[연수강좌]

일차진료의가 처방하는 항우울제, 항불안제

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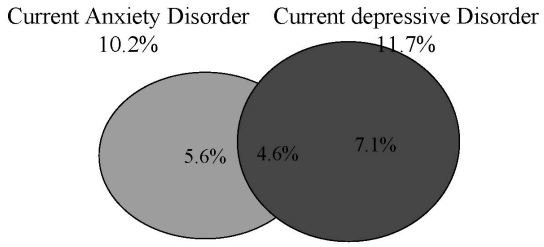
1차 진료에서 정신장애



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Anxiety and Anxiety Disorders

- Categories of Anxiety Disorder: DSM-IV
  - Panic Disorder 공황 장애
  - Phobic Disorder 공포 장애
  - Post-traumatic Stress Disorder (PTSD) 외상 후 스트레스 장애
  - Acute Stress Disorder 급성 스트레스 장애
  - Generalized Anxiety Disorder (GAD) 범불안장애
  - Anxiety Disorder due to general medical condition
  - AD NOS

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불안장애의 증상

- 정신증상
  - 극심한 공포
  - 죽음의 두려움
  - 불안, 초조
- 신체증상
  - 빈맥
  - 심계항진
  - 호흡곤란
  - 발한
  - 어지러움, 현기
  - 오심, 복통

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Antianxiety Drugs

- Classes
  - Benzodiazepines (BZDs)
    - 5 actions (SHAMA): Sedation, Hypnotics, Antianxiety, Muscle relaxant, Anticonvulsant
  - Non-BZD anxiolytics and hypnotics
    - Antihistamines (e.g., hydroxyzine)
    - Beta-blockers (e.g., propranolol)
    - Azaspirone anxiolytic (e.g., buspirone)
    - Barbiturates (e.g., amobarbital, phenobarbital)
    - Clonidine

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BZDs

		Anxiolyt.	Sed/Hypn.	Anti-convulsant	Potency
Short	Midazolam (M)	+	+++		-
	Triazolam (H)	+	+++		High
Intermediate	Alprazolam (X)	++	+	+	High
	Bromazepam (L)	++			High
	Lorazepam (A)	+++	++	++	High
	Clotiazepam (R)	+	+		Low?
Long	Chlordiazepoxide (L)	++			Low
	Clonazepam (R)	++	+	+++	High
	Diazepam (V)	+++	++	+	Medium
	Flurazepam (D)	+	+++	+	Medium

Approved Indications of Anxiolytics

- Mild to moderate anxiety, tension, agitation
- GAD
- Acute & chronic alcohol withdrawal
- Convulsions
- Insomnia
- Panic disorder (alprazolam)
- Muscle spasm, dystonia
- Other: endoscopy, bronchoscopy etc.

Pharmacokinetics of BZDs

- Marked inter-individual variation

Withdrawal Symptoms and Management

- Variable risk of physiological dependence
  - Individual/ Drugs potency/ Elimination half-life
- Symptoms
  - 1~2 days to 5~6 days following discontinuation
  - Insomnia, agitation, anxiety, perceptual changes, dysphoria, headache, muscle aches, twitches, tremors, loss of appetite, GI troubles, depression
- Management
  - Change to long-acting (diazepam or clonazepam)
  - Reduce by 25% per week
  - Carbamazepine or propranolol may aid
  - Alternative dosage if needed
  - Physical dependence and psychological dependence

AA: Alprazolam

- General description
  - Xanax 0.25mg, 0.5mg
  - Usual dosage: 0.5mg
  - Peak plasma level (p.o.): 1~2 hour
  - Lipid solubility: moderate
  - Elimination half-life: 9~20 hour
  - Rapid and complete absorption, 80% protein bound
- Clinical
  - Anxiety, agitated depression, panic attack prophylaxis
  - T.i.d. dosing
  - Frequent WD symptoms
  - Sleep stage 4, REM↓
  - Low degree of sedation

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AA: Diazepam

- General description
  - Valium 2mg, 5mg
  - Usual dosage: 5mg
  - Peak plasma level (p.o.): 1~2 hour
  - Lipid solubility: high
  - Elimination half-life: 14~70 hour / metabolites 30~200 hour
  - Quick and complete absorption, with rapid onset
- Clinical
  - Anxiety, sedative, anticonvulsant, akathisia, muscle relaxant
  - Sleep stage 4, REM ↓
  - High degree of sedation

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AA: Clotiazepam

- General description
  - Rize 5mg
  - Similar to diazepam with mild antianxiety effect
  - Less GI disturbance

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Non BZD AA: Buspirone

- General description
  - Buspar 5mg, 10mg
  - Azaspirone derivative
    - 5-HT1A agonist, no effect on GABA-BZD complex
- Clinical
  - Use: Anxiolytic
    - Antidepressant (40~90mg/day), augmentation for OCD Tx
    - No anticonvulsant or muscle relaxant effect
  - Advantage
    - Little or no sedative or psychomotor impairment
    - Low potential for abuse or addiction
    - No cross tolerance to BZDs
  - Disadvantage
    - Onset of action after 1~2 weeks; peak action in 3~4 weeks
  - Side effects
    - Dizziness, headache, nervousness

Hyp: Triazolam

- General description
  - Halcion 0.125mg, 0.25mg
  - Usual dosage: 0.25mg
  - Peak plasma level: (p.o.) 1~2 hour
  - Lipid solubility: moderate
  - Elimination half-life: 1.5~5 hour
  - High hepatic clearance: negligible accumulation
- Clinical
  - Hypnotic
  - Rebound insomnia and anxiety reported
  - Dose-related anterograde amnesia, rage, automatism reported

Hyp: Flurazepam

- General description
  - Dalmadom 15mg
  - Usual dosage: 15mg
  - Peak plasma level (p.o.): 0.5~1 hour
  - Lipid solubility: high
  - Elimination half-life: 0.3~3 hour / metabolites 40~250 hour
  - Quick and complete absorption, with rapid onset
- Clinical
  - Hypnotic
  - Increase stage 2 sleep; no effect on REM
  - Daytime sedation, hangover (+)

Hyp: Midazolam

- General description
  - Midazolam 7.5mg (iv 5, 15mg)
  - Usual dosage: 7.5mg,
  - Peak plasma level: (p.o.) 0.5~1 hour, (i.m.) 0.5~1 min
  - Lipid solubility: high
  - Elimination half-life: 1~4 hour, metabolites: 1~20 hour
- Clinical
  - Sedative, IV induction of anesthesia, post-ECT agitation, sleep GFS
  - Fast onset of action
  - Anterograde amnesia frequent

Non-BZD Hyp: Zolpidem

- General description
  - Stilnox, Ambien, 10mg

SSRIs

- Fluoxetine
  - Prozac (10, 20mg)
  - Usual dosage 10~60mg
- Paroxetine
  - Seroxat (10, 20mg), Paxil

NaSSA: Mirtazapine

- General description
  - Remeron: 15mg, 30mg
  - Usual dosage: 10~40mg
  - Presynaptic alpha2 antagonism → NE, 5-HT release↑
  - Postsynaptic 5-HT2,3 blockade → NE, 5-HT1A↑
- Clinical
  - Sedating antidepressant
  - Target symptoms: Anxiety and insomnia, depression
  - Advantage: No severe drug interaction
  - Disadvantage: Leukopenia, agranulocytosis?
  - Side effects: sedation, dizziness, orthostatic HoTN, weight gain

St John's wart : Jarsin

- General description
  - Jarsin: 300mg
  - Usual dosage: 900mg
- Clinical
  - Non sedating antidepressant
  - Target symptoms: Mild to Moderate depression, Anxiety, somatoform (dizziness, headache)
  - Advantage: Minor side effects
  - Side effects: GI trouble, photosensitivity

Other: Bupropion

- General description
  - Wellbutrin
  - NE RI + DA RI
- Clinical
  - Stimulating antidepressant
  - Target symptoms: anergia, anhedonia, psychomotor retardation, poor concentration
  - Advantage: in attention deficit patients, sexual dysfunction, anti-smoking agent
  - Side effects: anxiety, insomnia, weight loss, seizure

FAQ

- 불안증, 공황장애 등에서 BZD 사용기간?
  - Dose titration: 4~8 weeks
  - Maintain: 6~12 month
  - Taper to D/C: 6~12 month
  - Behavior + Cognitive Therapy important
- Xanax tapering 실패 시 대처방안
  - Symptom delineation
  - Change to / combine with longer acting BZD
  - For panic disorder: use SSRI

FAQ

- Insomnia에서 BZD 처방은 언제 고려?
  - Sleep disturbance with anxiety (initial insomnia)
  - Combined use of TCA
  - PRN use not recommended
  - Special case: night terror in children
- 수면제 복용 습관화된 환자들의 처치 방법
  - Sleep hygiene: non-pharmacological management FIRST!
  - TCA or new ADs provide better sleep profile
  - Use of antipsychotics in selected cases

FAQ

- 항 우울효과가 나타날 때까지의 manage
  - Acute stage: consider ECT
  - Weekly follow up
  - Drugs with rapid onset of action: SSRIs, NaSSA
  - Addition of ample Aas
- 우울증 치료 시 항우울제의 평균 사용기간?
  - Single episode: titration 4~8 weeks → Maintenance: 6 month → Tapering 3~6 month
  - Multiple episodes (recurrent MDD): at least 2 years in remission
  - Special cases