication, which may lead to relapse of the underlying psychiatric disorder. In addition, some side effects can cause secondary physical morbidity and mortality. For example, postural hypotension can lead to a fall and injury, hyperprolactinaemia may lead to osteoporosis, and weight gain contributes to type II diabetes, heart disease and stroke [Lean and Pajonk, 2003; Haddad and Sharma, 2007].

To prevent these outcomes it is important that patients treated with antipsychotics are monitored for potential side effects. If these are detected, their impact on the patient can be explored and potential avenues for treatment can be openly discussed in the clinical consultation. Treatment options will depend on the side effect, its impact on the patient and a careful assessment of both the benefits and drawbacks of continuing the current medication *versus* other strategies. The latter may include dose reduction of the antipsychotic, switching to an alternative antipsychotic or starting a treatment specifically tailored to counter the side effect in question, for example, prescribing an anticholinergic agent for antipsychotic induced parkinsonism.

A systematic approach to side effect monitoring is necessary otherwise side effects can be missed. Patients may be reluctant to discuss some side effects or to report nonadherence with medications because of side effects. Several schizophrenia guidelines have highlighted the advantage of a systematic approach to monitoring; for example, the National Institute for Health and Care Excellence (NICE) guidelines state that antipsychotic side effects should be monitored and recorded 'regularly and systematically throughout treatment, but especially during titration' [NICE, 2009] and the Clinical Standards Board for Scotland guidelines state that it is 'desirable' for antipsychotic side effects to be 'assessed using standardised methods and validated rating scales' [Clinical Standards Board for Scotland, 2001]. However, in clinical practice monitoring for antipsychotic side effects is often haphazard. A UK national audit of nearly 6000 patients prescribed depot antipsychotic medication in 2008 showed that 35% had no documented assessment of side effects in the previous 12 months. The proportion declined during a postaudit improvement programme but was still 18% in a repeat audit in 2011 [Barnes and Paton, 2012].

Some rating scales are designed to assess specific antipsychotic side effects, for example, the Simpson Angus rating Scale (SAS) assesses parkinsonism [Simpson and Angus, 1970], the Barnes Akathisia Scale (BAS) evaluates akathisia [Barnes, 1989] and the Abnormal Involuntary Movement Scale (AIMS) assesses tardive dyskinesia [Guy *et al.* 1976]. Other rating scales assess a range of side effects. For example, the Glasgow Antipsychotics Side-Effect Scale (GASS) covers 22 items (Waddell and Taylor, 2008), the Udvalg for Kliniske Undersøgelser (UKU) [Lingjaerde *et al.* 1987] evaluates 48 possible side effects, the Liverpool University Neuroleptic Side-Effect Rating Scale (LUNSERS) includes 41 items, plus 10 'red herring' items [Day *et al.* 1995] and the Systematic Assessment For Treatment Emergent Events (SAFTEE) has over 70 event terms [Levine and Schooler, 1986]. Some scales are clinician-completed and some are patient-completed.

Among current scales, the GASS is one of the most practical for clinical use (Waddell and Taylor, 2008). It is patient-completed, relatively short (21 items for men and women), global in its coverage, and rates both the frequency and distress of each item. Many of the other scales are impractical for use in routine clinical practice. Among the general scales, the UKU and SAFTEE are time-consuming and require the clinician to conduct a semi-structured interview (a patient-completed version of the UKU is available) [Lindström *et al.* 2001]. The LUNSERS, although patient-rated, is cumbersome. The movement-specific scales, including the AIMS, SAS and BAS, are primarily research tools to characterize in detail a narrow range of side effects.

The purpose of this paper is to describe the development of a short, easy-to-use checklist that could be used in routine clinical practice to screen for a range of common antipsychotic side effects. We emphasize that it is not primarily a research tool, but rather a clinical checklist to identify symptomatic side effects and facilitate subsequent clinician–patient discussion. If it is conducted together with a physical examination and biochemical blood tests, then it can form part of a more

comprehensive assessment of potential antipsychotic side effects.

Methods

Initial concept

An international group of 12 experts including psychiatrists, a general physician and a psychopharmacologist, with extensive collective experience in the treatment of schizophrenia and an interest in drug side effects and tolerability, held a series of discussions in 2008 and 2009 regarding the tolerability of antipsychotics in patients with schizophrenia. Early in these discussions the group concluded that an antipsychotic side effect checklist could be a valuable tool in routine clinical practice. As a next step the feasibility and clinical usefulness of a hypothetical side effect checklist was discussed at a meeting of 109 practising psychiatrists from across Europe, the Middle East and Africa (EMEA). During the discussions electronic voting was used to survey anonymously and to collate the opinions of this wider group on side effect monitoring. Two further meetings, also with electronic voting, were held at later stages in the development of the checklist and are reported subsequently. Key feedback from the first group meeting of 109 psychiatrists included the following:

- 85% of respondents indicated that they used tolerability rating scales or checklists in 25% or fewer of their patients with schizophrenia. The main reason cited for not doing so more often was a combination of limited time and resources.
- 86% felt that a need existed for a new, brief, patient-rated questionnaire for side effects monitoring; 75% recommended that a questionnaire consist of between 5 and 15 items.
- Respondents indicated that they thought that a self-completion checklist for patients to complete in the waiting room and then use in their meeting with their doctor would be a useful addition to currently available assessment instruments.

Development of the SMARTS checklist

Based on the information gathered during these discussions, the faculty developed a checklist termed SMARTS (Systematic Monitoring of Adverse events Related to TreatmentS). It is based on properties considered to maximize the clinical value of such a tool. These included the following.

1. Patient completion. The tool is designed to be completed by patients and as such it employs laypersons' language. It is envisaged that patients can complete it in the waiting room, prior to an appointment with their psychiatrist or other clinician.
2. Simple to use. It should only take a few minutes to complete. There are a total of 11 short questions addressing common and potentially important antipsychotic side effects, with the patient selecting items by circling, plus one open question for miscellaneous side effects (Table 1).
3. Questions apply to present state. This means that repeated use could allow the tracking of change over time. Ideally patients should have a baseline completion of the checklist immediately prior to starting a new antipsychotic.
4. Assesses patient's subjective viewpoint. This is achieved by focusing on symptoms that are 'troubling' the patient. Studies have shown that it is patient's perception of side effects, including the distress they cause, rather than their objective severity as assessed by a clinician, that is most relevant to medication adherence and quality of life [Fakhoury *et al.* 2001; Lacro *et al.* 2002; Lambert *et al.* 2004; Wong *et al.* 2011].
5. Questions refer to problems that 'may' be related to medication. This is because it is often difficult for the patient to be certain of what causes symptoms. Causality is best explored by the clinician when the patient is interviewed, supported by physical examination and blood tests when appropriate, including assessment of adherence with treatments.

In developing the final SMARTS checklist, the faculty took account of feedback on a draft version of the checklist that was discussed in a second meeting of 65 practising clinicians from the EMEA region. At this meeting 65% of attendees indicated they would use the draft tool if it were available.

The choice of 11 side effects to include in the questionnaire was based on the clinical experience of the faculty as well as the existing literature [Hamer and Haddad, 2007; Haddad and Sharma 2007; Lean and Pajonk, 2003]. Together the 11 questions encompass extrapyramidal symptoms (parkinsonism, akathisia), sexual dysfunction,

Table 1. Potential side effects of antipsychotics addressed by questions in the SMARTS checklist.

SMARTS checklist questions (Are you troubled by...)	Potential side effect addressed
1. Difficulties in your movement such as shaking, stiffness or muscle aches?	Parkinsonism, tremor
2. Changes in your weight or appetite?	Weight and appetite change
3. Problems with your sex life?	Sexual dysfunction (may reflect raised prolactin and/or other pharmacological mechanisms)
4. Changes in your periods or changes in your breasts?	Hyperprolactinaemia
5. Dizziness or light-headedness?	Postural hypotension
6. Tiredness or sleepiness?	Sedation
7. Restlessness or feeling fidgety?	Akathisia
8. Constipation, diarrhoea, nausea, stomach problems or dry mouth?	Gastrointestinal side effects (e.g. antimuscarinic side effects)
9. Difficulty passing water or passing water very frequently?	Urinary symptoms (e.g. antimuscarinic action may cause urinary retention; type 2 diabetes may cause polyuria)
10. Problems with your concentration or memory?	Sedation
11. Feeling anxious or depressed?	Affective side effects
12. Any other problems that you think may be related to your medication? Please state	Miscellaneous side effects

symptoms of hyperprolactinaemia, postural hypotension, sedation, appetite and weight change, gastrointestinal side effects, urinary symptoms and affective side effects (Table 1). The latter item was included as antipsychotic-induced dysphoria is a distressing though often neglected side effect [Voruganti and Awad, 2004]. Several of the items on the checklist can be caused by different mechanisms, for example, urinary symptoms ('difficulty passing water or passing water very frequently'; item 9) could include urinary hesitancy, an antimuscarinic effect of an antipsychotic, and urinary frequency, a symptom of type 2 diabetes caused by an antipsychotic. The 11 chosen side effects represented a shortlist of those that appear to be commonest, most clinically relevant and most troublesome for patients and their carers. A complete inventory of all possible side effects would be impractical, but enquiry about additional side effects should be considered during clinical interviews guided by answers to the 12 SMARTS questions as well as to the medications the patient is prescribed.

Early feedback on the SMARTS checklist

Following its development, the final SMARTS checklist was presented at a third meeting that was attended by 50 practising psychiatrists from across the EMEA region. Their feedback was very positive. Most respondents reported that the checklist covered relevant side effects that they encountered in their clinical work, that they would use it in their clinical practice and that the language was appropriate for patients. Subsequently, a number of attendees expressed an interest in translating the document into their own country's language for further dissemination. To date, the SMARTS checklist has been translated into Italian and Turkish. The SMARTS checklist is provided as an Appendix to this paper.

Discussion

The SMARTS checklist represents a simple, pragmatic tool and a useful start for patient–clinician discussion about potential side effects. The emphasis on tolerability (i.e. assessment of side effects that 'trouble' the patient) is deliberate as it is the subjective impact of side effects rather than an objective rating that is particularly relevant to adherence [Lacro *et al.* 2002]. The wording selected for the question stem in patient-completed questionnaires will never cover every clinical possibility that can be encountered. For example, a side effect may go unreported on the SMARTS if it does not 'trouble' the patient yet can still be clinically relevant. However, this is likely to be relatively rare and the faculty which developed SMARTS, and clinicians involved in the review process, were of the opinion that the wording adopted was understandable to patients and had the best

clinical utility of several options considered. It is intended that the checklist will help raise awareness amongst mental health professionals of the importance of monitoring side effects.

The development of the SMARTS checklist by experts in the area, with feedback obtained from clinicians during the process, provides face validity. The scale has not yet been formally assessed in terms of validity and reliability though work in this area is ongoing. It would be helpful for future research to compare the clinical utility of the SMARTS and other patient-completed global side effect rating scales such as the GASS (Waddell and Taylor, 2008) and LUNSERS (Day *et al.* 1995).

The SMARTS checklist is only one part of a full clinical assessment of side effects of antipsychotics. It needs to be complemented by other elements of side effect assessment including careful history taking to identify other, less common adverse effects of drugs, medication adherence, blood tests (especially fasting lipid and glucose levels) and physical examination (for example, determining body mass index and examination for abnormal movements) [American Diabetes Association *et al.* 2004]. The importance of monitoring patients with severe mental illness for cardiovascular risk factors and diabetes is well recognized [de Hert *et al.* 2009] but is often neglected in clinical practice [Fleischhacker, 2009]. The SMARTS checklist is not designed to detect or diagnose serious but rare adverse effects such as neuroleptic malignant syndrome or drug allergies.

Clinicians can use the SMARTS checklist in different ways. One option is for patients to complete it in the waiting room before an appointment with their psychiatrist or another member of the clinical team. It can then form the focus for a clinical discussion about side effects and tolerability. This will allow clarification and exploration of the patient's specific problems; this is important as some SMARTS items (e.g. item 8) encompass several possible side effects. Discussion will help clinicians to make a judgement about whether the symptoms reported on the SMARTS checklist are likely to be drug-related, symptoms of the underlying psychiatric illness, symptoms of a comorbid medical condition, or have a combined cause. Many patients who are prescribed antipsychotics will be simultaneously prescribed other psychiatric drugs, for example, antidepressants, valproate or lithium. These other drugs can cause side effects in their own right and sometimes a side effect such as tremor, sedation or weight gain may be the result of the combined effect of several drugs. The SMARTS checklist was developed primarily to assess antipsychotic side effects. However, we believe that the wide range of side effects it covers, plus the inclusion of a 12th open question, mean that it may be used to help assess side effects and tolerability in patients prescribed psychiatric drugs other than antipsychotics as well as patients prescribed antipsychotics in conjunction with other psychiatric medications. If it is used in this way the clinician will need to judge as to whether to enquire about additional specific side effects, depending on the drug(s) prescribed to that individual, during the consultation.

Management of side effects is best decided in partnership with the patient. Options will depend on the severity of symptoms, their impact on the patient and a weighing up of the benefits and drawbacks of continuing the current medication *versus* alternative options [Weiden and Buckley, 2007]. Potential strategies to manage side effects include reducing the dose of the antipsychotic, switching to an alternative antipsychotic, adopting life style changes (for example, sipping water if troubled by a dry mouth) or prescribing a specific treatment for the side effect (for example, an anticholinergic agent to treat antipsychotic-induced parkinsonism). Irrespective of whether a specific intervention is offered, the SMARTS checklist can be used to monitor change in side effects over time.

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Conflict of interest statement

The authors' involvement in this initiative was part of paid consultancy work with Janssen, which also provided travel expenses for authors to attend group meetings where the checklist was developed. In addition, in the past 3 years all the

authors except M.E.J.L. have received conference support and honoraria for lecturing and other consultancy work from Janssen and other pharmaceutical companies manufacturing antipsychotic drugs. During this period several authors have also received research grants from Janssen and/or other companies.

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Appendix: SMARTS

Systematic Monitoring of Adverse events Related to TreatmentS

Instructions:

We want to be sure that you are receiving the best treatment, and would like to check whether you have any problems which may result from taking your medications.

Please circle any of the following items that trouble you, so that your doctor or nurse can discuss them with you.

Are you troubled by:

1. Difficulties in your movement such as shaking, stiffness or muscle aches?
2. Changes in your weight or appetite?
3. Problems with your sex life?
4. Changes in your periods or changes in your breasts?
5. Dizziness or light-headedness?
6. Tiredness or sleepiness?
7. Restlessness or feeling fidgety?
8. Constipation, diarrhoea, nausea, stomach problems or dry mouth?
9. Difficulty passing water or passing water very frequently?
10. Problems with your concentration or memory?
11. Feeling anxious or depressed?
12. Any other problems which you think may be related to your medication?

Please state_____

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