NEW FINDINGS IN DEPRESSION

Ketamine use in Psychiatry—is it safe?

From a presentation by Dr. James Downar (Internal Medicine and ICU Specialist) at the CANMAT Mood & Brain conference 2014

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Pain involves central sensitization from chronic stimulation with 'wind up' and secondary hyper- analgesia involving influx of intracellular calcium and reduced opioid receptor availability. Dr. Downar (University of Toronto) discussed the use of ketamine as a potent non-competitive NMDA antagonist (calcium channel blocker). Chronic pain sufferers may be less reactive to opioids and thus require higher doses. Ketamine lowers intracellular calcium and as a result reduces pain experience and is an alternative choice to opioids. The s-ketamine isomer may be twice the potency of ketamine. The metabolism is thought to be CYP450 3A4. Ketamine has a t1⁄2 of 1-3 hours and norketamine a t1⁄2 of 4-12 hours. There is a strong first-pass effect of both drugs.

Dr. Downar outlined the main adverse effects with this treatment with sympathetic discharge including tachycardia, hypertension and increased intracranial pressure. There are psychomimetic effects including visual hallucinations, dissociative experiences (also known as k-hole). Prolonged recreational use may cause neurotoxicity and memory impairment. There is also ketamine induced vasculopathy. Inspite of these potential side effects, Dr. Downar noted that ketamine has proven to be an extremely safe drug and noted that it is widely used in very ill patients, and in children, in general outpatient settings.

The Bell Cochrane Review of over 250 patients showed 90% experienced pain relief. A systematic review by Blonk (2009) showed a good response in 30-50% of patients with opioid sparing and improved VAS (Visual Anologue Scale) pain reduction effects possible.

Oral ketamine in chronic pain with a starting dose of 0.5mg/kg oral dose which can be safely increased in 0.5mg/kg intervals with an oral dosing of 3-4 days. Ketamine for mucositis is very effective (20mg taken orally as “swish and swallow”). Oral use may involve a lollipop or lozenge.

There may be a bimodal response to ketamine in MDD with antidepressant response at 4 hours predictive of long-term response. May be similar effect in chronic pain with psychominetic effects.

Past use of cannabis will generally not have side-effects and likely to respond. Past dissociative experience may predict a poor response. Need to be cautious in psychotic patients due to risk of acute ketamine psychosis.

The third part of the afternoon was a practical discussion facilitated by Dr Sagar Parikh. There was discussion about the abusive potential of ketamine in comparison to cannabis. Given the evidence of the cautious use of cannabis for chronic pain, the panel suggested that ketamine and cannabis should be treated in a similar manner. The community use of ketamine was explored with the suggestion by Dr. Downar that the main risks of use lie with the dissociative effects rather than acute cardiovascular effects. He stated that response to ketamine in a patient with chronic pain can be difficult to differentiate as the mood altering effect may regulate chronic pain relief and vise-versa.