

University of Veterinary and Pharmaceutical Sciences



Pharmaceutical Care in Psychiatric Patients

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Workflow of this lecture



Patients diagnosed with:

- Schizophrenia
- Depression
- Bipolar Disorder
- Anxiety

Psychiatric medicines:

- Antipsychotics
- Antidepressants
- Anxiolytics

Special chapters:

- Peroral medicines (Cariprazine, Brexpiprazole)
- Injectable medicines (Paliperidone)
- Electroconvulsive therapy



Psychiatric patients



Psychiatric patients usually require a lifelong treatment

Pharmacological approach:

Long-term use of psychiatric medication is connected with many adverse effects (e.g. cardiovascular, metabolic, anticholinergic, and extrapyramidal effects, orthostatic hypotension, sedation, falls, and neuroleptic malignant syndrome)

Nonpharmacological approach:

Cognitive Behavioural Therapy (CBT) enhancing social cognition and perception, verbal communication, social skills, and interpersonal problem-solving skills in psychiatric patients

Schizophrenia



Schizophrenia is a **serious psychiatric disorder** in which people interpret reality abnormally, characterized by extremely disordered thinking and behavior that impairs daily functioning, and disabling

Positive Symptoms: hallucinations, delusions, disorganised thinking

Negative Symptoms: lack of emotions and interests, social withdraw, slow movement, poor memory, lack of concentration and poor hygiene

Causes: combination of **genetics**, brain **chemistry** and **enviroment** contributes

In men, symptoms typically start in the early to mid-20s, and in women, symptoms begin in the late 20s, it's uncommon for children to be diagnosed and rare for older than age 45 years

Schizophrenia



Risk factors:

- family history of psychiatric disease
- pregnancy and birth complications (e.g. malnutrition or exposure of toxins and viruses that may impact brain development)
- taking mind-altering drugs (psychoactive drugs)



Complications:

- suicide or aggressive behaviour
- depression or anxiety disorders
- abuse of alcohol and drugs (nicotine)
- inability to work or attend school
- financial problems and homelessness
- social isolation
- health and mental problems
- being victimized



Types of schizophrenia

1. Paranoid schizophrenia- the most common form of schizophrenia, may be developed later in life

Symptoms: hallucinations and delusions, but speech and emotions may not be affected

2. Hebephrenic schizophrenia- called disorganised schizophrenia, usually occurs between 15-25 years old

Symptoms: disorganised behaviours and thoughts, disorganised speech patterns

3. Catatonic schizophrenia- the rarest schizophrenia, characterised by unusual, limited and sudden movements

Symptoms: often switch being very active or not talk much, and may mimic other's speech and movement

4. Undifferentiated schizophrenia- some signs of paranoid, hebephrenic or catatonic schizophrenia, but it doesn't obviously fit into one of these types

5. Residual schizophrenia- history of psychosis in the past, only negative symptoms

6. Simple schizophrenia- rare to experience positive symptoms, dominant negative symptoms

7. Cenesthopathic schizophrenia- people experience unusual bodily sensations

8. Unspecified schizophrenia- symptoms meet the general conditions for a diagnosis, but do not fit in to any of the above categories



Treatment of schizophrenia

Changes in neurotransmitters, especially **dopamine**, serotonin, and glutamate

Different receptor bindings → different adverse effects

Typical antipsychotics (first-generation):

Phenothiazines:

Chlorpromazine, Levopromazine,
Fluphenazine, Perphenazine, Thioridazine

Thioxanthenes: Chlorprothixene, Thiothixene

Butyrophenones: Haloperidol, Droperidol

Adverse effects:

anticholinergic, extrapyramidal, sedative

Atypical antipsychotics (second-generation):

MARTA: Clozapine, Olanzapine, Quetiapine,
Asenapine, Zotepine

SDA: Risperidone, Paliperidone, Lurasidone,
Iloperidone, Ziprasidone

D₂/D₃: Sulprid, Amisulpirid

Aripiprazole, Brexpiprazole, Cariprazine

Adverse effects:

metabolic, cardiovascular, hyperprolactinemia

New options of the treatment



Cariprazine (2015)

Indication: schizophrenia, and mania or mixed episodes in bipolar disorder

Mechanism: act to D₂/D₃ receptors as a partial agonist, with high selectivity for D₃

Dose: 1.5-6 mg daily

Benefits: not impact prolactin levels, not increase the QT interval (ECG), low probability of extrapyramidal symptoms

Adverse effects: akathisia, insomnia, weight gain

Interactions: substrate of CYP2D6 and CYP3A4

Brexpiprazole (2015)

Indication: schizophrenia, and major depressive disorder

Mechanism: partial agonist D₂ receptors and serotonin-dopamine activity modulator (SDAM)

Dose: 1-4 mg daily

Benefits: less akathisia, restlessness and insomnia than other antipsychotics (include aripiprazole), not impact prolactin levels

Adverse effects: upper respiratory tract infection, akathisia, weight gain, nasopharyngitis

Interactions: substrate of CYP2D6 and CYP3A4

Long-acting injectable antipsychotics (LAI)

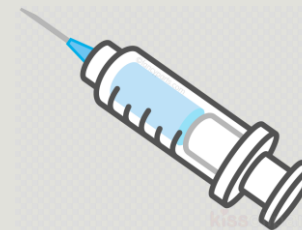
Evidence-based medicine (clinical trials) compared to oral medication LAI have shown significant improvement in:

1. reduction of illness relaps, in which is 3-5 times higher when patients stop taking medication
2. reduction of the frequent uncertainty between the drug response and patient adherence

Relaps is associated with repeated hospitalizations, social and work disruption, family burden and increased risks of harm to self and others

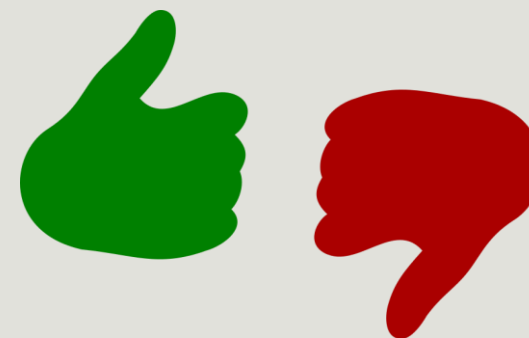
There is immediate **knowledge when a dose is missed**, and appropriate interventions can be implemented.

BENEFITS: Patients do not need to be reminded of their illness every day by taking a medication or do not need to make the daily decision to take it, there is only the one occasion of medication use every 2 to 12 weeks when medication administration is necessary.



Potential advantages

- Early identification of non-adherence
- Providing a mechanism for monitoring adherence with injections
- No need to remember to take medication every day
- Regular interactions between patient and medical staff
- Reduced relapse frequency and rehospitalization rates
- Clear attribution of the cause of relapse or non-response, discriminating between non-adherence or lack of response
- Reduce the risk of accidental or deliberated overdose
- Treating patients with more stable plasma concentrations than oral medications
- Avoidance of first-pass metabolism - better relationship between dose and blood level of drug
- Lower and less frequent peak plasma level - reduced side effects



Side effects:

- pain or soreness after injection
- dizziness, drowsiness, confusion
- uncontrolled movements
- skin rashes, rapid heartbeat, blurred vision...
- particular sedation
- post-injection delirium syndrome (less than 1%)



Paliperidone and injectable AP

Paliperidone is an active metabolite of the risperidone, efficacy from dopaminergic and serotonergic antagonism

Indication: schizophrenia, schizoaffective disorder

A long-acting injectable formulation, indicated once-every 1 or 3 months after an initial titration period

Dosing: initial dose 150mg (reduced in some cases), 100 mg in 8 days, and continuing monthly dosing (in demanded dose of 100, 75, 50, 25 mg)

Benefits: significantly less extrapyramidal symptoms and QT interval prolongation

Adverse effects: headache, tachycardia, somnolence, insomnia, hyperprolactinemia, sexual dysfunction

Fluphenazine decanoate

Haloperidol decanoate

Flupenthixol decanoate

Zuclopentixol decanoate

Risperidone microsphere (2002)

Olanzapine pamoate (2008)

Aripiprazole lauroxil (2013)

Paliperidone palmitate (2009, 3MPP 2015)

Comparable studies in 2013 have shown paliperidone is more effective than haloperidol, quetiapine, and aripiprazole, less effective than risperidone 11%, and clozapine 34%

Depression



Depression means a state of low mood and aversion to activity

Mood disorders characterized by depression include major depressive disorder and dysthymia

Changes in neurotransmitters: **serotonin**, norepinephrine, dopamine

Treatment phases:

Acute: 6-12 weeks

Continuation: 4-9 months
(this phase usually ends with 1st episode)

Maintenance: years
(this phase at least 5 years after 3rd episode)

Major depressive disorder (MDD), is a mental disorder characterized by at least 2 weeks of low mood, often accompanied by low self-esteem, loss of interest in enjoyable activities, low energy, pain without clear cause

Treatment: SSRI, SNRI, TCA

Dysthymia, known as persistent depressive disorder (PDD), is a state of chronic depression, which persists for at least 2 years, consisting in cognitive and physical problems, characterized by insomnia or hypersomnia, fatigue or low energy, eating changes, low feelings of hopelessness, poor concentration, difficult-making decisions

Treatment: SSRI, augmentation with lithium, thyroid hormone, amisulprid, buspirone, mirtazapine...



Find a right antidepressant

- **Particular symptoms:**
trouble sleeping (trazodone), anxiety (venlafaxine)
- **Possible side effects:** anticholinergic, metabolic...
- Whether it worked for a closed relative or in the past
- Interaction with other medications
- Pregnancy or breast-feeding
- Other health conditions: stop smoking (bupropion), pain (duloxetine), migraines (amitriptyline)
- Cost and health insurance coverage

How to recognize it works?

1. Be patient, and see results in few weeks
2. Take medicine consistently, and the correct dose
3. Explore options and consult with your doctor
4. Try psychotherapy
5. Don't stop taking medicine without talking your doctor (withdrawal-like symptoms)
6. Avoid alcohol and drug abuse
7. Other medications consult with your pharmacist



Treatment of depression

Selective serotonin reuptake inhibitors (SSRIs):

First-line antidepressants, well-tolerated

Citalopram, Escitalopram, Fluoxetine, Paroxetine, Sertraline, Fluvoxamine

Treatment of **major depressive disorder**, anxiety disorder, panic disorder, obsessive-compulsive disorder (OCD), eating disorders, chronic pain, premature ejaculation, posttraumatic stress disorder...

Serotonine-norepinephrine reuptake inhibitors (SNRIs):

Duloxetine, Venlafaxine, Desvenlafaxine

Tricyclic antidepressants: Imipramine, Nortriptyline, Amitriptyline, Trimipramine, Desipramine, Protriptyline, Doxepine

Very effective, but tend to cause severe side effects

Monoamine oxidase inhibitors (IMAOs):

Tranylcypromine, Selegiline*

Serious side effects, using require a strict diet (avoid tyramine in cheese, bananas, wine...)

Atypical antidepressants:

bupropion, mirtazapine, nefazodone, trazodone, vortioxetine...

Bipolar disorder

BP is a mental disorder characterized by periods of depression and abnormally elevated mood called mania (less severe is hypomania)

During mania, an individual behaves or feels abnormally energetic, happy, or irritable. Usually make impulsive decisions with little regard for the consequences

During depression, an individual often cries, has a negative outlook on life, and poor eye contact with others, a high risk of suicide

Prevalence of this disease increases with age, resulting in polypharmacy

Somatic comorbidities of BD including:

- metabolic syndrome (up to 50%)
- hypertension (45-69%)
- diabetes mellitus (18-31%)
- cardiovascular disease (9-49%)
- respiratory illness (4-15%)
- arthritis (16-21%)
- endocrine abnormalities (17-22%)
- atopic diseases (6-20%), such as allergic rhinitis and asthma



Treatment of the mania/depression

First-line: mood stabilizers

Lithium is preferred for long-term mood stabilization, but it can erode kidneys and thyroid hormones

Second-line: Olanzapine, Quetiapine

There is a limited evidence for the efficacy of antipsychotics, such as haloperidol, risperidone

Antidepressants are controversial in the treatment of BD, because of limited proofs for effectiveness, moreover venlafaxine and tricyclic antidepressants are associated with increased risk of triggering mania

Mania phase:

First-line: Lithium, Valproate, Carbamazepine

Second-line:

Olanzapine, Quetiapine, Aripiprazole

Depression phase:

Olanzapine (combined with fluoxetine)

Quetiapine, Lurasidone, Lamotrigine

Anxiety disorders



Generalized anxiety disorder (GAD)

Risk factors: gender (female), life events, chronic physical or mental disorders

Treatment of GAD lasts at least 12 months

First-line: SSRI, venlafaxine, pregabalin

Second-line: buspirone, hydroxyzine

Resistant GAD: augmentation of APII

risperidone, olanzapine, and quetiapine

Panic disorder

Benzodiazepines (short-term)

SSRI, venlafaxine, TCA (imipramine, clomipramine)

Social anxiety disorder

First-line: SSRI, venlafaxine

Specific phobia (e.g. fear of falling, spiders, elevator)

First-line: SSRI (escitalopram, paroxetine)

Posttraumatic stress disorder

First-line: SSRI, venlafaxine, TCA, mirtazapine

Obsessive-compulsive disorder (OCD)



Is a mental disorder in which a person feels the need to perform certain routines repeatedly (**compulsions**) or has thoughts repeatedly (**obsessions**)

Daily life is badly affected, this specific behaviour can take many hours per day, it can be hand washing, counting of things, checking the doors...

First-line: SSRI, TCA (clomipramine, amitriptyline)

Less efficacy of noradrenergic drugs (venlafaxine)

Resistant OCD:

- high dose antidepressants (sertraline 250-400 mg, escitalopram 50 mg)
- augmentation of AP II (risperidone, olanzapine, aripiprazole, quetiapine)
- electroconvulsive therapy (ECT)

Electroconvulsive therapy (ECT)



It has been one of the most effective treatments for severe **depressive and psychiatric disorders** (treatment-resistant)

- serves a vital role **in treating urgent illness** requiring expedient recovery, such as catatonia, or in patients with severe suicidal ideation or intent
- indicated in patients with **medication resistance or intolerance**
- remains a fairly **safe treatment option**, when medication options are limited

Results of ECT:

- improvement of symptoms after six treatments
- full improvement takes usually longer
- still you need ongoing peroral treatment to prevent a recurrence

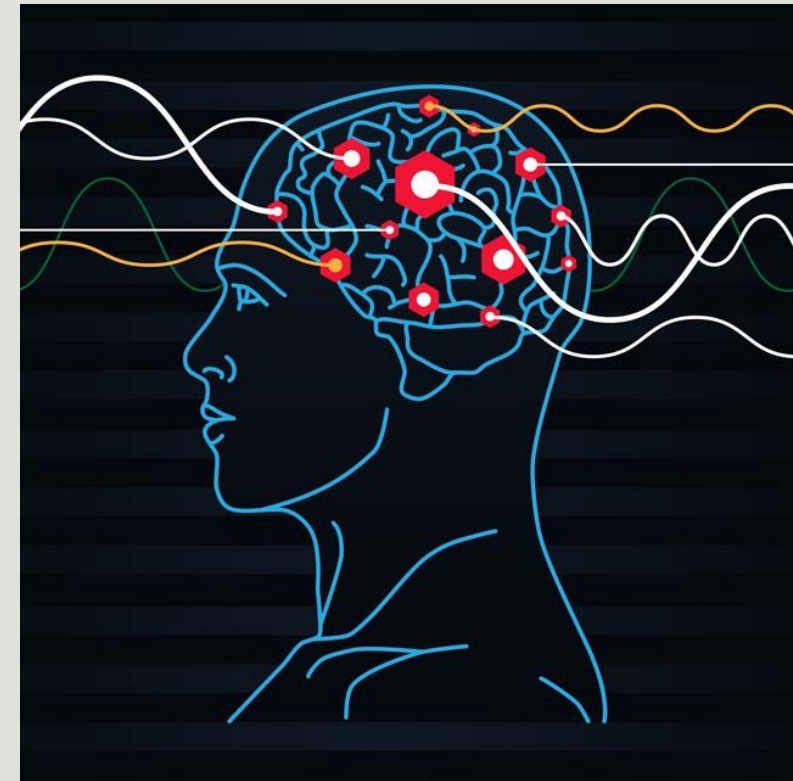
Risks of ECT:

- confusion (few minutes or hours)
- memory loss (events before treatment)
- nausea, headache, jaw pain, muscle ache
- medical complication after anesthesia, e.g may increase heart rate or blood pressure



ECT uses an electrical stimulus to induce depolarization of cerebral neurons, causing a generalized seizure in an anesthetized patient

ECT is a safe treatment option



Patient case 1



Gender: **Male** Age: **45 years** Diagnosis: **Schizophrenia**

Anamnesis: He was treated by risperidone, without effect.

Patient is hospitalized 3 weeks, because of worsen symptoms of schizophrenia (he quitted his job, because he felt persecuted). Now he starts to be depressed. He does not communicate with nurses and clinicians.

Medication/Dose	M	A	E
Olanzapine 10 mg			3
Aripiprazole 10 mg	3		
Sertraline 50 mg	2		
Clonazepam 0.25 mg	1		1

1. Control doses of used drugs, and evaluate if it is necessary to use them
2. Think if antipsychotics or antidepressants can be more effective in this patient, and comment your opinion
3. Find a drug which can have a good influence on his behavior
4. Explain your choice (influencing of receptors, find empirical literature)

Possible explanation:
can be depression itself
or negative symptoms
of schizophrenia

Patient case 2



Gender: **Female** Age: **30 years** Diagnosis: **Schizophrenia**

Anamnesis: She did not tolerate quetiapine in a higher dose than 600 mg (sedation), now she uses Xeplion 100 mg every 4 weeks

Patient has been hospitalized, because she had Séglas hallucinations. Clinicians decided to add a orally paliperidone 3 mg daily, but still without effect. Last laboratory test showed a decreased level of thyroid hormones and prolactin level 1131,2 mIU/L.

1. Find all drugs which can cause a hyperprolactinemia
2. Suggest a change of medication, because of a high prolactin level
3. Comment if it is possible to increase doses of used medicaments, and which you recommend to increase
4. Think which a new drug can be used (patient has hallucinations)

Medication/Dose	M	A	E
Paliperidone 3 mg	1		
Aripiprazole 10 mg	3		
Escitalopram 5 mg	3		
Lithium 100 mg	2	2	2
Quetiapine 100 mg	1	1	
Quetiapine ret 300 mg			1
Lamotrigine 25 mg	1		

Possible explanation:

Drugs caused a hyperprolactinemia, which is normally under 500 mIU/L (2-20 ng/mL)

**Take your medicine correctly,
being disorganized and depressed
is not a good plan for today.**

