EPI SET – Prescriber

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Objectives:

1. To review selection of antipsychotic medication in first-episode psychosis

2. Use measurement-based care to guide titration and side effect management

3. To apply strategies to promote adherence to antipsychotic medication for first-episode psychosis

Benefits of NAVIGATE in the RAISE trial

Compared with standard care, patients who received NAVIGATE:

- Had more improvement in overall symptoms, depression and quality of life
- Had more medication visits
- Were more likely to be prescribed an antipsychotic
- Were less likely to be prescribed an antidepressant
- Were less likely to experience side effects

Choice of initial antipsychotic

- Data from first episode or adolescent populations: aripiprazole, chlorpromazine, clozapine, haloperidol, olanzapine, quetiapine, oral risperidone, ziprasidone
- All equally effective for the treatment of positive symptoms of the initial episode (haloperidol less effective as maintenance vs SGA)
- Due to side effect profiles chlorpromazine, haloperidol, olanzapine should not be considered first, and clozapine considered for treatment resistant patients

Choice of initial antipsychotic (cont'd)

- Based on these considerations the first medication tried for NAVIGATE treatment should be either aripiprazole, quetiapine, risperidone, or ziprasidone (paliperidone does not have FEP dosing data but is closely related to risperidone)
- The broad range of side effect profiles allows for using another medication from this group as the second medication for patients unable to tolerate the first medication
- Consider long-acting injectable antipsychotic for maintenance treatment for all subjects

If a patient comes to the program on a non-preferred antipsychotic:

- Carefully evaluate the potential advantages and disadvantages of switching with the patient
- Consider that switching always has some relapse risk but generally, first-episode patients are very treatment responsive and all the aforementioned antipsychotics have the same efficacy
- Consider side effects the patient may have already developed (e.g., abnormal metabolic parameters)

Response to treatment

- Positive symptoms in first episode psychosis (FEP) patients often have a robust response to antipsychotic treatment
- FEP patients may respond to lower doses but take longer to respond than chronic patients
- Trial length to establish efficacy:

  - minimum of 8 weeks to establish efficacy recommended

  - insufficient trials lasting longer than 16 weeks not recommended

Clozapine

- should be considered for patients with persistent positive symptoms after adequate trials of 2 antipsychotics
- consider at earlier treatment stages for patients with persistent suicidal ideation

Treatment selection

- Evidence-based principles guide treatment selection based on:
  - Assessment of symptoms
  - Monitoring side effects (FEP patients may be more sensitive to adverse effects)
  - Monitoring adherence

- Shared decision making

Side effects

- Dose reduction is the first-line intervention if this is clinically possible
- If dose reduction is not possible, consider relative risks and benefits of switching antipsychotic vs adding a medication for side effect

Strategies for specific side effects

- Parkinsonism: dose reduction if possible, +/- anticholinergic (eg benztropine/Cogentin)
- Akathisia: dose reduction if possible or reduce speed of titration, +/- addition of a benzodiazepine, beta blocker or antihistamine
- Sedation: dose reduction if possible or change timing of dosing, consider waiting for tolerance to develop
- Hyperprolactinemia: consider switching to aripiprazole, quetiapine, or ziprasidone (for those stable on other antipsychotics consider addition of aripiprazole to their ongoing regimen)

Management of metabolic and cardiovascular side effects

- Cardiometabolic monitoring: fasting glucose and lipid measures at baseline, 3 months after starting a new antipsychotic and yearly thereafter if no abnormalities; weight, BMI, blood pressure at each visit
- Lifestyle interventions
- Consider aripiprazole or ziprasidone
- For patients who are overweight, obese, or experiencing rapid weight consider adding a medication such as metformin for weight loss

Using measurement-based care to guide titration and side effect management

- Patient self-report questionnaire to monitor symptoms, side effects, adherence, substance use and preferences about changing or keeping their current medications
- Physician rated scales:
  - Brief Psychiatric Rating Scale (BPRS) and Clinical Global Impressions (CGI) to monitor response to treatment
    - At least once monthly for all patients
    - When considering or making treatment changes
  - Validated rating scales at regular intervals to monitor and assess movement-related side effects
    - Abnormal Involuntary Movements Scale (AIMS) for tardive dyskinesia
    - Barnes Akathisia Rating Scale (BARS)
    - Simpson Angus Scale for medication-induced Parkinsonism

Nonadherence to medication

- **Prepare for nonadherence**
- Many factors contribute to the high risk of non-adherence in first episode population:
  - Level of response to antipsychotics is typically very good-can be interpreted by families and patients that medication is no longer needed
  - High rates of side effects in first episode patients
  - Patients and families ideas of “long-term” treatment
  - Stigma associated with taking medication

Enhancing Adherence to Medication

- prepare patients and families - provide information about both the course of treatment and specific antipsychotic medications available
- consider using long-acting injectable medications for all subjects
- shared decision making - engage patients and families in the decision making process
- NAVIGATE team-based problem solving
- as a prescriber, consider simplifying dosing schedule, use of dosette/blister packs, use of external reminders (eg alarm on phone)

Non-adherence

- When possible continue to follow patients who refuse medication
- If patients insist on discontinuing medication develop a monitoring and contingency plan
- Encourage patients and families to continue engaging in other components of the NAVIGATE intervention
- If regular prescriber appointments are declined keep the door open for return treatment
- Keeping a relationship during periods of non-adherence can decrease the risk of patients severely deteriorating before reaching out for treatment

References

NAVIGATE Psychopharmacological Treatment Manual

Robinson et al . Psychopharmacological Treatment in the RAISE-ETP Study: Outcomes of a Manual and Computer Decision Support System Based Intervention. *Am. J of Psychiatry* 175:2, February 2018

Mueser et al. The NAVIGATE Program for First-Episode Psychosis: Rationale, Overview, and Description of Psychosocial Components. *Psychiatric Services* 66:7, July 2015

Thank You

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