STANDARDS OF PRACTICE IN THE THERAPEUTIC USE OF SUBANESTHETIC KETAMINE REVISED JULY 30, 2020

The clinical use of ketamine as we know it today has been a collaboration between many different fields in healthcare. Starting with researchers and pharmaceutical companies in the 1960s, ketamine became FDA approved for anesthesia in 1970, and changed the landscape with its impact in the operating room as well as the battlefield. Anesthesiologists paved the way in perfecting the safe administration for decades. In the 1990s it became a staple for emergency medicine physicians as the drug of choice to safely sedate children for painful procedures, and although initially developed as an anesthetic, over the past several decades ketamine has been revealed to have greater potential in the field of medicine. A growing body of literature has demonstrated the clinical value of ketamine across diverse settings. In the early 2000s it broke out in the psychiatric world and would come to be known as the biggest breakthrough in 50 years for treatment-resistant depression. Over the past decade, doctors and therapists with various degrees and backgrounds have discovered and crafted the synergy of combining ketamine and psychotherapy to treat PTSD, anxiety disorders and other maladies. Clinicians of all specialties have tapped into ketamine's remarkable ability to treat addiction and pain. It is this symbiotic relationship between researchers, anesthesiologists, emergency and critical care physicians, pharmacists, family medicine physicians, advanced practice providers, psychiatrists, psychotherapists, nurses and many others, that has developed a revolution in advanced treatments for mood and anxiety disorders, PTSD, addiction and pain. The American Society of Ketamine Physicians, Psychotherapists and Practitioners recognizes and celebrates this collaboration, and seeks to protect and foster its growth.

There is much debate about which specialty is best suited to administer ketamine. Anesthesiologists and CRNAs, emergency and critical care physicians, psychiatrists and advanced provider mental health care professionals make up the majority of the current ketamine landscape today. At ASKP, we acknowledge that no one field of medicine can appropriately cover all of the bases, and there remains a need for continued learning and collaboration for all of us. This field requires a team approach with each specialty offering unique insights to a complex subject. One of ASKP's goals is to create and encourage a space where safe practices and standards are discussed, implemented and updated on a continuing basis that grows with the

needs of this rapidly expanding field. The fact remains that there are still substantial barriers to patients accessing this care. We recognize the danger of a medical board or other governing body regulating that only psychiatrists can provide ketamine for a psychiatric condition, or only anesthesiologists can provide IV ketamine. Significant devastation is likely to occur in the form of increased depression, addiction and suicides if care is restricted in this way. We assert that many specialties are capable and competent to provide ketamine within their state and licensure guidelines. However, with such a varied presence of providers, we recognize the urgent need of an updated Standards of Practice in the Therapeutic Use of Subanesthetic Ketamine to serve as a guideline for those using ketamine in their practices. They are intended to help clinicians provide safe and effective care, but not replace the individual providers clinical judgement. This document is also not intended to provide guidance on the use of ketamine for anesthesia, EMS or for procedural sedation, where higher doses of ketamine are administered, and higher levels of monitoring and support are needed.

1) Any clinician working with ketamine, in its various routes of administration, should practice within their scope, experience and comfort level. This will be different for each provider, as some will be more comfortable and appropriate to work with sublingual, intranasal or intramuscular ketamine at first. There will be opportunity through training programs, conferences and collaborations with anesthesia professionals or emergency medicine physicians to gain additional experience as they progress in their profession to expand their scope of practice. Others will be most comfortable working with IV ketamine at the start, but may need collaboration and training by psychiatrists and psychotherapists to safely treat certain conditions. In all cases, we do advocate for a thorough screening process and written consent, and for the clinician to seek out appropriate referral and collaboration when needed.

2) Any clinician working with ketamine needs to do a thorough medical assessment before deciding if a patient is appropriate for ketamine therapy. They need to be familiar with all side effects, both short and long term and how to manage them; clinical indications and contraindications; safety parameters to administer ketamine in its various forms; and when to seek collaboration with other specialites to safely and effectively provide treatment. A thorough review of all past and current medical problems should be done, including all past and current medications, past and current substance abuse, and recent vital signs including heart rate, blood pressure and pulse oximetry. This should include a discussion about medical causes of mood disorders, an assessment for cardiovascular risk factors, and recent laboratory studies if appropriate. Some patients with multiple comorbidities, extremes of age, or other conditions may require outside consultation. These collaborations may include family medicine practitioners to treat blood pressure and do laboratory testing; cardiology or pulmonology to assess underlying cardiopulmonary disorders in some patients; psychiatry for patients with a complicated psychiatric history or suicidal ideations; psychotherapists for patients with PTSD or certain anxiety disorders; in addition to other specialists as needed. Ongoing assessments to monitor for adverse effects should be conducted, and appropriate referrals should be made, if warranted.

3) Any clinician working with ketamine needs to do a thorough psychiatric evaluation before deciding if a patient is appropriate for ketamine therapy. If they are not able to provide this themselves, they need to refer to someone who can. This includes a review of all past and current diagnoses, both Axis I and Axis II, as well all past and current medications and treatments, and their response to each. Additionally this should include a review of all past and current substance abuse and suicidal ideations and whether there is intent or a plan. The use of standardized inventories for depression, anxiety, trauma, and substance use disorders is encouraged, but does not preclude the need for a professional assessment. The ability to closely monitor for behavioral emergencies such as the emergence or worsening of suicidal thoughts, psychotic or manic symptoms throughout the course of treatment is also of importance. For all patients, but particularly patients treated for PTSD, anxiety disorders and addiction, the concomitant use of psychotherapy is encouraged when possible.

4) Any clinician working with ketamine needs to obtain written informed consent that includes a discussion of short and long term side effects; evidence based information on the number of treatments necessary before patients tend to see improvement, and the percentage of patients that tend to benefit from ketamine therapy; disclose that most applications and routes of administration are done in an off label protocol; describe safety protocols such as no driving for a designated period of time, and how to manage side effects after a treatment including worsening of mood or suicidal thoughts; a list of alternative treatments available; and a disclosure that for most patients, ketamine therapy is a treatment and not a cure, and tends to require maintenance treatments, just like oral medications, TMS and ECT.

5) Any clinician working with ketamine needs to follow basic safety guidelines of monitoring patients during treatment. This often includes heart rate, pulse ox and blood pressure, as well as monitoring level of consciousness. Those working with higher doses of ketamine such as in treating pain conditions, may use additional monitoring techniques. The practitioner also needs to be knowledgeable and proficient in treating any potential side effects such as nausea, dysphoria, hypoxia, apnea and hypertension. Adequately trained health care providers must be immediately available to monitor and respond to adverse events. Spravato, a proprietary formulation of esketamine, has a REMS program with specific monitoring requirements and guidelines. We do not advocate the parenteral use of ketamine outside of direct medical supervision in the office or hospital setting, with the exception of palliative end of life care in some instances.

6) The majority of studies for depression are conducted with 0.5mg/kg administered IV over 40 min. However, it is standard practice amongst experienced clinicians to adjust dosing and infusion length for each patient in order to optimize response. Dose escalations and maximum dose is determined by the clinical judgement and experience of the provider. Additionally, dosing

and timing is also sometimes increased or decreased for the purpose of ketamine assisted psychotherapy.

7) Any clinician working with ketamine needs to keep appropriate documentation including what medications were given and in what doses. We do not advocate the use of “special formulas” or undisclosed medications. This documentation needs to be in a clear and concise format, and include the patient's weight, total dose of ketamine in mgs and volume, over what length of time and in what route of administration. It also needs to list all adjunctive medications that were given to the patient before, during or after the treatment.

Subanesthetic ketamine use for treatment resistant disorders has generated a great deal of excitement as well as providing a much needed rapid acting treatment. Development of best practices will be a dynamic process that continues to evolve as our knowledge base expands. Continuing to foster the collaboration and synergy of academic and clinical medicine is an essential step as this field progresses, and further research and data collection will greatly assist in providing this guidance.

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