Reviewer's report

Title: Subanesthetic ketamine for the treatment of children and adolescents with chronic pain: an outpatient longitudinal study

Version: 2 Date: 5 June 2015

Reviewer: Nicole Almenrader

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This is a further study reporting positive effects of low dose ketamine for treatment of chronic pain including CRPS. Unfortunately this is a retrospective analysis with a small number und vast heterogeneity of patients, which makes it difficult to draw any sound conclusion. Furthermore effects on long term pain relief are missing.

INTRODUCTION: a brief explanation of the role of NMDA receptors and NMDA receptor antagonists for chronic pain should be added.

METHODS: there can only be one primary outcome. All other measures are secondary outcomes (adverse effects included).

Regarding adverse effects of ketamine – have any ‘non psychotropic’ effects been assessed, such as hypertension, nausea, anorexia, insomnia, hepatic enzyme profile?

How was the percentage of pain relief calculated? Was NRS measured after each infusion or only after completion of the entire treatment? Was there a cumulative effect of pain relief?

How was the percentage of reduction in morphine consumption calculated?

Definition of inclusion / exclusion criteria is missing

RESULTS: should be presented in order: primary outcome followed by secondary outcomes.

Was morphine the only previous treatment that failed or were there other treatments? If so, which ones?

DISCUSSION: too long. Could be shortened by one third.

Please consider previous studies on low dose ketamine for chronic pain/CRPS in adults and see Dutch/UK guidelines for CPRS which rate the evidence for treatment with ketamine as ‘moderate’ or ‘level 3’. There is still insufficient evidence to suggest ketamine as part of routine clinical treatment for CRPS in adults (see Pickering et al Br J Clin Pharmacol 2013: 77;2: 233-238. Prolonged ketamine infusion as a therapy for CRPS: synergism with anatagosnism)

Please discuss mechanism of action / role of ketamine in the treatment of chronic pain /CPRS.
How do the authors explain a reduction in pain scores, but at the same time no reduction in morphine consumption?

How do the authors explain that they did not observe any psychotropic effect? This is in contrast with previous studies with a similar design (see reference 25)

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I DECLARE THAT I HAVE NO COMPETING INTERESTS