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Withdrawal Syndrome of Psychotropic Drugs



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ABSTRACT

Psychotropics are mainly prescribed to treat mental health disorders that have psychosis as a main symptom. There are certain categories of antipsychotics, First generation & second generation {Typical Antipsychotics & Atypical Antipsychotics}, antidepressants, mood stabilizers, Anti-anxiety, stimulants and some others for its treatment. Although you we have heard the term “withdrawal” the term “psychotropic discontinuation syndrome” may be new to us. Withdrawal syndrome of psychotropic drugs {Psychotropic discontinuation syndrome}, it is a name for the collection of the symptoms that may occur when someone suddenly stops psychotropic drugs or drastically lowers their dose. In the limited researches that does exists suggests that up to >50% of the people who stop taking psychotropics. There is no specific treatment other than reintroduction of the drug or substitution with the similar drug. The syndrome usually revolves in days or weeks also new neuropsychiatric symptoms including sensory changes, anxiety and agitation and all other symptoms as mentioned in the below introduction. This causes burden to the patient and his care takers, also impacts on mental health. A further compounding problem is the poor quality of care for many of those who do receive treatment. This article presents the various psychotropic drugs which causes complications and co-morbid psychiatric illness in brief with their respective discontinuation syndrome.



Figure No. 1: Introduction picture.

WITHDRAWAL STATE:

DEFINITION: A group of symptoms of variable clustering and degree of severity which occurs on cessation of use of a psychoactive substance that has been taken repeatedly, usually for a prolonged period or in high doses. The syndrome may be accompanied by signs of physiological disturbance. A withdrawal syndrome is one of the indicators of a dependence syndrome. It is also the defining characteristic of the narrower psycho-pharmacological meaning of dependence. The onset and course of the withdrawal syndrome are time-limited and are related to the type of substance and dose being taken immediately before reduction of use. Typically, the features of withdrawal syndrome are the opposite of those of acute intoxication. Sedative withdrawal syndrome have many features in common with alcohol withdrawal but may also include muscle aches and twitches, perpetual distortions and distortion of body image.

INTRODUCTION

Withdrawal syndrome, also known as discontinuation syndrome, occurs in individuals who have developed physiological dependence on drugs and who discontinue or reduce their use of it. Withdrawal occurs because your brain works like a spring when it comes to addiction. Drugs and alcohol are brain depressants that push down the spring. They suppress your brain's production of neurotransmitters like Noradrenaline.

The Existence of discontinuation syndrome following treatment with neuroleptic (antipsychotic) drugs was first outlined in the mid 1960s but the effects of such syndromes have been neglected since then.

Psychotropic drugs may cause withdrawal reaction which can occur after abrupt discontinuation or gradual tapering with a prevalence of greater than 60% among adults with a diagnosis of serious mental illness. A recent review of the literature suggested that benzodiazepines, Z-drugs ketamine, selective serotonin reuptake inhibitors (SSRIS), serotonin-norepinephrine reuptake inhibitors (SNRIS). Tricyclic antidepressants (TcAs), antipsychotics, monoamine oxidase inhibitors (MAOIs) and gabapentin are associated with withdrawal symptoms. Thus, it is confirmed what was previously reported in reviews focusing on specific drug classes. With regards to SSRIs and SNRI, the term “discontinuation syndrome” has been used for several transient, reversible years. However, this definition is no longer accepted, the term “withdrawal syndrome” is more relevant and there are no reason to believe that there are differences from other classes of psychotropic drugs.

Withdrawal of Benzodiazepines can cause you to feel anxious and on-edge for several weeks. You might feel irritable and hypersensitive to everything around you. Insomnia is also common. During the first week, you can also expect physical symptoms like headaches and hand tremors.

The withdrawal of MAOIs can result in severe anxiety, agitation, pressured speech, sleeplessness or drowsiness, hallucinations, delirium and paranoid psychosis.

SYMPTOMS:

Gleaned from the literature, Chouinard and Chouinard suggest in 2015 – 3 types of withdrawal syndrome for psychotropic medication.

1. New withdrawal symptoms
2. Rebound Symptoms
3. Persistent post-withdrawal symptoms.

1. **NEW WITHDRAWAL SYMPTOMS:** Usually short lasting, transient, reversible which are new to patient. New symptoms are usually the same, common to all psychotropic medication during withdrawal (eg: Nausea, headache, sleep disturbances).

2. **REBOUND SYMPTOMS:** Short-lasting, transient, reversible symptoms which represent a rapid return of the primary symptoms usually at a greater intensity than before treatment.

3. **PERSISTENT POST-WITHDRAWAL SYMPTOMS:** These are a set of long lasting, severe, potentially irreversible symptoms which entitle rebound primary symptoms or primary disorder at greater intensity and or new withdrawal symptoms and or new symptoms or disorders that were not present before treatment.

These symptoms include:

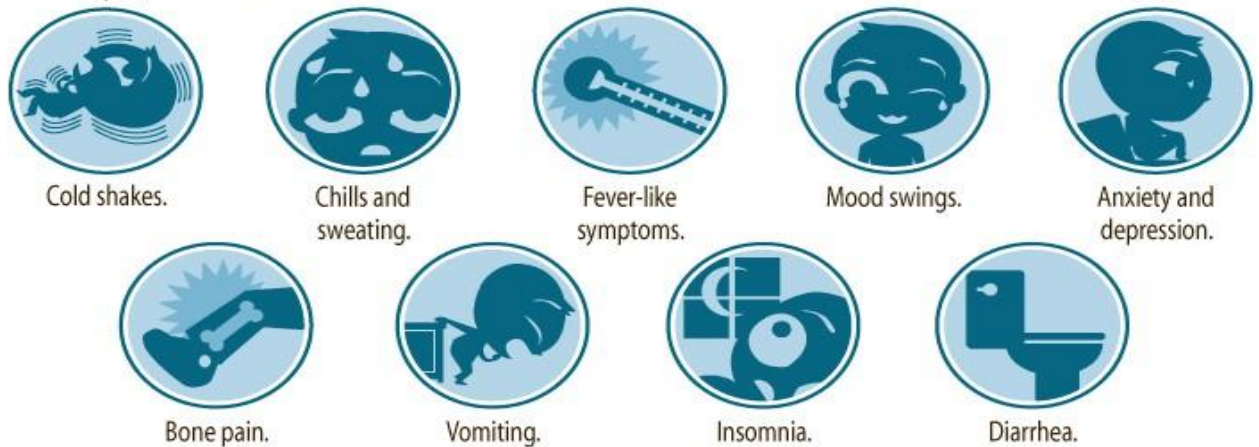


Figure No.2: Generalized symptoms of withdrawal condition

Table No. 1: New withdrawal symptoms following decrease, discontinuation or switch of psychotropic medications

Type	New withdrawal symptoms
Peak of onset	36-96 h (or later depending on drug duration of action)
Course	Transient
Duration	up to 6 weeks
Outcomes	Reversible, with complete recovery
Clinical manifestations	Appearance of new symptoms, that is symptoms which were not experienced Before the beginning of the treatment

Table No. 2: Rebound symptoms following decrease, discontinuation or switch of psychotropic Medications

Type	Rebound symptoms
Peak of onset	36-96h (or later depending on drug elimination half life)
Course	Transient
Duration	Up to 6 weeks (depending on drug elimination)
Outcome	Reversible, with complete recovery
Clinical manifestations	Return of the original symptoms at a greater intensity than before treatment

Table No. 3: Persistent post-withdrawal disorder following decrease, discontinuation or switch of psychotropic medications

Type	Persistent post-withdrawal disorder
Peak of onset	24h-6 weeks (or later depending on drug duration of action)
Course	persistent
Duration	More than 6 weeks (depending on drug elimination)
Outcomes	potentially irreversible
Clinical manifestations	Return of original symptoms at greater intensity and /or new withdrawal Symptoms persist over 6 weeks and /or appearance of new symptoms that were not present before

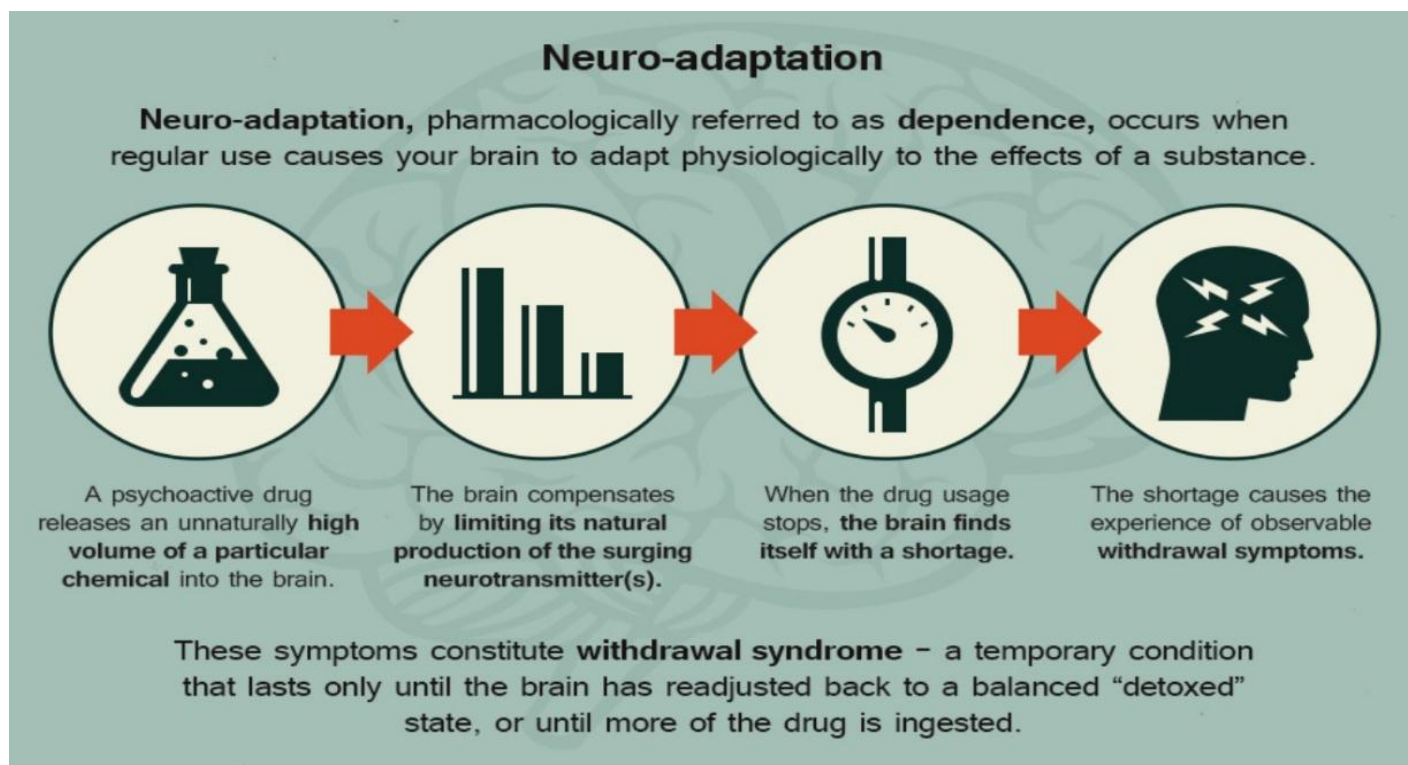


Figure No.3: Outlook of Withdrawal status

Epidemiology:-

When the outlook of all drugs is considered, here are some of majorly used psychotropic drugs with categories to treat various mental disorders and their withdrawal conditions and their prevalence.

1. ADHD {Amphetamines}:- After cannabis amphetamines are the most widely abused drug worldwide, almost 17million people are dependent on amphetamines and also 34.2 million people are using various kinds of stimulants global wise, overdose deaths are increased by 33% of stimulants. And there has been withdrawal symptoms of amphetamines in larger group of amphetamine users nearly 5-15% are prone to withdrawal syndromes and also psychosis.

2. Antidepressants{Citalopram}:- About >20% of patients have tendency of developing the withdrawal syndrome which is formally the antidepressant discontinuation syndrome, which its symptoms revolve around 3 days and last to 1-2 weeks {may persist up to one year}.

3. Anti-Anxiety {Benzodiazepines}:- Severe withdrawal syndromes can occur from these low doses of benzodiazepines even after gradual dose reduction. An estimated 30-45% of chronic low-dose benzodiazepine users are dependent and it has been recommended that

benzodiazepines even at low dosage be prescribed for a maximum of 7-14 days to avoid dependence.

4. Mood stabilizers {Lithium}:- Some research shows that patients taking lithium for bipolar disorder and when stopped taking it suddenly [i.e over the course of less than 14 days], then such conditions have a 50% [one in two] chance of becoming ill again within six months and a 90% [nine in ten] chance of becoming unwell again within three years.

Etiology:-

This syndrome is not specifically presents any cause as it is has the collection of symptoms that may occur when suddenly stops an psychic drug or drastically lowers the drug.

Reasons of stopping taking their psychic medication for various reasons, such as because the medications is [or is perceived] not effectively treating symptoms, because it is causing unbearable side effects, or because the person/patient does not think they should be taking the medication or do not agree with how they were instructed to take them.

The key causes are SWITCHING [switching one category of medication to the other immediately and discontinuing vice versa] and TAMPERING [inappropriate usage of a drug].

Other than these there are no ways to predict the patient related withdrawal condition and causes. Scientists are not exactly why some patients develop discontinuation syndrome while others do not.

Diagnosis:-

Physical examination:

Through physical examination is important, although a complete physical examination may have to be differed until after resuscitation treatment for seizures if present or sedation for severe agitation, this examination must be completed as soon as possible with the goal of detecting end organ damage resulting from the effects of withdrawal as well as underlying conditions.

Vital signs may include as following:

- The central adrenergic storm that occurs during withdrawal results in hyperventilation, tachycardia, hypertension, tremor, hyperthermia and diaphoresis.
- Paralysis of muscles can be noticed, tongue and skin becomes dry.

Chest findings:

- Tachycardia and hypertension, a murmur of tricuspid, Endocarditis.

Abdominal examination:

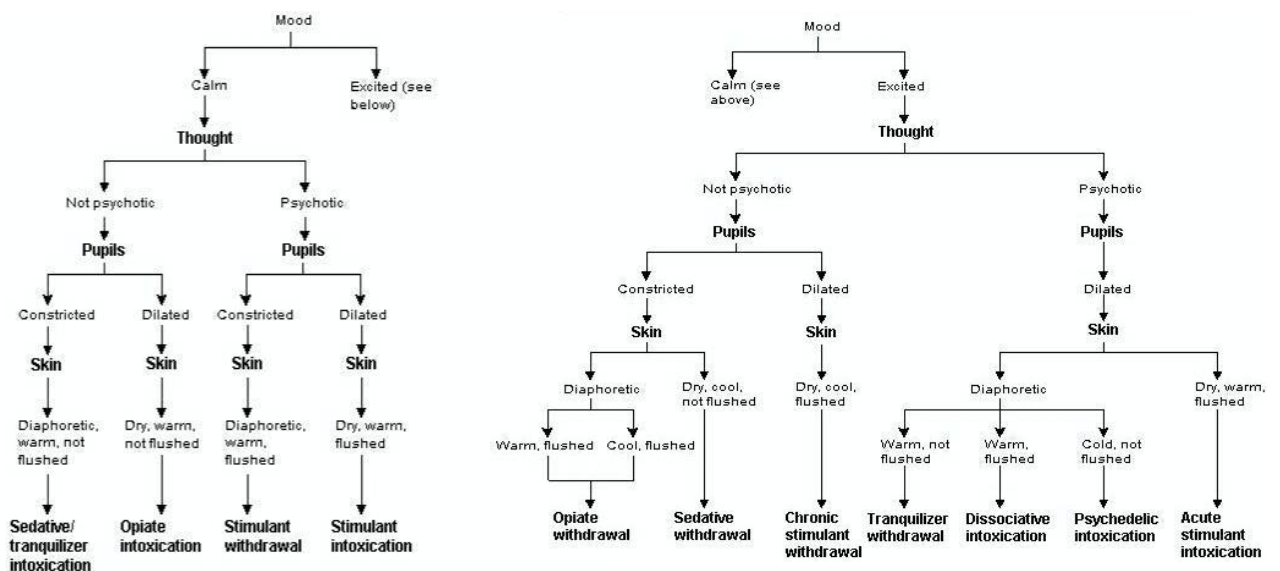
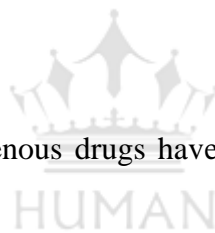
- Diffuse abdominal tenderness, GI bleeding, cramping and gastrointestinal distress.

Neurological examinations:

- Dysphoria, cranial nerve deficits, ataxia, in severe conditions peripheral neuropathy and focal neurological deficits may occur.

Skin findings:

- Piloerection, patients with intravenous drugs have evidence of injections, such as track marks.



Flow chart:- Showing physical examination (eyes and skin) of certain withdrawal symptoms and other drugs and their signs and symptoms

The following laboratory tests may be included to evaluate the underlying conditions:-

1. Serum glucose
2. Arterial blood gas analysis
3. CBC
4. Comprehensive metabolic panel
5. Urinalysis
6. Cardiac biomarker measurements
7. Prothrombin time
8. Toxicology screening

Pathophysiology:-

The body when exposed to any type of substance attempts to maintain homeostasis. When exposed, it produces counter regulatory mechanisms and processes that attempt to keep the body in balance. When the substance is removed, the residual counter regulatory mechanism produces unopposed effects and withdrawal symptoms.

Tolerance occurs when long term use of substance produce adaptive changes so that increasing amounts of the substance are needed to produce an effect. Tolerance depends on the dose, duration and frequency of use and is the result of pharmacokinetic [metabolic] or pharmacodynamic [cellular or functional] adaptation.

Comorbid disorders & complications:-

Even after treatment some unerased complications stay back in the withdrawal patients which are as follows, so at most care and control must be shown on these patients.



Figure No. 4: Explaining Co-Occurrence

Neonatal effects:- Historical long term [past] use of any benzodiazepines may cause stillbirths in pregnant women, therefore it is contraindicated in pregnant women, still it been misused and abused drug worldwide. In elders it cause dementia, impaired memories, hallucinations may come back even after its withdrawal treatment stated as comorbid conditions.

Some antipsychotic drugs may cause GAD, PSD, OCD & Social phobia.

GAD [Generalized Anxiety Disorder]:- As GAD symptoms can be mimicked by substance use or withdrawal, diagnostic complications may arise.

The treatment of this GAD can also be challenging as it is confused as the comeback symptoms and with the withdrawal symptoms, which is a natural and self suppressed symptom no specific treatment other than counseling or CBT [Cognitive behavioral therapy].

PSD [Posttraumatic stress disorder]:- It is the most commonly notable comorbid condition in the withdrawal patients which has no specific reason but the neurological feeling of not wellbeing of one's causes this condition it can be self suppressed if patient is shown at most care and the attention.

OCD [Obsessive compulsive disorder]:- This is the major comorbid sing in the specific sedative withdrawals individuals, it is restricted condition in these individuals as it is not shown as the comeback conditions in any other typical mental illness disorders.

Social phobia:- It is not as specific to the word comorbid but commonly occurring condition in all types of withdrawal conditions. Where certain individuals likely two out of three of

substance using individuals experience social phobia and lack of motivation, rehabilitation and giving their free space helps them to recovery says some limited research works.

Other complications include pessimism, neurological disturbances, abuse comebacks, increased sensitivity to stress, metabolic disturbances, hematological complications, major organ damages, cirrhosis of the injected sites etc.

Commonly Prescribed Psychotropic Medications (Antipsychotics, Antidepressants, Antipanic, Antianxiety, Mood stabilizers, Psychostimulants etc).

Antipsychotics (used in the treatment of schizophrenia and mania)	Anti-depressants	Anti-obsessive Agents
<p>Typical Antipsychotics Haldol (haloperidol) Loxitane (loxapine) Mellaril (thioridazine) Moban (molindone) Navane (thiothixene) Prolixin (fluphenazine) Serentil (mesoridazine) Stelazine (trifluoperazine) Thorazine (chlorpromazine) Trilafon (perphenazine)</p> <p>Atypical Antipsychotics Abilify (aripiprazole) Clozaril (clozapine) Risperdal (risperidone) Seroquel (quetiapine) Zyprexa (olanzapine)</p>	<p>Tricyclics * Anafranil (clomipramine) Asendin (amoxapine) Elavil (amitriptyline) Norpramin (desipramine) Pamelor (nortriptyline) Sinequan (doxepin) Surmontil (trimipramine) Tofranil (imipramine) Vivactil (protriptyline)</p> <p>SSRI's Celexa (citalopram) Lexapro (escitalopram) * Luvox (fluvoxamine) Paxil (paroxetine) Prozac (fluoxetine) Zoloft (sertraline)</p> <p>MAOIs Nardil(phenelzine) Parnate (tranylcypromine)</p> <p>Others Desyrel (trazadone)</p>	<p>Anafranil (clomipramine) Lubox (fluvoxamine) Paxil (paroxetine) Prozac (fluoxetine) Zoloft (sertraline)</p> <p>Antianxiety Agents</p> <p>Ativan (lorazepam) BuSpar (buspirone) Centrax (prazepam) *Inderal (propranolol) *Klonopin (clonazepam) Lexapro (escitalopram) Librium (chlordiazepoxide) Serax (oxazepam) *Tenorim (atenolol) Tranxene (clorazepate) Valium (diazepam) Xanax (alprazolam)</p> <p>*Antidepressants, especially SSRI's, are also used in the treatment of anxiety.</p>
<p>Mood Stabilizers (used in the treatment of bipolar disorder) Depakene (valproic acid) Depakote Eskalith Lithobid (lithium) Lithonate Lithotabs</p>		

<p>*Lamictal (lamotrigine) *Neurontin (gabapentin) *Tegretol (carbamazepine) *Topamax (topiramate)</p>	<p>Effexor (venlafaxine) Remeron (mirtazapine) Serzone (nefazodone) Wellbutrin (bupropion)</p> <p>Anti-Panic Agents</p> <p>Klonopin(clonazepam) Paxil(paroxetine) Xanax(alprazolam)</p> <p>Zoloft (sertaline) *Antidepressants are also used in treatment of panic disorder.</p>	<p>Stimulants (used in the treatment of ADHD)</p> <p>Adderall (amphetamine and dextroamphetamine) Cylert (pemoline) Dexedrine (dextroamphetamine) Ritalin(methylphenidate)</p> <p>*Antidepressants with stimulant properties, such as Norpramin and Wellbutrin, are also used in the treatment of ADHD.</p>
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TREATMENT:-

(Here we discussed majorly prescribed drugs which have potent withdrawal symptoms).

WITHDRAWAL SYMPTOMS OF SPECIFIC CATEGORY DRUGS:-

TYPICAL ANTIPSYCHOTICS:

HALDOL (HALOPERIDOL):



1. Elderly patients who present dementia-related problems should not be treated with haldol due to increased risk of death.
2. Haldol should not be combined with other medications or alcohol due to the risk of death caused by respiratory failure or other potentially fatal risks.

WITHDRAWAL SYMPTOMS:

Muscle spasms, tremors, shaking, unusual movements, hallucination, delusional thoughts, mental confusion. A return of original symptoms i.e., psychosis, mania, agitation etc.

DISCONTINUING /QUITTING:

Tardive dyskinesia like symptoms are more frequently seen when patients on maintenance level doses for a significant period of time withdraw from the drug for patients who have been on the medication for a longer duration.

TREATMENT:

A gradual tapering is generally recommended.

THORAZINE (CHLORPROMAZINE):

WITHDRAWAL SYMPTOMS:

Nausea, vomiting, shaking, tremors, delusions, hallucinations, return of psychosis, return of deep depression or mania, rage, excitability, aggressive, or violent behavior etc.

DISCONTINUING / QUITTING:

Quitting chlorpromazine should be discussed with your physician to look at other possible alternatives, but in any case, stopping chlorpromazine never be abrupt.

TREATMENT:

A Mild and gentle taper would be a safer and milder approach if the decision were made to stop the long term use.

ATYPICAL ANTIPSYCHOTICS:

ABILIFY (ARIPIRAZOLE):

WITHDRAWAL SYMPTOMS:

Nausea, feeling lightheaded, tachycardia, anxiety, diaphoresis (excessive sweating involving the entire body) insomnia, headaches, tremors, shakiness, flu-like symptoms.

DISCONTINUING/ QUITTING:

Quitting Ability symptoms may develop to severe and intolerable level. The preferred approach if possible would be taper while in residential care.

TREATMENT:

Tapering off the drug with medical oversight and guidance.



CLOZARIL (CLOZAPINE):

WITHDRAWAL SYMPTOMS:

Seizures, sedation, dizziness, cardiovascular issues (tachycardia, blood pressure, fluctuations). Insomnia, headaches, tremors, shakiness, flu-like symptoms.

DISCONTINUING / QUITTING:

Withdrawal of Clozaril may cause side effects like cardiovascular compromise, risk of stroke, signs of tardive dyskinesia and other severe reactions.

TREATMENT:

Gradually Clozaril tapering methods are recommended for coming off the drug.

MOOD STABILIZERS:

LITHOBID (LITHIUM):

WITHDRAWAL SYMPTOMS:

Mood disorders, return of mania, return of bipolar symptoms.

DISCONTINUING/ QUITTING:

Abrupt lithium withdrawal can cause pronounced episodes of returning mania as well as bipolar relapses.

TREATMENT:

At times, someone may choose to slowly convert from the prescription form of lithium (lithium carbonate) to lithium orotate as a way to bridge off to the drug. This is a pragmatic route for many, but it should be discussed with an integrative medical doctor before attempting.

TEGRETOL (CARBAMAZEPINE):

WITHDRAWAL SYMPTOMS:

Numbness in limbs tingling joint aches, Insomnia, Anxiety, weight loss, seizures.

DISCONTINUING/ QUITTING:

It is strongly recommended that individuals do not abruptly stop taking tegretol withdrawal symptoms as well as a worsening of side effects can take place if abrupt stopping occurs.

TREATMENT:

Do not stop taking carbamazepine without talking to physician. As physician may prescribe alternative drug for carbamazepine.

ANTI-DEPRESSANTS:

TRICYCLICS

NORPRAMIN (DESIPRAMINE):

WITHDRAWAL SYMPTOMS:

Nausea, headache, sensory disturbances, hyperarousal, weakness, gastrointestinal complaints.

DISCONTINUING/ QUITTING:

Antidepressant discontinuation syndrome may occur if you abruptly discontinue desipramine.

TREATMENT:

Do not stop taking desipramine without talking to physician as physician may decrease dose of the drug gradually.

ASENDIN (AMOXAPINE):

WITHDRAWAL SYMPTOMS:

Return of depression symptoms, anxiety, physical or mental fatigue, sleep disturbances, restlessness.

DISCONTINUING/ QUITTING:

Do not stop taking this medication abruptly. Abrupt discontinuation of amoxapine or cyclic should be avoided because it could precipitate symptoms of cholinergic rebound such as nausea, vomiting or diarrhea.

TREATMENT:

Tapering off of this medication may reduce the excessive and severity of withdrawal symptoms.

SSRI'S:

CELEXA (CITALOPRAM):

WITHDRAWAL SYMPTOMS:

Irritability, nausea, feeling dizzy, vomiting, nightmares, headache and paresthesia (prickling, tingling sensation on the skin), catatonia (a state of unresponsiveness).

DISCONTINUING/QUITTING:

Stopping citalopram abruptly may result mood changes, irritability, agitation.

TREATMENT:

Taper off your medication. Tapering involves adjusting your dose by a small amount.

*PSYCHOTHERAPY: Therapy can improve mood, reduce anxiety and soothe Irritability.

ANTI-ANXIETY AGENTS:

ATIVAN (LORAZEPAM):

WITHDRAWAL SYMPTOMS:

Headache, sweating, tremors (especially in the hands), difficulty concentrating/confusion, increase blood pressure, heart palpitations and a rapid heart rate, nausea, abdominal cramps, vomiting, weight loss, irritability, anxiety, mood swings & even panic attacks, seizure can occur [rarely].

DISCONTINUING/ QUITTING:

Discontinuing lorazepam may result changes in thoughts or behavior, while others may have seizures.

TREATMENT:

Tapering is the only safe way to stop taking your medication.

*cognitive behavioral therapy.

VALIUM (DIAZEPAM):

WITHDRAWAL SYMPTOMS:

Worsening of the original anxiety symptoms [rebound], emergence of apprehension, insomnia, ringing in the ears [tinnitus], pessimism, nausea, irritability, blurred vision, elevated blood pressure, increased heartbeat [tachycardia], muscle tension, agitation, severe restlessness, joint pain, hallucinations & grand mal seizures.

DISCONTINUING /QUITTING:

Stopping diazepam abruptly may results to post-acute withdrawal syndrome [PAWS] or protracted withdrawal syndrome.

TREATMENT:

Tapering off of this medication may reduce withdrawal symptoms.

*Detox programs.

STIMULANTS:

ADDERALL (AMPHETAMINE & DEXTROAMPHETAMINE):

WITHDRAWAL SYMPTOMS:

Irritability, depression, agitation, dreams that are often vivid, cravings, fatigue, sleep problems, impaired ability to focus, concentrate or maintain attentions, problems with short term memory, Inability to experience pleasure [anhedonia].

DISCONTINUING/ QUITTING:

Stopping Adderall abruptly may results to amphetamine withdrawal syndrome.

TREATMENT:

Detoxing under the supervision of medically trained professionals.

ANTI-PANIC AGENTS:

KLONOPIN (CLONAZEPAM):

WITHDRAWAL SYMPTOMS:

Anxiety, insomnia, restlessness, agitation & irritability, difficulty in concentrating, poor memory, muscle tension, muscle aches, depression, seizures.

DISCONTINUING/ QUITTING:

Sudden stopping of clonazepam after regular use can cause intense shaking, seizures and even death.

TREATMENT:

Tapering off the medication.

ZOLOFT (SERTRALINE):

WITHDRAWAL SYMPTOMS:

Nausea, vomiting, diarrhea, appetite loss, dizziness, lightheaded, mood swings, muscle pain, fatigue, anxiety, agitation, panic, irritability, suicidal ideation, anger, mania, bizarre sensations [like an electrical shock or shiver in your brain], tremors.

DISCONTINUING/ QUITTING:

Stopping abruptly may result in bizarre sensations, tremors & anxiety.

TREATMENT: *PSYCHOTHERAPY & Tapering off the drug is recommended.

MANAGEMENT:-

COGNITIVE BEHAVIORAL THERAPY [CBT]:

Cognitive behavioral therapy [CBT] is an umbrella term for a range of psychosocial interventions that are considered cognitive and or behavioral in nature. During CBT patterns of thinking that lead to substance use and the beliefs that direct those negative or destructive patterns of thinking to improve coping skills. Often, in addition to specific verbal CBT Communication techniques delivered by the CBT therapists during treatment sessions with

patients, practical exercises in real life environment outside the treatment venue and patient self- guided activities [e.g., keeping thought logs,] are also prescribed.

The overall aim of CBT is to help patients to understand negative thinking and to develop healthier thinking and improved coping skills which can be incorporated it into their lives.

POST TRAUMATIC STRESS DISORDER (PTSD) TREATMENT:

Eye movement desensitization and reprocessing (EDMR) is a fairly new non-traditional type of psychotherapy. It's growing in popularity, particularly for treating post-traumatic stress disorder (PTSD).

Exposure therapy is considered a behavioral treatment for PTSD. Thus exposure therapy targets learned behaviors that people engage in response to situations or thoughts and memories that are viewed as frightening or anxiety-provoking.

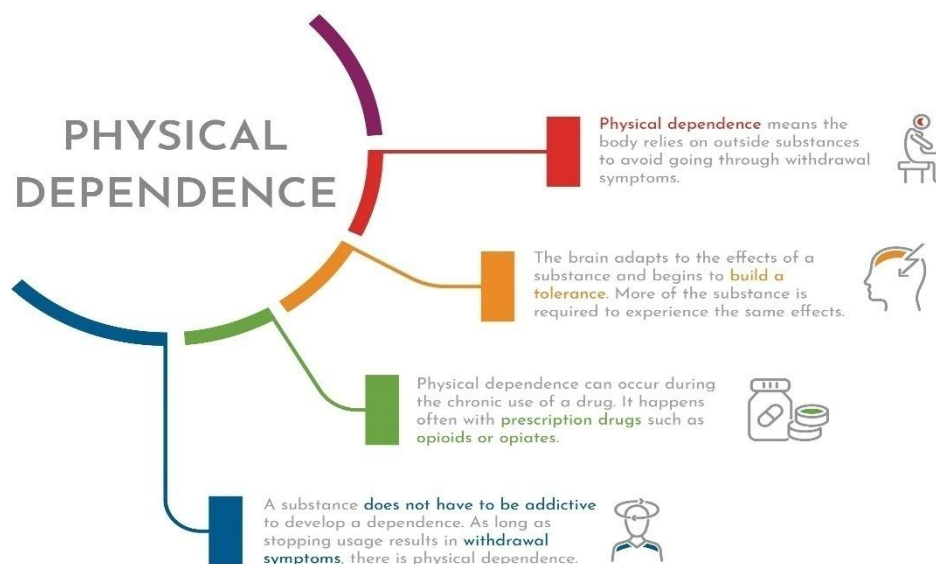





Figure No. 5: Physical Dependence

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