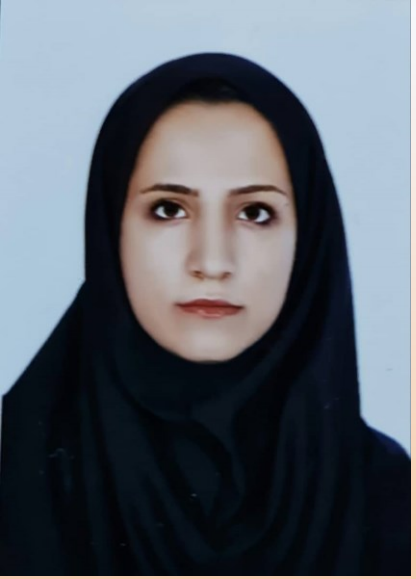

In the name of God

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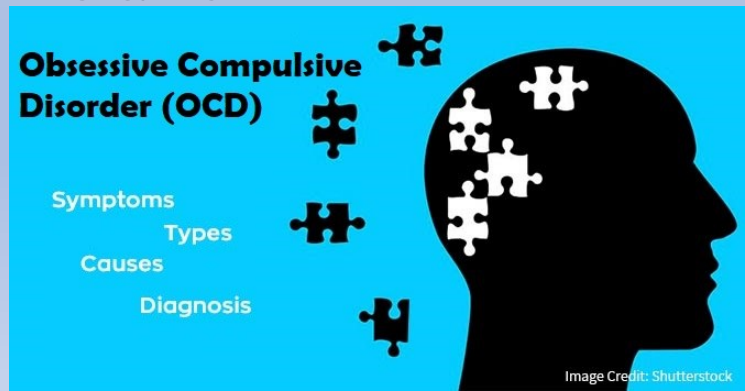
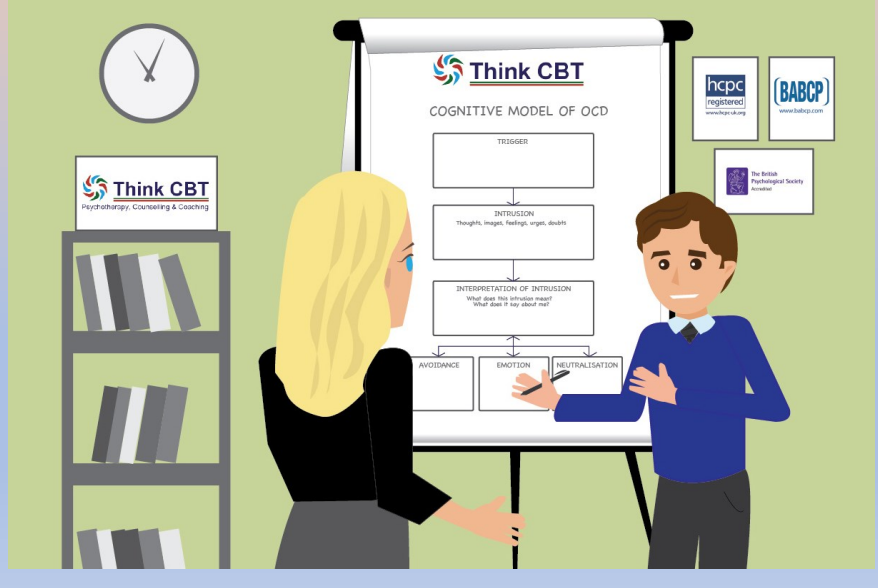


- What is **Obsessive-compulsive** disorder (OCD) treatment?

- Pharmacotherapy for OCD in adults:



Prescription:

- Tab fluvoxamine 100 mg
- هفته اول نصف موقع خواب
- هفته دوم یک عدد شب
- از هفته سوم نصف صبح، یک عدد شب
- Tab risperidone 1 mg

شبی نصف

Be effectively treated with:

1) Pharmacotherapy:
Serotonergic antidepressant

2) Non-Pharmacotherpy:
cognitive behavioral therapy

a type of psycho-social intervention, in which negative patterns of thought about the self and the world are challenged

serotonergic antidepressants:

- 1)**Selective serotonin reuptake inhibitors (SSRIs**) antidepressants:
- therapeutic dose ranges for OCD
- **Fluoxetine 40-80 mg/day**
- **Fluvoxamine 200-300 mg/day**
- **Sertraline 50-200 mg/day**
- **Paroxetine 40-60 mg/day**
- **Citalopram up to 40 mg/day (20 mg/day in age>60 years)**
- **Escitalopram 20-40 mg/day**
- No individual SSRIS more efficacious **than other SSRI** for OCD
- All SSRIs FDA approved for OCD **except:**
- 1)Citalopram
- 2)Escitalopram

Serotonergic/norepinephrin antidepressants:

2) Tricyclic antidepressant :

Clomipramine

2)**Serotonin nor epinephrine reuptake inhibitor (SNRIs) antidepressant**:

Venlafaxine

Administration & course of treatment:

- Studies:
- Serotonergic antidepressants in OCD:
- Higher doses, lead to greater response rates
- Dose response relationship shows:
- Higher doses, higher dropouts due to higher side effects
- So:
- Suggested **therapeutic** dose ranges

- Why must reduce the dose of **citalopram** in some specific population?

Max daily dose citalopram:

- Due to risk of QT prolongation
- Lower max daily dose:
- age>60 years
- Hepatic impairment
- Concurrently receiving medications increase citalopram levels (cimetidine, **omeprazole**)

- How to **start the SSRIs** in OCD patients at the first time?

Patients should be started:

- At a low dose to enhance tolerability
- *Tolerability* refers to the degree to which overt adverse effects of a drug can be tolerated by a patient.
- Fluvoxamine 50 mg 4 to 7 days at bedtime then, >100 mg in 2 divided dose, larger dose at bedtime
- The dose increased every week or every other week (as tolerated)

- What must we say to patients:

Its important to explain this to patients:

- **An adequate trial of medication for OCD as the max dose tolerated for a min of six weeks**
- **Until:**
- **Do not prematurely stop the medication before it has a chance to work**

Side effects of SSRIs:

- Generally well tolerated
- Potential side effects:
- 1)Gastrointestinal disturbances (nausea, diarrhea)
- 2) Agitation
- 3) Sleep disturbances (insomnia, vivid dreams)
- 4) increased sweat
- 5)sexual side effects(decreased libido, trouble ejaculating, delayed orgasm)

TCA (Clomipramine):

- Reduce symptoms OCD compared with placebo
- Less well **tolerated** than SSRIs & SNRIs
- Tolerability refers to the degree to which overt adverse effects of a *drug* can be *tolerated* by a patient.
- Clomipramine 100 to 125 mg/day

Side effects of Clomipramine:

Some patients may not be able to tolerate the side effects:

Sedation

Dry mouth

Constipation

Urinary delay

Orthostatic hypotension

Cardiac conduction delay

Head to head comparisons:

- Clomipramine Vs SSRIs:
- **Fluoxetine**
- **Fluvoxamine**
- **Sertraline**
- **Paroxetine**

Have not shown either **to be superior for** OCD

In general: SSRIs and clomipramine lead to improvement in 40 to 60 % OCD

On average, OCD patients who takes one of these agents, 20 to 40% reduction OCD symptoms

Typically amelioration than elimination of symptoms

SNRIs:

- Based on their mechanism & similarity to SSRIs, expect to be effective for OCD
- Limited study in OCD
- **Not FDA approved** for OCD
- Study1:
- Venlafaxine vs placebo in OCD, no significant reduction in symptoms
- Max dose limited to 225 mg/day
- Study2:
- Higher dose venlafaxine and compare with SSRI and clomipramine:
- Similar rate of response
- Larger study needed
- Venlafaxine 225 to 350 mg/day
- Duloxetine, no study in OCD

Side effects of SNRIs:

- Generally well tolerated
- The most common side effects:
- Nausea
- Constipation
- Dizziness
- Insomnia, sedation
- Sexual side effects
- Venlafaxine may cause:

1) elevated blood pressure
2) increase risk for Gastrointestinal bleeding

Duration of treatment:

- OCD patients who respond to an adequate trial of a serotonergic antidepressant should stay on that medication for:
  - **at least one to two years**

If decide to discontinue the medication:

- It should be slowly tapered
- 10 to 25% every one to two months

How to reduce 10 to 25% taper down?

- **Sertraline 50-200 mg/day**
- 200 mg
- 10% 200 mg: 20 mg
- 25% 200 mg:50 mg
- 200-50:150 mg for one to two months
- After one to two months taper again:
- 10% 150 mg:15
- 25% 150 mg:37.5
- (15…..37.5):25 mg reduced
- 150-25: 125 mg
- One tab 100 mg+1/2 tab 50 mg:125 mg
- After one month again reduce the dose

Other medications as monotherapy:

- Limited trials suggested:
- 1)mirtazapine:
- Antagonist alpha-2 adrenergic
- Antagonist 5-HT2, 5HT3 receptor
- 2)Tramadol
- Agonist mu opioid
- Modulator noradrenergic and serotonergic system
- 3)Stimulants
- D-amphetamine
- **All needed further study to determine efficacy in OCD**

Antidepressant

7.5, 15, 30, 45 mg
Indications:
Prophylaxis chronic tension-type headache
Major depression
Panic disorder
Withdrawal syndrome:
>3 lasted :
Taper to DC over 2 to 4 weeks
Side effects:
Dyslipidemia(Chol, TG even pancreatitis)
Sedation
Serotonin syndrome
Weight gain
Sexual dysfunction

Tramadol

- Analgesic, opioid
- Side effects:
- Addiction, overdose and death
- CNS depression (with BZD, alcohol)
- Respiratory depression
- Constipation
- Seizure (with SSRIs,TCSs, MAOi)
- Serotonin syndrome (drug interactions)
- Withdrawal syndrome
- Indications:
- Pain management moderate to severe
- Premature ejaculation (after SSRIs , topical anesthetics)
- Restless legs syndrome (refractory)

How about antipsychotic:

- There are no randomized trials of antipsychotic medications as monotherapy for OCD
- Small study: inconsistent results

- **Medication selection:**

Medication selection:

- SSRIs: as first line treatment
- Much greater support SSRI Vs venlafaxine
- SSRIs superior profile Vs clomipramine

- Which SSRIs must be chosen in OCD patients?

Note:

- None of the individual SSRIs advantage in efficacy for OCD
- Choice among the SSRIs based on:
- 1)prior treatment response
- 2)drug side effects
- 3)acceptability to patients
- 4)drug interaction

Comorbidity:

- Depression
- Anxiety disorder
- Commonly co occur with OCD
- A beneficial aspect of serotonergic antidepressants for OCD:
- Effective treatment for several depressive and anxiety disorder

no response

- If no response with one SSRI?

no response:

Patient should be given:

Another Monotherapy with:

1) A different SSRI
2) Clomipramine
3) Venlafaxine

Patients change to another SSRI:

- Less than ½ patients will benefit from switching from one SSRI to another
- Response diminishes as the number of failed adequate trials increase

partial response

- If partial response with one serotonergic antidepressants ?

Augmentation of this agent

- To augment medications with partial response in OCD
- Adding:
- 1)Cognitive behavioral therapy (CBT)
- 2) Risperidone or another antipsychotic medication
- 3)a low dose of clomipramine (ADD to SSRI or SNRI)

Antipsychotic augmentation:

- Efficacy to reduce OCD symptoms **when add** to an SSRI or clomipramine
- None of Antipsychotic medication FDA approval for OCD treatment

- **Which** Antipsychotic medication could be use as augmentation?

Antipsychotic

- Haloperidol
- Risperidone
- Quetiapine
- Olanzapine
- Aripiprazole
- In RCT augment SRI response

- **When** Antipsychotic medication should be add as augmentation ?

Antipsychotic augmentation administration:

- Delayed onset of action SSRIs or clomipramine
- Antipsychotic augmentation should be added only after the patients not responded at least 12 weeks at the max antidepressant dose tolerated

- **How much** Antipsychotic medication could be added as augmentation?

Dose of antipsychotic augmentation:

- Most of these trials used low doses (risperidone 0.5 to 2 mg/day)
- Short term used only
- Low antipsychotic doses appear effective:
- 0.5 to 3 mg for risperidone

- When antipsychotic should be terminated?

- Should be terminated **after one month if** the patient dose **not show a clear benefit**

Antipsychotic augmentation side effects:

- Greater:
- weight gain
- Sedation
- Than SSRI or clomipramine monotherapy
- Side effects:
- 1)Metabolic syndrome
- 2)Extrapyramidal symptoms
- 3)Tardive dyskinesia
- 4)Neuroleptic malignant syndrome

Other pharmacologic augmentation:

- 1) Clomipramine <75 mg/day (low dose) as augmentation may be effective in add to SSRIs
- 2) Add in serotonergic antidepressants, Did not show clear efficacy:
- Lithium
- Buspirone
- Clonazepam
- Pindolol
- Desipramine
- Ondansetron

Continue:

- 3) some shown some promise, but **further study in RCT needed**:
- 1)Caffeine
- 2)Lamotrigine
- 3)Celecoxib
- 4)Pregabalin
- 5)NAC
- 6)Memantine
- 7)Riluzole
- 8)Minocycline

- OCD in **pregnancy** and **lactation:**

OCD treatment in pregnant or lactation:

- should be based on, weighing of benefits over risks:
- 1)severity, impair patient and family functioning
- 2)untreated illness has risk to mother or baby
- 3)risk medication present to baby

OCD in pregnant, lactation:

✓If mild OCD:

Without immediate risks to mother or baby:

CBT

✓If moderate-severe OCD

Requires informed consent via discussion among the physician, patient family :

weighing of benefits over risks:

First line:

serotonergic antidepressants

✓if refractory to first line:

- 1) augmentation with CBT
- 2)Switching to different class of serotonergic antidepressants
- 3)augmentation atypical antipsychotic

- The efficacy medication in OCD for pregnant or nursing woman not tested in RCT
- No published studies of any type these medication in this population
- Study1:
- Quetiapine augmentation to SSRI in 17 nurse woman
- After 12 weeks 11/17 experienced a 50% or greater reduction in symptoms

postpartum

- Non RCT
- Compared CBT+ paroxetine Vs paroxetine alone:
- In 35 mothers with comorbid depression+ anxiety disorders:
- No difference

Postpartum

- Comorbid postpartum depression +OCD
- First line:
- Serotonergic antidepressant
- At the start of treatment:
- BZD (lorazepam or clonazepam) can ne used to treat anxiety and insomnia

- Treatment of OCD disorder in **children and adolescents**:

Treatment:

- 1) medication (serotonergic reuptake inhibitors)
- 2) psychotherapy
- 3)combination (more severe, comorbid, refractory)

Mild to moderate cases of pediatric OCD:

- First line:
- CBT
- If CBT not available, cases preference:
- First line:
- serotonergic reuptake inhibitors

More Severe cases of pediatric OCD:

- First line:
- Combination serotonergic reuptake inhibitors + CBT
- serotonergic reuptake inhibitors Decrease OCD-anxiety symptoms, so CBT can be effective
- Combination, lead to:

1) needed lower doses of serotonergic reuptake inhibitors,

2) so reduce side effects

Pharmacotherapy:

Monotherapy:

- SSRIs: fluoxetine, fluvoxamine, sertraline
- TCA: clomipramine

When medication is used for pediatric:

Suggest:

- One SRIs as first line

Treatment refractory pediatric OCD:

- SSRI
- A second SSRI
- Augmentation with atypical antipsychotic
- Clomipramine
- Combination SSRIS +clomipramine

SSRI in pediatric OCD:

- Initial medication of choice
- Efficacy, generally well tolerated side effects
- Fluoxetine
- Fluvoxamine
- Sertraline

SSRI in youth OCD:

- Paroxetine
- Citalopram
- Escitalopram
- Efficacy Citalopram, Escitalopram not established
- In RCT Paroxetine was effective in pediatric OCD
- But no efficacy in depression youth
- Paroxetine **not FDA approve** for children
- If used:
- Child with OCD without depression
- And
- First degree relative well response to paroxetine

Side effect SSRI in children & adolescents:

- Well tolerated
- Side effects dose dependent
- Many are transient, finish over time
- Headache
- Abdominal pain
- Nausea
- Diarrhea
- Sleep changes
- agitation

Suicidality:

- There is controversy about the relationship between SSRI & suicidality in children
- Slightly increased risk of suicidal thought
- The evidence is inadequate

Comorbid conditions:

- Fluoxetine FDA approved for **major depression**
- RCTs show:
- Sertraline
- Fluvoxamine
- Fluoxetine
- Effective in pediatric **anxiety**

Administration:

- SSRIS typically initiated:
- At a low dose (25 mg sertraline) for the first week
- Titrated up (every two to four weeks) to therapeutic dose
- 12 weeks
- Not adequate:
- Gradual adjustment to max efficacy and min toxicity for additional six to twelve weeks

Therapeutic dose:

- Fluvoxamine 50-200 mg/day children OCD
- Fluvoxamine 50-300 mg/day adolescent OCD
- START:
- 25 mg daily one week
- 50 mg daily for 12 weeks
- 100 mg
- Dose fluoxetine higher in pediatric OCD (20-60) than major depression(10-20)

Selected characteristics:

- Fluvoxamine:
- Girls needed lower maintenance dose
- Give in divided dose+meal+bedtime: to min side effects
- Sertraline:
- Diarrhea more frequent
- Paroxetine:
- Mild anticholinergic side effect
- Clomipramine:
- Only TCA with efficacy in pediatric OCD
- ECG before to initiating
- Anticholinergic side effects(sedation, dry mouth, constipation)
- Irritability and vomiting
- Give in divided dose+meal+bedtime: to min side effects

- Fluoxetine:
- Prolonged half life
- Improvement OCD symptoms more slowly than others
- More than 8 weeks on a therapeutic dose

Clomipramine vs SSRIs:

- Although, Clomipramine **more efficacious** than SSRIs in pediatric OCD

SSRIs preferred treatment Due to:

- Better tolerated
- Safer

- In adult:
- Either drug **not to be** superior for OCD

Using clomipramine:

- Avoid grapefruit/ grapefruit juice
- Raise concentration
- Caution:
- Add clomipramine to SSRI (serotonin syndrome):
- Mental changes (agitation, hallucination, delirium)
- Autonomic instability (tachycardia, HTN, dizziness, flushing)
- Neuromuscular changes(tremor, rigidity)
- Seizure
- GI symptoms (nausea, vomiting, diarrhea)

Refractory case of pediatric OCD:

- 1)SSRI, or add CBT
- 2) A second SSRI
- 3)Clomipramine
- 4)Augmentation SRI with atypical antipychotic
- 5)Combination SSRI+clomipramine

Medication augmentation:

- Response insufficiently monotherapy
- 1)Atypical antipsychotic (risperidone)
- Augment SSRI or clomipramine
- Side effect to pre adolescent:
- Metabolic side effects
- Weight gain
- Diabetes
- Insulin resistance

First generation antipsychotic:

- Typically not consider as first line
- Side effect & limited study
- Haloperidol
- **Better metabolic** side effect than atypical

Other augmentation strategies:

- Negative results
- 1)lithium + SSRI and clomipramine
- 2)Buspirone +SSRIs
- 3)Thyroid hormone +clomipramine

- Complementary and alternative treatment for **anxiety symptoms**

- None of the herbal remedies shown in clinical trials to be clearly effective or ineffective:
- Kava and chamomile:
- Reduce anxiety in GAD
- Valerian, passion flower, St/John's wort:
- Either mixed or negative

Note:

- May wrongly equate herbal remedies with:
- Good
- Weak
- Healthy
- but: some herbs can be:
- Potent
- Poisonous
- Addictive
- Potentially Side effect:
- Hepatotoxicity with kava
- Anticoagulation with chamomile
- The mechanisms of action for anxiety reduction is partially understood

Kava kava

- Piper methysticum
- 2 meta analysis multiple RCT:
- Reduce anxiety
- Side effects:
- Headaches
- Sedation
- Sleepiness
- Reports:
- Severe hepatotoxicity
- Liver failure
- Within a few weeks to up to two years
- FDA:
- use with caution in :
- 1)Preexisiting liver disease
- 2)at risk of liver disease

Valerian

- Was not found to reduce anxiety, side effects valerian vs placebo
- Side effects:
- Drowsiness
- Dizziness
- Risk respiratory depression:
- Valerian + sedating drug (alcohol)
- In large dose:
- Abdominal pain

Passion flower:

The anxiolytic effects of passion flower **milder than** :

Kava

Valerian

Side effects:

Rare

Drowsiness

Sedation

Nausea/vomiting

Dizziness

Chamomile:

- **Matricaria Recutita**
- Research in animals:
- Anti-inflammatory
- RCT Mix results for GAD
- Anticancer
- Reported:
- Increase anticoagulation properties of other medication
- Use with caution in patients receive anticoagulant

Saffron:

- Use for treatment:
- Cramps
- Depression
- Asthma
- 2RCT:
- Reduce anxiety and depression better than placebo
- 60 patients with depression + GAD
- Fluoxetine, sertraline + saffron/placebo

St. John’s wort:

- Hypericum perforatum
- Widely prescribed as :
- Antidepressant
- Anxiolytic remedy
- The mechanism unknown
- Weak MAOI
- No evidence of efficacy in anxiety disorder
- RCT for OCD: negative result
- There are no trials for anxiety as a primary outcome
- Secondary anxiety reduction (major dep, somatization disorder)
- Note:
- Combination with SSRI: serotonergic syndrome
- avoided

Dietary supplements:

- Nutrients:
- Vit
- Minerals
- Omega3
- Amino acids
- Fruits, vegetable, nuts, seafood

ESSENTIAL NUTRIENTS:

- THEY ARE NEEDED FOR BODYS BIOLOGIC PROCESS
- But are not produce in adequate amounts by body
- Must be obtained through dietary
- Nutrient deficiencies:
- Zinc deficiency and OCD
- Vit B12 deficiency and OCD
- RCT:
- Found benefit of zinc supplement of fluoxetine for OCD