Talking to Patients and Their Families About Clozapine

The Care Transitions Network

National Council for Behavioral Health
Montefiore Medical Center
Northwell Health
New York State Office of Mental Health
Netsmart Technologies
Clinicians (N=144) primarily cite patient factors as barriers to prescribing clozapine.
What is important to patients may differ from clinician priorities
Patients may value benefits other than direct antipsychotic effects
Perceptions of patients (N=80) taking clozapine

<table>
<thead>
<tr>
<th>Positive Effects</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall improvement</td>
<td>30.0%</td>
</tr>
<tr>
<td>Improved sleep</td>
<td>27.5%</td>
</tr>
<tr>
<td>Calming effect</td>
<td>27.5%</td>
</tr>
<tr>
<td>Antipsychotic effect</td>
<td>18.7%</td>
</tr>
<tr>
<td>Anxiolytic effect</td>
<td>7.5%</td>
</tr>
<tr>
<td>Improved functioning</td>
<td>7.5%</td>
</tr>
<tr>
<td>Recovery</td>
<td>5.0%</td>
</tr>
<tr>
<td>Stabilization</td>
<td>5.0%</td>
</tr>
<tr>
<td>Reduction of cognitive deficits</td>
<td>5.0%</td>
</tr>
</tbody>
</table>

Angermayer et al, Psychological Medicine 2001
Clozapine has side effects and these are important to patients.
**Perceptions of patients (N=80) taking clozapine**

<table>
<thead>
<tr>
<th>Negative Effects</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue/sedation</td>
<td>56.2%</td>
</tr>
<tr>
<td>Lack of motivation</td>
<td>21.2%</td>
</tr>
<tr>
<td>Hypersalivation</td>
<td>21.2%</td>
</tr>
<tr>
<td>Anticholinergic effects</td>
<td>16.2%</td>
</tr>
<tr>
<td>Weight gain</td>
<td>15.0%</td>
</tr>
<tr>
<td>Orthostatic hypotension</td>
<td>11.2%</td>
</tr>
<tr>
<td>Cognitive deficits</td>
<td>11.2%</td>
</tr>
<tr>
<td>Restlessness</td>
<td>5.0%</td>
</tr>
<tr>
<td>Increased perspiration</td>
<td>5.0%</td>
</tr>
<tr>
<td>Sexual dysfunction</td>
<td>5.0%</td>
</tr>
</tbody>
</table>

Angermayer et al, Psychological Medicine 2001
It is important to know the patient’s priorities about side effects. For example, clinicians often do not think about clozapine’s favorable motor side effect profile.
Perceptions of patients (N=80) taking clozapine

<table>
<thead>
<tr>
<th>Advantages over standard antipsychotics</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>No parkinsonism</td>
<td>27.5%</td>
</tr>
<tr>
<td>No akathisia</td>
<td>12.5%</td>
</tr>
<tr>
<td>No acute dystonia</td>
<td>12.5%</td>
</tr>
<tr>
<td>No restlessness</td>
<td>11.2%</td>
</tr>
<tr>
<td>Reduced sedation</td>
<td>8.7%</td>
</tr>
</tbody>
</table>

Angermayer et al, Psychological Medicine 2001
What we need to do

• Clozapine has special properties—both in terms of potential benefits and also side effects

• Patients and their families need a thorough discussion of the benefits and risks in order to make informed decisions

• Besides conveying medical knowledge, we need to make sure that in our discussions we carefully address patient and family goals and concerns
The decision process

• Patients and their families often need several visits to make a decision about clozapine treatment

• Clozapine is indicated for the treatment of persistent symptoms. If patients and their families do not think that clozapine is a good option at one time point, they may have a different evaluation at a later time (e.g. after a relapse requiring hospitalization).
Clozapine indications

- FDA approved
  - Treatment-Resistant Schizophrenia
  - Reduction In The Risk Of Recurrent Suicidal Behavior In Schizophrenia Or Schizoaffective Disorder
- Not FDA approved but included in the 2009 PORT guidelines
  - People with schizophrenia with persistent symptoms of hostility or who display persistent violent behaviors
Applying medical based indications to patient experience
REAP model

• Recognize goals
• Explain how clozapine supports goals
• Acknowledge patient concerns
• Provide accurate information to patients and their families to allow them to make informed choices about clozapine treatment
Patient goals

• Some patients will have as a goal reduction of one or more of the symptoms that are listed in the indications for clozapine.

• Others may have a goal that is not directly tied to the clozapine indications but can be furthered by clozapine treatment.

• Find out what is important to your patient:
  • For example, a decrease in auditory hallucinations may be beneficial for school performance if the patient has school problems.
REAP model

- Recognize goals
- Explain how clozapine supports goals
- Acknowledge patient concerns
- Provide accurate information to patients and their families to allow them to make informed choices about clozapine treatment
Frequently expressed goals that may be furthered by clozapine treatment

• Help with positive, suicidal or hostility symptoms
• Help with anxiety or depressive symptoms
  • Determine whether these are the result of distressing psychotic symptoms
• Help with concentration or focus
  • Determine whether intrusive psychotic symptoms are interfering with concentration
• Help with social isolation
  • Is social isolation secondary to paranoia or other psychotic symptoms?
• Help with role functioning
  • Are psychotic symptoms interfering with school or work functioning?
REAP model

• Recognize goals
• Explain how clozapine supports goals
• **Acknowledge patient concerns**
• Provide accurate information to patients and their families to allow them to make informed choices about clozapine treatment
Patient concerns

• It is important to find out what the patient’s baseline knowledge is about clozapine and their concerns about a clozapine trial
  • Some patients will have accurate perceptions based upon knowing other patients taking clozapine or from reading reliable materials
  • Some patients will have been exposed to inaccurate information through sources such as the internet
REAP model

• Recognize goals
• Explain how clozapine supports goals
• Acknowledge patient concerns
• Provide accurate information to patients and their families to allow them to make informed choices about clozapine treatment
Provide accurate information

• During the discussion on how clozapine can further goals, you should provide information about clozapine positive effects and the likelihood that a patient will experience a positive effect

• It is important to discuss potential benefits first
  • If a patient does not see any potential benefits to clozapine treatment, they are unlikely to want a clozapine trial
Discussing side effects

• It is important to give patients and their families the proper context for a discussion of the risk to benefit ratio for clozapine treatment
  • Clozapine does have more side effects than other antipsychotics
  • But the patient has already tried several other antipsychotics without full benefit
  • Side effect risk must be considered in relation to the serious symptoms (e.g. suicidal ideation) that the patient is experiencing
Discussing side effects

• Clozapine has side effects that are medically serious and others that can be troubling but are not medically serious. The medically serious ones are much less frequent than the ones that are not medically serious. It is important that patients and families are clear about this distinction.

• It is important that patients and families are knowledgeable about management strategies
Discussing side effects

• A detailed discussion of clozapine side effects is provided in the companion materials

• In the following slides we will review selected side effects
Agranulocytosis

- The estimated risk is 7 patients out of 1000
- With proper monitoring, fatal agranulocytosis has become extremely rare
- The risk is highest between week 12 and 16 of treatment
- 80-95% of cases occur within the first 6 months
- The blood test monitoring schedule is designed to minimize the risk of agranulocytosis with the fewest blood tests possible. Test occur weekly for 6 months, every 2 weeks to month 12 and monthly thereafter
Myocarditis

• Risk is estimated to be in the range of 2 out of 1000 to 2 out of 10,000 patients
• Occurs within the first months of treatment
• Flu-like symptoms, fever, fatigue, and dyspnea are the most common symptoms
• Other symptoms include: Chest pain/pressure; orthopnea, peripheral edema, persistent palpitations, nausea/vomiting and diaphoresis
Neuroleptic malignant syndrome (NMS)

• A rare adverse effect

• With most antipsychotics, NMS presents with abrupt onset of fever, autonomic instability, extrapyramidal signs (EPS) and altered mental state. These may be accompanied by raised serum creatine kinase, impaired liver function tests, leukocytosis, electrolyte disturbance, renal impairment, altered coagulation studies and electrocardiogram abnormalities

• NMS with clozapine is less likely to present with EPS
Seizures

- Estimate of risk is between 1% and 5%
- Higher risk associated with higher clozapine dose and more rapid titration of dose
- If needed, anticonvulsants can be added to clozapine
Metabolic effects

• The metabolic syndrome is a group of cardiovascular risk factors including obesity, hypertension and disturbances of lipid and glucose metabolism

• Rates of the metabolic syndrome are around 50% for patients taking clozapine versus around 20% for matched control subjects

• Healthy lifestyle training, monitoring of metabolic syndrome components and in some cases medications to treat abnormalities are useful
Sedation

- Very common side effect
- Occurs early in treatment
- Patients often develop tolerance to the sedative effect
Sialorrhea

• A frequent side effect (between 30% and 80% of patients)
• Often occurs early in treatment
• It is often manageable with non-pharmacological approaches
Nocturnal Enuresis

- The reported incidence ranges from <1% to over 40%
- Generally occurs within the first 3 months of treatment
- Non-pharmacological management includes:
  - Limit fluid intake during the evening
  - Void at bedtime
  - Schedule a middle-of-the-night awakening to empty the bladder
  - Enuresis alarms can also be used
Tachycardia

• Occurs early in treatment in around 25% of patients
• Tolerance usually occurs by 4-6 weeks
• Treatment is not usually needed but if needed, a beta blocker can be effective
Constipation

• May occur in up to 60% of patients
• May be severe
• Treatment can include hydration, stool softeners and laxatives
Orthostatic hypotension

• Is a common side effect
• Usually occurs early in treatment and resolves in days or weeks
Pain/fear of needles

• It is important to acknowledge that no one likes needles
• BUT millions of people get blood draws around the world
• If the patient acknowledges potential benefits to clozapine but has fear of needles, it is often beneficial to focus the conversation on what supports the patient feels they would need to get the required lab tests
  • With identified supports, one can determine if the clinic can supply them
  • For example, often staff going with the patient to the first blood collection is a simple but powerful support for patients
Summary

• Making a decision about clozapine treatment involves integrating a lot of information
  • Give patients and their families enough time to thoroughly understand the material
• Find out what are the important issues for the patient and family
• Explore potential benefits first--if the patient and family do not see any potential benefits there is no reason to review risks
Summary

• Clozapine has a range of side effects
  • It is important to convey the frequency and severity of each potential side effect. Otherwise, patients and families cannot get an accurate understanding of risk
  • There is a lot of material to master so patients and families may need several sessions for review

• Peers who take clozapine can be helpful to patients and families to get a patient perspective of what taking clozapine is like

• Patient and family priorities often change over time. Patients who decline clozapine at one point may agree at a later time
  • Periodic review of clozapine benefits and risk is useful for patients who have an indication for clozapine treatment
Summary

• It is important that patients and families understand that we cannot predict the extent of response to clozapine, but OVER 50% of patients will have a meaningful clinical improvement.

• At the same time, some patients have a VERY dramatic improvement on clozapine.

• We don’t know the extent of improvement until we try it and only then can we really assess the benefit-to-risk ratio.

• We will generally know within three months how well it is going to work, but improvement can continue well beyond that.

• It would be a shame if we miss the opportunity to experience a real benefit.
Thank you!

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