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## Survey of clozapine use by consultant old age psychiatrists

### AIMS AND METHOD

The aim of the survey was to assess the attitudes of specialists in old age psychiatry towards the use of clozapine in elderly patients. A postal questionnaire was sent to a random sample of 155 consultant old age psychiatrists in England.

### RESULTS

The response rate was 87%. A majority of respondents felt that clozapine had a useful place in the treatment of elderly patients, although they expressed concerns about the lack of published data and about safety and practical difficulties in monitoring. Prescribers of

clozapine ( $n=45$ ) were significantly more positive about its role in treating older patients than those who had not used it.

### CLINICAL IMPLICATIONS

The findings suggest that familiarity with and confidence in clozapine and practical difficulties in monitoring are important determinants of its use in older patients.

With increased life expectancy the number of older patients with psychoses is expected to rise (Jeste *et al*, 1996). Antipsychotic drugs are the most effective treatment for late-onset psychosis; however, a significant proportion of patients do not respond to conventional and/or atypical antipsychotics, and treatment resistance may be more common in elderly people than in younger adults with schizophrenia (Tran-Johnson *et al*, 1992). Clozapine is an atypical antipsychotic that is widely used in treatment-resistant psychosis and significantly improves quality of life and social functioning (Bachana, 1995). Case reports, open-label studies and double-blind comparison studies have concluded that clozapine at a relatively low mean dosage (134 mg per day) is safe and effective for elderly patients with treatment-resistant psychosis and that patients are able to continue treatment for extended periods (Sajatovic *et al*, 1997; Barak *et al*, 1999; Howanitz *et al*, 1999). Agranulocytosis owing to clozapine is more frequent than in younger adults and should be monitored carefully. Active monitoring of patients treated with clozapine has reduced predicted agranulocytosis rates (Honigfeld, 1996) and ensured adherence (Munro *et al*, 1999). Reports suggest that clozapine may be successfully used to treat psychosis associated with Parkinson's disease (Poewe & Seppi, 2001). However, a recent study from the UK found that clozapine usage was proportionately lower among older patients with psychosis compared with adults of working age (Woodall *et al*, 2004). To explore why this might be so, a postal questionnaire was devised to survey the practices and attitudes towards clozapine of consultants in old age psychiatry in England.

### Method

The questionnaire covered the following areas: consultants' own experience of using clozapine; their views of clozapine's usefulness in elderly patients; and their views on the barriers to using clozapine in older adults. In addition, the questionnaire included a section for written open comments.

It was sent initially to 10 local consultants in old age psychiatry to pilot its suitability and ease of use. The questionnaire was modified based on their responses and sent by post to a representative sample of consultants in old age psychiatry in England ( $n=155$ ) in April 2005, along with a covering letter explaining the purpose of the study and a stamped addressed envelope. The sample was taken randomly from a national database of old age psychiatrists updated in 2004 by the Policy and Social Services Research Unit of the University of Manchester (Professor D. Challis). Questionnaires were marked with a code so that non-responders could be identified but anonymity was maintained. A reminder was sent to non-responders 6 weeks later.

For questions seeking an opinion, a five-point Likert scale was used, ranging from 'definitely' to 'definitely not', or 'strongly agree' to 'strongly disagree'. The data were analysed using the Statistical Package for the Social Sciences, version 13.0 for Windows. The  $\chi^2$  test was used to examine categorical responses.

### Results

One hundred and thirty-five replies were received, representing a response rate of 87%. The characteristics of respondents are shown in Table 1, and their responses are analysed in Tables 2 and 3.

Sixty-one consultants (45%) had patients who were prescribed clozapine under their care. Of these consultants, two-thirds ( $n=39$ ) had initiated clozapine treatment themselves (29% of the whole sample). Almost all consultants had used clozapine for treatment-resistant schizophrenia. A very small proportion had used it for other indications, including schizoaffective disorder, Parkinson's disease, Lewy body dementia, bipolar affective disorder and other organic psychosis. There was no statistically significant difference between consultants' age, experience, gender and whether or not they had patients on clozapine under their care. Likewise, there was no statistically significant difference between consultants' age, gender or experience and their views

**Table 1. Characteristics of respondents**

	Respondents	
	<i>n</i>	(%)
Age, years		
30–39	17	(12.6)
40–49	70	(51.9)
50–59	42	(31.1)
> 60	5	(3.7)
Data missing	1	(0.7)
Gender		
Male	78	(57.8)
Female	54	(40.0)
Data missing	3	(2.2)
Experience as consultant		
< 10 years	87	(64.4)
11–20 years	37	(27.4)
> 20 years	9	(6.6)
Data missing	2	(1.5)
Patients treated with clozapine	61	(45.2)
If so, initiated by respondent	39	(28.9)

about clozapine having a useful place in the treatment of the elderly.

A majority of respondents (between 57% and 90%) expressed concerns about the lack of published data, and the safety and side-effects of clozapine in the elderly, or were concerned about physical comorbidity – even though two-thirds (67%) indicated that clozapine had a useful place in the treatment of elderly patients (Table 2). Those who had patients under their care treated with clozapine were more likely to say that it had a useful place in the care of the elderly than consultants who had no patient taking the drug (83.6% v. 51%;  $\chi^2=14.12$ ,  $P<0.0001$ ). Around two-thirds of the consultants agreed or strongly agreed that limited personal experience with clozapine was a reason for its limited use (Table 3). A third

of respondents would consider using clozapine more if a community phlebotomy service were available and a fifth would consider using clozapine more in the light of UK restrictions on the use of atypical antipsychotics in patients with dementia or cerebrovascular risk factors (Committee for the Safety of Medicines, 2004).

Twenty-five additional written comments were made, with two themes emerging: the practical difficulties of regular blood monitoring and a lack of evidence specifically in older patients.

## Discussion

The high response rate from a nationally representative sample of old age psychiatrists in consultant posts is encouraging. The majority of consultants agreed that clozapine is effective in the elderly but under half had recent experience with its use. There was a range of concerns regarding its use in older patients, but this survey suggests that familiarity and confidence of consultants are important determinants of its use in older patients. However, there were also concerns about a lack of published data regarding elderly patients and practical difficulties in blood monitoring. Given the community orientation of old age psychiatry in England, there was a specific concern about a lack of community phlebotomy services.

Although not a comparative study, this survey adds to the data that suggest that older patients with schizophrenia are prescribed clozapine less often than younger adult patients (Woodall *et al*, 2004). This does not appear to be offset by the prescription off-label of clozapine in other psychotic disorders which occur often in later life, such as the Lewy body–Parkinson's psychosis spectrum. In part this is a reflection of the lack of data specific for older adults which many respondents highlighted. It seems especially important to advocate such research

**Table 2. Consultants' responses to questions concerning the use of clozapine (n=135)**

Question	Definitely/ probably % <sup>1</sup>	No opinion %	Probably not/ definitely not %
What do you think are the indications for clozapine?			
Schizophrenia in patients < 65 years old	95.5	2.2	0.7
Schizophrenia in patients > 65 years old	73.4	6.7	18.5
Schizoaffective disorder	51.9	21.8	25.2
Bipolar affective disorder	7.4	17.8	72.6
Parkinson's disease	43.0	14.1	42.2
Dementia	19.3	8.1	71.9
Do you think clozapine has a useful place in treating elderly patients?	66.6	7.4	24.5
Would you consider using clozapine more in the light of CSM recommendations? <sup>2</sup>	21.4	10.4	68.1
If there was a community phlebotomy service, would you consider using clozapine more?	34.1	13.3	51.1

CSM, Committee for the Safety of Medicines.

1. Not all rows add up to 100% because of missing data.

2. In the UK in 2004 the CSM advised against use of atypical antipsychotics in the treatment of patients with dementia, whether psychotic or not, and cautioned against their use in patients with cerebrovascular risk factors.



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**Table 3. Consultants' views on possible reasons for the limited use of clozapine in elderly patients (n=135)**

	Strongly agree/ agree % <sup>1</sup>	Neutral %	Disagree/ strongly disagree %
Concerns about efficacy	17.8	20.0	62.2
Concerns about safety	90.4	3.0	6.6
Concerns about anti-cholinergic side-effects	57.0	31.1	8.1
Concerns about agranulocytosis	82.3	11.9	5.1
Concerns about cardiovascular side-effects	68.9	26.7	3.0
Concerns about medical comorbidity	79.3	17.0	2.9
Practical difficulties in monitoring WCC	71.8	8.9	19.2
Limited published data	84.4	13.3	2.2
Limited personal experience	73.3	11.9	14.9

WCC, white cell count.

1. Not all rows add up to 100% because of missing data.

given an anticipated rise in overall numbers of older patients with psychotic disorders. The results are consistent with a recent survey of the prescription of clozapine to adolescent patients, with similar reasons for non-use cited (Cirulli, 2005).

A further issue identified in our survey concerns the natural tendency of clinicians to feel confident about prescribing treatments they have used successfully and, conversely, reluctance to use ones with which they are unfamiliar such as clozapine. This might be best addressed by training within the context of continuing professional development. Finally, practical barriers to blood monitoring, especially a lack of community phlebotomy services, should be addressed.

## Declaration of interest

None.

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