

## Ketamine Therapy Overview

Ketamine - one of the safest anesthetics in medical history - has been traditionally used for the induction and maintenance of anesthesia since 1970. In recent decades, its anti-depressive properties have been well demonstrated through research, and it has emerged as a promising agent for the treatment of psychiatric disorders, including major depressive disorder (MDD), anxiety disorder, bipolar disorder, post-traumatic stress disorder (PTSD), addiction, migraines, as well as post-operative and chronic pain management.

Ketamine infusion therapy involves intravenous (IV) administration of ketamine for the management of above-mentioned psychiatric and pain disorders.

### Ketamine:

- Invented in 1962
- One of the most common and widely-used anesthetics
- On WHO's list of "Essential Medications"
- Classified as a "Dissociative"
- Safety - it is considered the most "cardiopulmonary stable" anesthetic agent known to man
- 2019: Ketamine was approved by the FDA for use in patients with Treatment-Resistant Depression
- OFF LABEL uses:
  - Chronic Pain, Migraines, PTSD, Anxiety disorder, Additional Mood Disorders, Addiction
  - Unfortunately, very few insurance companies cover the treatment due to the "off-label" nature of the treatment
- NON-ADDICTIVE: when used in the pulsed protocol administered in controlled outpatient settings
- Excellent side effect profile

### Ketamine Mechanisms of Action in Treatment of Depression:

- NMDA receptor antagonism
- Effects on multiple pathways
  - Brain-derived neurotrophic factor (BDNF)
  - Glutamate release: A vital amino acid in signal transmission at nerve connections
- Increases **synapse repair and function**
- Promotes **dendritic spine formation**
  - Reformats thought patterns, memory orientation and filtering
  - Directly repairs "mood centers"
  - Restructuring Locus Coeruleus (brain activation center)
- Inhibits GABA interneurons: allows for **nerve cell recovery and regeneration**
- Affects **global brain connectivity**
- Changes Brain Wave patterns, enhancing **Gamma Wave** - the highest frequency brain wave associated with insight, peak focus & expanded consciousness

### Ketamine Therapy Advantages in the Treatment of **Depression**:

- Immediate results – often after a single dose
- 80% response rate
- > 50% improvement in symptoms
- Instantaneous reversal of suicidal ideation
- Significantly increases synaptic activity/branching, improving neuroplasticity
- Huge increases in BDNF levels (proven through seeing no effects in mice with mutation that lacks BDNF action)
- Utilizes multitude mechanisms to alter brain activity, as opposed to mainstream medications that usually involves a single mechanism
- Patients often achieve significant insights into their lives and a sense of clarity, as the treatment facilitate patients into a deep meditative state
- No longterm side effects as compared to mainstream medications

### Ketamine is Highly Effective in **Chronic Pain** associated with:

- Complex Regional Pain Syndrome (CRPS), i.e.. “Reflex Sympathetic Dystrophy”
- Migraine Headaches
- Stress-Induced Arthritic pain
- Chronic Back pain and Neuropathy
- Fibromyalgia
- Intestinal Inflammation such as in Crohn’s Disease, Ulcerative Colitis
- Lyme Disease
- Other neuropathic sensations and pain
- Any other conditions associated with abnormal levels of involvement of the sympathetic nervous system

### Ketamine Mechanisms of Action in the Treatment of **Chronic Pain**:

- NMDA receptor antagonism reduces Central Sensitization
  - Increasing “inhibitory” GABA interneurons reduces firing rates at the synapse in the Dorsal Root Ganglion
- Increased glutamate concentration in the synapse
  - Resets the hyper-excited pathway that’s been stuck in the ‘ON’ position
- Direct Pain Relief through:
  - K opioid receptors
  - AMPA sites
  - Ion-gated Calcium channels
- Anti-inflammatory action
- Increased synaptic repair via higher levels of BDNF

## What Can Patients Expect from Ketamine Treatments

Each infusion lasts approximately 1 hour for depression/PTSD/anxiety/addiction, or 2-3 hours for chronic pain/migraines.

### Before Treatment:

- Patient will remain in street clothes throughout the process.
- Patient will be comfortably seated in a recliner in one of the private treatment rooms, and provided with eye mask and headphone
- After placement of a small IV catheter in patient's vein (22-24g), the infusion therapy can begin
- Patient will NOT receive ketamine therapy with another patient unless under special circumstances where the patient chooses to do so with his/her significant other or family member.

### During Treatment:

- As the ketamine experience begins, patient will feel relaxed, mildly euphoric, and many experience a very calm, dissociative feeling, described as a "therapy session with oneself."
- Some will experience a mild, pleasant, psychedelic experience. This is often an important indicator that the dosing is appropriate and effective.
- The treatment gives each individual an opportunity to self-examine in a relaxed and safe place
- Patient will be constantly monitored for vital signs. A health professional will continue to monitor the patient, yet seek to disturb the patient as little as possible.
- The sensory deprivation helps to maximize the therapy's success.
- Patients can dissociate from the familiar "movie" about their own lives, and can examine their thoughts and states of being as an impartial observer
- Patients are empowered to calmly and objectively process information and rework thought processes without the rush of secondary anxieties, negative rumination, self-judgement or stress responses
- Patients may feel a sense of connectedness to something greater than themselves, much like what many people experience during deep meditation

### After Treatment:

- When the infusion ends, patients will begin to feel like their normal selves within 15-30 minutes.
- Patients may continue to relax in the room or the recovery lounge.
- There is persistent ketamine level in your bloodstream after the patient awakens, thus another 30-90 minutes of continued relaxation is recommended, to maximize the therapeutic effect.
- IV access will be painlessly removed. Healthcare provider will then sit with patient to discuss his/her experience in detail.

## General Post-Treatment Recommendations

- Participate in intensive, skill-based **psychotherapy** alongside ketamine therapy
- Avoid any stress-provoking stimuli or exposure to violent movies/television
- Reduce consumption of social media, news, negative conversations or gossip
- All benzodiazepines and GABAergic medications may be tapered *to maximize response*. (However, this is not required)

## Patient screening

### Inclusion criteria:

- h/o depression, anxiety, OCD, PTSD, addiction, migraines, chronic pain.
- May also include bipolar disorder patients who is taking adequate dose of mood stabilizers.
- Can also help patients who seek clarity in life and spiritual connectedness, or people who struggle with fear of death.

### Exclusion criteria:

- History of psychosis
- Active mania
- History of increased intracranial pressure
- Pregnancy or breastfeeding
- Uncontrolled hypertension, congestive heart failure, severe coronary artery disease
- Allergy (extremely rare) or previous negative response to ketamine
- **Current illegal substance use.** At times a *negative urine toxicology screening may be required prior to the initiation of treatment given risk of precipitated mania.*
- ***Bipolar patients are NOT excluded, provided they have adequate mood stabilization.***
- ***Personality Disordered Patients are NOT excluded***

## **Ketamine Therapy Protocol**

### Dosage:

Multiple factors are used to determine ketamine dosages, including the patient's body weight, drug metabolism, and past psychedelic experiences

### Duration:

- Mental Health Disorders: 1 hour (50 min actual infusion time)
- Chronic Pain/Migraines: 2-3 hours (100-150 min actual infusion time)

### Frequency:

- **Initial phase:**
  - 2 infusions per week x 3 weeks (in some cases, may change to 3 infusions per week x 2 weeks); then
  - 1 infusion per 1 week x 4-8 weeks
- **Maintenance phase:**
  - 1 infusion every 2 weeks x 4-8 weeks; then
  - monthly infusions