

# Clinical Applications of Antidepressants in Anxiety Disorders

성균관의대  
 삼성서울병원 정신과  
 유 범 희

SMC

---

---

---

---

---

---

---

---

## Antidepressants for panic disorder

SMC

---

---

---

---

---

---

---

---

## SSRIs

- TCAs나 benzodiazepine 제제들에 비해 항공황 효과 우수
- 치료효과  
 약물투여 후 4주 후부터 본격적으로 나타남  
 일부에서는 8-12주가 걸리는 경우도 있음
- 유지요법  
 8-12개월 유지  
 이후 4-6개월에 걸쳐 약물을 감량해서 중단함  
 tapering시 증상의 재발과 일시적인 rebound 현상의 강별  
 필요 → 감퇴 위해 최소한 3주 정도 증상 경과관찰 필요
- 약물 중단시 2회 이상 증상이 재발하면  
 인지행동요법을 병용하면서 다시 약물 감량을 시도  
 무기한 약물요법을 지속함

SMC

---

---

---

---

---

---

---

---

### Selective serotonin reuptake inhibitors (SSRIs)

- Fluoxetine : 5mg/day→ 20mg/day
- Sertraline : 25mg/day→ 200mg/day
- Paroxetine : 10-20mg/day→ 40mg/day
- Fluvoxamine : 50mg/day→ 300mg/day
- Citalopram : 10mg/day→ 20-30mg/day

SMC

---

---

---

---

---

---

---

---

---

---

### Paroxetine

- 현재 가장 널리 사용되는 공황장애 치료제로서 국내 환자들의 경우 대개 20-40mg의 용량에서 panic-free state를 보임(up to 80-85%)
- 다른 SSRI 제제에 비해 asthenia, 구갈, 변비, 체중증가 같은 부작용이 더 흔하게 나타남
- (1주) (2주) (3주) (4주)  
10mg→ 20mg→ 30mg→ 40mg
- 드물게 일부에서는 10mg/day 에서도 과민반응을 보임
- 가끔 skin allergic reaction 등의 부작용이 나타나기도 한다.

SMC

---

---

---

---

---

---

---

---

---

---

### Sertraline

- 적정용량  
대개 50-100mg/day이 적절
- Paroxetine을 쓰기 어렵거나 부작용이 예상되는 환자에서 우선적으로 일차약물로 권장됨
- 특히 오심, 설사 같은 소화기계 부작용이 흔함
- 초기용량은 대개 25mg/day가 적절함

SMC

---

---

---

---

---

---

---

---

---

---

**제 3 부 불안장애의 생물학적 치료 I**

**Fluoxetine**

- 급성기 치료효과 → 50%  
1년 정도 치료시 치료효과 → 76%
- 일반적으로 paroxetine보다는 다소 치료효과가 낮다는 보고가 있으나 paroxetine을 쓰기 어려운 환자들에 유용할 수 있음
- 초기사용시 불안이나 흥분 같은 부작용이 많아 치료에서 조기탈락할 가능성이 높음
- 시작용량 5mg/day → 10mg/day → 20mg/day

SMC

---

---

---

---

---

---

---

---

**Fluvoxamine**

- 대개 150mg-300mg/day가 적절용량으로 알려짐
- 위약군은 물론, 인지행동요법 치료군에 비해서도 치료효과가 더 좋게 보고됨
- 초기 시작용량은 50mg/day로 시작함
- 흔한 부작용  
오심, 두통, 졸림, 어지럼증, 구갈, 불안, 불면, 초조감, 떨림 등

SMC

---

---

---

---

---

---

---

---

**Citalopram**

- 대개 20-30mg/day가 적정용량으로 알려짐
- 초기용량은 10mg/day가 권장됨  
불안증상을 일시적으로 악화시킬 가능성 있음
- 오심, 두통, 발한 등의 부작용이 흔함
- 8주 F/U 시 치료반응율 → 약 67%  
40주 F/U 시 치료반응율 → 약 78%

SMC

---

---

---

---

---

---

---

---

### Common side effects and withdrawal syndrome of SSRIs

- **Side effects**  
Headache, Irritability, Nausea, Other GI complaints, Insomnia  
Sexual dysfunction, Increased anxiety, Drowsiness, Tremor
  - **Withdrawal syndrome due to abrupt discontinuation**  
Dizziness, Incoordination, Headache, Irritability, Nausea
- Begin within 1 day  
Peak at day 5  
Resolve by day 14

SMC

---

---

---

---

---

---

---

---

### Venlafaxine

- 50-75mg/day – 150mg/day에서 항공황 효과를 보임
- GAD와 병발시 특히 효과가 좋을 수 있음
- 최근 antipanic drug으로 미국 FDA의 승인을 받음

SMC

---

---

---

---

---

---

---

---

### Mirtazapine

- 20-30mg/day에서 항공황 효과를 보임  
(74% of patients were responders)
- Fluoxetine과의 비교임상에서 다른 증상의 호전에 있어서는 차이가 없으나 phobic anxiety는 오히려 mirtazapine이 더 효과가 좋게 나옴
- SSRIs를 사용할 수 없는 경우 대체요법으로 고려

SMC

---

---

---

---

---

---

---

---

### 제 3부 불안장애의 생물학적 치료 I

#### Monoamine oxidase inhibitors

- Moclobemide : 450mg/day  
Phenelzine : 45mg/day
- 충분한 항공황 효과 판정을 위해서는 최소한 몇 주간 관찰이 필요 (따론 12주 정도까지)
- 다른 공황장애 치료제에 반응을 보이지 않는 환자에서 좋은 치료효과를 보일 수 있음
- Serious drug interactions with tyramine-rich diet, sympathomimetic amines, decongestants, dextromethorphan, SSRIs  
→ acute hypertensive crisis

SMC

---

---

---

---

---

---

---

---

#### TCA's

- TCA 사용시 증상의 호전 순서  
공황발작 증상 → 예기불안 → 공포증적 회피 증상
- 대개 4주 이상 지나야 약물효과를 기대, 일부에서는 8-12주 정도가 걸리기도 함. 따라서 약 6주 정도는 치료효과를 기다려보는 것이 좋음
- Imipramine, clomipramine이 좋은 치료효과를 보임  
Imipramine: start with 12.5mg/day → increase up to 150mg/day  
Clomipramine: start with 10-25mg/day → increase up to 150mg/day
- 장기추적연구에서 SSRI보다 치료효과가 떨어진다고 보고됨

SMC

---

---

---

---

---

---

---

---

#### Factors to predict antipanic effects

20-40% of panic patients are non-responders to pharmacotherapy

(Predictors of non-responders)

- Long duration of illness
- Agoraphobic avoidance
- Personality disorder or personality trait
- Comorbid depression or other anxiety disorders
- Genetic polymorphism: COMT L/L type
- Reduced HRV: Reduced total spectrum and low frequency power

SMC

---

---

---

---

---

---

---

---

Antidepressants for GAD

SMC

---

---

---

---

---

---

---

---

**Venlafaxine XR Efficacy, Tolerability, and Safety**

- SNRI and originally approved for treatment of major depression
- Effective and well tolerated
- Most common side effects  
nausea, somnolence, dry mouth, dizziness, sweating, constipation, anorexia,  
occur in first 2-3 wk and decrease over time
- Low potential for drug-drug interactions

SMC

---

---

---

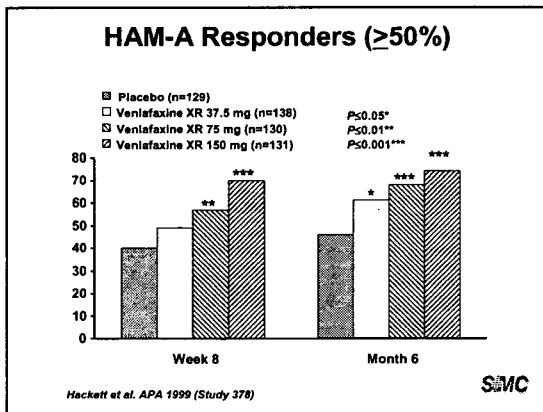
---

---

---

---

---




---

---

---

---

---

---

---

---



## Paroxetine

- The second agent to be indicated in the treatment of GAD
- Response rate → 72%, Remission rate → 43%
- Potential risk of long-term weight gain  
: >7% gain of initial weight in 20-25% of patients
- Withdrawal symptoms  
(Serotonin discontinuation syndrome)  
: agitation, nausea, dysequilibrium, dysphria

S/MC

---

---

---

---

---

---

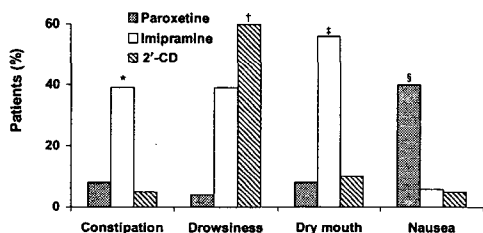
---

---

---

---

## Side effects of paroxetine and TCA



Rocca P et al. Acta Psychiatr Scand 1997;95:444

S/MC

---

---

---

---

---

---

---

---

---

---

## TCAs

- Equivalent to or greater than anxiolytic effect of Bdz
- Slower onset and more effective in psychic symptoms rather than somatic ones
- Treat depressive symptoms, too
- Adverse effects  
Sedation, hypotension, edema, anticholinergic effects,  
potential of toxic or lethal overdose

S/MC

---

---

---

---

---

---

---

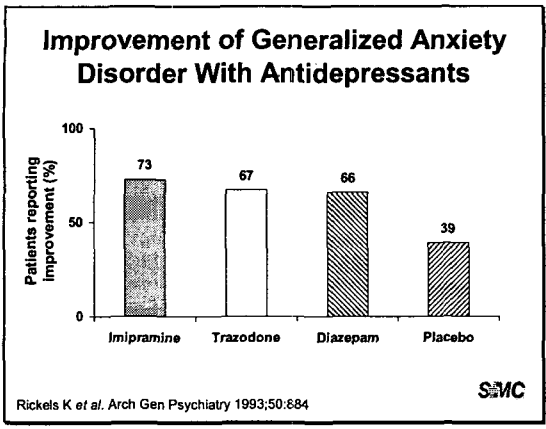
---

---

---



제 3 부 불안장애의 생물학적 치료 I



---

---

---

---

---

---

---

---

---

---

### Antidepressants for OCD

SMC

---

---

---

---

---

---

---

---

---

---

- ### OCD의 약물치료 원칙
- Optimal drug
  - Optimal dose
  - Optimal compliance
  - Optimal duration
- SMC

---

---

---

---

---

---

---

---

---

---

### SSRIs for OCD

- **SSRIs**  
 Clomipramine : up to 250mg/day  
 Fluoxetine : up to 80mg/day  
 Fluvoxamine : up to 300mg/day  
 Sertraline : up to 200mg/day  
 Paroxetine : up to 60mg/day

SMC

---

---

---

---

---

---

---

---

---

---

### TCAs and MAOIs for OCD

**IV pulse loading or gradual infusion of clomipramine**  
 난치성 강박신경증에 치료효과가 있다는 보고

**MAO inhibitors**  
 phenelzine이 강박증에 효과적이라는 보고 있었으나 아직 논란의 여지가 있음 (symmetry obsession에만 효과가 있다는 보고도 있음)

SMC

---

---

---

---

---

---

---

---

---

---

### OCD의 약물치료 원칙

- 평균 치료반응률은 40-60% 정도에 불과하다.
- 치료기간은 최소 10-12주 이상의 장기간 치료를 권장한다.
- 약물치료 효과에 대한 중요한 예측인자
  1. Early onset of illness
  2. Presence of  
 Schizotypal p.d.  
 Borderline p.d.  
 Avoidant p.d.

SMC

---

---

---

---

---

---

---

---

---

---

### 제 3 부 불안장애의 생물학적 치료 I

#### SRI + Augmentation therapy

- **SRI + fenfluramine (serotonin releaser/reuptake blocker)**  
: 효과가 있을 가능성 있으나 신경독성과 pulmonary hypertension과 valvular disease 의 위험성이 문제
- **SRI + lithium (enhance presynaptic serotonin release)**  
: still questionable / 우울증이 동반된 경우엔 효과 있을 수 있다.
- **SRI + buspirone (5-HT<sub>1A</sub> agonist)**  
: still questionable / 범불안장애가 동반된 경우에 효과적일 수 있다.
- **SRI + pindolol (nonselective beta-adrenergic antagonist & 5-HT<sub>1A</sub> agonist) antagonize 하는 기능)**  
: still in debate / 치료반응을 앞당겨 줄 가능성이 있음

SMC

---

---

---

---

---

---

---

---

#### SRI + typical antipsychotics

- **Effective in OCD with a comorbid chronic tic disorder**  
Haloperidol + Fluvoxamine  
Pimozide + Fluvoxamine
- **Effective in OCD with a comorbid schizotypal personality disorder (not confirmed)**

SMC

---

---

---

---

---

---

---

---

#### SSRI + Atypical antipsychotics

- **Risperidone**은 소량을 SRI 제제와 병용투여 할 시 효과적일 수 있다.
- **Clozapine augmentation**은 강박증 증상을 치료하는데 별 도움이 안 된다.
- **Risperidone, clozapine**은 OCD 증상을 유발하거나 악화시킬 수도 있다고 보고됨.
- **Olanzapine**은 강박증 치료에 효과적일 수 있으나 좀더 체계적인 연구가 앞으로 필요하다.
- **Risperidone, Olanzapine, Clozapine** 모두 단독치료는 강박증 치료에 효과가 없다.

SMC

---

---

---

---

---

---

---

---

Antidepressants for Social phobia

SMC

---

---

---

---

---

---

---

---

약물치료의 종류

- Venlafaxine-XR
- MAOIs
- SSRIs
- Benzodiazepines
- Beta-blockers

SMC

---

---

---

---

---

---

---

---

Venlafaxine-XR(1)

- In 271 generalized social anxiety disorder patients, 173 patients completed the 12 week placebo-controlled study

Venlafaxine dose: 75-225mg/day

Response rate: 44%(vs. 30% for placebo) p=0.018  
Remission rate 20%(vs. 7% for placebo) p<0.01

Liebowitz, et al. J Clin Psychiatry 2005

SMC

---

---

---

---

---

---

---

---

제 3 부 불안장애의 생물학적 치료 I

Venlafaxine-XR vs.Paroxetine

- In 440 generalized social anxiety disorder patients, 318 patients completed the 12 week-comparative study.

Venlafaxine-ER(mean dose: 201.7mg/day)  
Paroxetine(mean dose: 46mg/day)

Response rate  
Venlafaxine-ER vs. Paroxetine vs. Placebo  
58.6%                      62.5%                      36.1%

Liebowitz, et al. Arch Gen Psychiatry 2005



---

---

---

---

---

---

---

---

Escitalopram

- Patients with generalized SAD were randomized to receive placebo(n=171) or 10-20mg escitalopram(n=181) in a 12-week, double-blind trial

Response rate: Escitalopram vs. Placebo(54% vs. 39%, p<0.01)

Kasper, et al. Br J Psychiatry 2005

- 5-20mg of escitalopram are effective and well tolerated in generalized SAD patients  
20mg escitalopram is superior to 20mg paroxetine

Lader, et al. Depression & Anxiety 2004



---

---

---

---

---

---

---

---

Fluoxetine

- 295 patients with generalized social anxiety disorder were randomized to fluoxetine, placebo, CBT, or (CBT+fluoxetine) group

Response rate  
Fluoxetine: 50.9%  
CBT: 51.7%  
CBT+Fluoxetine: 50.8%  
Placebo: 31.7%

All active treatments were superior to placebo after 12 weeks  
Combined treatment did not yield any further advantage

Davidson, et al. Arch Gen Psychiatry 2004



---

---

---

---

---

---

---

---

### MAOIs

- Irreversible, Nonselective MAOIs  
Phenelzine(45-90mg/day)→ 64-91% response rate
- Reversible MAO-A inhibitors  
Moclobemide(300-600mg/day) → 18-67% response rate  
Brofaromine → 효과 있었으나 안전성 문제로 개발 중단
- Selective MAO-B inhibitor  
Selegiline→ questionable effect

SMC

---

---

---

---

---

---

---

---

### SSRIs

- Paroxetine  
40-60mg/day→ 55-70% response rate
- Fluoxetine  
20-60mg/day→ 58-71% response rate
- Fluvoxamine  
150-200mg/day→ 43-47% response rate
- Sertraline  
50-200mg/day→ 53% response rate

SMC

---

---

---

---

---

---

---

---

### Antidepressants for PTSD

SMC

---

---

---

---

---

---

---

---

제 3부 불안장애의 생물학적 치료 I

TCA & MAOIs

- Amitriptyline may have a preferential effect on avoidant symptoms(50-300mg/day)
- Imipramine may affect intrusive symptoms
- Serotonergic antidepressants are more effective than noradrenergic antidepressants(desipramine, nortriptyline)

SMC

---

---

---

---

---

---

---

---

MAOIs

- Phenelzine has superior efficacy to imipramine (30-90mg/day)
- One study reported no difference between phenelzine and placebo
- Moclobemide is effective and has little adverse effect such as acute hypertensive crisis

SMC

---

---

---

---

---

---

---

---

SSRIs

- Fluoxetine(20-80mg/day) improved both intrusive and avoidant symptoms
- Sertraline(50-200mg/day) resulted in global improvement in PTSD symptoms
- Paroxetine(mean dosage=42.5mg/day) was effective in hyperarousal and avoidant symptoms
- Fluvoxamine(50-200mg/day) produced significant reduction in all PTSD symptom clusters

SMC

---

---

---

---

---

---

---

---

### Other antidepressants

- Mirtazapine: not so encouraging
- Venlafaxine: promising, but still not proved
- Nefazodone: may be effective but has hepatotoxicity
- Bupropion: not effective

SMC

---

---

---

---

---

---

---

---

### Conclusion

- Antidepressants are among the most effective anxiety agents available
- SSRIs are effective for all anxiety disorders and are very well tolerated
- Venlafaxine are effective for PD, GAD, and probably for SP, and possibly for PTSD
- TCAs are effective for PD, GAD, OCD, and PTSD, but the use of TCAs is restricted due to many adverse effects
- MAOIs are effective for PD, and SP, and possibly for OCD and PTSD
- Mirtazapine can be used as a 2<sup>nd</sup> line treatment for PD

SMC

---

---

---

---

---

---

---

---