

Daily oral ketamine for the treatment of depression and anxiety in patients receiving hospice care: A 28-day open-label proof of concept trial

Reference:

Irwin SA, Iglewicz A, Nelesen RA, Lo JY, Carr CH, Romero SD, and Lloyd LS. 2013. Daily oral ketamine for the treatment of depression and anxiety in patients receiving hospice care: A 28-day open-label proof of concept trial. *Journal of Palliative Medicine* 16(8): 958-65.

Presented by: Shauna Turnbull R3, October 21, 2015

Abstract:

Background: Depression and anxiety are prevalent and undertreated in patients receiving hospice care. Standard antidepressants do not work rapidly or often enough to benefit most of these patients. Ketamine has many properties that make it an interesting candidate for rapidly treating depression and anxiety in patients receiving hospice care. To test this hypothesis, a 28-day, open-label, proof-of-concept trial of daily oral ketamine administration was conducted in order to evaluate the tolerability, potential efficacy, and time to potential efficacy in treating depression and anxiety in patients receiving hospice care.

Methods: In this open-label study, 14 subjects with symptoms of depression or depression mixed with anxiety warranting psychopharmacological intervention received daily oral doses of ketamine hydrochloride (0.5 mg/kg) over a 28-day period. The primary outcome measure was the Hospital Anxiety and Depression Scale (HADS), which was used to rate overall depression and anxiety symptoms at baseline, and on days 3, 7, 14, 21, and 28.

Results: Over the 28-day trial there was significant improvement in both depressive symptoms ($F_{5,35} = 8.03$, $p = 0.002$, $g_2 = 0.534$) and symptoms of anxiety ($F_{5,35} = 14.275$, $p < 0.001$, $g_2 = 0.67$) for the eight subjects that completed the trial. One hundred percent of subjects completing the trial responded to ketamine for both anxiety and depression. A significant response in depressive symptoms occurred by day 14 for depression (mean $D = 3.5$, $d = 1.14$, 95% CI = 1.09–5.9, $p = 0.01$) and day 3 for anxiety (mean $D = 2.4$, $d = 0.67$, 95% CI = 1.0–3.7, $p = 0.004$). These improvements remained significant through day 28 for both depression (mean $D = 4.0$, $d = 1.34$, 95% CI = 2.3–5.9, $p = 0.001$) and anxiety (mean $D = 6.09$, $d = 1.34$, 95% CI = 3.6–8.6, $p < 0.001$). Side effects were rare, the most common being diarrhea, trouble sleeping, and trouble sitting still.

Conclusions: Patients who received daily oral ketamine experienced a robust antidepressant and anxiolytic response with few adverse events. The response rate for depression is similar to those found with IV ketamine; however, the time to response is more protracted. The findings of the potential efficacy of oral ketamine for depression and the response of anxiety symptoms are novel. Further investigation with randomized, controlled clinical trials is necessary to firmly establish the efficacy and safety of oral ketamine for the treatment of depression and anxiety in patients receiving hospice care or other subject populations.

Strengths:

- Extensive use of symptom assessment tools to capture multiple outcomes (cognition, pain, adverse events, suicidality, quality of life, and functional status)
- Strong inter-rater reliability between those conducting data collection
- Use of oral drug formulation which improves potential for administration in the study population

Weaknesses:

- Very small study from a single centre ($n=8$ for analysis)

- Excluded patients who dropped out of study from analysis – this will have inflated the significance values of their findings
- Didn't take into account potential effects of other medications the patients may have been on to improved mood/anxiety
- Potential for placebo effect given no control group

Applicability to Palliative Care:

Depression and anxiety are common symptoms amongst the palliative care population. Attempts to alleviate these symptoms are often challenging in the palliative care population because of short expected survival time and long time to effect for traditional anti-depressants/ anxiolytics. Having an alternative option that acts through a different mechanism of action (NMDA receptor antagonism) is beneficial as is the fact that ketamine appear to work much more quickly than traditional antidepressants.