



evolve

ketamine 101

It's history, science, use, and how to prepare for your first session...

Introduction

As a nation, we're depressed. You've probably already heard the numbers: 1 in 10 people over the age of 12 are taking an antidepressant. These stats alone suggest that you, or someone you know, has battled (or is battling) with depression.

Depression is not *one-size fits all*, yet there's really only one medical option: **antidepressants**. Antidepressant medications are the second most commonly prescribed drugs in the US, bringing in more than \$200 billion a year for the pharmaceutical companies, yet depression (and suicide) rates continue to climb.

Between 30-70% of patients on antidepressants see no improvement in their symptoms, and at least 60% have significant side effects (like sexual dysfunction, weight gain, and thoughts of suicide).

The vast majority of antidepressants work on monoamine neurotransmitters - that's serotonin, norepinephrine and dopamine. In the last 30 years we have become fixated on this theory of depression, a theory that is just that: *theory!* It has never been proven in a single human study that low neurotransmitters cause depression.

Because of this fixation, there has not been a true new drug for depression in over 30 years. We are desperate for something new. Recently, in the past 10-20 years there has been a resurgence of old knowledge and we have rediscovered what has been under our noses for 60 years for the treatment of depression: ketamine.

In my practice I see patients at the end of their rope; they've seen every specialist imaginable, tried several medications and medication cocktails, and are at the point where they just don't know who they are anymore. They are hopeless for a cure.

Enter Ketamine

Ketamine was first synthesized in 1962 as an anesthetic agent. Fast-tracked for FDA approval due to its incredible safety profile, ketamine was a miracle drug for soldiers in the Vietnam War, ensuring they could be transported to medic centers without suffering undue pain, and without compromising their breathing (this was a huge breakthrough in anesthesia medicine).

By the 1970s, as more physicians were becoming familiar with ketamine and its uses, case reports began surfacing noting its antidepressant effects. At first reported as a "side-effect" of anesthesia, some physicians began using it specifically for depression. Yes, ketamine has been used as an antidepressant for the last 50 years.

Eventually there were enough observations to catalyze a formal study in 2000. The first placebo-controlled clinical trial of an infusion of ketamine for treatment-resistant depression showed powerful antidepressant effects - within 4 hours.

In a randomized controlled trial published in 2006, ketamine's rapid-onset antidepressant effects were reproduced (*National Institute of Mental Health*). A whopping 35% of the patients from this trial sustained these effects for 7 days following a single infusion. One week of no depression without any remaining drug in their system in patients who previously had no relief.

The success rate and speed of results shown in the first studies were astonishing, and have now been reproduced in numerous clinical trials. There are hundreds of publications indicating ketamine has the power to effectively treat depression, with estimates of up to 70% of patients showing significant improvement. Some studies report up to 62 weeks of symptom relief after a single dose!

So, what is Ketamine?

Ketamine is a schedule III controlled substance that has been used primarily as an anesthetic (sedative) and analgesic (pain reliever). It is a psychoactive compound, meaning it is capable of "affecting the mind."

Chemically ketamine has a variety of actions. It's a dissociative analgesic, sedative, stimulant and antidepressant. It affects glutamate, serotonin, dopamine, opioid, acetylcholine, GABA, cannabinoid systems and more.

Ketamine is also often labeled a "psychedelic" because it produces a non-ordinary state of consciousness (NOSC) due to its dissociative effects. However, it should not be coupled with the classic psychedelics -- psilocybin, mescaline, LSD, and DMT (the active compound in ayahuasca). It is chemically and experientially quite distinct from these compounds.

In depression one loses the number and functionality of neuronal connectivity, and ketamine increases that connectivity. It can literally heal the brain.

Who is Ketamine for?

Ketamine is not for everyone. It has been formally studied for major depressive disorder, bipolar depression, PTSD, OCD and treatment-resistant depression. However, it has specifically shown significant promise for treating suicidal ideation.

Ketamine is likely not helpful for individuals with recent manic episodes, psychotic disorders like schizophrenia, and it should be used very cautiously in patients with high addictive potential. Ketamine treatment should be considered on a case-by-case basis by a qualified health professional.

Ketamine can raise blood pressure while it's in your system, and long-term use can cause bladder issues. If you have uncontrolled hypertension, kidney, or bladder disease, your doctor may decide ketamine is not a good option for you.

How is Ketamine given?

There are many different ways to administer ketamine, and it is not clear presently whether different routes of administration (ROA) provide different results, or are superior to the others. The vast majority of studies researching ketamine have used infusion protocols, i.e. intravenous. Other ROAs are: intramuscular (IM), sublingual (SL), and intranasal.

Sublingual tablets are a preferred method for some clinicians due to the ease of use. Dr. Phil Wolfson, MD, author of *The Ketamine Papers*, routinely uses ketamine as sublingual tabs and teaches other clinicians this method. It's important to note that no matter the route of administration, ketamine should be taken under direct supervision of a doctor.

A common treatment regimen for all routes – infusion, intramuscular, nasal spray and sublingual – is two times per week for three weeks, with a maintenance session every 4-12 weeks, or as needed.

How does Ketamine work?

There is much debate on how ketamine works as an antidepressant. The most accepted theory is that it inhibits glutamate (a neurotransmitter, not in the monoamine family) via the NMDA receptor. But, like most things, it's not so simple.

As mentioned earlier, ketamine has many different functions in the brain, not least of which is creating an altered state wherein the individual may have a transformative experience with new insights and perspective shifts.

Remember, ketamine is a dissociative anesthetic. Dissociating from what, you may ask? In simple terms: **your thoughts from your emotions**. As one scientist explains (paraphrasing) 'when on ketamine, you may have negative emotions, but you don't care.' That's a rather glib way of saying: ketamine offers you space from your emotions.

Because it dissociates part of the limbic system from the cortex, it allows you to experience unpleasant memories or feelings without being *triggered* by them. This means you can do deep

psychological work without your ego defenses getting in the way. The effect of which makes one feel as if they've done "5 years of therapy in 5 hours."

Anatomically, it is clear that ketamine reconnects neurons. Neuroscientists performing functional MRIs while patients are on ketamine see an increase in functional connectivity of neurons. We know that depressed patients have less connections, so it follows that with more connections, you have less depression.

What are the side effects of Ketamine therapy?

The most common side effects of ketamine while you are under its influence are: nausea, vomiting, high blood pressure, urinary urgency, visual disturbances, ataxia (unbalanced walking), feelings of dissociation, and agitation.

A small amount of patients (less than 5%) cannot tolerate the nausea and vomiting experienced even with anti-nausea medication. Bladder conditions including cystitis are well established as an effect of long-term use, though the mechanism is unclear.

This all sounds rather unpleasant, but in general, ketamine is well-tolerated by most. In practice we prepare for many of these potential side effects by giving anti-nausea medication, dimming the lights to help with visual disturbance, and of course someone is with you at all times to make sure you don't get up and walk around!

How can I best prepare for my Ketamine session?

To avoid the common side effect of nausea, it is recommended patients go without food 4-6 hours prior to their session. You should wear comfortable clothing and secure a ride to and from the facility.

Before your session, you should read through all materials provided by your doctor or clinic and have all of your questions answered prior to your first session. You should always feel safe and comfortable with your ketamine guide.

The most important part is that you are mentally and emotionally prepared.

You have a clear intention.

You have set aside time to integrate after each session (and not packed your schedule the day following).

You have scheduled appointments with your therapist or doctor for at least the three weeks of your ketamine treatment.

You have prepared your life as much as possible for low stress and time for self-care over the course of your treatments.

And, most importantly, you arrive with an open mind, ready to dive into a transformative experience.

The Ketamine experience

Disclaimer: Administration and technique varies among clinics and physicians. Described below is how I perform sessions in the office.

When performed as part of therapy, the individual is given a dose of ketamine that creates a non-ordinary state of consciousness (NOSC) similar to a psychedelic "trip." The intensity of this experience varies, and is dose and individual dependent.

At low doses and in the beginning of your session, you may experience sensory changes such as feelings of tingling, lightness, heaviness, numbness, and altered perception of your body. As the ketamine increases in dose, awareness of the body dissolves as you become increasingly internal in orientation. This is generally well received and pleasurable.

This is a result of the dissociative nature of the drug: the brain regions of the thalamus dissociate from frontal cortex, allowing the limbic system (emotion) and frontal cortex (cognition) to communicate with little ego interference (as mentioned above). Ego defenses and judgments cease and one experiences pure being without added narration.

Many patients find the experience of dissociating essential to healing, not just a "side effect." One may have visions, insights, discoveries or other experiences in the dissociative state, which prove incredibly beneficial - if not necessary - for recovery.

What can I expect after my session?

No one can tell you what you will experience with ketamine; it is uniquely personal. You may feel "out of it" directly after your session and wish to have a cozy night at home with some good food and your favorite book. You will likely have an immediate shift in your state that is more positive, and if not positive, at least neutral.

You may notice normal depressive symptoms are absent. You may wish to discuss what you experienced in the session with your guide. You may want to journal, play music, be with a loved one, or simply remain quiet. All are equally right.

You may feel the antidepressant effects immediately, but it also may take a few sessions. Do not be discouraged if you "don't feel any different" right after your first session. There are certainly many individuals who require 4-6 sessions to feel a shift, and this is perfectly normal.

A note about depression treatment, in general

We must be aware of falling into the trap of substituting one drug for another. The treatment of depression is multi-modal, requiring a combination of approaches – dietary, lifestyle, psychotherapy - depending on the individual.

Ketamine provides a window for change. It is not a "one-shot wonder" and those who understand this and view ketamine as a part of their overall treatment plan have better rates of recovery and remission. It is important to continue therapy and self-care as needed between ketamine sessions.

Conclusion

In my clinic I have seen first-hand the power of ketamine to bring people back to life. I can barely hold back tears even now as I remember a suicidal 23-year old, a single mother shut-in, and many others severely disabled by their depression have the lights come back on after ketamine therapy.

Light exists in each of us, but under the veil of depression we can't see or feel or even believe it's possible to know that light anymore. Ketamine gives us that chance. It reorganizes the neuronal connections in the brain, providing an experience of hope and pleasure to people who have forgotten what that even means.

The most common thing I hear as people re-emerge from ketamine treatment is, "I didn't know I could feel that way again." For those with depression and TRD (a population with very little hope) not offering this treatment is doing harm.

If you are interested in experiencing the transformative effects of ketamine therapy, you can [Book A Free Discovery Call](#) to see if ketamine may be a good option for you.

In good health,



Dr. Katelyn Kalstein, MD MsC

*Please note, Ketamine Therapy is available only for patients at Dr. Kalstein's Los Angeles clinic -

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