Antipsychotic Medications and Prolactinemia

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Learning Outcomes

• 1. Participants will have a better understanding of the pathways of effectiveness related to antipsychotic medications
• 2. Participants will have a better understanding of drug induced prolactinemia
• 3. Participants will be introduced to the latest antipsychotic agents.

Nomenclature of Antipsychotics

Typical
• Limited efficiency (primarily positive sxs)
• High risk for movement disorders.

Atypical
• Decrease risk of movement disorders
• Increased risk of metabolic disorders

<table>
<thead>
<tr>
<th>Category</th>
<th>Efficacy</th>
<th>EPS/TD</th>
<th>Prolactinemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>First Generation</td>
<td>Pos sxs only</td>
<td>High</td>
<td>Elevating</td>
</tr>
<tr>
<td></td>
<td>(Haldol, Thorazine etc)</td>
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<tr>
<td>Second Generation</td>
<td>Both pos/neg sxs</td>
<td>Dose dependent</td>
<td>Elevating</td>
</tr>
<tr>
<td></td>
<td>(Resperidal, Geodon)</td>
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<tr>
<td>Third Generation</td>
<td>Broad spe.</td>
<td>Low</td>
<td>Sparing</td>
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<tr>
<td></td>
<td>(Clozaril, Zyprexa, Seroquel)</td>
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</tbody>
</table>

**Antipsychotic Mechanism of Action**

- 4 relevant dopamine pathways
- 1. Mesolimbic tract- Antipsychotic efficacy
- 2. Mesocortical tract
- 3. Tuberinfundibular tract-Prolactin elevation
- 4. Nigrostriatal tract-Movement disorders

* 5 types of dopamine receptors (D1-5) D2 is found in all the pathways

**Mechanism of Action**

- Blockage of Dopamine pathways, (catch 22)
- Serotonin is also a modulator of dopamine
- If 5HT 2a is blocked this can lead to an increase of dopamine
- Antipsychotics are reliant on their affinity for dopamine and serotonin
Seeman & Tellerico (1998)

- Studied how tightly antipsychotics bound to the dopamine D2 receptor
- **Conclusion:** that more tightly bound to D2 the more likely to elicit movement disorders (Haldol, Thorazine, Geodon, Resperdal, Prolixin)
- More loosely bound, less movement disorders, (Zyprexa, Seroquel, Clozaril)

Dopamine Pathways

Prolactin

- Luteotropic Hormone, secreted by the pituitary gland
- Only known function-to induce milk production
- Unknown in males
- Ranges: Males 4-23ng/ml
- Females 4-30ng/ml; preg 2-215ng/ml
- Post menopausal 2.4-24ng/ml
Luteotropic Hormone

Prolactin elevators

- First Generation Antipsychotics and Resperdal (due to mech of action) (tightly bound)
  Clozaril, Seroquel and Zyprexa have less impact on prolactin increase. (spare available dopamine in the tuberoinfundibular pathway and the nigrotriatal pathway)

Potential Health Problems

- **Women:**
  - **Short term:** Menstrual disturbances, galactorrehea, breast engorgement, sexual dysfunction, infertility
  - **Long Term:** decreased bone density, deficiency in estrogen, CV dx, Cancer

- **Males:**
  - **Short Term:** loss of libido, erectile dysfunction, gynecomastia
  - **Long Term:** decreased bone density, CV dx, Cancer

*G. A. Maguire (2002).*
Pituitary Tumors

- Study by, A. Szarfman, J. Tonning, J. Levine, P. M. Doraiswamy (2005)
- Concluded: high potency D-2 receptor antagonists may be associated with pituitary tumors
- The long term effect of antipsychotic associated hyperprolactinemia in humans is not well studied.

Product Update

- Iloperidone (Fanapt), structurally similar to Risperdal
- Asenapine (Saphris), modification of a tetracyclic antidepressant
- Lurasidone (Latuda) derivative of Buspar


Iloperidone/Fanapt

- Similar to other SGA
- Dose range 12-24 mg/day
- Use cautiously with pts who have renal or liver impairment
- EPS and Prolactin elevation at higher doses
Asenapine/Saphris
• For manic and mixed bipolars
• High affinity for dopamine
• Minimal anticholinergic effects
• Dose range 10-20mg /day (SL administration with decreased bioavailability if swallowed)
• Avoid liver and renal impaired pts

Lurasidone/Latuda
• Similar to other SGA, blocks D2 receptors
• Minimal anticholinergic effects
• High affinity for serotonin
• Dose range 40-80mg/day
• Careful use with renal and liver impaired pts.

Questions???
References


References


- Special thanks to Joyce Bowens R.Ph. SC. Department of Mental Health