TREATMENT OF PSYCHOSIS, PART 1:
STABILIZING ACUTELY PSYCHOTIC PATIENTS

From Psychiatry Update 2012: Solving Clinical Challenges, Improving Patient Care, presented by Current Psychiatry and American Academy of Clinical Psychiatrists, and jointly sponsored by Duke University School of Medicine and Quadrant HealthCom Inc.

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Background on stabilization of acute psychosis: occurs in context of many different conditions; defined by acute onset of delusions, hallucinations, disorganized speech, or disorganized behavior (≥1 of 4 required for diagnosis); consequences — significant disturbance in self-care; sleep disturbance accompanied by agitation; propensity toward violent behavior; threats to personal safety; represents psychiatric emergency (particularly when presenting with agitation); associated diagnoses — schizophrenia; schizoaffective disorder; psychotic mood disorders; delusional disorder; substance-induced psychotic disorder; psychosis secondary to general medical condition

Importance of diagnosis: influences treatment choices; has impact on issue of emergency (since psychosis may signify, eg, unidentified medical crisis); during differential, consider diagnoses known to overlap with psychosis and psychotic disorders (eg, dementia [behavioral disorganization or agitation], delirium, developmental disability [with psychosis, agitation, and/or aggressive behavior])

Speaker’s views on state of treatment: patient’s needs often unmet due to serious limitations of current therapies; many new therapies have not lived up to initial promises; consequently, speaker has developed conservative attitude toward claims made about new treatments; data can help determine ideal treatment, but may also mislead through selective presentation; clinicians must assess all available data through critical lens and attempt to distill data into clinical application

Classification and criteria of psychotic disorders: different psychotic disorders, and psychotic or nonpsychotic disorders (eg, psychotic obsessive-compulsive disorder [OCD] vs standard OCD, body dysmorphic disorder vs delusional disorder), often have indistinct boundaries; clinicians have often responded to indistinct boundaries by ignoring distinctions and treating based on general discretion (which has led to discrepancies between diagnosis and treatment); since disorders do not remain stable over time, patient’s diagnosis may change after each hospitalization; some diagnoses offer less guidance about treatment

Changes to classification and criteria in Diagnostic and Statistical Manual of Mental Disorders (Fifth Edition; DSM-5): less emphasis on subtypes of schizophrenia (due to lack of clinical relevance); number of diagnoses reduced (with focus on adding greater meaning and distinctions to remaining disorders); introduces concept of dimensions to existing disorders (eg, positive symptoms, negative symptoms, cognitive symptoms, mood symptoms); treating specific dimensions in specific patients allows more targeted and individualized care; early diagnosis and intervention — remains controversial (inclusion in DSM-5 uncertain); improving diagnosis of schizoaffective disorder — currently criteria associated with low diagnostic stability, poor reliability of diagnosis between different clinicians, and questionable validity; partial delinking of catatonia from schizophrenia — catatonia itself has unique implications and specific treatments (eg, benzodiazepines, electroconvulsive therapy)

Important diagnostic considerations: recent substance use; contributing general medical condition(s); recent stressors or life changes; most urgent — medical stability, imminent medical risk, and safety of patient and those in contact with patient

Violence and schizophrenic illness: schizophrenia shows association with increased violence in broad epidemiologic data, but only in context of untreated psychosis; lack of treatment and presence of substance abuse most significant predictors for violent behavior

Legal considerations: physicians must establish patient’s competence to consent; if found incompetent, party responsible for consent must be determined; in emergencies, physicians may issue emergency treatment order without consent; determine voluntary or involuntary treatment status and necessity of inpatient admission

Setting of care: patients with acute psychosis may present to emergency departments (EDs), nonpsychiatric hospital floors, or outpatient clinics; setting of care may be highly germane to assessment of patient, since obtaining information may be difficult in context of acute psychosis (due to

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Educational Objectives
The goal of this program is improve the management of acute psychosis. After hearing and assimilating this program, the clinician will be better able to:

1. Recognize conditions commonly associated with psychosis.
2. Minimize safety and legal risks when treating psychotic patients.
3. Compare efficacy and hazards associated with first-generation and second-generation antipsychotic agents.
4. Reduce agitation in patients with psychosis.
5. Prevent side effects associated with antipsychotic medications.

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patient’s lack of cooperation); physicians must attempt to rapidly obtain comprehensive information about patient; in ED, information may be obtained by coordinating with ED provider, ED physician, or nursing staff; due to medical biases, many EDs attempt to rapidly discharge psychotic patients (because of perceived potential for disturbances); attempt to collect collateral information from all possible sources (eg, police department [if involved]); providers of nonpsychiatric care must be educated about collecting as much information as possible

Primary objectives: reduce acute symptoms as rapidly as possible; maintain patient safety (ie, medical safety, psychiatric safety, and safety of others); address specific cause of psychosis (if present); treat agitation before attempting to stabilize acute psychotic state; consider maintenance treatment after stabilization; provide specific treatments for refractory schizophrenia in patients with refractory symptoms

Psychosis vs agitation: treating agitation alone has poor outcomes, since patients may discontinue medications due to side effects or enter crisis related to unidentified and underlying medical condition; since psychosis drives agitation over time, physicians must initiate specific antipsychotic treatment; using one agent to control psychosis and aggression may be ideal, but dual medications may be preferable to extremely high-dose monotherapy (in patients with resistant agitation); agitation often related to psychosis, but may have different timeframe for response to treatment

Background on antipsychotic medications: encompass 65 agents (51 first-generation [or typical] antipsychotics and 14 second-generation [or atypical] antipsychotics [AAP]); 10 typical antipsychotics and 10 AAP currently available in United States; multiple studies have disputed superiority of AAPs over first-generation agents; Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) — olanzapine showed some superiority; however, other AAPs showed no differences when compared with typical agents; substantial number of patients taking olanzapine, risperidone, and other AAPs before study; patients who had poor responses before enrollment and then received same medication had better outcomes than patients who switched; when controlling for variables associated with pretreatment and remaining on medication, olanzapine fails to show superiority; despite selecting for patients at low risk for extrapyramidal symptoms (EPS), 4% of 8% patients developed new EPS over 18 mo (6% with perphenazine, 8% with olanzapine and risperidone, and 4% with ziprasidone and quetiapine); anticholinergics used to treat EPS in 4% of patients on quetiapine (7%-10% in other arms); patients receiving perphenazine showed somewhat higher rates of discontinuation due to EPS (8%, compared with 4% in other arms); total rates of EPS remained low overall, with no difference in rate seen with AAPs vs typical agents; however, study design excluded patients with history of significant akathisia or other EPS, and patients with existing tardive dyskinesia (231 of 1460 participants) received only AAPs

Critical lessons from CATIE: dosing of medication has significant importance; prioritize avoidance of EPS (ideally without anticholinergics); avoiding EPS may be easier with AAPs; when balancing efficacy and tolerability, different agents present different challenges; clozapine affirmed as gold standard for refractory patients; switching medications presents risks; antipsychotics show roughly equal efficacy but unique side effects and pharmacokinetics; since individual patients respond differently, finding correct agent remains challenging; patients who develop EPS while on AAPs reap no benefit from choice of AAP over typical agent

Selecting appropriate antipsychotic medications: each agent presents unique challenges in dosing (in terms of, eg, rapidity of escalation); assessing each medication’s side effect profile should have primary importance; attempt to match patient’s vulnerabilities with side effect profile

Keys to effective treatment: sequence; achieve proper dose of selected agent; allow adequate duration of trial; dosing — critical; must maximize potential efficacy while minimizing adverse effects; trials — consider switching if no benefit after 3 wk; if partial response seen after 3 wk, avoid switching; 6- to 8-wk trial (or slightly longer) required for clozapine (recommended for patients who fail to respond on 2-3 other medications); remain at starting dose for ≥3 wk; differences between agents may require variations in titration (eg, olanzapine may be initiated at target dose of 10-15 mg daily, but quetiapine or risperidone [and other agents with potent affinity for antagonism of α1 receptor] must be titrated slowly due to concerns about hypotension); target dose may vary significantly (eg, 2 mg daily of risperidone may be sufficient for first episode of schizophrenia, but chronic schizophrenia may require 4 mg daily); consider modifiers relevant to agent’s pharmacokinetics (eg, dosing with food doubles availability of ziprasidone)

Other forms of medication: have relatively limited role in management of psychosis; antidepressants — recommended for significant depression, but otherwise of limited use; anticonvulsants — have limited role outside context of bipolar disorder; benzodiazepines — have significant role in treatment of agitation

Background on psychotic agitation: treatment of acute psychosis should be separated from treatment of agitation (speaker considers agitation analogous to impending myocardial infarction, which requires immediate treatment independent of that for underlying cardiovascular causes); rationale for treating agitation as emergency — propensity for aggression (directed at self or others); potential harbinger of impending medical crisis requiring immediate attention

Important environmental aspects of care: eye-to-eye contact; safe egress from encounter with patient; soft voice; calmness; confidence; authoritative demeanor; sufficient personnel in vicinity

Pharmacologic strategies: oral vs injectable medications — determined by patient’s level of compliance; oral agents have better adherence over long term; other considerations — for severe agitation, antipsychotics superior to benzodiazepines (according to all available data); dosing extremely important when using injectables (eg, haloperidol typically requires fewer repeat injections); however, injectable olanzapine, ziprasidone, haloperidol all have comparable efficacy (aripiprazole slightly less efficacious); sedation vs tranquilization — speaker dismisses this dichotomy and considers sedation irrelevant to efficacy; high-potency agents (eg, haloperidol) do not have superior efficacy, but may have fewer side effects; for both psychosis and agitation, high-potency and low-potency agents have comparable effects (eg, injectable ziprasidone and haloperidol cause less sedation than olanzapine, but have similar efficacy)

Safety precautions: patients receiving injectable antipsychotics require monitoring in ED until patient no longer at risk for short-term respiratory depression, cardiac arrhythmia, and hypotension; all injectables show similar rates of cardiac and respiratory side effects when combined with benzodiazepines (eg, lorazepam)

Minimizing cost of care: haloperidol — associated with lowest rates of repeat injections and overall costs, and shorter inpatient and ED admissions; compares favorably with
Superiority of haloperidol over AAPs: speaker does not believe superior efficacy of haloperidol due to stronger blockade of dopamine D2 receptor (attributes it to better understanding of dosage parameters [10-mg dose established over 40 yr of use]); ideal doses of injectable ziprasidone, olanzapine, and aripiprazole remain undetermined (data limited to establishment of superiority of 20-mg dose of ziprasidone over 10 mg, and of 10-mg dose of olanzapine over 5 mg)

Use of benzotropine with antipsychotics: anticholinergic blockade may cause medical emergency in patients with certain undiagnosed medical conditions (disadvantage when combining with drug other than lorazepam)

Preventing EPS: since haloperidol has relatively long duration, effects of anticholinergics (e.g., diphenhydramine) may dissipate too quickly and leave patients with dystonia; however, anticholinergics should not be given over long periods of time; since injectable olanzapine and ziprasidone only inferior in terms of repeated dosing requirements, speaker utilizes all injectable antipsychotics in practice

Long-acting injectable antipsychotic agents: have important role in long-term treatment of schizophrenia

Suggested Reading


Acknowledgements

Dr. Tandon spoke at Psychiatry Update 2012: Solving Clinical Challenges, Improving Patient Care, held March 29-31, 2012, in Chicago, IL, and presented by Current Psychiatry and American Academy of Clinical Psychiatrists, and jointly sponsored by Duke University School of Medicine and Quadrant HealthCom Inc. For information about next year’s Psychiatry Update, visit currentpsychiatry.com/aacp. The Audio-Digest Foundation thanks Dr. Tandon and the sponsors for their cooperation in the production of this program.

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Estimated time to complete the educational process:
Review Educational Objectives on page 1 5 minutes
Take pretest 10 minutes
Listen to audio program 60 minutes
Review written summary and suggested readings 35 minutes
Take posttest 10 minutes
1. A diagnosis of acute psychosis requires that the patient have ______ of 4 primary symptoms (ie, delusions, hallucinations, disorganized speech, disorganized behavior).
   (A) 1   (B) 2   (C) 3   (D) 4

2. Which of the following descriptive variables associated with schizophrenia will be de-emphasized in the Diagnostic and Statistical Manual of Mental Disorders (Fifth Edition; DSM-5)?
   (A) Dimensions   (C) Positive symptoms
   (B) Subtypes   (D) Negative symptoms

3. ______ will be partially delinked from schizophrenia in DSM-5.
   (A) Hebephrenia   (B) Paranoia   (C) Catatonia   (D) Alogia

4. The highest rates of violence are seen in schizophrenic patients who are:
   (A) Not receiving treatment   (C) Having hallucinations
   (B) Abusing substances   (D) A and B

5. When treating an acutely psychotic patient with agitation, a physician should attempt to:
   (A) Give first priority to stabilizing the acute psychosis
   (B) Give first priority to reducing agitation
   (C) Treat psychosis and agitation simultaneously
   (D) None of the above

6. Specific antipsychotic treatment is required to reduce agitation.
   (A) True   (B) False

7. After controlling for pretreatment and superior outcomes in patients who remained on their pre-study medications, which of the following showed superiority over typical antipsychotics in Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE)?
   (A) Olanzapine   (C) Quetiapine
   (B) Ziprasidone   (D) None of the above

8. Which of the following medications is considered the gold standard for patients with refractory schizophrenia?
   (A) Clozapine   (B) Perphenazine   (C) Haloperidol   (D) Olanzapine

9. Patients should generally be switched to another antipsychotic agent if they fail to show a response after:
   (A) 2 wk   (B) 3 wk   (C) 4 wk   (D) 6 wk

10. The necessity of injectable agents is primarily determined by:
    (A) Severity of illness   (C) Patient’s level of compliance
    (B) Presence of agitation   (D) Patient’s general medical health

Answers to Audio-Digest Psychiatry Volume 41, Issue 13: 1-B, 2-A, 3-A, 4-C, 5-B, 6-D, 7-D, 8-B, 9-B, 10-A