PHARMACOTHERAPY OF PERSONALITY DISORDERS

Dr Mohammadreza Shalbafan

Assistant Prof. Psychiatry, Iran University of Medical Sciences

- In general, patients with PD require a multifaceted treatment plan that often combines psychotherapy and pharmacotherapy.
- Psychotherapy is the primary treatment, as it promotes the maturation of character and ultimately the development of the patient's capacity to develop better adaptive solutions.
- However, psychotherapy is very hard to implement in the setting of unstable affects and risky or self-destructive behaviors, all very common in the initial stages of treatment.
- During these early stages, pharmacotherapy achieves a relatively prompt control of affects and behaviors.

- As the first step, pharmacotherapy stabilizes affects and ensures safety of the patient, which interferes with psychotherapy.
- Common assumption is that pharmacotherapy "works" only at the biological level and psychotherapy works only at the psychological level.
- However, psychotherapy can modulate structural CNS characteristics, such as receptor activity and expression in brain tissue through epigenetic mechanisms.
- On the contrary, pharmacological improvement of depressed mood or symptoms of psychosis can restore complex psychological phenomena, such as integration of identity, in Major Depression or Postpartum psychosis.

- In comparison to psychotherapy, medication is more effective in treating mood or modulating aggression then in changing internalized concepts about self and the world.

PREVENTABLE ERRORS IN TREATING INDIVIDUALS WITH PERSONALITY DISORDERS

- There are three major barriers to effective treatment of PD, but all are preventable errors within the control of the health care provider.
- The first is the frequent loss of professional objectivity, signaled by the development of strong emotions (positive or negative) and called positive or negative countertransference. This inappropriate personal involvement is a red flag to reassess diagnosis and treatment.
- Frequent discussions and counseling with colleagues are useful because even strong countertransference feelings sometimes persist unrecognized.

PREVENTABLE ERRORS IN TREATING INDIVIDUALS WITH PERSONALITY DISORDERS

- The second preventable error in PD management is to believe the myth that PDs cannot be treated effectively.
- Belief in the untreatability of a patient creates a self-fulfilling prophecy. For example, many controlled studies indicate that even severe PDs, such as borderline or antisocial PDs, can be effectively treated with an appropriate condition, such as a cooperative therapeutic alliance.

PREVENTABLE ERRORS IN TREATING INDIVIDUALS WITH PERSONALITY DISORDERS

- The third preventable error in PD management is to give direct advice on personal and social problems.
- This is counterproductive in patients with PD because they usually become dependent, noncompliant, or resentful.
- Occasionally, direct advice may be offered to some antisocial, narcissistic, and schizoid patients who are at low risk of developing dependency and need precise structure and direction initially.
- However, it is most beneficial to provide guidance and support without giving direct advice.
- In summary, supporting these patients involves joint evaluation of options and encouragement to practice skills in solving problems.

MOOD DYSREGULATION AND ANXIETY

- Emotional instability and mood swings are usually responsive to lithium or valproates (for patients with frequent episodes of euphoria) or lamotrigine (for patients with more frequent depressive episodes).
- Lowdose atypical psychotropics may be used to stabilize mood or improve depression as the second-line medications.
- Tricyclic antidepressants (TCAs), like imipramine, sometimes increase impulsivity and anger in emotionally unstable patients (e.g., borderline, narcissistic, histrionic, dependent).
- TCAs are extremely dangerous in an overdose, so these drugs ought to be used with caution in patients with PD.

MOOD DYSREGULATION AND ANXIETY

- Atypical depression and dysphoria are very frequently observed in patients with any subtype of PD. The "first-line" medications used here are selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), monoamine oxidase inhibitors (MAOIs), or low-dose atypical psychotropics, such as aripiprazole, ziprasidone, lurasidone, or clozapine.
- TCAs are not recommended as at least half of the PD subjects suffering from atypical depression worsen on TCAs.

MOOD DYSREGULATION AND ANXIETY

- Patients with PD often present with both cognitive anxiety (anticipatory worry) and somatic anxiety (concerns about bodily pains and psychophysiological reactions).
- Treatment of choice for chronic cognitive anxiety is psychotherapy, especially various forms of CBT.
- With respect to pharmacotherapy, chronic cognitive anxiety is most responsive to SSRIs, MAOIs, SNRIs, GABA analogues (such as valproates, pregabalin, gabapentin), and (with caution) long half-life benzodiazepines.
- Chronic somatic anxiety is more responsive to MAOIs, SNRIs (e.g., venlafaxine or duloxetine), and buspirone.

MOOD DYSREGULATION AND ANXIETY

- Avoidant traits can be also effectively treated with either SSRIs or MAOIs.
- Some components of somatic anxiety, such as sweating, palpitations, diarrhea, and tremor, can be treated with betablockers.
- Severe, psychotic-like anxiety responds to low-dose neuroleptics, especially drugs with low D2 affinity (e.g., quetiapine).
- Recent reports indicate that a number of medications used to treat depression and anxiety, for example, SSRIs, stimulate neurogenesis in the hippocampus and thereby restore hippocampal control of the HPA axis.

AGGRESSION

- Multiple double-blind trials have shown efficacy of lithium carbonate in the treatment of affective aggression.
- Lithium salts help impulsive– aggressive individuals to be more reflective, that is, to think about consequences before acting on impulse.
- Likewise, low-dose atypical neuroleptics may be useful in setting the stage for the patient to modify old habits and assist him or her in reducing affective aggression.
- Anticonvulsants, such as valproates, lamotrigine, carbamazepine, and oxcarbazepine, reduce both the intensity and the frequency of unprovoked angry outbursts in many patients regardless of normality of their EEG.

AGGRESSION

- Psychostimulants and catecholamine agonists, such as methylphenidate, are often beneficial in the treatment of inattentive and hyperactive adults who are impulsive and aggressive, especially when the symptoms have begun in early childhood.
- In accord with postulated serotonergic mechanisms in aggressive behaviors, antidepressants (particularly SSRIs and SNRIs) are considered by many to be beneficial for certain subtypes of impulsive PD (e.g., borderline, histrionic).

AGGRESSION

- There is no effective pharmacotherapy for predatory, premeditated, and cold-blooded aggression.
- Low-dose traditional neuroleptics (haloperidol) or low-dose novel psychotropics (Risperdal, quetiapine) may help tone down predatory aggression.
- Of note, antipsychotic-level doses have not been shown more effective here and are not recommended.
- When accompanied by impulsivity, predatory aggression may improve if treated with beta-blockers.

- Lithium should not be given to antisocial persons without aggression and impulsivity because it does not diminish nonaggressive antisocial behaviors (such as lying, cheating, and stealing) and is poorly tolerated by anxious schizoid individuals.
- Likewise, benzodiazepines and alcohol have disinhibiting effects on violence, reduce conditioned avoidance behavior (“loosen inhibitions”), and further impair passive avoidance learning in impulsive antisocial persons.
- The use of benzodiazepines seems appropriate only in nonaggressive asocial behaviors, for example, patients with schizoid PD.

SOCIAL AND EMOTIONAL DETACHMENT

- In some cases, emotional detachment or disinterest may respond to novel psychotropics, such as aripiprazole, risperidone, quetiapine, clozapine, olanzapine, or ziprasidone. These medications may help reduce social withdrawal and other features of "aloof" PDs with less risk of extrapyramidal symptoms than with typical neuroleptics.
- In cases in which emotional disinterest reflects an underlying depression, antidepressants (SSRIs or MAOIs) frequently help.
- One should be cautious with TCAs in schizotypal PD, because they may worsen and/or trigger psychosis.

COGNITIVE-PERCEPTUAL DISTORTIONS; PSYCHOTIC SYMPTOMS

- In cases in which these symptoms persist and interfere with everyday functioning despite psychotherapy, medications are occasionally needed, usually novel atypical psychotropics (such as aripiprazole, quetiapine).
- Acute, brief reactive psychoses may complicate most subtypes of PD. These are treated symptomatically, according to accepted pharmacological practices, most frequently with second-generation atypical psychotropics due to much better safety and tolerability.

Table 26–24.
Choice of Drugs According to Target Symptoms of Personality Disorders

Target Symptom	Drug/Treatment of Choice	Not Recommended
I. Mood dysregulation and anxiety		
Anxiety		
Chronic cognitive	PSYCHOTHERAPY SSRIs, SNRIs, MAOIs LOW-DOSE NOVEL PSYCHOTROPICS (aripiprazole, quetiapine) Valproates and other GABA analogs clonazepam, buspirone	Benzodiazepines and ethanol (risk of abuse/addiction)
Chronic somatic	MAOIs, SNRIs (duloxetine, milnacipran) Pregabalin and other GABA analogs TCAs, beta-blockers	If used—benzodiazepines with long half-life and short trials preferred
Obsessions	SSRIs, PSYCHOTROPICS (quetiapine) TCAs (clomipramine) Mild NMDA antagonists (riluzole, memantine)	
Acute and severe	MIRTAZAPINE, NOVEL PSYCHOTROPICS (quetiapine, aripiprazole, clozapine) TCAs, clonazepam, valproates, lithium	
Depression		
Atypical depression/dysphoria	MAOIs, SSRIs, SNRIs, ARIPIPRAZOLE Lurasidone, ziprasidone, quetiapine	TCAs
Classical depression	STANDARD ANTIDEPRESSANTS TCAs (males) SSRI (females) Atypical psychotropics (as monotherapy or augmentation)	
Emotional lability/rapid cycling	LITHIUM, LAMOTRIGINE, VALPROATES Lower-dose novel psychotropics (olanzapine, aripiprazole, clozapine, ziprasidone)	TCAs ("catecholamine stress") Standard antidepressants (risk of switching to mania)
II. Behavior dyscontrol		
Aggression/impulsivity		
Affective aggression "Hot temper" with normal EEG	LITHIUM, SSRIs, ANTICONVULSANTS Low-dose novel psychotropics	Benzodiazepines (disinhibition)
Predatory aggression (cold blooded revenge/cruelty)	NO EFFECTIVE PHARMACOLOGICAL Tx Novel psychotropics, lithium, valproates, beta-blockers	BENZODIAZEPINES (disinhibition)
Organic-like aggression (traumatic brain injury)	BETA-BLOCKERS, VALPROATES, QUETIAPINE, CARBAMAZEPINE TCAs, cholinesterase inhibitors (donepezil)	BENZODIAZEPINES (disinhibition, delirium)
Ictal aggression (abnormal EEG)	CBMZ, DIPHENYLHYDANTOIN, VALPROATES Benzodiazepines (clonazepam)	TCAs LOW-POTENCY TYPICALS (both increase risk of seizures)
III. Social and emotional detachment		
Chronic asociality and disinterest	LOW-DOSE PSYCHOTROPICS (aripiprazole, olanzapine, low-dose	

Blunted affect	clozapine, sulpiride)
IV. Cognitive-perceptual distortions/psychotic symptoms	
Acute and brief psychotic episodes	NOVEL PSYCHOTROPICS (Risperdal, olanzapine) Typical neuroleptics (for the duration of psychosis)
Chronic and low-level psychotic-like symptoms	NOVEL PSYCHOTROPICS

SHALBAFAN.MR@IUMS.AC.IR