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Characteristics of patients expressing an interest in ketamine treatment: results of an online survey

Jolien K. E. Veraart, Sanne Y. Smith-Apeldoorn, Hayley Trueman, Marrit K. de Boer, Robert A. Schoevers and Rupert McShane

Background
Off-label ketamine treatment has shown acute antidepressant effects that offer hope for patients with therapy-resistant depression. However, its potential for integration into treatment algorithms is controversial, not least because the evidence base for maintenance treatment with repeated ketamine administration is currently weak. Ketamine is also a drug of misuse, which has raised concerns regarding the target population. Little is known about which patients would seek ketamine treatment if it were more widely available.

Aims
To explore some of the characteristics of the patients actively seeking ketamine treatment.

Method
An online survey containing questions about duration of current depressive episode, number of antidepressants used and other comments was completed by patients who were exploring the internet regarding the possibility of ketamine for depression.

Results
Of the 1088 people who registered their interest, 93.3% reported depression, 64.3% reported a chronic course of their symptoms and in the past 10 years, 86.3% had tried at least two antidepressants. Desperation was a common theme, but this appeared to be competently expressed. A small minority (<8%) reported experience of illegal ketamine use.

Conclusions
It cannot be ruled out that patients with different degrees of treatment resistance and comorbidities will seek treatment with ketamine. This stresses the urgency to perform larger randomised controlled trials as well as to systematically monitor outcomes and adverse effects of ketamine, that is currently prescribed off-label for patients in need.

Declaration of interest
R.M. is consulting and is Principal Investigator for Janssen trials of esketamine and is consulting for Eleusis.

Keywords
Ketamine; antidepressant; depression; treatment resistant; off label.

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Method
A simple survey was constructed that contained the following questions.

(a) Do you suffer from depression?
(b) How many different antidepressant drugs have you taken in the last year? (0, 1, 2, 3, 4, 5, more than 5)
(c) How many different antidepressants have you taken in the last 10 years? (0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more)
(d) How long ago were you last free from depression for more than a month?
(e) Are you currently under the care of a psychiatrist or mental health team?
(f) Employment status
(g) How old are you? (Under 20, 21–40, 41–60, 61–70, 71 or over)

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A link to the survey was posted on the website of RedKITE (http://www.red-kite.org.uk) and in an article reporting the publication of results of case series\textsuperscript{13} published on the website of an National Health Service (NHS) hospital trust.\textsuperscript{14} RedKITE was a collaboration between clinicians and researchers across the UK exploring the use of ketamine as a possible treatment for depression. This survey link therefore could only be found by those who were very active in exploring ketamine as a treatment for depression. It was not directly discoverable through standard internet searching. Completion of the survey was invited thus: ‘The study team (i.e. for the published case series) would like to hear from patients and others who are interested in this area. Please register this interest at https://www.surveymonkey.com/r/9RQP5KL’. The answers of this survey were collected from the 2 April 2014 until the 5 February 2017. Basic descriptive statistics (such as frequencies) were used to describe the results of the survey. The qualitative, free-text comments were assessed for comments about the following topics: poor effect, intolerable side-effects or other adverse comments considering regular antidepressant medication, desperation and suicidality, former ketamine use and negative opinions about ketamine. The Health Research Authority decided that this project was not considered to be research and did not require review by an NHS research ethics committee.

### Results

#### Depression

The online survey regarding people’s interest in treatment with ketamine for depression was filled out 1088 times. Most (93.3\%) reported having depression (Table 1). The other 6.7\% were filled in on behalf of relatives or by people with a professional interest in treatment of depression with ketamine. Of those reporting depression, most (88.1\%) were in the age category of 21–60 years old, 8.7\% were older than 60 years old and 3.2\% of the people were younger than 21 years old (Table 1).

#### Duration of current depressive episode

Of the people reporting depression, 64.3\% had not been free from depressive symptoms for more than 2 years (chronic depression) and half of these reported unrelenting depression for more than 10 years (32.6\%). Of the people reporting current depression, 19.4\% had been free from these symptoms for more than a month within the past 2 years (Table 1). Other patients (16.3\%) did not answer the question or could not recall when they were last free from depression, with the latter answer suggesting a chronic course. However, only 51.9\% of the patients were currently under the care of a psychiatrist or a mental health team.

#### Antidepressants

No regular antidepressant medication was used within the past year by 32.4\% of patients reporting depression and 39.1\% had not used antidepressants in the past 10 years (Table 1). Most people reporting depression had used at least two antidepressants in the past year (54.0\%) and 9.6\% had tried five or more antidepressants. Over the past 10 years, 86.3\% had used at least two antidepressants, of which 47.2\% had tried five or more. In the group of patients who reported chronic depression, 87.9\% had used at least two antidepressants in the past 10 years.

#### Summary of other comments

A free-text ‘comments’ field was completed by 499 respondents (49.2\% of patients reporting depression). Of these, 221 (44.3\%) reported poor effect or intolerable side-effects from their current or previous antidepressant medication (Fig. 1). A further 22 respondents (4.4\%) made other adverse comments: that drug companies are withholding clinical trial evidence; or that antidepressants make you feel falsely happy or only mask the depressive symptoms. Desperation was not uncommon (n = 63, 12.6\%). Reference to suicidal thinking was relatively uncommon (n = 33, 6.6\%). Some reported that they felt that their psychiatrist gave up on them (n = 12, 2.4\%).

A small minority (n = 39, 7.8\%) described previous use of ketamine, most of which was through illegal routes, and 16 respondents (3.2\%) reported self-medicating with other drugs or alcohol. Nine patients (1.8\%) reported longer-term self-medicating with ketamine (for example for 3, 6 and 15 years).

Comments about former ketamine experiences included feeling less depressed for several weeks, feeling peaceful or more capable of facing certain aspects of life. Patients found ketamine to be very effective in relieving depressive symptoms. It was called the only thing that had helped thus far and a way to see life from a more gentle and clear perspective. Other patients mentioned ketamine as alleviating their feeling of endless misery and reducing their suicidal thoughts. Further comments stated that ketamine helped them feel alive again, enabled them to function as a normal person and made them aware of themselves in a different way. One patient declared it made him feel like the person he lost years ago. One respondent expressed the opinion that being depressed is a ‘mood’ instead of a ‘condition’ and should not be treated with any kind of medication.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All respondents</td>
<td>1088</td>
</tr>
<tr>
<td>Depression status</td>
<td>1015 (93.3)</td>
</tr>
<tr>
<td>Employment status*</td>
<td>1012</td>
</tr>
<tr>
<td>Currently receiving mental healthcare</td>
<td>1008</td>
</tr>
<tr>
<td>Duration of depressive episode</td>
<td>1015</td>
</tr>
<tr>
<td>Amount of antidepressants in the past year</td>
<td>1005</td>
</tr>
<tr>
<td>Amount of antidepressants in the past 10 years</td>
<td>1009</td>
</tr>
</tbody>
</table>

\*The sum of these percentages are >100 because some people were in more than one category.
improved after at least two adequate trials of different classes of usually considered treatment resistant when an episode has not explain their interest in alternative treatment options. Depression is persistent symptoms despite regular antidepressant treatment can patients can therefore be regarded as treatment resistant. Their tried at least two antidepressants in the past ten years. This group of least two antidepressants. Of all patients reporting depression, 64.3% Our results among patients seeking information on ketamine treat-

Main findings

Discussion

Our survey suggests that 86.3% of those who actively seek ketamine treatment would qualify as resistant to treatment (inadequate response to at least two antidepressants) and they clearly voice a pressing need for more effective antidepressant treatments. It is also clear that, despite the optimism ketamine publications have inspired, patients and clinicians should be cautious in drawing conclusions from small, uncontrolled open-label studies\textsuperscript{16,17} and larger randomised controlled trials are warranted. In addition, there is an urgent need to set up national or international registries to systematically collect data on effectiveness, long-term safety outcomes, tolerance, misuse and illegal diversion of off-label ketamine treatment in a situation where prescriptions are rapidly expanding.\textsuperscript{12,18}

Limitations

The main limitation of this descriptive study is the selective nature of the population completing the survey. Respondents had to be sufficiently motivated to come across the survey link and it may be that the profile of other interested individuals is different from those who did. However, it is likely that this survey does reflect the population of those who would be willing to use such a new treatment in a controlled manner.

A second limitation is that the self-report design is prone to recall bias, for example when patients are asked when they were last free from depression for more than a month. Furthermore, depressive symptoms experienced by patients might not always correspond with the diagnosis of a depressive episode by a specialist and based on regular classification criteria. It is likely that some patients reporting ‘depression’ in the questionnaire could have other diagnoses such as dysthymia, anxiety disorders or personality disorders. However, a large majority of the respondents report having had several treatments for depression. Moreover, the self-report information about depressive symptoms, for instance as used in the Inventory of Depressive Symptomatology Self-Report (IDS-SR), has shown to be highly related to the assessment of depressive symptoms by a trained clinician using the Hamilton Rating Scale for Depression.\textsuperscript{19}

Another important limitation is that the current survey information is not sufficient to judge whether the former antidepressant treatment strategies had been adequate. In current daily clinical practice, factors such as non-adherence to treatment, poor psychoeducation and limited time to evaluate and treat depression are unfortunately common. Prescription of medication is often inadequate in terms of dosage and length of treatment.\textsuperscript{20,21} The survey

![Fig. 1 Qualitative analysis of free-text comments. Percentage of the total respondents that filled in a free-text entry (n = 499).]
also does not contain information about psychotherapy, even though several evidence-based psychotherapeutic interventions are available for the treatment of depression.

**Implications**

This survey suggests that most patients who are actively seeking ketamine as an antidepressant have chronic, treatment-resistant depression. Many have given up on conventional therapies and on mental health services. Their tenacity in exploring treatments with evidence for efficacy, and the reports of self-medication with illegally obtained ketamine, suggest that excessively tight restrictions on medically controlled ketamine use could risk fuelling an expansion of illegal use. This risk needs balancing against the risks associated with long-term, repeated, medically controlled, use – which have yet to be quantified. Rapid large-scale aggregation of real-world clinical data, as well as randomised trial evidence is therefore needed if policy is to develop rationally.

**References**


