

PHARMACOLOGY

☒ Sheet

☐ Slide

☐ Handout

Number

3

Subject

Schizophrenia

Done By

Sondos Alkhateeb

Corrected by

Doctor

Malek Zihlif

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Price:

Order of this sheet will be a little bit different from the record .

This sheet was written according to sec 3 record

First 10 min of the record was mentioned in the previous sheet , so i didn't mention it here

Schizophrenia

Some facts about it :

- Males are affected more than females by this disease
- Its percentage is 1% of the population which is not low , it is becoming very popular which is not nice
- It is not a genetic disease , genes may have an effect on the disease but it is not the main cause of It , so we can say that its pathogenicity is unknown but there is genetic predisposition and familial cases account for only 10% of the overall number .
- *For further understand to this point , genetics doesn't exert its effect on schizophrenia by it self as a disease , it actually affect the ability of person's body to tolerate bad situations and stress.
- Onset of the disease mostly in twenties (20-28)

General role :

There is no disease without genetic risk factors which is totally different from genetic diseases . for example asthma, hypertension and diabetes all have genetic risk factors but that doesn't mean that they are genetic diseases .

Another evidence that schizophrenia is not a genetic disease :

If you bring a twins its very common that one of them has schizophrenia and the other doesn't , twins have the same genetic component , so if schizophrenia is a genetic disease both of them should be affected with this disease because they have exactly the same genetic material .

Schizophrenia has four components

1- **Negative component** (exactly like depression) :

- doesn't laugh on jokes
- doesn't have any reason or passion to continue his life
- always asking why I'm here ? , why all this world is even exist ? and all this type of questions .

2- **Positive component**

- hallucinations ,delusions, perception disturbances , disorganized thoughts , inappropriate emotions

3- **Cognition component**

- some loss of memory
- difficulty in learning not because they cant learn but because they don't want to .

4- **Mood symptoms**

- can be considered as part of negative component also
- loss of motivation
- withdrawal from life
- suicidal thoughts which is the biggest problem

* The most obvious characteristic symptom of schizophrenic patient is **positive component** , that the patient really cannot bring events of single story together , so you see him linking unrelated events in the same story like saying for example I was in the university then I fell down then I went to my brother wedding and pray in Mecca , absolutely you can notice the disconnection between these events . Schizophrenic patients are linked in some manner to strange ideas like saying that he is " Almahdi , the expected " and some ideas about philistine freeing , and something about that they are very important persons " وإنه المخابرات بتلاحقهم " . schizophrenic patients also has things toward muttering and talking to themselves .

Treatment :

Before talking about drugs we have to know that these drugs aren't curative , they only reduce the symptoms but they don't cure schizophrenia , unlike depression which we cure totally by antidepressant drugs .

Treatment of schizophrenia is for life , there is **NO** remission (the drug have to be taken all life) why we have to treat schizophrenia ?

Because if left without treatment , the case will progress becoming a very dangerous situation not only for the patient itself (by doing **suicide**) , but in greater level for other people around him in the society , even if the patient is not responding to our treatment , you must not leave him without treatment .

All crimes we heard about last days , about guy who killed his wife and kids or son who killed his mother , and a lot of other heart breaking stories , are typical examples of untreated cases of schizophrenia .

So we can conclude reasons behind schizophrenic patients treatment necessity in :

- 1- suicidal thoughts they have
- 2- their very dangerous effect on society because they are not safe persons to deal with .

Schizophrenic theories

1- Dopaminergic theory (old theory) :

This theory said that schizophrenia is a result of too much dopamine in the brain , because of increase the activity of dopaminergic system , this leads to symptoms of this disease . in this situation there is greater occupancy of D2 receptors by dopamine .

2- Serotonin theory (newer one) :

This theory said that in addition to increase in dopamine , there is increase in serotonin also , so its not only a dopaminergic activity , it is also a serotonergic activity increment in the brain .

Depends on the first old theory treatment of schizophrenia is D2 receptors antagonist, but depends on the newer ones, treatment now contains combined antagonism of D2 receptors as well as 5-HT2 receptors which are serotonin receptors .

Antipsychotic Drugs

Are they good drugs ?

No, they are not , they produce a very bad side effects , so again and again you have to convince your patient to take them although the bad side effects appear a long time before therapeutic effects of these drugs , and this is a very difficult job .

Classification

A- Typical drugs (pure D2 antagonist)

- 1- haloperidol
- 2- chlorpromazine

These old drugs (depends on the old theory in treatment) generally have effects on the positive symptoms **NOT** the negative ones , so if you are antagonizing the dopaminergic activity you will affect the positive symptoms only.

Are they in use up to now ?

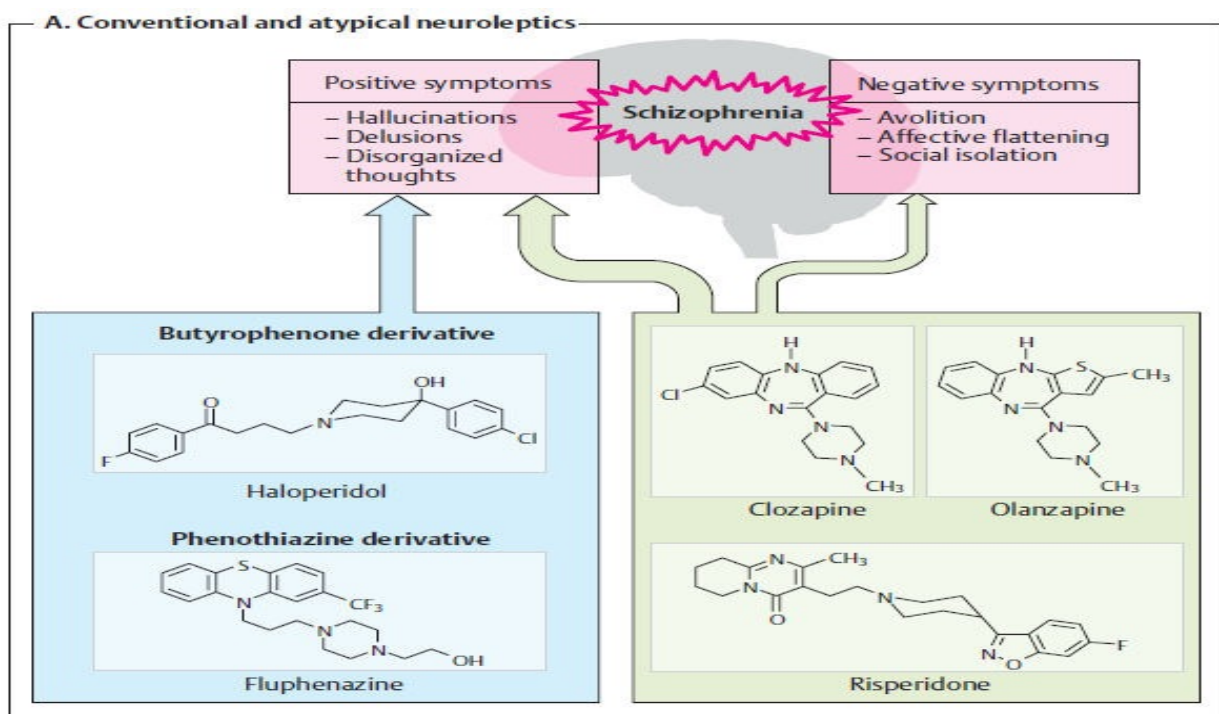
Yes, they are in use until now , because some patient don't respond to the new drugs (Atypical ones)

B- Atypical drugs (combined D2 and 5-HT2 receptors antagonist)

- 1-clozapine
- 2-risperidone
- 3-sulpiride
- 4-olanzapine

However , new drugs whom have combined antagonism against dopamine and serotonin have their greater activity on positive component and small activity against negative component .

So negative thoughts is the problem here because we can control positive thoughts with drugs but we have least effect on negative thoughts . see the pic below



What's the difference between the two categories ?

1- The most important difference is the target ; that typical ones targets D2 receptors , but Atypical type targets D2 receptors as well as serotonin receptors 5-HT2 so they have more activity toward the negative symptoms as we said earlier .

2-Their side effects;

We all know the motor system depends on dopamine , so when you give the patient pure D2 antagonists , this absolutely will affect movements of the patient .

Further explanation to this point :

When we use such drugs the first side effects appear on the patient are Parkinson like effects (remember that parkinsonism happens when there is depletion of dopamine from CNS , and it is just like when you block the dopamine receptors by these antagonists) , However with continuous using of these drugs it will cause something called extrapyramidal side effects which are involuntary movements begins in mouth area called flight tongue or flight kisses (generally its tremor in tongue) and if it gets more complicated the patient will suffer from involuntary movements in his/her limbs also .

This side effect appears with typical drugs therapy much more than with Atypical ones,

So because of extrapyramidal side effects of chlorpromazine and haloperidol don't use them till you really need them .

***In Jordan we use haloperidol injections despite its bad side effects just because it is cheap!**

- This motor system dysfunction can appear also in this representations (neurological side effects) :

***Acute dystonia** which is spasm of the muscles of face , neck and tongue (stiffness in these places) ,which appears after 1 to 5 days of usage .

***Akathisia** which is restlessness disease , the patient cannot sit (بقدرش يقعد وبضل يحوس زي ام العروس) but it is not anxiety or agitation , which appears after 5 to 60 days of usage.

***Parkinsonism** which appears after 5 to 30 days of usage.

Our body maintain these things in normal situations by maintains balance between acetylcholine as activator and dopamine as inhibitor , so when you disturb this balance by giving the patient dopamine antagonist these effects above will appear , and to treat them you have to restore the balance by restoring the normal ratio between Ach and dopamine by decreasing the concentration of Ach , this achieved by **antiparkinsonian agents** .

***Tardive dyskinesia** which is oral- facial dyskinesia ;

This symptom differ from the above ones in some extent :

1-lit needs months to years of therapy with typical antipsychotic drugs to appear.

2- Above ones caused by decreased dopamine by antagonizing it , but in tardive dyskinesia there is excess in dopamine function , **How this could be ?**

With long usage of these drugs , the body will adapt by increase the number of receptors of dopamine (up regulation) so increasing in dopaminergic activity in the CNS , thus it couldn't be treated by antiparkinsonian because it will worsen the case even more .

why dopaminergic activity increases although dopamine is little ?

Because the number of receptors is really increased dramatically so even little dopamine can exert super activity which worsening with withdrawal , **why ?**

Because when the number of receptors increases dramatically part of them will be occupied by the antagonizing drug , and when you stop the drug abruptly , all this huge number of receptors will be exposed to dopamine which will increase dopaminergic activity even more , so you have to tapering the drug .

*general concept

- With long usage of antagonism number of receptors goes up (up regulation)
- With long usage of agonism number of receptors goes down (down regulation)

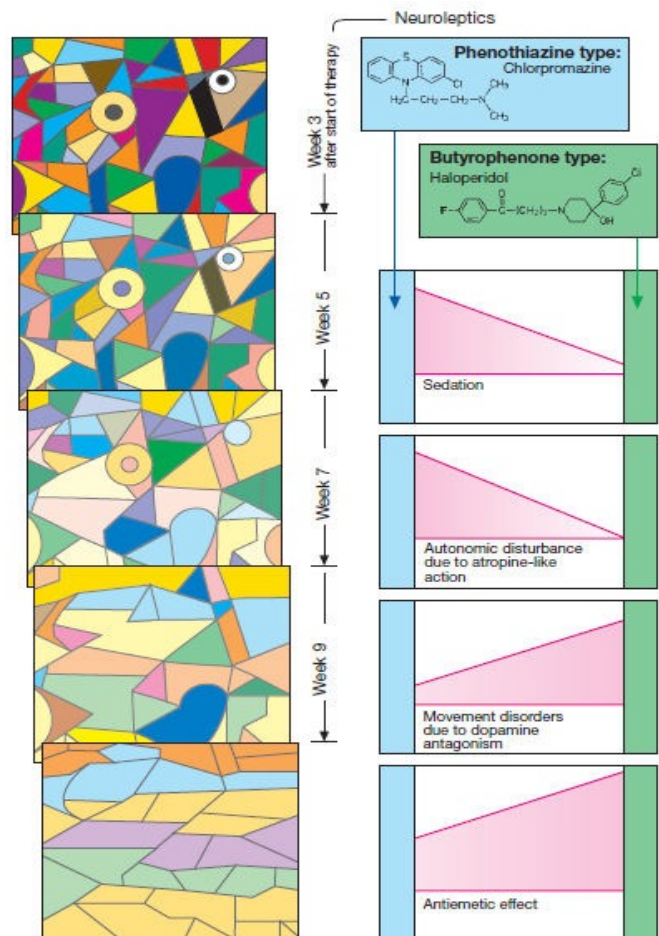
How long it will take for an antipsychotic drug in general to work ?

Just like antidepressants , now what we think that schizophrenia and also depression are disturbances at the level of neurotransmitters (this is what all world expect) , but in reality they are not , the evidence on this in case of depression for example that if you increase dopamine and serotonin today you won't have effect before very long period of time , this because in depression there is also something wrong with connections of neurons with each other as result of low level of dopamine and serotonin , so it will take long time like approximately 6 weeks for these connection to recap again and that why we observe the effect of antidepressant drugs after at least 4 weeks of usage , PDNF is the theory which has explained this .

Now in case of schizophrenia , we don't have a theory that explain the long time needed for observing the effects of the drugs , but its difficult to change the way of thinking in your patient from non straight forward (circuitous thinking) to a straight forward thinking this is why it will take 4 to 6 weeks for the antipsychotic drugs to work in a schizophrenic patient, see this pic which show you how these drugs convert thinking of schizophrenic patient from circuitous thinking to straight forward thinking (more organized thinking)

Now, why we need psychologists ?

Because we need someone to convince schizophrenic patients to take the drugs



Tolerance and dependence to antipsychotic drugs :

- No addiction , because they don't cause Euphoria , although haloperedol can produce some hallucinations but not happiness .
- Physical dependence
- Relapse in psychosis when discontinued abruptly (there is withdrawal symptoms) which are nausea and vomiting , headache and insomnia , these symptoms may persist up to 2 weeks , they can be minimized by tapering reduction of drug dosage .
- Most of these drugs will exert their activity on alpha1 and alpha2 receptors as well as histamine receptors

Activity on histamine receptors = sedation effect , but the nice thing about it that it develops tolerance to this sedative effect . so these antipsychotic drugs are not just a D2 antagonists (old ones) or D2 /5-HT2 antagonists (new ones) , it will bind also other places (alpha 1 and 2 and histamine receptors) this means that they are **NOT** selective .

So most antipsychotic drugs have two problems :

- 1- sedative effects (as result of their activity on histamine receptors)
- 2-postural hypotension (as result of their activity on alpha 1 and 2 receptors)

Notes

*Postural hypotension also will develop some kind of tolerance , but what is more important is the tolerance which develops against sedative effect in second or third week of usage .

*You are not just targeting a receptor by these drugs , you are changing the physiology of the brain that's why treatment takes long time to exert its effect .

THE END

Wish you all the best 😊