Quetiapine modified-release versus immediate-release in early psychosis

Marlene Kelbrick MBChB, MRCPsych, PGCert, MRes

Antipsychotic treatment choice in first-episode psychosis is multifaceted with a need to focus on all aspects of recovery. There are clear differences between quetiapine immediate-release (IR) and modified-release (MR) that may have clinical significance in this patient group.

Antipsychotic medication is an effective treatment for first-episode psychosis, both in the acute phase, and as maintenance treatment for the prevention of subsequent future episodes.1–3 Antipsychotics have a shared therapeutic action associated with dopamine receptor antagonism (D2-blockade),4 however, there are small but potentially clinically significant differences in efficacy (the exception that of clozapine with superior efficacy in treatment-resistant schizophrenia), variation in individual response, and substantial differences in tolerability amongst the different antipsychotics available.2,5,6.

Quetiapine is an antipsychotic with a relatively broad receptor binding profile, including affinity to dopamine (D1 and D2), serotonin (5HT2A), histaminergic (H1), alpha-adrenergic (alpha2) and muscarinic (M1) receptors.7 It has proven efficacy not only for psychosis but also bipolar affective disorder mood episodes, and growing evidence for anxiety related disorders.8–11 Quetiapine is available in two forms, immediate-release (IR) given as twice daily dosage, and modified-release (MR) given as once daily dosage.

Important aspects and challenges for first-episode psychosis

Patient characteristics

Patients with first-episode psychosis represent a diagnostically heterogeneous group of psychotic disorders, including substance-induced, non-affective and affective psychoses.12,13 Patients are mostly young adults with relationships, families, and either in education and/or employment, or seeking employment.14

High rates of disengagement, relapse and increased sensitivity to side effects

Rates of disengagement amongst those with first-episode psychosis are high,15 and although response and remission rates with antipsychotic medication are good, risk of relapse remains high in the context of elevated rates of nonadherence to medication (one of the most robust predictors for relapse) and substance misuse.16–18 Sensitivity to antipsychotic medication side-effects is also increased in those with first-episode psychosis.19,20

The advantage of quetiapine modified-release versus immediate-release in first-episode psychosis

Fast titration and once-daily dosage

Quetiapine modified-release (MR) has a simple and fast titration24 (see Table 1). This is of significant benefit where there is often urgency for reaching therapeutic dose and steady state in the acute phase of illness, with quetiapine MR more often used in therapeutic doses compared with immediate release (IR), and its once-daily dosing enhances adherence with less treatment

Table 1: Differences in titration (adapted from the BNF)25

<table>
<thead>
<tr>
<th>Quetiapine MR</th>
<th>Quetiapine IR</th>
</tr>
</thead>
<tbody>
<tr>
<td>300mg nocte day 1</td>
<td>25mg bd day 1</td>
</tr>
<tr>
<td>600mg nocte day 2</td>
<td>50mg bd day 2</td>
</tr>
<tr>
<td>100mg bd day 3</td>
<td>100mg bd day 3</td>
</tr>
<tr>
<td>150mg bd day 4</td>
<td>150mg bd day 4</td>
</tr>
</tbody>
</table>
cessation in patients prescribed quetiapine MR.26,27

Less daytime sedation and overall side-effect profile
In young people who want to drive, work, study, or are young parents with children, sedation as a side-effect of antipsychotic medication is a significant problem. In a multicentre, prospective, double-blind, crossover study in patients with stable schizophrenia, quetiapine MR was associated with less daytime sedation, and better overall treatment satisfaction, compared with IR.28 Similar to previous study findings,29,30 in addition to the fact that quetiapine MR has less daytime sedation compared with IR, the sedation that it does potentially cause is mostly in the first seven hours post-dose, which with a night-time only dosage can improve sleep as an advantageous effect.29,30 Quetiapine MR has a more favourable plasma concentration level with overall less frequency of other common side-effects, including dry mouth, dizziness, headaches and nausea.29

Cost comparison between quetiapine MR and IR
There is still a significant cost difference between quetiapine MR and IR despite patent expiry. British National Formulary quoted comparisons include Sondate XL 300mg tablets, one month’s worth £24.99 versus quetiapine IR 300mg tablets, one month’s worth £3.33.25 However, when considered, this should be balanced against cost of ‘wasted’ medication (covert nonadherence), acute psychiatric admission cost, and costs to the person including loss or interruption of employment/education, impact on relationships and cost of relapse on future prognosis.

Matching patient and antipsychotic medication choice
Antipsychotic medication choice should be individualised to the person in order to achieve a balance between efficacy and tolerability.5,33 Factors to consider include previous treatment choice and response/tolerability, presenting symptom profile (for example, where, in addition to psychotic symptoms, there is a need for mood-stabilising properties, or to address sleep difficulties and comorbid anxiety), urgency for achieving therapeutic dose, risk profile, individual personal circumstances (employment, driving, etc) and individual antipsychotic side-effect profile (both undesirable and advantageous side-effects). In addition to these, there should also be consideration of factors likely to enhance adherence to treatment.

Conclusion
Antipsychotic prescribing choice in first-episode psychosis is based not only on efficacy but importantly also on tolerability, and focussed on enhancing medication adherence and overall functioning. Quetiapine MR has a more favourable side-effect profile compared with quetiapine IR in first-episode psychosis, especially in terms of less daytime sedation, as well as the advantage of fast titration, improved ability to achieve therapeutic dose and likely better adherence, and should be the preferred choice when using quetiapine in this patient population.

Declaration of interests
No conflicts of interest were declared.

Dr Kelbrick is Consultant Psychiatrist, Early Intervention in Psychosis, Northamptonshire Healthcare NHS Foundation Trust.

References