Journal Watch

# An Intravenous Ketamine Test as a Predictive Response Tool in Opioid-Exposed Patients with Persistent Pain.

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Chronic pain patients who are treated with opioid therapy represent a significant challenge to medical professionals. When pain recurs in the face of a previously effective opioid regimen, treatment options include dose escalation, opioid rotation, drug holidays, and the addition of adjuvants. Some experts advocate the use of *N*-methyl-d-aspartate receptor (NMDA-R) antagonists to combat tolerance. Recently, the use of an intravenous (i.v.) ketamine infusion to predict the response to a dextromethorphan (DX) treatment trial has been described. In this study, 56 opioid-exposed patients with recurrent pain were treated with a low-dose (0.1 mg/kg) i.v. ketamine test followed by a DX treatment course. Using previously designated cutoff values for a positive response to ketamine (67% or more pain relief) and DX (50% or more pain relief), the sensitivity, specificity, positive predictive value, and negative predictive value for an i.v. ketamine infusion to predict subsequent response to DX treatment were 72%, 68%, 52%, and 85%, respectively. The observed agreement between analgesic responses was 78%, indicating a highly significant correlation ($r = 0.54$, $P = 0.0001$). Subgroup classification revealed no significant differences in the response to either ketamine or DX treatment based on pain classification (i.e., nociceptive, neuropathic, or mixed) or placebo response. In contrast, a weaker correlation between ketamine and DX response was found in subjects requiring high-dose rather than low-dose opioid therapy. A significant correlation also was noted between the development of side effects for the two NMDA-R antagonists. Based on these results, we conclude that an i.v. ketamine test may be a valuable tool in predicting subsequent response to DX treatment in opioid-exposed patients. with persistent pain.

Study Strengths:

This is a prospective trial which is partially blinded to the subjects. It provided robust statistically significant data that suggests the need for larger RCT's to strengthen the data.

Study Weaknesses:

This study is also a sSingle arm, unblinded, small study, with a multitude of opportunities for bias. The method and procedure were not well outlined, although this information may be available in the authors' previous publications.

Relevance to Palliative Care

This was not a palliative, or malignant pain population, however the test subjects were an opioid treated with neuropathic, nociceptive or mixed pain etiologies. Other studies have suggested these pain pathways may play a role in malignant pain. As further research is conducted in this area the relevance of the NMDA receptor pathway to palliative care patients may be further elucidated.