بسم الله الرحمن الرحيم

Treatment of psychosis in geriatric patients

Two Preliminary Points

1-In older adults, for all conditions:
think "Comorbidity"

2- Any new psychiatric conditions or change in symptoms ,Must assume physical cause until proven otherwise

Management Factors

Age-related pharmacokinetic changes (absorbtion,distribution,metabolism , elimination)

Age -related pharmacodynamics

(body response to medication , including clinical response and adverse reactions)

Comorbidities and concurrent use of medications

Safety and efficacy issues of pharmacological treatments, such as FDA black box warnings and limited efficacy

Acute or subacute?

Primary or secondary disorder?

THERE IS NO RELIABLE PATHOGNOMONIC SIGNS TO DISTINGUISH PRIMARY OR SECONDARY PSYCHOSIS (NEED TO RULE OUT SECONDARY CAUSES)

Primary psychotic disorders:

Schizophrenia and related disorders :

Schizophrenia

Schizoaffective disorder

Delusional disorder

Affective psychoses :

Bipolar disorder with psychotic features

Unipolar depression with psychotic features

Secondary psychotic disorders:

Psychotic symptoms associated with dementia :

Alzheimer's Disease with psychoses
Vascular dementia with psychoses
Lewy Body Disease with psychoses
Other dementing disorders with psychoses

Psychotic symptoms during delirium

(*Psychotic symptoms due to medical and surgical disorders)*

Psychotic symptoms associated with medications and substance abuse

Primary psychotic disorders:

Schizophrenia and related disorders

Schizophrenia

Schizoaffective disorder

Delusional disorder

Affective psychoses

Bipolar disorder with psychotic features

Unipolar depression with psychotic features

late life schizophrenia

1- Early onset

2-Late onset

3- Very-late-onset schizophrenia-like psychosis

late life schizophrenia

Early onset schizophrenia became Chronic schizophrenia

Gradual decline in positive symptoms and an increase of negative symptoms , correlating with cognitive deficits and depressive symptoms , poor physical health , low income and diminished network support.

late onset (after 40 -60year) became Chronic schizophrenia

Good premorbid and good outcome ,response to lower dose

Decreasing the dose of medications to the lowest effective dosage should be attempted

late life schizophrenia

Non-pharmacological interventions

Education for patients and family

Cognitive behavior therapies (CBT)

Family interventions to subside conflicts in caregiving

Assertive community treatment

Training for social skills

Supporting socioeconomic approaches to enhance treatment adherence

Medical care (cardiovascular,metabolic,frailty,bleeding,sedation,EP….)

For new drug start in late life schizophrenia

Individualize choice of drug on basis of:

- Patient's comorbidities
- Drug's side-effect profile
- Patient's sensitivity to these effects
- Drug's potential for interacting with other medications

The starting dose of the drug being 25–50% of the dose used in young patients

Starting dosage for late onset persons **25%** of the recommended adult dose and

Maintenance doses effective **25-50%**

Effective dose **50-75%**

common adverse effects

include sedation

- frequent falls

anticholinergic effects

cardiovascular effects(QT prolongation)

- extrapyramidal symptoms and tardive dyskinesia
- metabolic effects

hyperprolactinemia, agranulocytosis, and neuroleptic malignant syndrome

Risperidone	0.25–0.5	2–3
Aripiprazole	2.5- 5	5-20
Olanzapine	1–5	5 –15
Quetiapine	12.5–25	100–200
Clozapine	6.25	50–100
(Ziprasidone	15–20	80–160)
Typical antipsychotics:		
Haloperidol	1-2	1.5-5
Perphenazine	2-4	4-16

The dosage of medications for treating symptoms was significantly higher for early-onset schizophrenia but lower for late-onset and very late-onset groups .

The risk of tardive dyskinesia was found to be predominantly high for patients with very late-onset schizophrenia

Decreasing the dose of medications to the lowest effective dosage should be attempted

- electrocardiography,QT prolongation(aripiprazole,olanzapine ,quetiapine),
  poor feeding ,female, IHD, hypomagnesemia are risk factors of qt prolongation
- laboratory tests, weight gain

Long acting injective drugs:

30-50 percent of young dose (alert about EP. Qt prolongation, over sedation and falling)

ECT : bilateral (hospitalized and monitoring of electrolyte and cardiac)

Very Late onset schizophrenia

Neurodegenerative

Some research groups have reported more impaired function in learning and memory retention in individuals with very late-onset schizophrenia, suggesting the possibility of an association with neurodegeneration.

The dosage of medications for treating symptoms was significantly lower for late-onset and very late-onset groups

Risperidone	0.25–0.5	2–3
Olanzapine	1–5	5 –15
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Unipolar depression with psychotic feature (primary psychiatric disorder)

Psychotic feature in late life depression occur in about 4 percent of depressed older outpatients and 45 percent of hospitalized older depress patients

Ect : Standard for psychotic depression in older adults; response rates 80%

ECT : Is most important of the non pharmalogical somatic treatments,and is the treatment of the choice in certain older patients with severe depression due to poor tolerance of psychotropic medications, psychotic features , significan comorbid medical conditions ,or marked disability associated with depression

Treatment of choice for psychotic major depression

Treatment of choice for psychotic major depression:

1-An antipsychotic plus antidepressant

2-Electroconvulsive therapy

Second line : antidepressant alone or mood stabilizer plus antipsychotic

Combination of antidepressant and antipsychotic:

Risperidone	0.25–0.5	2–3
Olanzapine	1–5	5 –15
Quetiapine	12.5–25	100–200
Aripiprazol	2-5	5-15

Psychotic depression in bipolar

The use of quetiapine as monotherapy has been chosen as first line treatment of acute bipolar depression and the prevention of mania/hypomania switching

Electroconvulsive therapy is a treatment of choice for patients with bipolar major depression who are **severely ill** (e.g., persistent suicidal ideation with a plan) and have not responded to multiple (e.g., three to five) pharmacotherapy trials.

ECT AND elderly MDD

ECT : Is most important of the non pharmalogical somatic treatments,and is the treatment of the choice in certain older patients with severe depression due to poor tolerance of psychotropic medications, psychotic features , significan comorbid medical conditions ,or marked disability associated with depression

Management

Admission to hospital is required to prevent self

harm and to ensure adequate hydration and nutrition. Treatment comprises either electroconvulsive therapy and/or a combination of antipsychotic and antidepressant medications.

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These medications should be continued for at least 1 year. Patients with relapsing depressive psychoses require life long combined pharmacotherapy. Antidepressants very occasionally trigger mania. If this happens, the antidepressant should be stopped immediate

Secondary psychosis

Alzheimer's disease

Dementia with Lewy bodies and Parkinson's disease.

- In Alzheimer's disease and Lewy body dementia, psychotic symptoms are thought to be related to the underlying pathophysiology of the condition.
- In Parkinson's disease, which commonly presents with motor symptoms and dementia, anti Parkinsonian medication is the most frequent cause of psychotic symptoms .

Psychosis in major neurocognitive disorders

Behavioral and psychologic symptoms of dementia(BPSD)

The most prevalent BPSD are apathy, depression, irritability, agitation and anxiety, delusions , hallucinations, and disinhibition. euphoria ,Agitation , disinhibition

In a systematic review of meta-analyses that evaluated the use of antipsychotics among individuals with dementia, the investigators found that antipsychotics had modest efficacy in treating psychosis, aggression, and agitation.

There is also significant controversy regarding the use of antipsychotics among older adults who present with severe psychosis due to dementia. The FDA has a boxed warning indicating an association between the use of antipsychotics among older adults with dementia and increased risk for mortality.

Increases the risk for cerebrovascular adverse events, metabolic side effects, and pneumonia, when compared with age-matched controls who were not prescribed these drugs

Antipsychotic medications should be discontinued as soon as clinically possible to avoid serious adverse effects among older adults.

BPSD

Choice of treatments

Non-pharmacological interventions as first-line treatment followed by the least harmful medication for the shortest time possible

Non-pharmacological treatment of psychotic symptoms in dementia

positive stimulation through auditory sensations such as music and tactile sensations such as touch and massage may also prove useful

Reducing sensory deprivation

Reducing inappropriate inner sensory stimulation: reduce stimulations that produce psychotic symptoms.(Examples include removing mirrors if reflections cause the delusion of having phantom boarders in the house, or drawing a curtains over windows if the patient has a delusion of being spied on or followed.)

Non-pharmacological treatment of psychotic symptoms in dementia

Sensory enhancement

structured activities

Social contact

Behavior therapy

Cognitive/emotion-oriented interventions (reminiscence therapy, simulated presence therapy, validation therapy

Aromatherapy, light therapy, massage/touch, music therapy

Non-pharmacological treatment of psychotic symptoms in dementia

- Provide eyeglasses, hearing aids, mobility support, etc.
- Consider approaches based on patient history/preferences: hand massage, pet therapy, music listening

- Caregiver education: skills targeting behavioral challenges, and enhancing coping techniques

Antipsychotics

- First, psychosis related to cognitive disorders presents differently than primary psychotic disorders.
- Secondly, psychosis in late life may be a harbinger of the cognitive disorder even in the absence of other overt symptoms.
- Third, many times the psychotic symptoms in cognitive disorders may not always need antipsychotic treatment.
- In many instances the psychotic symptoms may be harmless and not distressing to the patient, and treatment with an antipsychotic may present more risks than benefits, thus antipsychotics should only be considered when the symptoms themselves are distressing to the patient or lead to other problems such as agitation or aggression.

APA recommends that in the absence of delirium, if nonemergency antipsychotic medication treatment is indicated, haloperidol should not be used as a first-line agent.

APA recommends that in patients with dementia with agitation or psychosis, a long-acting injectable antipsychotic medication should not be utilized unless it is otherwise indicated for a co-occurring chronic psychotic disorder.

APA recommends that in patients with dementia with agitation or psychosis, if there is no clinically significant response after a 4-week trial of an adequate dose of an antipsychotic drug, the medication should be tapered and withdrawn.

Pharmacologic treatments

Currently, antipsychotic medications in patients with dementia are recommended only :

There is substantial risk for harm to self or others

After all non- pharmacological measures have failed

This approach is apparently justifiable in the case of minor hallucinations in PDD or DLB, to which patients are usually insightful, and which rarely lead to patient suffering or to behavioral changes. Early treatment of minor psychotic symptoms in PD has been suggested by some authors to attenuate psychiatric deterioration

Barriers for the adoption of the FDA's warnings were lack of alternative treatments :

lack of guidance, lack of evidence regarding pharmacological treatments, and poor availability of data

Treatment of behavioral symptoms in dementia :

Placebo effects???

The natural course of illness? ??

Symptomatic decline over time ???

Important points before starting treatment

Poly pharmacy

Falling

Qt prolongation

Poor feeding and dehydration

Main organs

Secondary psychosis

After non pharmacological intervention

Recommended doses:

Medication	Initial dose	Usual dosage
	mg/day	mg/day
Risperidone	0.5	0.5-2
Olanzapine	2.5-5	5-10
Quetiapine	25	200-250
Aripiprazole	5	5-15
Clozapine	6.25-12	50

Brexpiprazole (Rexulti®) is the only atypical antipsychotic that is FDA-approved for agitation associated with dementia due to Alzheimer's

Other effective drugs in agitation with and without psychosis

Escitalopram 5-15mg

Citaloperam 10-20

Anticonvulsants

BZ

Cholinesterase inhibitors (Rivastigmine, donepezil and galantamine)

Improving psychotic symptoms and may be value in preventing or reducing psychotic symptoms in Alzheimer's disease

The treatment of psychotic symptoms in Lewy body dementia remains a challenge and most often requires a treatment plan tailored to the characteristics of individual patients.

This should strike a balance between use of anti-Parkinsonian medication, which improves motor disorder but may induce psychotic symptoms, or not treating motor symptoms and cautiously treating the psychotic symptoms.

Parkinson's Disease

Critical to adjust anti-parkinsonian medication

Quetiapine :12.5mg to 150mg has been effective for psychotic symptoms

Clozapine : 6.25mg to 50mg has been effective.

pimavanserin has been proven effective and well-tolerated for psychosis symptoms in PD and LBD ,being approved by the FDA for this indication

pimavanserin ,an inverse agonist and antagonist of the serotonin 5-HT2A receptor which lacks the dopamine receptor blocking effects of other antipsychotics ,

Comorbid conditions

- Bipolar patients with MCI or early stage of Major Neurocognitive Disorder

Bipolar mood disorder comorbid with PD

Major depressive disorder with late onset

Depressive or anxiety symptoms as prodromal stage of M.N.Cognitive Disorder or PD

- Patients with dementia are especially vulnerable to delirium
- If patients with long standing psychotic illnesses develop dementia, doses of antipsychotic medications may need to be reduced.

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