Promoting the Discussion of the Beneficial Effects of Ketamine to Treat Refractory Depression

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To the Editor

We read a recent article published by CNN titled “Ketamine offers lifeline for people with severe depression, suicidal thoughts” with great interest. The article traces the story of a man with a 35-year history of severe refractory depression, suicidal ideation, and recent suicide attempts who was successfully treated with ketamine as a last resort after failing dozens of other pharmacologic psychiatric medications, including selective serotonin reuptake inhibitors, serotonin and norepinephrine reuptake inhibitors, and tricyclic antidepressants. This incredible medical success story is not isolated to this gentleman. In fact, there has been significant data, with seven placebo controlled randomized clinical trials (RCT), that have shown the beneficial effects of ketamine infusion therapy on refractory depression. However, ketamine therapy for refractory depression in practice is still very limited since it continues to be an off-label use of ketamine.

Unfortunately, there are currently no large scale, randomized controlled clinical trials that demonstrate the safety or durability of ketamine therapy. Another limiting factor is that patient selection criteria is limited to major depressive disorder (MDD) without psychotic features with effects lasting up to 1 week, as this is the only population and timeline successfully studied. However, there is evidence that other patients and repeated dosing could be significantly beneficial but there are no clinical trials to fully support this theory. Due to the limitations of trials demonstrating the above factors, the on-label approval of ketamine for psychiatric illness has not undergone scrutiny by the FDA.
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As anesthesiologists and pain specialists, we regularly use ketamine in a multitude of settings, including the perioperative surgical home, inpatient wards, and the chronic pain clinic. As such, we are the clinicians most familiar and comfortable with ketamine administration, and we wholeheartedly support the usage of this medication to help patients with psychiatric comorbidities. There is enough positive data thus far to believe that ketamine is a medication that can really change a patient’s life for the better. Now is the time for psychiatrists, anesthesiologists, and pain management specialists to collaborate to create RCTs that will hopefully show evidenced-based results that ketamine does in fact help in certain psychiatric illnesses, including MDD, with the goal of ultimately becoming an on-label, allowable drug to use.

We feel strongly that ketamine infusions for refractory depression and other psychiatric conditions is an exciting new avenue to help patients who have been suffering without relief. In addition, we feel that this is an area that is perfect for collaboration between psychiatrists, anesthesiologists, and pain specialists to deliver the most evidenced-based, safe patient care. We hope that this letter will promote conversation and discussion on this very important topic that will hopefully in the future yield another avenue to help patients in need.

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**References**