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A qualitative study of the attitudes of patients in an early intervention service towards antipsychotic long-acting injections

Amlan K. Das, Abid Malik and Peter M. Haddad

Abstract

Objectives: The objective of this study was to investigate attitudinal themes to antipsychotic long-acting injections (LAIs) in patients in an early intervention team (EIT).

Methods: Interviews were carried out with outpatients purposively sampled from an EIT to represent patients currently prescribed antipsychotic LAIs, oral antipsychotics and those not prescribed antipsychotic medication. Interviews were conducted and analysed according to grounded theory. Recruitment stopped when saturation of themes was reached.

Results: Interviews from 11 patients were analysed (median age 24 years). Attitudes to LAIs were condensed into three key categories: therapeutic alliance and the psychiatrists' recommendation of antipsychotic medication; patients' knowledge and beliefs about LAIs; and patients' views regarding the appropriateness of LAIs. Participants valued their psychiatrist's recommendation as to the most appropriate antipsychotic. Attitudes to LAIs varied but were most positive among those currently receiving a LAI. Among those not prescribed LAIs, some were open to considering a LAI if their clinician recommended it but others were opposed to such treatment and preferred tables. There was a lack of awareness of LAIs as a treatment option among those not prescribed a LAI. Delay in being offered a LAI was reported in the group currently prescribed a LAI. Several participants associated oral antipsychotics, LAIs and mental illness with stigma. Some not prescribed a LAI had misperceptions about the nature of this treatment. Participants regarded the advantages of LAIs as convenience and avoiding forgetting to take tablets, while disadvantages included injection pain, fear of needles and coercion.

Conclusion: Lack of knowledge, misperceptions and stigma related to LAIs and other treatment options should be addressed by providing patients with accurate information. This will facilitate patients being involved in choices about treatment, and should they decide to accept medication, which drug and formulation is most appropriate for their needs. Clinicians should avoid making assumptions about patients' attitudes to LAIs; attitudes vary but some early intervention patients not prescribed LAIs are open to considering this treatment. Antipsychotic prescribing should result from a shared decision-making process in which clinicians and patients openly discuss the pros and cons of different formulations and drugs. The themes identified in this qualitative study require further exploration using quantitative methodology.

Keywords: adherence, antipsychotics, attitudes, depot, first-episode psychosis, long-acting injection, schizophrenia

Correspondence to:
Peter M. Haddad, MD, FRCPsych
Consultant Psychiatrist, Greater Manchester West Mental Health NHS Foundation Trust, UK
Honorary Reader, University of Manchester, Cromwell Road, Eccles, Salford M30 0GT, UK
peter.haddad@gmw.nhs.uk

Amlan K. Das, MRCPsych, FRCPC
PTSR Program, Homewood Health Centre, Guelph, and McMaster University, Hamilton, Ontario, Canada

Abid Malik, PhD, MRCPsych
Greater Manchester West Mental Health NHS Foundation Trust, University of Manchester, Salford, UK

Introduction

In clinical practice the effectiveness of maintenance antipsychotic medication in reducing the risk of relapse in schizophrenia is often reduced by nonadherence [Novick *et al.* 2012]. A Finnish observational study found that less than half of patients admitted to hospital for the first time with schizophrenia were continuing medication

30 days post discharge [Tiihonen *et al.* 2011]. A wide range of strategies to manage nonadherence with antipsychotic medication are available, including the use of antipsychotic long-acting injections (LAIs), but the strategy or strategies chosen must be tailored to the individual [Haddad *et al.* 2014]. Observational studies generally report longer continuation rates or reduced rehospitalization rates for patients treated with LAIs compared with those treated with oral antipsychotics, though randomized controlled trials (RCTs) show no significant difference in relapse rates [Kishimoto *et al.* 2014; Kirson *et al.* 2013].

Rates of LAI use vary between countries, but some observational studies found that only a minority of patients with known nonadherence to oral antipsychotics were switched to a LAI [Ascher-Svanum *et al.* 2009]. Rates of LAI use are particularly low in early intervention services [Heres *et al.* 2011]. A significant proportion of clinicians, varying from 34% in a UK study [Patel *et al.* 2010b] to 71% in a German study [Heres *et al.* 2006], regard LAIs as inappropriate for patients with first-episode psychosis. When psychiatrists identified the optimal patient profile for a LAI, first-episode psychosis ranked as one of the least important of 14 potential factors [Heres *et al.* 2008]. In another study, less than 10% of surveyed psychiatrists reported that they offered a LAI after a first episode of psychosis [Jaeger and Rossler, 2010]. Clinicians' beliefs may act as a prescribing barrier to the use of LAIs in early schizophrenia and contribute to LAIs being reserved as a treatment of last resort for patients with chronic schizophrenia who have had repeated hospital admissions secondary to nonadherence with oral medication ('resolving door' patients). The belief that LAIs are inappropriate for patients with first-episode psychosis seems to partly stem from clinicians presuming that such patients are unlikely to accept a LAI [Heres *et al.* 2011; Jaeger and Rossler, 2010]. Another reason may be that some treatment guidelines for schizophrenia emphasize relapse secondary to nonadherence with oral medication as the main indicator for LAI use (e.g. Lehman *et al.* 2004]. In contrast, the National Institute for Health and Care Excellence guideline [NICE, 2014] takes a broader view, recommending that LAIs are considered when avoiding covert nonadherence is a priority or when a patient would prefer a LAI to oral medication.

Research on patient attitudes to LAIs has focused almost exclusively on patients with chronic schizophrenia [Kirschner *et al.* 2013; Waddell and Taylor, 2009]. The lack of data on the attitudes of patients with first-episode psychosis to LAIs prompted the current study. This aimed to explore the attitudes of patients in an early intervention service to antipsychotic LAIs using qualitative methodology. This methodology aims to identity key categories or themes that underlie patients' attitudes; it does not attempt to quantify them.

Methods

Recruitment

The study was conducted in 2010/2011. The only inclusion criterion was that subjects were outpatients under the care of an early intervention team (EIT) serving an urban catchment area in the northwest of England. The team accepts patients within 3 years of the diagnosis of a psychotic illness and aged 18–35 years at entry. The exclusion criteria for the study were as follows:

1. Lacking capacity to consent to be interviewed.
2. Too unwell to participate in the interview process.
3. Insufficient command of English to participate in the interview.

Patients from the EIT were 'purposively' sampled to represent the following groups:

1. Patients prescribed either a LAI or an oral antipsychotic. Both first-generation antipsychotics (FGAs) and second-generation antipsychotics (SGAs) were represented within the LAI and oral groups.
2. Patients who had opted not to take antipsychotic medication and with different levels of insight.
3. Male and female patients.
4. White patients and patients from ethnic minority groups.

The study received ethical and research governance approval and all subjects gave signed consent to take part. All potential subjects were informed that the interviews were confidential and anonymous.

Interview process and analysis

Face-to-face interviews were conducted by the researcher (AD) who was not known clinically to

any of the participants. Interviews were conducted either in the patient's home or a consultation room in a community mental health centre. The interviews were audio recorded or if the patient did not agree to this, written notes were taken. Recordings were transcribed verbatim as Microsoft Word documents using standard notation for pauses and nonverbal communication [Strauss and Corbin, 1990]. For patients who did not agree to be taped, the handwritten notes were typed as Microsoft Word documents. After transcription the audio files and any original hand written notes were destroyed. All identifiable data were removed from the transcripts.

The first three interviews were conducted using a semi-structured questionnaire that explored key areas thought to be relevant to patients' attitudes to antipsychotic formulation based on a literature review. Questions/topics included whether the patient was currently taking antipsychotic medication or had in the past, was aware of LAIs, whether they had been offered a LAI in the past, their views about the information they were given about antipsychotic medication and choice of formulation, their views about the advantages and disadvantages of oral medication and LAIs, whether they would consider switching to a LAI in the future etc. Cues offered by the participants were used to inform the style and direct further lines of questioning during the interviews. The raw data (transcripts) from the first three interviews were analysed following grounded theory methods [Strauss, 1987].

The analysis identified meaningful segments, labelled each with a code and then condensed these into meaningful categories. A key feature was that the data were analysed as they emerged, checked against data already collected, with the researcher actively looking to identify new themes that characterized the patients' attitudes and views towards LAIs. The resulting information allowed the topics/questions that guided subsequent interviews to be refined, modified and developed, a process that continued with each subsequent interview. In looking for new categories the researcher tried to avoid being unduly biased by assumptions that originated from the existing literature. In keeping with grounded theory, recruitment continued until a point of saturation of themes was achieved, that is, no new concepts emerged from new interviews. Previous studies using this methodology indicate that 10–20 participants are required to achieve this [Strauss and Corbin, 1990].

Results

Sample

Thirteen patients were recruited but one was considered to be too mentally unwell to complete the interview and a second patient withdrew consent during the interview. In summary, data from 11 patients were analysed. Recruitment was stopped after 11 completed interviews as the last two interviews did not reveal any new themes, that is, saturation had been reached. Most interviews were 30–45 min in duration. Among the 11 participants the median age was 24 years (range 18–40 years) and all but one patient was aged under 30 years. Six patients were male, 10 were white and one was Asian. Seven of the participants had been in contact with the EIT for less than 1 year, three for between 1 and 3 years and one for over 3 years. None of the patients were subject to a community treatment order, that is, all patients who were taking medication did so voluntarily. Three participants were prescribed a LAI, four were prescribed an oral antipsychotic (one took this in liquid form) and four were not currently taking antipsychotic medication, though they had in the past. Only one patient currently taking medication reported his recent adherence as poor.

Analysis showed that attitudes to antipsychotic LAIs could be condensed into three categories: therapeutic alliance and the psychiatrists' recommendation of antipsychotic medication; patients' knowledge and beliefs regarding LAIs; and patients' views about the appropriateness of LAIs. These will be considered in turn.

Therapeutic alliance and the psychiatrists' recommendation of antipsychotic medication

A repeated theme was that patients trusted their treating psychiatrist to advise them or help them choose an initial antipsychotic medication and a new antipsychotic should a change be necessary. This trust encompassed advice on LAIs and oral antipsychotic medication. Several participants highlighted that accepting the psychiatrist's advice on medication had been particularly important to them as they had been too unwell when medication was initiated to be fully involved in the decision.

Patients' knowledge and beliefs regarding LAIs

Of those not currently prescribed a LAI, half stated that they knew little and the other half that

they knew nothing about the option of taking antipsychotic medication as a LAI prior to the interview. All reported that this option had either not been discussed with them by their clinical team, or if it had, they could not remember such a discussion. Comments included 'did not have enough information', 'did not know other forms of medication were available' and 'doctors did not tell me'. Lack of knowledge was also evident in the group prescribed a LAI. One patient prescribed a LAI reported that he had been in treatment for 3 years but had only learnt about the option of a LAI 3 months previously when his psychiatrist discussed it with him. He stated he would have chosen a LAI earlier had he received the information sooner. Several participants said that side effects, including weight gain and sedation, influenced their choice of antipsychotic whatever the formulation. LAIs were not seen as causing either more or fewer side effects than oral antipsychotics.

Several misperceptions about LAIs were voiced by those not prescribed a LAI. A patient, currently on no medication but in remission, feared that he might get 'addicted' to a LAI as it was administered by an injection. This view related to him associating 'addiction' with injectable 'street drugs'. He did not have psychosis and this concern was rational to him. Another patient queried whether a LAI needed to be injected daily 'like insulin'. One subject, who paid for her prescriptions of oral antipsychotic medication, was concerned that the prescription cost for the patient may be higher for a LAI than for an oral medication. Most subjects did not have an idea of comparative costs of LAI *versus* oral antipsychotic medication. Three participants regarded LAIs as being associated with stigma as evidenced by statements including 'people on the street might look at you differently' or think your illness is 'really severe' or think 'you're weird' (if they know you are taking an injection). Stigma was not unique to LAIs. One participant regarded oral medication as more stigmatizing than LAIs as tablets need to be taken daily. Two patients believed antipsychotic medication was associated with stigma but that the formulation was irrelevant to this. One highlighted the stigma of severe mental illness itself.

When the ideal frequency of administration of a LAI was discussed most participants indicated that once a month would be ideal. Two patients, one male and another female, expressed a preference for the deltoid rather than gluteal injection site. Several female participants stated that if they were prescribed a LAI in the future they would prefer a female nurse to administer the injections.

Patients' views regarding the appropriateness of LAIs

Views about the appropriateness of LAIs varied irrespective of whether patients were currently prescribed a LAI. Among those not currently prescribed a LAI, most (n = 6/8) were open to the possibility of considering a LAI rather than oral medication in the future should this be recommended by their psychiatrist and, for those not taking medication, should they decide to take medication. The remaining two patients, one on oral medication and one taking no medication, were adamant that they would not want to be prescribed a LAI. Within the group taking a LAI (n = 3), two patients stated that they clearly preferred a LAI to oral antipsychotics. This included one participant who stated that he would recommend a LAI to others. The third patient prescribed a LAI regarded the treatment as coercive and said that he was taking it as he 'would be given it anyway'. He had limited insight into his psychotic illness.

Most participants were able to identify advantages and disadvantages of the two formulations. Ease of use and avoiding forgetting taking tablets were repeatedly cited as advantages of LAIs, though one patient stated that having to leave home to receive a LAI, a reference to attending a 'depot clinic', was a downside. Disadvantages of LAIs that were given included injection site pain, fear of needles and the perceived stigma of taking an injection. Pain and fear of needles were not widespread concerns and were predominantly reported by those not prescribed LAIs. Advantages of oral medication given by participants included privacy, greater control of medication taking and greater dignity but reported disadvantages included requiring prompts from relatives to take medication, the risk of forgetting medication and tablets being a daily reminder of their illness.

Discussion

This is the first study we are aware of that specifically investigates the attitudes of patients in an early intervention service to LAIs. A strength of the study is the use of purposive sampling to

recruit patients encompassing a range of demographic characteristics and different degrees of medication adherence, as well as individuals prescribed oral antipsychotics, LAIs and those not taking antipsychotic medication. The researcher conducting the interviews (AD) was not clinically known to any of the participants; this was to encourage participants to be frank and to reduce a tendency towards social desirability in their responses. Grounded theory tries to guard against the researcher's preconceptions and to explore responses from a neutral perspective. Further work is needed to confirm our results, which should be regarded as preliminary due to sampling from a single service, and to quantify the themes we have identified. However, the results have resonance in previous research. The three identified categories that underlie attitudes to LAIs provide clinicians with a framework to understand and improve access to LAIs and potentially improve adherence and clinical outcomes in early psychosis.

Therapeutic alliance and the clinician's recommendation on medication emerged as crucial themes. A positive therapeutic relationship with clinicians is known to be associated with better medication adherence in schizophrenia [Dassa *et al.* 2010; McCabe *et al.* 2013; Weiss *et al.* 2002] and the current study extends this to patients in an early intervention service and to LAIs. Our data also suggest that the psychiatrist's recommendation of treatment will influence the likelihood of it being accepted by a patient. Conversely if a clinician conveys a negative view about a LAI to a patient it may lead to rejection of the treatment. This is a concern given that a significant proportion of psychiatrists do not regard LAIs as appropriate in first-episode psychosis [Kirschner *et al.* 2013].

A striking finding was that participants who were not prescribed a LAI reported having little or no prior awareness of this treatment option while those prescribed LAIs reported a delay in receiving information about LAIs. Patient recall of treatment decisions made in consultations is poor, even in the short term [Skinner *et al.* 2007] and it may be that participants had forgotten information that they had been given about LAIs. However, even if this is the case, it highlights the importance of repeated discussions, when clinically relevant, between the psychiatrist and patient about choice of medication, including formulation. Our results are consistent with a Swiss study in which two-thirds of patients with schizophrenia, and nearly 80% of those not prescribed an LAI, reported not receiving information about the availability of depot antipsychotics from their psychiatrist [Jaeger and Rossler, 2010]. The NICE schizophrenia guideline states that a LAI should be considered if a patient has a preference for such treatment [NICE, 2014]. Patient preference can only be exercised if patients have information on the alternatives available. Psychiatrists need to ensure that patients are given comprehensive information about medication choices, including the range of formulations available.

In terms of beliefs about LAIs, injection pain and fear of needles was raised as a downside of LAIs but was not a major theme. Injection site pain is the most common injection site complication of LAIs but is not persistent and tends to reduce with successive injections [Haddad and Fleischhacker, 2011]. Several patients perceived LAIs as being associated with stigma, in particular that receiving a LAI would lead others to think that their illness was severe. Stigma was not restricted to LAIs, with some regarding antipsychotics in general and psychosis as stigmatizing. Furthermore one participant regarded a LAI as less stigmatizing than oral medication on the basis that tablets need to be taken daily. Several participants not prescribed LAIs held misperceptions, including querying whether a LAI could be addictive (an association was made with intravenous drug misuse) or needed to be administered daily (an association was made with insulin). One patient was concerned that the prescription cost for patients could be higher for a LAI than for an oral antipsychotic. In reality, most patients with schizophrenia in the UK are not required to pay prescription charges, irrespective of the formulation, and if a charge was due it would not differ by formulation for National Health Service patients. The results highlight the importance of providing patients with accurate information about treatment options and of mental health organization continuing to combat stigma, which is a major challenge in mental illness, particularly in patients with first-episode psychosis [Windell and Norman, 2013].

Most participants were able to identify advantages and disadvantages of the two formulations. Among those currently prescribed oral medication, or not taking antipsychotic medication, most expressed an openness to consider a LAI in the future should this be recommended by their

doctor. Conversely a smaller number were strongly opposed to considering a LAI and preferred oral medication. Attitudes towards LAIs were most positive in those currently prescribed a LAI, though one patient prescribed a LAI reported feeling coerced to take this treatment. Patel and colleagues found that patients prescribed LAIs were more likely to report feeling coerced to take medication than those prescribed oral medication [Patel *et al.* 2010a]. Antipsychotic prescribing, irrespective of formulation, needs to result from a shared decision-making process.

Conclusion

The lack of knowledge and misperceptions about LAIs that were identified indicate that patients need to be provided with balanced and accurate information about LAIs. Information can be provided by the clinical team in existing meetings as well as in more formal psychoeducational programmes [Rummel-Kluge and Kissling, 2008]. Patients may benefit from peer to peer education from another patient prescribed a LAI, though as far as we are aware the effectiveness of this approach has not been formally investigated for LAIs. The fact that a proportion of patients, managed within an early intervention service, report being willing to consider a LAI means that clinicians should avoid making negative assumptions about patients' attitudes to LAIs. Conversely, some patients regard LAIs as stigmatizing and coercive, confirming the view of previous researchers that LAIs have an 'image problem' for some patients as well as clinicians [Patel *et al.* 2003]. Reserving LAIs as a treatment of last resort for 'revolving door' patients is likely to reinforce negative perceptions. Two recent systematic reviews found evidence that LAIs can be effective in patients with first-episode psychosis [Emsley *et al.* 2013; Taylor and Ng, 2013]. The data included a national cohort study in which outcomes were better for those treated with LAIs than the identical antipsychotics in oral form [Tiihonen *et al.* 2011]. The lack of a large well conducted RCT comparing a LAI with oral antipsychotic medication in first-episode psychosis remains a significant gap in the current evidence base. Despite this, the existing evidence base plus the relatively positive attitudes to LAIs seen among a proportion of early intervention patients suggest that LAIs should be discussed more widely as a potential treatment option within this population.

The importance that patients place on therapeutic alliance and the clinician's recommendation of medication highlights the responsibility that clinicians have when discussing medication options with patients. Antipsychotic prescribing should result from a shared decision-making process in which clinicians and patients openly discuss the pros and cons of different formulations and drugs. Medication is only one element of the treatment of schizophrenia and should be accompanied by psychosocial interventions. The themes identified in this qualitative study require further exploration using qualitative methodology.

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Conflict of interest statement

PMH has received expenses to attend conferences and fees for lecturing and consultancy work (including attending advisory boards) from various pharmaceutical companies, including some that manufacture antipsychotic LAIs: Eli-Lilly, Janssen, Lundbeck and Otsuka. AM has received conference expenses from Eli-Lilly, Bristol-Myers Squibb and Nutricia. AD has no conflicting interests.

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