

KETAMINE THERAPY

Educational Presentation Transcription

Slide 1: WHAT IS KETAMINE?

- Anesthetic developed in the 1960s, known for high level of safety regarding cardiovascular and respiratory function.
- Most common anesthetic in pediatrics, veterinary medicine, and battlefield medicine, and possibly worldwide.
- Termed a “dissociative anesthetic” for the separation of mind and body the patient may experience.
- On the World Health Organization’s list of essential medications.
- Considered a psychedelic due to the powerful psychoactive effects, though it works through different mechanisms than the classical serotonergic.

Slide 2: WHAT CAN KETAMINE TREAT?

- Ketamine is FDA approved only for use in anesthesia.
 - Off-label uses came after expiration of patents, so there’s little financial incentive to conduct studies for FDA approval.
- Off label uses include:
 - Pain
 - Acute pain, Fibromyalgia, Chronic Regional Pain Syndrome, Chronic Neuropathic Pain, Migraine Headaches, Post-Herpetic Neuralgia, etc.
 - Mood disorders (especially disorders involving rumination)
 - Major Depression, Postpartum Depression, Treatment-Resistant Depression, Suicidal Ideation, Bipolar, Anxiety, Unresolved Emotional Trauma, PTSD, OCD, end-of-life distress, etc.

Slide 3: HOW DOES KETAMINE WORK?

- Ketamine is a “promiscuous drug,” interacting with many receptors, but is primarily an NMDA receptor antagonist.
- NMDA receptors work with glutamate, the brain’s primary excitatory neurotransmitter.

- Through use-dependent blockade of NMDA receptors and reducing action of inhibitory neurons, ketamine interrupts rumination and promotes communication through alternative neural pathways.
- Action on NMDA receptors causes signaling pathway cascade increasing brain-derived neurotrophic factor (BDNF).
- BDNF causes an increase in neuroplasticity through increased synaptogenesis.
- Several other potential mechanisms.

Thomas (Dr. Swahn)'s additional oral input/comments:

Other potential mechanisms that have been proposed: anti-inflammatory effects, estrogen receptor, serotonin receptor or opioid receptor activity, or its neuroexcitatory effects in general, which are similar to electroconvulsive therapy.

Slide 4: IS KETAMINE SAFE?

- Ketamine was added to the U.S. Controlled Substances Act in 1999 as a Schedule III substance due to the view that it was being improperly used as a recreational substance.
- At high doses, harmful effects such as respiratory depression can occur, but ketamine has been shown to have a robust safety profile over the last 50 years of use in anesthesia, which is at doses many times higher than for mood and pain disorders.
- Mild side effects such as nausea, dizziness, and anxiety occasionally occur, but are short-lived and contained to the administration period and shortly after.
- Distress from the psychoactive effects is rare when the patient and environment are appropriately prepared for the experience.
- Ketamine studies have shown no physiologic addictiveness, though it can, like any other positive experience, create a psychological dependence when used inappropriately and must be used cautiously and respectfully.
- The World Health Organization reports very low rates of abuse or addiction worldwide and recommends ketamine not be labeled a controlled substance to ensure adequate access and supply.
- Contradictions include uncontrolled hypertension, increased intracranial pressure, glaucoma, and active psychosis such as schizophrenia.

Slide 5: HOW IS KETAMINE ADMINISTERED?

- Ketamine is usually administered via intravenous (IV), intramuscular (IM), oral (PO), sublingual (SL), and intranasal (IN) routes.
- IV infusion is the optimal route.

- 100% bioavailability. Direct control of intensity. Very short duration of action.
- IM injection has other advantages.
 - 93% bioavailability. Simple to administer. Longer duration. Patient is fully committed to the experience once injected.
- PO/SL/IN are less common
 - 25-50% bioavailability. Unpredictable absorption, onset, and duration.

Thomas (Dr. Swahn)'s additional oral input/comments:

IV infusions have such a short duration of action, so should any complications arise, the drip can be stopped and within a few minutes the intensity is starting to wear off.

Slide 6: IS TREATMENT COVERED BY INSURANCE?

- Because ketamine is off-label for mental health or chronic pain, insurance companies are not obligated to cover it.
- A form of ketamine called esketamine is approved by the FDA for depression, but the manufacturer charges much higher prices for the medication (\$590-&885 per dose compared to <\$10 for ketamine) despite a lack of evidence that it is any more effective than racemic ketamine.
- The FDA requires 2 hours medical observation and several other additional restrictions for esketamine, raising the consumer cost.

Thomas (Dr. Swahn)'s additional oral input/comments:

The short answer is no, treatment is not covered by insurance.

Slide 7: HOW LONG IS THE TREATMENT?

- IV Infusion
 - ~90 minute appointments, ~40 minute infusion, immediate onset and peak at 10-15 minutes, residual effects for 2-3 hours after.
- IM Injection
 - ~2 hour appointments, usually 2 separate injections about 30-45 minutes apart, onset within 3-5 minutes and peak around 15 minutes, residual effects for ~3 hours.
- Most patients see some benefit immediately after first treatment.
- Treatment-resistant conditions may take several treatments for benefits to become apparent.

- Commonly requires six infusions over 2-4 weeks, with many patients achieving significant symptom remission and improved quality of life.
- Maintenance doses are usually required about once a month.

Slide 8: WHAT IS THE KETAMINE EXPERIENCE LIKE?

- Dependent on the dose.
- Four proposed experience levels:
 - Empathogenic experience, out-of-body experience, near-death experience, and ego-dissolving transcendental experience.

Thomas (Dr. Swahn)'s additional oral input/comments:

During an empathogenic experience, users usually report an increased feeling of connection and serenity. During the out-of-body experience, people feel disconnected from their physical form but still retain most of their personal identity and experiences. Beyond that is the near-death experience where the user starts to feel a complete disillusion of their physical form, and that's often construed as a sense of having died, though this usually is reported to have a cathartic quality to it. Beyond *that* is the ego-dissolving transcendental experience where patients begin to lose any reference points for their existence as a human being.

- The psychedelic experience has been portrayed in a variety of ways:
 - Powerful, incredible, strange, transcendent, spiritual, mystical, surreal.

Thomas (Dr. Swahn)'s additional oral input/comments:

There also seems to be a noetic quality which gives abstract thoughts a concrete feeling and this can enable patients to act upon the insights they gain during their experiences. The dissociative effects can also help patients with trauma gain a new perspective of the past and finally process and address these memories. There's a sense of being able to peek behind the curtain of reality and see their universe how it truly is.

Some patients report feeling that the experience was much longer, or even completely removed from time, even feeling infinite.

Slide 9: COMMON PATIENT CONCERNS

- Is ketamine legal?

- Ketamine is a Schedule III controlled substance under the U.S. Controlled Substances Act.
- Ketamine therapy is legal under a healthcare provider with controlled substance authority.
- It is illegal to use without a prescription just like any other controlled substance such as prescription painkillers.
- What if I'm drug tested?
 - Ketamine therapy under the supervision of a healthcare provider is treated like any other prescribed controlled substance.
 - Ketamine is not on any common drug screen panels.
 - Ketamine's half-life is 2.5 hours, so it is effectively cleared from the body in about 10-12.5 hours (4-5 half-lives).

Slide 10: HOW TO GET THE MOST OUT OF TREATMENT

- Incorporating psychotherapy before or after ketamine treatments can help patients prepare for their mental journeys, create intentions, learn grounding skills to use during treatment, and integrate their experiences after each session.
- Ketamine's interruption of rumination and increase in synaptogenesis give the opportunity for patients to progress more rapidly in eliminating troubling thoughts/behaviors and in developing positive neural pathways and coping skills.
- Some patients may benefit from ketamine-assisted psychotherapy, where a smaller dose of ketamine is used as an adjuvant to psychotherapy as a "psychoolytic," helping bypass mental barriers and difficult emotions so they can process traumatic memories with the help of a therapist.

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