Management of treatment resistant schizophrenia in medium secure care

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Thirty-one percent of patients within a male medium secure unit (MMSU) were identified with treatment resistant schizophrenia. Almost half of these patients had not received clozapine treatment at least once during the course of their treatment history. The authors recommend that early identification of these patients and the appropriate use of therapeutic treatments, including clozapine, could lead to better outcomes for patients and significant cost savings for the NHS.

T
reatment resistant schizophrenia (TRS) is relatively common, in that between a fifth and a third of service users show a disappointing response to adequate trials of conventional antipsychotic drugs.\(^1\)\(^-\)\(^3\) The economic burden of this is considerable, both in direct health care costs and loss of productivity due to patients being unable to work. The Schizophrenia Commission report identified the employment rate of patients with schizophrenia as being around 8% in the UK, within a range of 5–15%, against a national UK employment rate of 71%.\(^4\) A prospective longitudinal study of TRS patients identified 47 of 59 (79.7%) patients were unemployed at baseline. However, over a 12-month period of clozapine therapy, 23 (48.9%) additional patients were able to gain paid or volunteer jobs, or attend school.\(^5\)

The average total direct health care costs of treating each patient with schizophrenia amounts to £1670 per year.\(^6\) For all patients in the UK, this represents £310 million annually, of which hospital and residential care account for 74% of the total.\(^7\) It was initially thought that the target length of stay in medium security hospitals should range between 18 months and two years.\(^8\)\(^,\)\(^9\) However, several studies have identified that a significant proportion of the medium secure population have treatment needs that extend beyond the two-year duration.\(^10\) Prolonged stay of these patients, many of whom have been transferred from high security psychiatric hospitals, has led to sifting up of medium secure beds with inherent consequences for patient flow through the care pathway.\(^11\)

An earlier study found that, among 21% (25 out of 122) of medium secure male patients who had been admitted for five years or longer, there were high levels of comorbidity and treatment resistance.\(^12\) The primary aim of our study was to determine the prevalence of TRS within the male medium secure unit (MMSU). Secondary aims were to establish what factors contributed to long stay, and to use these data towards future service redesign.

**Method**

The MMSU is a 134-bedded hospital comprising two acute adult...
admission wards – one for challenging behaviour, one for vulnerable adults (learning and physical disabilities) – and four wards for rehabilitation.

In all, 125 patients were identified with International Classification of Diseases 10th revision (ICD-10) diagnoses of schizophrenia and schizoaffective disorder. We analysed these patients’ notes for details of drug treatment, and residual positive and negative symptoms. We used the National Institute for Health and Care Excellence (NICE) definition for treatment resistance – defined as failure to respond to an adequate, sequential trial of two different antipsychotics, at least one of the drugs being a non-clozapine second-generation antipsychotic.13 Patients who were admitted within the private sector and those recently discharged were excluded from the study for pragmatic reasons.

Figure 1 shows the study inclusion/exclusion criteria. The 39 patients identified were anonymised for confidentiality. Demographic details, mental health diagnoses, physical health, treatment and engagement data were collected through interview with a member of the multidisciplinary team and perusal of electronic records. We used the Camberwell Assessment of Need – Forensic Version (CAN-FOR).14 This is an individual needs assessment scale designed to identify the needs of an individual with mental health problems in contact with forensic services. It assesses need over 25 domains. The primary nurse or the patient’s associate nurse assisted in its completion. The nurse’s ratings were completed as ‘carer’s ratings’ on numbered forms.

Peer approval from the trust’s clinical governance and audit department was obtained prior to the start of the study.

Results

Of the total 135 inpatients on the MMSU, 125 were identified with a diagnosis of schizophrenia (92%) and schizoaffective disorder (8%). Of these, 39 patients fulfilled NICE criteria for TRS. Table 1 lists the demographics of the 39 patients included in the study. Patients’ mean age was 43 years and four months, with a wide range (24–72 years, standard deviation 12 years). One in five patients were of black Caribbean ethnicity. Fifty-nine percent of patients were detained under Section 37/41 of the Mental Health Act with 92% having committed a serious violence against the person as their index offence. The median length of stay was three years (interquartile range 5.75, range 1–6 years); Table 2. Thirty-nine percent of patients were admitted on rehabilitation wards, with 28% on acute admission wards, and 21% admitted onto the wards for patients with challenging behaviours. We also noted that, compared to the other wards, the rehabilitation wards had the longest median duration of stay (six years).

Ninety-seven percent of patients, according to the CAN-FOR, had residual psychotic symptoms despite pharmacological and psychological interventions. The most common residual positive symptoms were persecutory delusions (n=20) and second-person auditory hallucinations (n=16); Table 3. Although we did not look for specific negative symptoms in patients’ records, the CAN-FOR suggested that a large group of these patients require consistent and sometimes quite intensive practical support from staff to attend to their self-care (18%) and activities of daily living (49%).

When we looked at pharmacological treatment in this group, we found that 41% (n=16) of patients...
had not received clozapine treatment at least once during the course of their treatment history. Patients’ refusal of this treatment was the most common reason that prevented treatment with clozapine; Table 4. Of the 23 patients who had a trial of clozapine, only five remained on clozapine at the time of this study. Among these, amisulpride was used to augment clozapine in two patients, with the other two patients augmented with either haloperidol or risperidone.

The remainder of the patients discontinued clozapine due to poor tolerance (26%), poor compliance (22%) and serious side effects (17%). We found that, on average, patients who discontinued clozapine had remained on it for only a few months.

Referral for psychological treatments and therapeutic activities
Seventy-two percent (n=28) of patients had been referred for formal psychological treatment including: individual psychology sessions (27%); cognitive behavioural therapy (CBT) for psychosis (18%); anger management; enhanced thinking skills; psycho-educational group therapy; and psychological treatment for substance misuse. However, 21% were not referred, with the most common reason being that they were too unwell at the time. Of those who had been referred, we found that 19% had below average engagement with psychological therapies.

CAN-FOR data for daytime structured activities showed that 95% of patients had needs for provisions in areas of psychological therapies, exercise and occupational therapy, further education, day centre activities and employment opportunities.

All of the men had been referred for a variety of other therapeutic activities including: occupational therapy; art therapy; music therapy; drama therapy; work rehabilitation; education; and the gym. With regard to these groups, we found that occupational therapy groups (14%) and CBT for psychosis (11%) had a greater than average attendance. All of the men were reported to be expected to attend ward-based community (milieu) meetings.

Comorbidity with physical health problems
Sixty-four percent (n=25) of the group had at least one chronic physical health problem. The most common problem was obesity (26%, n=10). We found that hypertension was the second most common problem, seen in 23% (n=9), followed by diabetes in 15% (n=6) of patients. Chronic dermatological problems such as psoriasis and eczema were seen in 8% (n=3). Chronic respiratory diseases, neurological disorders, ischaemic heart disease and dental problems were each seen in 5% (n=2 each). Twenty-eight percent (n=11) of the men had more than one physical health problem.

CAN-FOR results
A total of 540 met and unmet needs were identified for the 39 patients in the sample. On average each patient had seven met and seven unmet needs. Patients were found to have most unmet needs in domains of treatment and psychotic symptoms. Figure 2

<table>
<thead>
<tr>
<th>Variable</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary diagnosis</strong></td>
<td></td>
<td></td>
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<tr>
<td>Paranoid schizophrenia</td>
<td>36</td>
<td>92</td>
</tr>
<tr>
<td>Schizoaffective</td>
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<td>8</td>
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<tr>
<td><strong>Secondary diagnosis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Personality disorder</td>
<td>14</td>
<td>61</td>
</tr>
<tr>
<td>Learning disability</td>
<td>2</td>
<td>9</td>
</tr>
<tr>
<td>Depression</td>
<td>2</td>
<td>9</td>
</tr>
<tr>
<td>Dementia</td>
<td>2</td>
<td>9</td>
</tr>
<tr>
<td>Post-traumatic stress disorder</td>
<td>2</td>
<td>9</td>
</tr>
<tr>
<td>Obsessive compulsive disorder</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td><strong>Residual psychotic symptoms</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Persecutory delusions</td>
<td>20</td>
<td>36</td>
</tr>
<tr>
<td>Delusions of grandeur</td>
<td>7</td>
<td>13</td>
</tr>
<tr>
<td>Auditory hallucinations (2nd person)</td>
<td>16</td>
<td>29</td>
</tr>
<tr>
<td>Auditory hallucinations (3rd person)</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Formal thought disorder</td>
<td>11</td>
<td>20</td>
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</table>

Table 3. Diagnoses and residual psychotic symptoms

<table>
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<tr>
<th>Treatment</th>
<th>No.</th>
<th>%</th>
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<tr>
<td><strong>Clozapine treatment</strong></td>
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<td></td>
</tr>
<tr>
<td>On clozapine</td>
<td>5</td>
<td>22</td>
</tr>
<tr>
<td>Discontinued (poor compliance)</td>
<td>5</td>
<td>22</td>
</tr>
<tr>
<td>Discontinued (poor tolerance)</td>
<td>6</td>
<td>26</td>
</tr>
<tr>
<td>Discontinued (serious side effect)</td>
<td>4</td>
<td>17</td>
</tr>
<tr>
<td>Ineffective</td>
<td>2</td>
<td>9</td>
</tr>
<tr>
<td>Unknown</td>
<td>1</td>
<td>4</td>
</tr>
</tbody>
</table>

Table 4. Clozapine pharmacotherapy
summarises CAN-FOR data for all of the TRS patients.

**Discussion**

Our finding that a third of patients within the sample group had a diagnosis of TRS is in keeping with available literature. The patients’ ethnic backgrounds were not surprising given the catchment area for the unit. This spans eight London boroughs with diverse communities, and over 100 first languages spoken. In addition, it contains areas of affluence as well as areas of significant socio-economic deprivation. We therefore replicated the finding that admission rates to both high- and medium-security services demonstrate a linear correlation with measures of socio-economic deprivation in patients’ catchment areas of origin.15

With the help of the CAN-FOR we were able to analyse the characteristics of the TRS group with a median length of stay of three years, and found that ‘psychotic symptoms’ and ‘treatment’ were areas of unmet need. The low take-up for clozapine in this group was disappointing given that the superior effectiveness of clozapine is supported by two major independently funded studies, the Clinical Antipsychotic Trial of Intervention Effectiveness (CATIE) and the Cost Utility of the Latest Antipsychotic Drugs in Schizophrenia Study (CUtLASS).16,17 The latter study found that clozapine was significantly superior to non-clozapine second-generation antipsychotics with regard to symptoms, and exhibited a trend towards superiority regarding quality of life (p=0.08).18

Patient refusal was found to be a major factor that contributed to patients not being treated with clozapine. All of our study population was compulsorily detained under the Mental Health Act, within the medium secure unit. It must be recognised here that treatment under compulsion can be not only difficult, but also counterproductive. Positive reinforcement often predicates successful treatment of these patients.19 Service users indicated treatment adherence is enabled by collaborative care with professionals who listen and enable them to take helpful medication.20

Moeller and Kelly et al. found that clozapine treatment was more likely to be discontinued in African-Caribbean patients largely because of pre-existing low neutrophil counts – a condition known as benign ethnic neutropenia.21,22 Perhaps specific interventions may be required to improve insight into this group with a view to improving uptake of clozapine.

Almost all of our sample group (92%) were admitted having committed a serious violence against the person. Our CAN-FOR data showed that, despite the prolonged period of admission, ‘safety towards others’ remained an unmet need. It has already been established that, in patients with schizophrenia, clozapine is more effective in reducing violent behaviour and hostility than standard antipsychotic therapy, further validating the need for more emphasis on clozapine initiation and maintenance for this group of patients.23–25

Interestingly, of the patients referred for various psychological and therapeutic activities, only about one in five had a below average attendance at these

![Figure 2. Summary of CAN-FOR data for all treatment resistant schizophrenia patients](image-url)
programmes. However, when we looked at the CAN-FOR data for daytime structured activities, 95% of patients had needs for provisions in areas of psychological therapies, exercise and occupational therapy, further education, day centre activities and employment opportunities. This clearly highlights the challenge that implementation of psychological and allied therapies poses to this group of patients. NICE’s updated guideline on interventions in the treatment and management of schizophrenia in primary and secondary care recommends the use of psychological interventions, such as CBT, family interventions and arts therapies for the treatment of people with schizophrenia. CBT, if delivered over a period of at least six months, will reduce positive and, to some extent, negative symptoms in otherwise treatment resistant schizophrenia. This would indicate that more needs to be done to optimise rehabilitation programmes available to these treatment refractory groups of patients.

Conclusions

This study has identified a distinct population of patients within a medium secure service who have TRS, with half of the group having not had a trial of clozapine. As a result, they have several unmet needs besides the persistence of psychotic symptoms. We identified a unique opportunity within the service to develop a treatment programme specifically aimed at addressing treatment resistance more effectively. Early identification of these patients, with appropriate use of therapeutic treatments including clozapine, could lead to significant cost savings for the NHS.

The White Paper, Reforming the Mental Health Act, highlighted the need for staff: ‘Where individuals are detained as a result of their mental disorder, they must be held in a therapeutic environment which is designed to address their needs effectively. This is not just a matter of new places but also properly trained staff, new approaches to assessment and treatment and a rigorous programme of research and evaluation.’ This study suggests that specific secure services could be developed for this group.

We recommend three possible changes to the service to address the complex needs of this client group. The first is the development of a ward, possibly within the low secure setting, specially tailored to meet their needs. This engenders the ‘therapeutic community’ concept which is multidisciplinary team led and provides a combination of psychological and optimal treatment with neuroleptic medication. The second could be the development of a non-ward based service within the unit, which comprises professionals with a special interest in the treatment of patients with TRS. And, finally, a third alternative involves a combination of both of the above.

There is already evidence which supports the establishment of such units, towards improving implementation of clozapine in TRS patients. Longer treatment continuation has been found in hospitals where greater numbers of patients are prescribed clozapine. It may be that clinicians, who have more experience of using clozapine, develop expertise in encouraging patients to continue with clozapine, especially when faced with side effects in the initial phase of treatment. Patients who complete a year of clozapine treatment have a higher rate of continuation to two or more years than those who discontinue treatment at an early stage. This may be due to the length of time it takes for beneficial effects to become evident.

We hope that service innovation in this area can improve the care of TRS patients within secure settings, by enhancing their treatment and alleviating the distress they suffer, and, in the long term, afford them a better quality of life.

Limitations of the study

As this investigation was descriptive, we did not seek to draw statistically significant conclusions from this small sample size, restricted to one service. We did not use a control group for comparison. Smoking, a potentially modifiable risk factor for treatment resistance was not considered in detail in this study.

Finally, further research is necessary to investigate whether there are distinct groups within this longer-term cohort with differing treatment and rehabilitation needs.

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Declaration of interests

There are no conflicts of interest declared.
Original research

Treatment resistant schizophrenia

References

News

Forensic services initiative to reduce seclusions wins 6Cs NHS England award

Taking the action to seclude patients in Forensic Services can have a dramatic effect on both staff and patients. Whilst in some cases, this may be necessary to maintain levels of safety for other patients and the clinical team, seclusion brings with it some degree of stigma for the patient and can significantly damage the overall therapeutic relationship.

The healthcare professional team at Fir Ward at The Chichester Centre, a Low Secure Unit within Sussex Partnership NHS Foundation Trust, looked into the practice of using seclusion as an intervention in the management of violence, with a view to developing strategies that would lead to a reduction in seclusion episodes. The initiative they developed won the NHS England 6Gs award for September (6Gs standing for care, compassion, competence, communication, courage and commitment - which was launched by the Chief Nursing Officer of England in December 2012).

The multi-disciplinary team looked at various situations that could potentially lead to an episode of seclusion within the context of ‘Relational Security’ – the knowledge and understanding staff have of a patient and of the environment; and the translation of that information into appropriate responses and care. From this, the team arrived at some key interventions that would become part of Fir Ward’s philosophy and clinical functioning.

Examples included making one-to-one time with patients more effective and involving greater liaison with multi-disciplinary colleagues. Training, particularly in the areas of de-escalation and conflict management, was set in motion as was building a greater understanding of attachment theory and boundaries. Other improvements included improving the clinical environment, making sure assessment was a team exercise and developing collaborative care planning designed around the needs of the patient.