An evaluation of subjective experiences, effects and overall satisfaction with clozapine treatment in a UK forensic service

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Abstract

Objectives: Patients prescribed clozapine were surveyed to assess (a) the effects, both positive and adverse, and overall satisfaction with clozapine in comparison to previously prescribed antipsychotics and (b) the relative significance of effects experienced, both positive and adverse, in terms of impact on subjective well-being.

Methods: A total of 56 male patients prescribed clozapine at a forensic psychiatric hospital were surveyed using a 27-item questionnaire. All patients had been prescribed clozapine for a minimum of 3 months. Respondents were asked to rate effects and satisfaction with clozapine treatment in comparison with previously prescribed antipsychotic medication on a five-point scale. Respondents were also asked to rate effects experienced with clozapine treatment in terms of impact on subjective well-being on a five-point scale.

Results: A total of 89% of respondents reported greater satisfaction with clozapine than with previously prescribed antipsychotic medication. A majority of patients reported positive effects in terms of an improvement in their quality of life (68%) and social abilities (52%) with clozapine in comparison with previously prescribed antipsychotics. Nocturnal hypersalivation (84%) and weight gain (57%) were the most common adverse effects. Hedonic responses were assessed for each effect in order to determine the associated subjective experiences. The most positive hedonic responses were for quality of life, mood and alertness. In terms of adverse impact on subjective well-being, nocturnal hypersalivation ranked highest.

Conclusions: Patients in a UK forensic sample are largely satisfied with clozapine treatment. The subjective effects of clozapine treatment should be taken into account by clinicians when assessing response. This may provide an opportunity to highlight the positive changes and prioritize management of the most undesirable adverse effects, which is likely to promote compliance and improve longer term treatment outcomes.

Keywords: clozapine, forensic, side effects, subjective experience

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Introduction

Clozapine is an atypical antipsychotic used in the treatment of resistant schizophrenia with an established efficacy superior to other antipsychotics [Wahlbeck *et al.* 1999]. Clozapine is associated with a range of side effects including those which are rare and life-threatening such as cardiomyopathy [Hagg *et al.* 2000], and others that are relatively common such as hypersalivation [Syed *et al.* 2008] and weight gain [Wirshing *et al.* 1999]. Discontinuation of clozapine is not uncommon in the first year [Ciapparelli *et al.* 2000], with a large proportion due to side effects experienced [Taylor *et al.* 2009].

Clinicians tend to place greater emphasis on adverse effects that are in fact of lesser importance to patients, such as the frequent blood tests required with clozapine treatment [Hodge and Jespersen, 2008]. Additionally previous reports of the adverse effects of clozapine treatment have largely reported on their prevalence and not assessed the subjective importance attributed to them by patients [Angermeyer *et al.* 2001]. The

aim of this survey was to assess patient satisfaction with clozapine in comparison with previous antipsychotics and patients' experience of the side effects of clozapine treatment as well as its impact on subjective well-being.

Method

The survey was undertaken at a forensic psychiatric hospital in the north-west of England. All patients prescribed a stable dose of clozapine for a minimum of 3 months were approached to take part in the survey. Of the 67 patients approached, 84% of patients agreed to participate in the survey and data were collected by medical staff who were part of the patient's care team.

The survey sample consisted of 56 men, with a mean age of 37.9 years [standard deviation (SD): 10.6, range: 22–59 years). A total of 42 respondents were White British, while the remainder included: 3 Other White; 3 White or Black Caribbean; 2 Black Caribbean; 2 Black African; 2 Pakistani; 1 Black or White African; and 1 Other Asian Background. The mean daily dose of clozapine was 349.3 mg (SD: 134.0 mg, range: 125–850 mg) and the mean length of prescription was 520.1 days (range: 93–2074 days).

A 27-item questionnaire was used to assess subjective experiences with items adapted from a North American survey [Waserman and Criollo, 2000]. Respondents were asked to rate side effects and satisfaction with clozapine in comparison to previously prescribed antipsychotic medication on a five-point scale (much worse, worse, no different, better, much better). We also asked respondents to rate the effects experienced in terms of hedonic response (how they felt about them) on a five-point scale (very unhappy about it, unhappy about it, don't mind either way, happy about it, very happy about it).

All data were gathered in accordance with the service evaluation standards of the responsible institutional review board (Research Governance Committee, Mersey Care NHS Trust).

Results

Respondents were largely positive about clozapine treatment: 86% of respondents reported that treatment with clozapine was better than treatment with previous antipsychotics and none thought it worse; 89% of respondents reported greater satisfaction with clozapine; and 96% reported better compliance with clozapine treatment than with previously prescribed antipsychotics.

Ratings of changes in side effects as a result of clozapine treatment are shown in Table 1. Responses revealed the most positive effects with clozapine treatment were in the domains of quality of life (mean: 3.93) and social abilities (mean: 3.59); 68% of patients (n = 38) reported their quality of life had improved and 52% of patients (n = 29) reported an improvement in their social abilities. A total of 46% of respondents (n = 26) reported improvements in 'thinking' (a marker for cognitive ability) since starting clozapine treatment but 13% (n = 7) reported a deterioration in 'thinking'. Similarly, 48% (n = 27) reported improvements in sleep but 20% (n = 11) reported worse sleep than before. An improvement in mood was reported by 43% (n = 24) of the patients.

Nocturnal hypersalivation was overwhelmingly the most frequently reported negative side effect, reported by 84% of patients (n = 47) (mean: 1.72); 57% of the patients (n = 32) also reported weight gain (mean: 2.29), 41% (n = 23) reported deterioration in daytime salivation and 39% reported an increase in constipation (n = 22). In addition, 27% of patients also reported a worsening of thirst (n = 15).

To assess the subjective experience of effects associated with clozapine, hedonic responses were grouped into those patients for whom the effect had improved and those for whom it had deteriorated. The hedonic ratings were then averaged for each of the two groups. To maintain reliability of the ratings, only groups that included at least 20% of patients were included (see Table 2). Whilst many side effects deteriorated for many patients, the hedonic impact of this deterioration varied. For example, patients disliked the change in weight (mean hedonic rating: 1.81) more than they disliked the change in appetite (mean hedonic rating: 2.18). However, the most adverse impact on subjective well-being by far was deterioration in nocturnal salivation (mean hedonic rating: 1.72).

Effects that improved as a result of clozapine treatment included a range of responses. For example, when patients perceived an improvement in quality of life, they reported being slightly happier about this (mean hedonic rating: 4.37)

Table 1. Subjective experiences of side effects: ratings of clozapine treatment compared with previous antipsychotic treatment ($n = 56$).

After starting clozapine, did the following change?	Number of responses					Mean rating
	Much worse [1]	Worse [2]	No different [3]	Better [4]	Much better [5]	
Nocturnal salivation	26	21	7	2	0	**1.72**
Weight	14	18	19	4	1	**2.29**
Daytime salivation	7	16	33	0	0	**2.46**
Constipation	7	15	30	4	0	**2.55**
Thirst	1	14	39	2	0	**2.75**
Dry mouth	4	9	40	1	2	**2.79**
Itchiness	1	10	45	0	0	**2.79**
Unusual movements	2	10	42	2	0	**2.79**
Sweating	1	8	47	0	0	**2.82**
Dizziness	0	11	43	2	0	**2.84**
Wetting yourself – night	2	7	46	0	1	**2.84**
Vision	1	9	43	2	1	**2.88**
Abdominal pain	1	5	49	1	0	**2.89**
Breathing	1	7	45	2	1	**2.91**
Energy levels	1	20	21	11	3	**2.91**
Headache	2	1	52	1	0	**2.93**
Unusual sensations	1	5	48	1	1	**2.93**
Urination	0	6	48	1	1	**2.95**
Wetting yourself – day	0	1	54	0	1	**3.02**
Alertness	1	7	32	15	1	**3.14**
Activity level	0	10	26	16	4	**3.25**
Appetite	0	11	22	17	6	**3.32**
Sleep	2	9	18	21	6	**3.36**
Mood	0	5	27	16	8	**3.48**
Thinking	1	6	23	12	14	**3.57**
Social life	1	1	25	22	7	**3.59**
Quality of life	0	2	16	22	16	**3.93**

Note: Change ratings were on a 5-point scale where 1 = 'much worse than before' and 5 = 'much better than before'.

Table 2. Mean hedonic ratings of side effects with clozapine treatment grouped by deterioration and improvement ($n = 56$).

Effects that **deteriorated** for 20% or more of patients			Effects that **improved** for 20% or more or patients		
	mean hedonic rating	*% patients (n)*		*mean hedonic rating*	*% patients (n)*
Nocturnal salivation	1.72	84% (47)	Quality of life	4.37	68% (38)
Weight gain	1.81	57% (32)	Activity level	4.35	36% (20)
Daytime salivation	1.83	41% (23)	Alertness	4.31	29% (16)
Constipation	1.86	39% (22)	Social life	4.24	52% (29)
Unusual movement	2.00	21% (12)	Mood	4.21	43% (24)
Energy	2.14	38% (21)	Thinking	4.19	46% (26)
Dry mouth	2.15	23% (13)	Energy levels	4.14	25% (14)
Appetite	2.18	20% (11)	Sleep	4.07	48% (27)
Itchiness	2.27	20% (11)			
Sleep	2.27	20% (11)			
Thirst	2.40	27% (15)			
Appetite	2.87	41% (23)			

Note: Feelings rated on a 5-point scale: 1 = very unhappy about it; 2 = unhappy about it; 3 = don't mind either way; 4 = happy about it; 5 = very happy about it.

than about the improvement in energy levels (mean hedonic rating: 4.14). Similarly, despite the fact that social abilities received the second highest mean change rating (mean change rating: 3.59), patients were as happy about this (mean hedonic rating: 4.24) as they were about the change in alertness (mean change rating: 3.14; mean hedonic rating: 4.31).

Discussion

We could not find any previous published survey that sought to explore the effects and overall satisfaction with clozapine and the relative significance of effects experienced, both positive and adverse, in terms of impact on subjective well-being. In this survey in a UK forensic mental health service, 86% of the respondents reported treatment with clozapine as very positive in comparison with previous medication and 68% of the patients reported improved quality of life.

These are important findings for clinicians within a forensic setting, particularly where there has been a delay in commencing clozapine [Howes *et al.* 2012] and our findings are similar to a survey in a non-forensic sample [Taylor *et al.* 2000]. In our survey, nocturnal hypersalivation was the most commonly experienced adverse effect and this is consistent with a previous survey of the prevalence of adverse effects in North America [Waserman and Criollo, 2000].

The added contribution that our survey makes is in asking respondents about the associated significance attached to each side effect; responses indicated clear differences in terms of impact on subjective well-being. For example, nocturnal hypersalivation was the most distressing side effect experienced by our sample of patients followed by weight gain. In terms of positive effects when patients perceived an improvement in quality of life, they reported being slightly happier about this than about the improvement in energy levels. Patients also attributed a large subjective significance to improvement in mood.

Patients' subjective experiences of medication are important and it is recognized that these are powerful predictors of adherence [Fujikawa *et al.* 2008], which in turn influences treatment outcomes [Hellewell, 2002]. However, many patients with a diagnosis of schizophrenia discontinue their medication in the first few years, citing their experience of side effects as a crucial aspect of their decision [Kampman and Lehtinen, 1999]. We suggest that clinicians should be aware of the relative impact of different side effects. Several instruments have been developed to evaluate perceived side effects of antipsychotic treatment: Medication and Adherence Rating Scale [Thompson *et al.* 2000]; Self-rating Scale to Measure Subjective Well-being under Neuroleptic Treatment [Naber, 1995]; and Patient Assessment Questionnaire [Mojtabai *et al.* 2012]. We are not aware of these being used in routine clinical practice and it might be worth exploring the use of such instruments whilst patients wait in clozapine clinics and the responses discussed at subsequent clinical reviews.

This was a survey of patients established on clozapine therapy with a minimum duration of treatment of 93 days and mean duration of 520 days, indicating the sample is positively biased in favour of clozapine therapy. Additionally, the relatively small number of respondents in this survey may not be representative of patients in other forensic services. However, we had an encouraging response rate and our population of a broad ethnic mix of patients, although exclusively male, is unlikely to be significantly different from other male forensic populations.

In conclusion, clinicians should routinely explore not only the presence of effects of clozapine treatment, both positive and negative, but also their subjective importance in terms of impact on well-being. This may provide an opportunity to highlight the positive changes and to prioritize management of the most undesirable adverse effects, which is likely to promote adherence to medications and improve longer term treatment outcomes.

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Conflict of interest statement

The authors declare no conflicts of interest in preparing this article.

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