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Progressing an Evidence-Base Beyond Case Series

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Dear Editor:

We read with interest in the latest edition of this journal the four case reports reporting dramatic responses to sub-anaesthetic doses of ketamine in patients with complex pain syndromes poorly responsive to escalating doses of opioids.[1]

The management of complex pain such as this remains challenging and at times most clinicians struggle with cases such as these. Treatment plans in these situations tend to be guided by physician experience and local practice and therefore vary greatly between centres as there is often little quality evidence to guide practice decisions.

Although it is of great interest to read of cases such as these, there is a concern that the experience presented by the publication of case reports cannot be used as an "evidence base" to guide future management. Instead, it should be used as a basis for properly blinded prospective studies.

Placebo response rates as high as 75% have been reported in chronic pain studies.[2] This may be because of patient expectation of benefit, a reflection of the extra care and attention given to patients on trials or the fact that patients are generally put on new treatments when their pain is at its worst and a number will improve over time to a baseline level without treatment. Significant placebo response rates should always be anticipated and considered when initiating any new analgesic intervention.

It is well documented that uncontrolled trials may greatly vary from subsequent point estimates in controlled studies often with over estimates of effect[3] especially if it is not a consecutive series of cases that is presented. Conversely, case series of people given ketamine who experience negative outcomes are unlikely to be written or published.

Randomized trials are also needed for a true estimate of adverse effects. The authors of this case series note few "serious effects," yet report in two patients acute confusion (presumed delirium), somnolence, and psychomimetic effects. The other two patients were proactively treated with benzodiazepines that may have masked toxicity and equally was associated with toxicity in themselves. In case series it is less easy to standardize prior treatment such as opiods or adjuvants.

High-quality randomized trials in hospice and palliative care are achievable[4] to provide quality evidence to guide our practice especially if several sites work together to conduct the trial.[5] Palliative medicine is a specialty that is contributing more and more to the care of patients with life limiting disease. It is time we based this practice on high-quality evidence and that can only come with high-quality research.

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