Emergent Treatment of Schizophrenia

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Overview

Schizophrenia is a chronic psychotic disorder, either persistent or episodic, whose hallmark features may include delusions, hallucinations, disturbed thinking processes, flattening of affect, and abnormal behaviors. Affecting approximately 1% of the members of all cultural groups globally, schizophrenia is a catastrophically disabling illness with heavy social and economic costs on its sufferers and society.

It is essential in the emergency department (ED) not to confuse the thought and behavioral disturbances of organically based acute delirium with any of the psychotic disorders. The avoidance of this confusion is the primary reason for "medical clearance" examinations and drugs-of-abuse screening.

Because of the variability of symptom expression, diagnostic requirements of chronicity, and lack of pathognomonic features, an ED diagnosis of schizophrenia should be provisional at best. As a diagnosis-by-exclusion, schizophrenia must be distinguished from the numerous psychiatric and organic disorders that also can lead to psychotic disturbances in thinking and behavior.

Psychosis and schizophrenia are not equivalent, although they are commonly mistaken as such. Psychosis is a disorder of thinking and perception in which information processing and reality testing are impaired, resulting in an inability to distinguish fantasy from reality (delusions and hallucinations). Schizophrenia is one of several psychiatric disorders for which psychosis is a major feature. Other psychiatric disorders that can be mistaken for schizophrenia include the following:
- Bipolar disorder in a manic phase
- Delusional disorders
- Brief psychotic disorder
- Schizophreniform illness, schizoid and schizotypal personality disorder
- Borderline personality disorder
- Posttraumatic stress disorder (PTSD)
- Transient, drug-induced psychosis; alcoholic hallucinosis; and drug or alcohol withdrawal syndromes
- Major depression with psychotic features
- Delirium

The most common etiologies for severe mental status changes in the ED are organic, not psychiatric. They include medications, drug intoxication, drug withdrawal syndromes, and general medical illnesses causing delirium.

Take a careful medication history; many commonly prescribed medicines can occasionally cause psychotic reactions.

Medical clearance examinations are medicolegally risky. These evaluations are typically brief and rarely sufficient to rule out organic etiologies.

Go to Schizoaffective Disorder, Childhood-Onset Schizophrenia, and Schizophreniform Disorder for complete information on these topics.

**Patient History**

The onset of schizophrenia is insidious in approximately one half of all patients. The prodromal phase can begin years before the full-blown syndrome and is characterized by losses of functioning in home, society, and occupation (eg, poor school or work performance, deterioration of hygiene and appearance, decreasing emotional connections with others, behaviors that would have been odd for the individual in the past).

A gradual onset indicates a more severe and prolonged course of illness.

An abrupt onset of hallucinations and delusional, bizarre, or disorganized thinking in patients who previously functioned normally may result in a better intermediate and long-term outcome. Such patients arriving in a psychotic crisis that requires immediate management may not have been diagnosed with psychiatric illness previously. They often present diagnostic dilemmas involving organic versus psychiatric etiology and primary psychotic versus affective disorder diagnosis. Treatment may be complicated further by the presence of alcohol or drug intoxication.

Often, the history obtained in the ED relates to a complication of treatment (medication adverse effects) or a crisis arising from socioeconomic factors secondary to schizophrenia (eg, poverty, homelessness, social isolation, failure of support systems).

While the primary diagnosis of schizophrenia rarely is made de novo in the ED, several historical features can be helpful in distinguishing the illness from the many medical and psychiatric conditions that can mimic it.
Two or more of the following must have been present over the prior month for a significant period (unless treated with medication):

- **Delusions** - Bizarre or illogical false beliefs, which often have a paranoid, grandiose, persecutory, or religious flavor; false interpretation of normal perceptions
- **Hallucinations** - Typically auditory (visual or tactile strongly suggest an organic etiology), often involving malevolent or taunting voices commenting on the patient's actions or character, often with a sexual flavor; voices giving commands (ie, command hallucinations); 2 or more voices discussing or arguing with each other; audible thoughts; thought withdrawal (feeling that thoughts are being removed from head), thought broadcasting, or thought interference by an outside agent
- **Disorganized speech** - Tangential, incoherent, rambling speech; neologisms (new word creation); loosening of associations
- **Behavior** - Grossly disorganized or catatonic
- **Negative symptoms** - Poverty of speech (ie, alogia), emotional and/or social withdrawal, blunting of affect, avolition

Loss of a previously held level of occupational, social, or self-care functioning must have occurred since the onset of illness.

Presence of an affective disorder (eg, major depression, **bipolar disorder**, **schizoaffective disorder**) must be excluded; these conditions can be mistaken for schizophrenia and have very different prognoses and therapies. Additionally, an organic etiology (eg, drug intoxication, medical illness) must be ruled out.

One of the following problems with antipsychotic medications commonly is the chief complaint:

- Acute dystonia (muscle rigidity and spasm), oculogyric crisis (bizarre and frightening upward gaze paralysis and contortion of facial and neck musculature), akathisia (dysphoric sense of motor restlessness)
- Parkinsonian symptoms of stiffness, resting tremor, difficulty with gait, and feeling slowed-down
- Orthostatic hypotension caused by alpha-adrenergic blockade
- Dry mouth, fatigue, sedation, visual disturbance, inhibited urination, and sexual dysfunction, which can be adverse reactions to antipsychotic medication or to anticholinergic drugs taken for prophylaxis of dystonia

Obtain the following information when an acutely psychotic patient presents to the ED:

- The potential danger the patient presents to himself or herself or to others
- Prior medical and psychiatric records, including past hospitalizations and medication therapy
- His or her baseline level of functioning
- Current or recent substance abuse
- Current use of prescribed, over-the-counter (OTC), and herbal medications
- Compliance with current psychiatric medications
A paranoid schizophrenic, in response to delusions and command hallucinations, can be extremely dangerous and unpredictable.

Find out about threats made to others, expressions of suicidal intent, and possession of weapons at home or on the person.

**Physical Examination**

Depending on the reason for ED presentation, the patient with schizophrenia may present with wildly agitated, combative, withdrawn, or severely catatonic behavior. Conversely, the patient may appear rational, cooperative, and well controlled (perhaps with only some blunting of affect). The person also could be subtly odd, unkempt, or frankly bizarre in manner, dress, and/or affect.

Perform a general physical examination on all patients, with attention to vital signs, pupillary findings, hydration status, and mental status.

A comprehensive physical examination and laboratory evaluation is required when an organic etiology or drug intoxication may be related to mental status changes.

Pay particular attention to fever, tachycardia (which, in association with rigidity, can be a sign of neuroleptic malignant syndrome), heatstroke (antipsychotics inhibit sweating), and other medical illness.

Look for signs of dystonia, akathisia, tremor, and muscle rigidity.

Tardive dyskinesia is a common and often irreversible sequela of long-term (and sometimes brief) antipsychotic use. It involves uncontrollable tongue thrusting, lip smacking, and facial grimacing.

Mental status testing should typically reveal clear sensorium and orientation to person, place, and time. Assess attention, language, memory, constructions, and executive functions. Absence of clear sensorium and/or orientation may indicate the presence of acute delirium, a medical condition.

**Differential Diagnosis**

Conditions to consider in the differential diagnosis of schizophrenia include the following:

- Delirium, dementia, and amnesia
- Depression
- Encephalitis
- Neuroleptic malignant syndrome
- Panic disorders
- Personality disorders
- Acetaminophen toxicity
- Hallucinogen toxicity
- Hallucinogenic mushroom toxicity
Neuroleptic agent toxicity
Phencyclidine toxicity
Sympathomimetic toxicity

Laboratory Studies

No specific laboratory findings are diagnostic of schizophrenia. However, performing some studies may be necessary to rule out possible organic etiologies for psychosis or to uncover complications of schizophrenia and its treatment.

Blood levels of certain psychiatric drugs, specifically lithium and the mood-stabilizing antiseizure medications (eg, valproic acid, carbamazepine), can be used to confirm compliance or rule out toxicity.

Serum alcohol levels and drugs-of-abuse screening can be useful when substance abuse is suspected.

Interpreting the results of a fingerstick blood glucose determination is a rapid and inexpensive method of ruling out a diabetic emergency masquerading as an exacerbation of a psychotic illness; similarly, measuring oxygen saturation levels can help to disclose hypoxia resulting in behavioral or central nervous system (CNS) disturbance.

Electrolyte measurements may reveal hyponatremia secondary to water intoxication (ie, psychogenic polydipsia). This is common in undertreated or refractory schizophrenia.

Laboratory abnormalities observed in neuroleptic malignant syndrome may include leukocytosis with left shift and elevated skeletal muscle creatinine kinase (CK) and aldolase levels.

Other Studies

Computed tomography (CT) scanning, magnetic resonance imaging (MRI), and positron emission tomography (PET) scanning can disclose abnormalities of brain structure and function in schizophrenia. Although these studies are of interest for research, they have limited clinical relevance. Various psychological and neurobiologic tests, such as absence of smooth eye-tracking, may be helpful in studying schizophrenia but are not useful in the ED setting.

Prehospital Care

Safe transport of a patient with acute psychosis may require physical or chemical restraints.

Be familiar with restraint and sedation protocols in your emergency medical service (EMS) area and hospital.

Know your state's regulations or statutes regarding involuntary transport, treatment, and hospitalization of psychiatric patients.

Document your concerns regarding imminent risk to the patient or others resulting from the patient's psychiatric condition.
File appropriate application for involuntary transport/treatment when indicated.

**Emergency Department Care**

Evolving from the efficacy of modern antipsychotic medications and the subsequent widespread budget cutting of psychiatric services over the past 2 decades, deinstitutionalization of patients with schizophrenia has had a major impact on emergency medicine. Patients with schizophrenia now are frequent visitors to the ED, presenting with problems ranging from symptom exacerbation to medication noncompliance, adverse effects to medications, and socioeconomic crisis arising from substance abuse, poverty, homelessness, or a failed support system.

Depending on the reason for the patient's ED visit, care may be limited to diagnosis and treatment of an urgent or nonurgent medical complaint; a brief medical evaluation followed by consultation with psychiatric, crisis, or social service personnel; evaluation and treatment of an adverse reaction to a psychiatric drug; or physical and chemical restraint of a patient with acute psychosis in coordination with a workup, when indicated, to rule out organic etiologies.

Remember that psychiatric and organic illness can coexist and interact at the same time in the same patient. Furthermore, acute psychiatric symptoms and difficulties obtaining a reliable history from the patient can mask serious organic illness.

A brief medical clearance examination is limited in usefulness and insufficient to rule out organic etiologies.

**Use of restraints and involuntary commitment**

Failure to talk down or intimidate (with a show of force) a severely agitated patient may require physical restraint of the patient, followed by chemical restraint (ie, sedation).

Proper physical restraints and individuals trained in their application should be available at all times. Document reasons for restraining a patient (mention patient/staff safety and protection), the type of restraint used (eg, locked room vs 4-point leather), the maximum duration of restraint, and reasons for involuntary commitment\(^1\); follow all Consolidated Omnibus Budget Reconciliation Act (COBRA) regulations when transferring patients to another facility for psychiatric care.

Be familiar with ED and hospital regulations, Health Insurance Portability and Accountability Act (HIPAA) rules, regional statutes, and Emergency Medical Treatment and Labor Act (EMTALA) requirements regarding the use of physical restraints, involuntary psychiatric commitment, and transfer.

Do not order "restrain prn." Give specific reasons for applying and removing restraints. Personally ensure that restraints are applied safely. Use the least restrictive measures that are effective. The patient should be monitored continuously while restrained either physically or chemically. Restraint and seclusion orders should be renewed at regular intervals not to exceed 4 hours.
In most cases, chemical restraint (ie, sedation) is preferable to physical restraint when prolonged behavioral control is necessary or when the patient is severely combative. Any physical restraint of a combative patient can lead to serious injury or death (eg, from aspiration, sudden cardiac death, rhabdomyolysis).

**Tranquilization**

Rapid tranquilization (chemical restraint) may be carried out as follows here.

Typically, a combination of lorazepam 2 mg mixed in the same syringe with haloperidol 5 or 10 mg is administered intramuscularly or intravenously. Benztropine (Cogentin), 1 mg, may be added to counteract dystonia ("5-2-1"). Elderly patients typically require lower doses. Repeat doses can be administered in 20-30 minutes as needed to control continued severe agitation. Haloperidol dose can be doubled each time up to 20 mg if prior dosing is inadequate for severe agitation.

An alternative to the haloperidol component is droperidol at the same dosages. Droperidol is more sedating, faster in onset, and somewhat shorter acting. The downside is the black-box warning about prolonged QT syndrome, which rarely occurs at higher doses than those typically utilized for acute behavioral control. Cardiac monitoring is recommended, but some experts believe these warnings to be overly cautious. Following the black-box warning, most physicians continuing to utilize droperidol for acute behavioral control reserve it for special situations requiring somewhat faster onset and greater sedation than would be achieved with similar doses of haloperidol. Droperidol, therefore, may be considered useful, yet second-line to haloperidol in the emergency department.

In certain cases, sedation can be administered orally and may consist of lorazepam 2 mg plus haloperidol 2-5 mg or risperidone 2 mg PO (by mouth). An alternative is olanzapine (Zyprexa Zydis), which is an oral, rapidly disintegrating tablet, 5-10 mg.

If the patient has haloperidol or droperidol sensitivity, ziprasidone 10-20 mg (administered intramuscularly) can be substituted (20 mg is the typical dose). Exercise caution regarding prolonged QT syndrome and multiple drug-drug interactions. Ziprasidone may be somewhat slower in onset than haloperidol and droperidol but has excellent sedating qualities with less propensity for dystonia. A single repeat dose of 20 mg in 4 hours may be necessary (maximum 40 mg/d IM). A 10 mg dosing can be repeated in 2 hours. Reduced pricing now makes ziprasidone an excellent first-line alternative to the older, conventional antipsychotics, especially in younger patients who are more likely to develop dystonic reactions.

Lorazepam alone is sometimes sufficient for lesser degrees of agitation or anxiety and can be given sublingually for more rapid onset. The recommended dose for anxiety and mild agitation is 1-2 mg administered orally or sublingually.

**Consultations**

When available, consult with a psychiatrist (ideally, who can immediately and personally evaluate the patient in the ED) when assistance is needed with proper diagnosis and/or management of acute symptoms or severe behavioral disturbances.
Crisis liaison teams, typically made up of clinical social workers, psychologists, and/or psychiatric nurses, are available in many EDs 24 hours a day through the hospital or local psychiatric agencies. Their primary role is assessment for appropriateness of psychiatric hospitalization and to determine availability of inpatient beds in compliance with the patient's insurance coverage. Such clinicians can also assist in arranging prompt outpatient follow-up when hospitalization is not necessary.

Emergency clinicians always should examine each patient personally, assessing their suicide risk or threat to others and documenting all reasoning. A medical clearance evaluation must be performed in order to rule out organic illness that may be causing psychiatric symptoms or will preclude admission to a psychiatric bed.

The emergency clinician should speak directly with the crisis consultant and read his or her evaluation notes. Then, based on the evaluation and the information has been obtained, the crisis consultant's disposition proposals should be confirmed or modified. The final decision as to patient disposition should always be confirmed by the emergency physician. Such decision-making should never be abrogated to or overruled by a crisis liaison worker. Ultimately, the emergency clinician is medically and legally responsible for the patient and his or her disposition until a psychiatrist or other provider assumes the primary responsibility for care.

Do not delay necessary sedation of a patient with acute psychosis for the diagnostic benefit of psychiatric crisis consultants not yet present in the ED. Treatment delays can lead to injuries and can increase morbidity and worsen prognosis. In these situations, the crisis consultant must rely on the presedation assessment.

**Transfer**

Psychiatric transfers from the ED to other hospitals are common because of bed shortages and insurance considerations. These transfers should be treated as medical transfers by documenting the patient's stability, the reason for transfer, and other factors required to meet COBRA obligations.

Sedating patients with severe agitation and/or acute psychosis is essential to prevent potential injury to the patient and staff en route.

**Medication**

Antipsychotic medications (previously referred to as neuroleptics or major tranquilizers) have revolutionized the treatment of and prognosis for schizophrenia. All block dopamine (especially D2) receptors in the brain.

The newer, atypical agents also affect serotonin transmission. These newer agents (eg, risperidone, clozapine, olanzapine, quetiapine, ziprasidone, aripiprazole) are less likely to produce dystonia and tardive dyskinesia and are more likely to improve negative symptoms. However, they are not more effective than traditional agents (eg, haloperidol, droperidol, fluphenazine), with the possible exception of clozapine in the treatment-resistant patient. Some newer agents cause serious weight gain and may raise the risk of insulin resistance and diabetes
mellitus. Studies show a slightly increased death rate in elderly patients with dementia using atypical agents. However, the risk was even higher with the older, conventional agents.

Benzodiazepines also have a role in schizophrenia, especially in the emergency care of a patient with acute psychosis.

Anticholinergic medications (ie, benztropine, diphenhydramine) are used to counteract the dystonic and parkinsonian adverse effects (extrapyramidal symptoms [EPS]) of the antipsychotics, particularly the higher-potency agents that are less sedating but more EPS-producing.

For further information, see the Practice Guideline for the Treatment of Patients with Schizophrenia.[3]

References

