

공황장애 약물치료에서 새로운 식견

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Treatment of Panic Disorder



- Historically, panic disorder was first treated with TCAs and MAOIs.
- TCA : Anticholinergic and adverse cardiovascular effects.
- MAOI : Strict dietary restrictions and overall poor tolerability.
- ➔ Decrease overall patient compliance.

Treatment of Panic Disorder



- Benzodiazepines
- ⊙ Rapid onset of action.
- ⊙ Long-term use may lead to dependency and withdrawal.
- ⊙ Potentially lethal danger in overdose when combined with alcohol.

Treatment of Panic Disorder



- Currently, SSRIs are indicated as the first-line treatment for panic disorder.

The APA's Practice Guideline for the Treatment of Patients With Panic Disorder

- SSRI : Safer in overdose
 - Significantly lower rate of adverse events
 - Lower risk of causing physiological dependence

Treatment of Panic Disorder



- SSRI and TCA are equally effective in reducing panic severity and the number of attacks.
- The choice of antidepressant should be based on side effect profiles and patient preferences.

Medications Used in the Treatment of Panic Disorder

- TCAs
- MAOIs
- Benzodiazepines
- SSRIs
- Other agents - Escitalopram / Paroxetine-CR
 - Venlafaxine / Duloxetine
 - Mirtazapine / Reboxetine
 - Olanzapine ...

Escitalopram



- Escitalopram is the active S-enantiomer of RS-citalopram.
- Escitalopram 10-20mg/day produced significantly greater improvements in standard measurements of antidepressant effect.
- Consistently significant improvements for all efficacy parameters were also observed in patients with GAD, SAD, and panic disorder.

- Continued

- Escitalopram has a rapid onset of symptom improvement and has a predictable tolerability profile of generally mild adverse events.
- Escitalopram is indicated for use in patients with panic disorder in Europe.
- A/E : Nausea, ejaculatory problems, diarrhea, insomnia, dry mouth, headache, URI

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- Adverse events profile from in patients with GAD, SAD or panic disorder receiving escitalopram was similar to that observed in patients with MDD.



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- The recommended dosage of escitalopram for the treatment of MDD is 10mg/day which, depending on the individual patient response, may be titrated to maximum dosage of 20mg/day.
- In Europe, Panic disorder – the recommended initial dosage is 5mg/day for 1 week then titrated to 10mg/day. The dosage may be further increased to 20mg/day, dependent on patient response to treatment.

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- Administration is once daily in the morning or evening and escitalopram may be taken with or without food.
- In elderly patients or patients with hepatic impairment, the maximum recommended dosage is 10mg/day (In Europe – 5 mg/day).
- Escitalopram should be used with caution in patients with severe renal impairment.

Paroxetine Controlled Release



- A controlled-release(CR) formulation of the SSRI paroxetine has been developed. This CR formulation delays the release of paroxetine until the tablet has passed through the stomach ; the drug is then released over 4-5 hours.
- Paroxetine CR demonstrated efficacy in three well designed studies in patients with panic disorder with or without agoraphobia.

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- The incidence of nausea was lower with paroxetine CR than paroxetine IR during the first week of treatment.
- The recommended starting dose is 12.5mg/day in patients with SAD, panic disorder, and PMDD.
- The dosage can be increased in 12.5mg/day increments (at intervals of >1 week).
... 25 - 37.5 - 62.5 - 75mg/day

Venlafaxine



- Venlafaxine (Effexor) - 1993, FDA
- Extended-release form (Effexor XR) - 1997, FDA
- The observation that both serotonergic and noradrenergic activity is important in the pathophysiology of PD raises the issue of the possible efficacy of SSNRIs.
- Venlafaxine could be an option for PD even for refractory patients and at relatively low doses.

Duloxetine



- Duloxetine is a new drug with selective serotonin and norepinephrine reuptake inhibitor antidepressant profile.
- Efficacy ... depression (anxiety & physical Sx),
panic disorder
- Duloxetine might currently be considered a second-line treatment for PD

Int J Neuropsychopharmacol. 2005 Nov 17:: 1-2

Mirtazapine



- Mirtazapine, a newer antidepressant with a novel mechanism of action enhancing both norepinephrine and serotonin levels without reuptake inhibition, is a good candidate for the treatment of panic disorder.
- 7 of 10 demonstrated an acute response.

Ann Clin Psychiatry. 1999 Jun; 11(2): 81-6

- Continued

- The results of this open label study in panic disorder suggest that mirtazapine seems to be a fast and effective treatment alternative for SSRIs in panic disorder. (74% - responders)
- The results support the hypothesis that mirtazapine is an antipanic agent with an effectiveness comparable to that of fluoxetine.

Int Clin Psychopharmacol. 2001 Nov; 16(6): 363-8.

Braz J Med Biol Res. 2001 Oct; 34(10): 1303-7.

Reboxetine



- Reboxetine, a selective norepinephrine reuptake inhibitor, is effective in treating depression and may alleviate depression-related anxiety.
- Reboxetine appears to be effective in the treatment of SSRI-refractory panic disorder patients.

Hum Psychopharmacol Clin Exp 2002; 17: 329-333

Reboxetine vs citalopram

- The advent of 5-HT reuptake inhibitors and more recently, selective noradrenergic reuptake inhibitors has provided potentially important avenues of treatment for panic disorder.
- Citalopram and reboxetine led to significant improvements in panic attack severity. Citalopram demonstrated superior efficacy in treating depressive symptoms.

Int Clin Psychopharmacol. 2003 Sep;18(5): 279-84.

Alprazolam extended-release in panic disorder



- Alprazolam-XR is an extended-release formulation of alprazolam designed to deliver sustained therapeutic concentrations for 24 h after once-daily dosing.
- Plasma concentrations gradually decline as the time for the next dose approaches, but still remain above therapeutic minimum levels.

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- The main advantage of the new extended-release formulation appears to be its greater tolerability and safety.
- Alprazolam-XR does not exhibit the sudden increases in plasma concentration characteristic of the original formulation of alprazolam.
- A reduced liability of abuse and a reduced incidence of sedation and cognitive and psychomotor impairment during acute therapy.

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- The once-daily dosing reduces clock-watching, increases compliance and it eliminates the penalty of breakthrough anxiety and panic that many patients experience.
- It should be noted that long-term therapy with alprazolam-XR carries the same risk of dependence and withdrawal during discontinuation as the original formulation of alprazolam.

Olanzapine



- Several animal studies have demonstrated anxiolytic action of olanzapine.
- Olanzapine has some demonstrated effectiveness for anxiety in humans.
- There are two reports of two cases each where panic attacks were ablated when olanzapine was added to other anti-panic medications.

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- Refractory panic disorder patients required a wide dose range averaging 12.3mg/day of olanzapine to significantly improve or ablate panic attacks. Olanzapine is potentially effective and safe in panic disorder.

Depression and anxiety 21: 33-40(2005)

- Olanzapine might be particularly beneficial for the refractory patient with hypomania, irritability, and insomnia, who also has demonstrated acute SSRI hypersensitivity.

Psychopharmacol Bull. 2001 Spring; 35(2):97-110.

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- The experts did not recommend using an antipsychotic in geriatric panic disorder & geriatric generalized anxiety disorder.

J Clin Psychiatry 2004;65 suppl 2



SSRI



- Increased aggression and suicidality has been reported in association with the SSRIs, particularly paroxetine, but is an uncommon event.
- A direct comparison of sertraline and paroxetine suggested that both were of equivalent efficacy but that sertraline was significantly better tolerated and was associated with significantly less worsening during taper.

J Clin Psychiatry. 2004 Mar;65(3):405-13.

- Continued

- Combined treatment with paroxetine and clonazepam resulted in more rapid response than with the SSRI alone, but there was no differential benefit beyond the initial few weeks of therapy.
- Initiating combined treatment followed by benzodiazepine taper after a few weeks may provide early benefit while avoiding the potential adverse consequences of long-term combination therapy.

J Psychopharmacol. 2003 Sep;17(3):276-82.

Buspirone



- It is slow in onset of action.
- Apart from nausea, it is well tolerated.
- Efficacy has not been established for buspirone in panic disorder.
- Buspirone may also play a role in the long-term pharmacotherapy of anxiety disorders.

Schweiz Rundsch Med Prax. 1998 Sep 23;87(39):1252-4.

Beta-blocker



- Beta-blocker can be helpful in anxious patients when physical symptoms such as palpitations and tremor are prominent.
