

Pharmacological Treatment for Social Phobia (Social Anxiety Disorder)

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Pharmacotherapy

Indication of Medication

- Rapid response is crucial
- Patient is unwilling to do CBT work
- Patient can not perform the homework assignments
- CBT is ineffective after 3 months trial

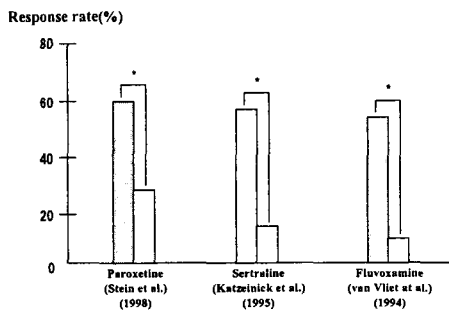
Medications

- SSRIs(paroxetine, sertraline, fluvoxamine, fluoxetine, citalopram)
- SNRI(venlafaxine)
- MAOIs(phenelzine)
- RIMAs(moclobemide)
- New Antidepressants
 - : nefazodone(?), mirtazapine(?), bupropion(?)
- Benzodiazepines(clonazepam)
- Beta blockers
- Others
 - Buspirone
 - Clonidine
 - Gabapentine, Pregabalin

Selective Serotonin Reuptake Inhibitors(SSRIs)

- First choice drug
- Favorable side effect profile
- Delayed onset of effects
- Dose
 - fluoxetine : 20-80 mg/day
 - sertraline : 50-200 mg/day
 - paroxetine : 40-60 mg/day
 - fluvoxamine : 100-150 mg/day

Comparing Response Rate of SSRIs



SNRI(Serotonin Noradrenergic Reuptake Inhibitors)

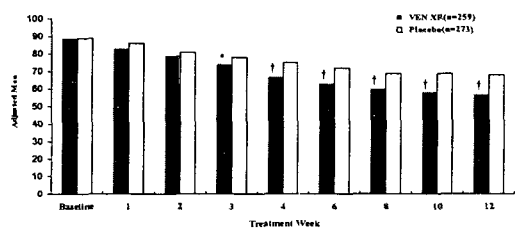
Venlafaxine XR

- Efficacy : proved by multi-center, placebo-controlled study
- Dose : flexible(75-225mg/d)
- Favorable side effects

Venlafaxine XR in Social Anxiety Disorder

- N = 271, Time : 12 weeks
- Multicenter, randomized, double-blind, placebo-controlled study
- Dose : flexible(75-225mg/d)
- Efficacy Variables : LSAS, SPIN, CGI

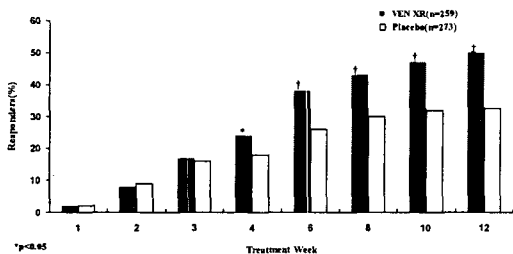
LSAS Total Score



*p<0.01
†p<0.001

Davidson et al, 2002

Responder Rate



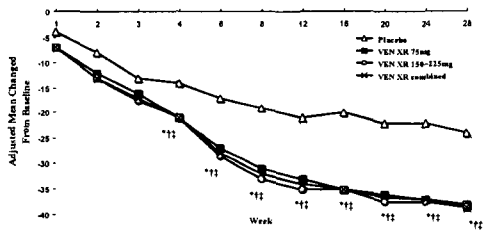
*p<0.05
†p<0.01
‡p<0.001

Davidson et al, 2002

Long-Term Treatment of Generalized Social Anxiety Disorder with Venlafaxine XR

- N = 386, Time : 28weeks
- Multicenter, randomized, double-blind, placebo-controlled study
- Dose : fixed(75mg/d) & flexible(150-225mg/d)
- Efficacy Variables : LSAS, CGI-S, SPIN

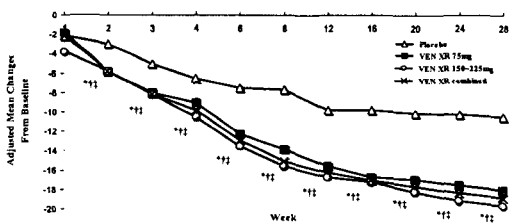
LSAS Total Score(LOCF)



*p<0.05 VEN XR 75mg vs placebo
 †p<0.05 VEN XR 150-225mg vs placebo
 ‡p<0.05 Combined vs placebo

Data on File, Wyeth, Janssen Pharmaceuticals

SPIN Scores(LOCF)



*p<0.05 VEN XR 75mg vs placebo
 †p<0.05 VEN XR 150-225mg vs placebo
 ‡p<0.05 Combined vs placebo

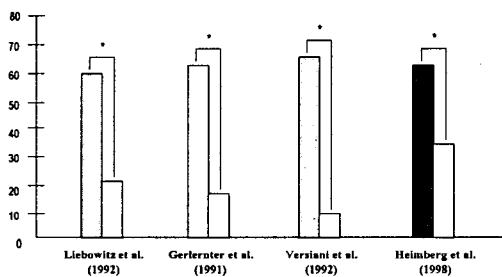
Data on File, Wyeth, Janssen Pharmaceuticals

Irreversible Monoamine Oxidase Inhibitors

- Best established
- Highly effective
- Dietary restriction needed
 - adverse effects (hypertensive crisis, weight gain, sedation, postural hypotension)
- Delayed onset of action
- Dose
 - phenelzine : 30-90 mg/day
 - tranylcypromine : 30-50 mg/day

Phenelzine

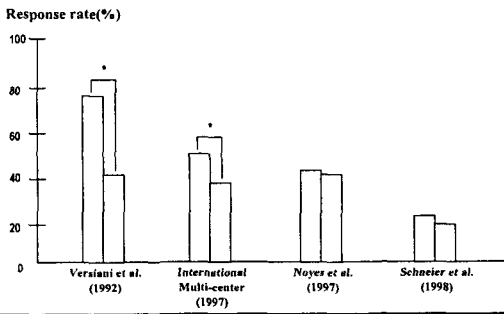
Response rate(%)



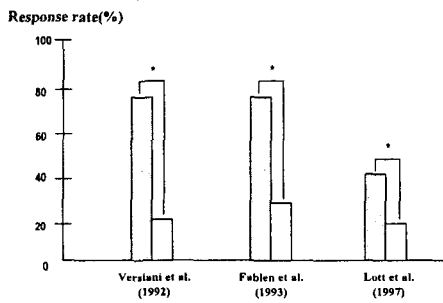
Reversible Monoamine Oxidase Inhibitors(RIMAs)

- Selective for A iso-enzyme of MAO
- Bind selectively
- Minimal side effects including hypertensive crisis
 - : no need of dietary restriction
- Dose
 - moclobemide : 300-600mg
 - brofaromine : 50-150mg

Moclobemide



Brofaromine

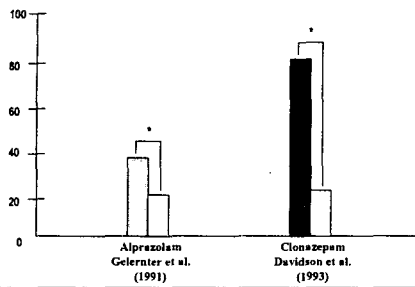


Benzodiazepines

- Rapid onset of action
- Favorable side effect profile
- Multiple doses for short-acting agents
- Dose
 - clonazepam : 1-3 mg/day
 - alprazolam : 2-5 mg/day

Benzodiazepines

Response rate(%)



Others

- Buspirone
- Gabapentine
- β -blockers
- Clonidine

Buspirone

- Serotonine Agonist Anxiolytic
- Use for non-responder to better established treatment
- Use for augmentation of a partial response
- Dose : 30-60 mg/day

Beta-blockers

- Diminish performance anxiety
 - With prn medication(1hr before performance situation)
 - Predictable feared situation, not occur so frequently
- Most effective for tachycardia(mediated by beta-1 receptors) and tremor(mediated by beta-2 receptors)
- Mediated by combination of physiologic and psychologic factors
- Dose
 - Propranolol : 20-80 mg/day
 - Atenolol : 25-100 mg/day

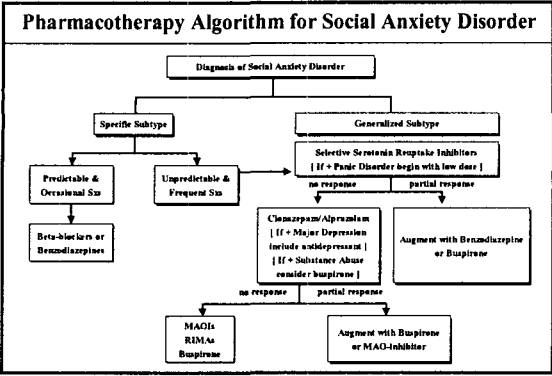
Augmentation Strategies

- 1) SSRI/SNRI + Benzodiazepine
- 2) SSRI/SNRI + Beta blocker
- 3) SSRI/SNRI + Buspirone
- 4) MAOI + Benzodiazepine
- 5) MAOI + Beta blocker
- 6) Benzodiazepine + Beta blocker
- 7) Antidepressant(SSRI/SNRI or MAOI) + Benzodiazepine + Beta blocker

Summary of Placebo-Controlled Studies in Social Anxiety Disorder

Drug	No. of studies	Efficacy	Main side effects	Others
Phenelzine	4	+++	sleep disturbances, risk of hypertension	diet restriction
RIMAs	7	++	insomnia, daytime sedation dry mouth, light headedness	not marketed in U.S.A
SSRIs	5	+++	sexual dysfunction, nausea	slow tapering
Benzodiazepines	2	+++	sedation, impaired coordination memory impairment	probably useful in performance anxiety
Atenolol	2	--	bradycardia, hypotension	Can be used with SSRIs
Buspirone	2	--	nausea, dizziness, insomnia	

(Carles Blencoe et al, 2002)



- ### Medication Treatment Algorithm for Social Anxiety Disorder (Effective Treatment 2004, February)
- | | |
|---|--|
| <p>1) Antidepressant</p> <ul style="list-style-type: none"> a) SSRI, Venlafaxine, Moclobemide b) MAOI <p>2) Benzodiazepine</p> <ul style="list-style-type: none"> a) Clonazepam b) Clonazepam + Antidepressants | <p>3) Augmentations(1 or more)</p> <ul style="list-style-type: none"> a) Modafinil(Provigil) b) Nefazodone c) Gabapentine d) Lamotrigine e) Bupropion f) Methylphenidate g) Alprazolam h) Caffeine |
|---|--|

Duration of Medication Treatment

Acute treatment

2-4 weeks to achieve optimal dosage

6-8 weeks at an adequate dosage

: 8-12 weeks

Maintenance treatment

: 6 months – 1 year

Treatment Decisions for Social Anxiety Disorder

Decision 1 Treatment of choice	SSRI ₁			
Decision 2 Switching	SSRI ₂	MAOI	RIMA	Venlafaxine
Decision 3 Augmentation	Buspirone			
Decision 4 Other options	HPBZ	Gabapentin		
Decision 5 To be discussed	Nefazodone	SNRI		
Decision 6 Experimental	Ondansetron	■	NAP	
Decision 7 Long term	Continue medication at the same dosage with which remission was achieved, for 1 year, followed by very gradual down-titration (20-30% every 6-8 weeks)			
<input type="checkbox"/> Intervention supported by consistent randomized trials <input type="checkbox"/> Intervention supported by limited controlled data <input type="checkbox"/> Intervention supported by uncontrolled data <input checked="" type="checkbox"/> Intervention that have been found to be ineffective. (*SSRI ₁ denotes treatment of choice; SSRI ₂ suggests using a second SSRI after a therapeutic attempt with SSRI ₁ has failed.)				
