# Antipsychotics use in elderly: the good, the bad and the weird

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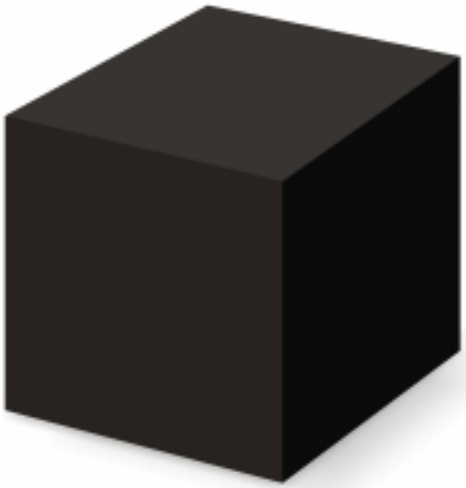
# Antipsychotics?



**WARNING**

Increased Mortality in Elderly Patients with Dementia-Related Psychosis — Elderly patients with dementia-related psychosis treated with atypical antipsychotic drugs are at an increased risk of death compared to placebo. Analyses of seventeen placebo-controlled trials (modal duration of 10 weeks) in these patients revealed a risk of death in the drug-treated patients of between 1.6 to 1.7 times that seen in placebo-treated patients. Over the course of a typical 10-week controlled trial, the rate of death in drug-treated patients was about 4.5%, compared to a rate of about 2.6% in the placebo group. Although the causes of death were varied, most of the deaths appeared to be either cardiovascular (e.g., heart failure, sudden death) or infectious (e.g., pneumonia) in nature. [this drug] is not approved for the treatment of patients with dementia-related psychosis.

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# Antipsychotics?

**Indications**

Antipsychotic drugs are first-line agents for managing psychotic symptoms in elderly patients. Conventional antipsychotic drugs have been used to treat elders with schizophrenia (Tran-Johnson et al., 1992) and late-onset chronic psychoses (Post, 1966). They also have a role in the management of manic states, of psychotic depression, and of behavioral disturbance in the context of brain disease. Because of their side effect profile, atypical antipsychotics are now drugs of first choice for these same indications.

*Geriatric Psychiatry 3rd*

# THE GOOD

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# Efficacy

- Paucity of researches on elderly

- Reasonable in the management of acute symptoms or in the long-term treatment of psychotic disorders in elderly.

# Schizophrenia

- Schizophrenia 환자가 나이 든 경우
  - Effective as younger pts.
- Late onset schizophrenia and Very Late Onset Schizophrenia Like Psychosis(VLOSLP)
  - No reported randomized RCT
  - Antipsychotics relieve some target symptoms, the overall treatment response to medication is modest.

# Psychotic Sx을 조절하는데 젊은 성인과 유사한 효과를 보인다.

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# THE BAD

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# Risks in Elderly

- Drug-Drug Interactions

**Table 2** Possible isoforms of CYP involved in atypical antipsychotic drugs metabolism

| Enzyme | Substrates | Inhibitors | Inductors |
|---|---|---|---|
| CYP1A2 | Antipsychotics: clozapine,* olanzapine, asenapine, haloperidol | Ciprofloxacin | Barbiturates |
| | Antidepressants: imipramine, amitriptyline, clomipramine, | Fluvoxamine | Carbamazepine |
| | fluvoxamine, mirtazapine | | Phenytoin |
| | Methylxanthines: theophylline, caffeine | | Rifampicin |
| | Various drugs: paracetamol, R-warfarin, tacrine | | Tobacco |
| CYP3A4 | Antipsychotics: clozapine,* risperidone, ziprasidone,^ sertindole, | Erythromycin | Barbiturates |
| | quetiapine, aripiprazole, asenapine, haloperidol | Fluconazole | Carbamazepine |
| | Antidepressants: venlafaxine, clomipramine, citalopram, mirtazapine | Fluvoxamine | Felbamate# |
| | Benzodiazepines: diazepam, bromazepam | Grapefruit juice | Hypericum |
| | Non-benzodiazepine anxiolytics: buspirone | Itraconazole | Oxcarbazepine# |
| | Antiepileptics: carbamazepine, felbamate, tiagabine | Ketoconazole | Phenytoin |
| | Calcium antagonists: nifedipine, diltiazem, verapamil | Nefazodone | Rifampicin |
| | Various drugs: terfenadine, astemizole, cyclosporine, erythromycin, | | Topiramate# |
| | clarithromycin, tamoxifen, amiodarone, quinidine | | |
| CYP2D6 | Antipsychotics: risperidone, clozapine, olanzapine, aripiprazole, asenapine | Asenapine° | No known agent |
| | zuclopenthixol, haloperidol, thioridazine, perphenazine, fluphenazine | Fluoxetine | |
| | Antidepressants: amitriptyline, clomipramine, imipramine, desipramine, | Paroxetine | |
| | fluvoxamine, nortriptyline, fluoxetine, paroxetine, fluvoxamine, | Perphenazine | |
| | citalopram, venlafaxine, mirtazapine, mianserin | Propafenone | |
| | Opioids: codeine, dextromethorphan, tramadol | Quinidine | |
| | β-blockers: metoprolol, timolol, pindolol, propranolol | Thioridazine | |
| | Antiarrhythmics: encainide, flecainide, propafenone | | |
| | Various drugs: debrisoquine, sparteine, phenformin | | |

**Notes:** *Also metabolized via CYP2C19. ^Also metabolized via aldehyde oxidase. °Weak inhibitor. #Weak enzymatic inductors.
**Abbreviation:** CYP, cytochrome P450.

Gareri, et al. 2014

# Risks in Elderly

- Physical changes in elderly may influence the effect of a drug in elderly.
- Older people are known to be more sensitive to the actions of antipsychotics, these drugs have a stronger sedative effect at lower plasma concentrations than is seen in younger people.

# Risks in Elderly

- Metabolic side effects
- QTc prolongation
- Hypotension and orthostatic hypotension
- DVT

# Risks in Elderly

- Risk of cerebrovascular accidents
  - Risperidone and olanzapine
  - Conventional antipsychotics
  - Elderly subjects with dementia
- Increased risk of all-cause mortality and sudden death compare to nonuse
- The risk of pneumonia is higher in patients treated with antipsychotics.

# THE WEIRD

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# Can we use antipsychotics In dementia pts?

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# BPSD

- Pharmacological treatment should be used only when non-pharmacologic approaches have failed to adequately control symptoms.
- Neither conventional nor atypical antipsychotics as class of drugs are approved for the treatment of BPSD.

- HOWEVER…….

# BPSD

- Effectiveness?
- Health costs?

# BPSD

- Antipsychotics may be more effective for particular symptoms, such as anger, aggression, and paranoid idea.
- For global behavioral symptoms associated with dementia, small but statistically significant benefits were observed for aripiprazole, olanzapine and risperidone.
- Antipsychotics do not appear to improve functioning, care needs, or quality of life.

# Antipsychotics

- Mortality?
- Cerebrovascular Accident?

# Which one?

- Conventional vs Atypical?
- Which medication?
- How much?

- Single most effective and safe treatment option does not exist.

# Antipsychotics

Clinicians should continue
to assess
the potential risk
and benefits.

# Delirium

- Current evidence does not support the use of antipsychotics for prevention or treatment of delirium.
- There is limited evidence that second-generation antipsychotics may lower the incidence of delirium in postop pt.
- Second generation antipsychotics have a benefit for the treatment of delirium with regard to efficacy and safety compared with haloperidol.

# Long-acting injectable AP

- There are few studies regarding the use of long-acting injectable AP.
- Favorable; EPS, TD의 위험이 낮음.

- Long-acting injectable AP medication should be considered for older pts. For whom long-term treatment is indicated.

# Antipsychotics?

THE GOOD?

THE BAD?

THE WEIRD?

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# Antipsychotics?

- 임상의의 개별화된 환자별, 상황별 고려가 필요함.