Prescribing in First Episode Psychosis

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Images courtesy of paulsonabend.com
What is special about clients with FEP?

• Antipsychotic naïve clients more sensitive to the pharmacological effects of medication\textsuperscript{1,2,3}  
  – more frequent side-effects, eg EPSE, weight gain  
  – often need lower doses

• Dopamine receptor super-sensitivity  
  – prolonged prescription of potent dopamine antagonist antipsychotics can induce changes in dopamine receptors leading to super-sensitivity  
  – can diminish the effectiveness of antipsychotic medication over time, increase EPSE (TD) and reduce chance of being well & medication free at 7 years

• Naïvety + supersensitivity = Less D2 blockade required  
  – Start low + go slow

• Cardio metabolic syndrome  
  – Partial agonists vs (potent) antagonists
Need for evidence-based guidance

- Medication experiences at the beginning of treatment can have a lasting impact on future attitudes towards medication, compliance and outcomes\(^1\)
  - critical time to optimise medical treatments
  - maximise the chance of a positive outcome for the patient
  - better efficacy, tolerability and compliance
  - positive interactions and engagement with mental health professionals\(^2,3,4,5\)

- Medication choice is complex and evidence-based information is essential to assist prescribers in medicine optimisation
  
  Initial presentation
  Which first-line medication, at what dose, for how long, when to switch if there is no response, which second AP, how long, role of LAI, is it ever appropriate to combine psychotropic medications?

  Maintenance of remission
  Which antipsychotic medication is recommended for the maintenance of remission, duration of treatment, dose, etc

  Treatment resistance
  When should Clozapine be considered, dose, duration, what is Clozapine does not work?
Audit
Audit standards

• NICE guidelines

• Maudsley guidelines

• Recent guidelines produced by South London & Maudsley NHS Trust
<table>
<thead>
<tr>
<th>Audit Criteria</th>
<th>% compliance</th>
</tr>
</thead>
<tbody>
<tr>
<td>The patient should be involved in the choice of antipsychotic</td>
<td>40</td>
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<tr>
<td>Treatment of FEP to be commenced by a specialist in secondary care</td>
<td>87</td>
</tr>
<tr>
<td>A second generation antipsychotic used as first line treatment</td>
<td>96</td>
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<tr>
<td>Antipsychotic medication trialled at optimum dosage for 4-6 weeks</td>
<td>13</td>
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<tr>
<td>Medication reviewed and documented in the notes, including side effects</td>
<td>84</td>
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<td>Clozapine to be offered if no response following 2 different antipsychotic drugs</td>
<td>25</td>
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</tbody>
</table>
Audit

• No Trust-wide guidelines for prescribing for patients experiencing FEP
  – Prescribing practice can vary greatly

• Bath and North East Somerset (BaNES) locality working group
  – Protocol and recommendations
New Trust-wide Prescribing Protocol

Medicines Guideline: Prescribing Protocol for First Episode Psychosis (MG17)

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Review cycle
Review every two years or sooner if guidance changes.
Next review

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This guidance should be read in conjunction with the following Trust documents:
AWP Medicines Policy - P060
AWP Procedure for the prescribing, administration and monitoring of clozapine (Med20)
Guidance for Monitoring Psychotropic medications (MG11)
Interactions between tobacco smoke and medication (MG10)
Procedure for the prescription of medicines (Med02)
**Population**
What’s so special about patients with FEP?
- Neuroleptic naïvety - > sensitivity
- <D2 blockade required?
- High response rate
- High rates of substance use/misuse
- Adherence is more problematic
  (Buchanan et al, 2010; Lieberman et al, 2013)

**Critical period (first 2-3 years)**
Long term 'treatment resistant' symptoms develop during the 'critical period' so assertive treatment required.
Studies of psychosis show that long term, persistent, troublesome symptoms develop within the 'critical period'
  (Mason et al, 1995; Harrow et al, 1995).
There is now a growing recognition that the treatment approach required for a young person with a newly diagnosed psychotic illness, is in many ways quite different to the approach which may suit a person with more long-standing illness. Studies have identified younger, treatment naïve, patients with FEP as a population highly vulnerable to adverse metabolic ‘derangements’ from second generation antipsychotics (Pramyothin & Khaodhia, 2010; Correll, 2011).
**Antipsychotic free initial assessment (up to 7 Days) with baseline investigations.**
If possible delay antipsychotic medication for at least two days until the diagnosis of psychosis is confirmed and organic causes are excluded. Benzodiazepines (e.g. diazepam 10 to 30mg daily for agitation) can be used for sedation and behavioural control during this period and beyond this time as required (Taylor et al, 2016).

**Assess response after 2-3 weeks**
- Sooner if the patient is experiencing adverse effects
- If no response after 2-3 weeks choose alternative antipsychotic with patient involved in choice (Kinson et al, 2010); if some response continue
- Provide information and practical help to promote and monitor concordance
  (Murray et al, 2016; Taylor et al, 2016; NICE CG155 and CG178)

**Re-assess after further 2-3 weeks**
- Continue with effective dose; slowly increase/adjust depending on individual response
- Following inadequate response to two antipsychotics consider Clozapine
- Ensure patient is receiving NICE psychosocial interventions alongside medication eg CBTp, Family Interventions
- Ensure physical health checks continue as per guidelines
- Combinations of antipsychotics should not be prescribed (Buchanan et al 2010; Essock et al, 2011; Murray et al, 2016; Taylor et al, 2016; NICE CG155 and CG178)

**When to cease medication**
- Please consider on a case by case basis with advice from an EI prescriber
- After single episode review pros and cons of stopping at 18 months (slowly taper over at least 3 weeks)
- Multiple episodes – advise continued treatment
- Ensure appropriate monitoring in place
- Discuss use of depot when appropriate (Taylor et al, 2016)

**Disturbed behaviour**
Try to avoid use of antipsychotics.
Use Benzodiazepines e.g. Lorazepam 1-2 mg oral.
  (Taylor et al, 2016).
If rapid tranquillisation is needed refer to Trust Guidelines for rapid tranquillisation.
If patient is antipsychotic naïve use Lorazepam 1-2mg (AWP Rapid Tranquilisation Procedure, Med 23).

**Why treat people with FEP in a specialised manner?**
With sustained assertive treatment over 85% of people in first episode achieve remission of symptoms within 6 months. Full remission takes time, but will occur in the majority of patients. Overall, around 60% of patients will respond by 12 weeks and another 25% will respond more slowly.
(Murray et al, 2016)

**After 7 days**
Choose antipsychotics following discussion of benefits and side effect profile with patient and family where possible. If patient is an inpatient or with Intensive Service discuss prescribing decision with prescriber in EI Team prior to initiating antipsychotic.
Choose a second generation antipsychotic with low side effect profile (NICE CG155 and CG178)

Start with low dose and increase slowly:
- Aripiprazole 5mg OD increasing to 10mg OD
- Olanzapine 2.5 mg noite increasing to 10mg noite
- Quetiapine 50mg daily increasing to 300mg daily
- Risperidone 0.5mg daily increasing to 2mg OD
- Amisulpride 25mg BD increasing to 200mg BD
Rapid Tranquilisation Policy Updated

Guidelines for Rapid Tranquilisation (Adults aged 18-65 years): Page 1

Non-Pharmacological Measures
- De-escalation e.g. distraction, talking down, providing privacy, change of environment, time out

Before prescribing pharmacological measures you must:
- Check medication given in last 24hrs: ensure BNF limits are not exceeded
- Check advance statements and any 12/13s paperwork: offer service user opportunity to make informed choice of treatment
- Consider other medical conditions: asthma, diabetes, acute infection, intoxication, hydration, low body weight, epilepsy, hypocalaemia, abnormal ECG, respiratory disease, disabilities, pregnancy

Pre rapid tranquilisation

Consider oral PRN medication
- If insufficient info to guide choice of medication or the service user is on a regular antipsychotic, is antipsychotic naive or in non-psychiatric context, preferable to use lorazepam alone
  - Lorazepam 1mg - 2mg
- Alternatives include an oral antipsychotic if service user has previously had antipsychotic treatment and ideally not on a regular antipsychotic. Typical doses are:
  - Haloperidol 5mg or Olanzapine 5-10mg or Risperidone 2mg or Quetiapine 50mg
  - or oral - Promazine 25-50mg (slower acting but effective sedative, off label)
- If insufficient effect repeat doses once after minimum 30-60mins (1-2hrs for promazine)
- Check Physical Health Observations (PHO) are recorded prior to possible IT

Consider short acting IM medication
- If refusing oral medication, if two oral doses fail or if increasing risk to self or others
- Prescribe initial IM rapid tranquillisation medication as a single dose
- Only repeat when effect of initial dose reviewed
- Each prescription must state: dose, frequency, max dose 24hrs and minimum interval between doses

IM Rapid Tranquilisation

Antipsychotic not indicated
- Lorazepam IM 1-2mg or second line option (depending if sensitive to benzodiazepines
- Promazine IM 25-50mg or haloperidol IM 2-5mg

Antipsychotic indicated
- No history of cardiovascular disease and/or antipsychotic naive
- Aripiprazole IM 7.5-9.75mg

Antipsychotic indicated
- Haloperidol IM 2.5-5mg or olanzapine IM 5-10mg and/or promazine IM 25-50mg
- Partial response: consider further dose after minimum of 30-60mins

Initiate post rapid tranquilisation Physical Health Monitoring
- When IM medication is being used, a senior medic should review all medication at least once a day

If no response consider
- Aripiprazole or olanzapine IM or haloperidol plus promazine or ketamine

If no response consider
- Lorazepam IM, if not already used in this episode

If no response consider
- Lorazepam IM, if not already used in this episode or alternative antipsychotic

If still no response, seek advice from senior medic and/or pharmacist
Next steps

- Guidance MG 17 now fully operational across the Trust

-> Plan to re-audit in 6 months
References


9. Keating, Dolores; Hynes, Caroline; Madigan, Kevin; Lawlor, Elizabeth; Clarke, Mary 2017. Pharmacological guidelines for schizophrenia: a systematic review and comparison of recommendations for the first episode. BMJ Open 7:e013881. doi: 10.1136/bmjopen-2016-013881