



Letter to the Editor

Ketamine infusion for sedation in ICU, response to Dr Mion



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We thank Dr. Mion [1] for his comments on our recent article [2], published in *Anaesthesia Critical Care and Pain Medicine*, on the effect of ketamine infusions on opiate consumption and delirium incidence during sedation of ICU patients. He highlights the following relevant issues that deserve discussion.

First, we must apologise for a typo error in the abstract section, the continuous infusion of ketamine in the interventional arm was at the dose of 0.20 mg/kg/h (or 3.3 µg/kg/min) as mentioned in Patients and Methods section, and not 2 mg/kg/h.

Second, we disagree with Dr. Mion that ketamine advantages for sedation of critically ill have been pointed out since many years [1]. To our point of view, referring to studies published between 20 and 30 years ago [3,4], including 10 and 17 patients by arm, with one of these studies published in German with no available access to the full text article, is more related to shamanism than medicine. We need proofs of ketamine effects in ICU; we advocate for randomised control trials in ICU using ketamine to move from beliefs to evidence based medicine. Our study has several limits, but it remains one of the first RCT involving ketamine for sedation of ICU patients.

Third, Dr. Mion described three different concentrations curves modelled with Rugloop II® software [1]. He hypothesised that concentration ranges are higher with bolus + infusion than with infusion only and more than with bolus only (as used in the PODCAST study [5]). Thus he made a second hypothesis that ketamine effects are directly related to plasmatic, or brain, concentration. One more time, it is really difficult to compare data from retrospective analysis of postoperative patients with prospectively enrolled ICU patients in a RCT. This is particularly true in the field of sedation and analgesia due to subjective clinical managements and outcomes. In our study [2], patients who received a ketamine bolus of 2.5 mg/kg for tracheal intubation presented a lower delirium incidence compared to those receiving only ketamine infusion. We must highlight that this is a post-hoc

analysis, these are data used to generate hypothesis. We agree with Dr. Mion that this could pre-establish a possible concentration-effect relationship between delirium incidence and plasmatic ketamine concentrations, but it must be evaluated prospectively. On a statistical point of view, hypotheses suggested by a given dataset, when tested with the same dataset that suggested them, are likely to be accepted even when they are not true; this is a model of circular reasoning.

In conclusion, we share with Dr. Mion the idea that ketamine is probably a useful drug for ICU patients. We have some proof in the field of intubation [6], the results of our study have generated some hypothesis that in addition to others, as the concentration-effect hypothesis, may help researchers to design new studies to move from beliefs to evidences.

Disclosure of interest

The authors declare that they have no competing interest.

References

- [1] Mion G. Ketamine infusions for sedation in ICU. *Anaesth Crit Care Pain Med* 2018. <http://dx.doi.org/10.1016/j.accpm.2018.11.010> [pii: S2352-5568(18)30440-5, Epub ahead of print].
- [2] Perbet S, Verdonk F, Godet T, Jabaudon M, Chartier C, Cayot S, et al. Low doses of ketamine reduce delirium but not opiate consumption in mechanically ventilated and sedated ICU patients: A randomised double-blind control trial. *Anaesth Crit Care Pain Med* 2018. <http://dx.doi.org/10.1016/j.accpm.2018.09.006> [pii: S2352-5568(18)30325-4, Epub ahead of print].
- [3] Kolenda H, Gremmelt A, Rading S, Braun U, Markakis E. Ketamine for analgo-sedative therapy in intensive care treatment of head-injured patients. *Acta Neurochir (Wien)* 1996;138(10):1193-9.
- [4] Adams HA, Claussen E, Gebhardt B, Biscopling J, Hempelmann G. [The use of ketamine and midazolam for analgesia and sedation in ventilated patients subject to obligatory treatment with catecholamines]. *Der Anaesthesist* 1991;40(4):238-44.
- [5] Avidan MS, Maybrier HR, Abdallah AB, Jacobsohn E, Vlisides PE, Pryor KO, et al. Intraoperative ketamine for prevention of postoperative delirium or pain after major surgery in older adults: an international, multicentre, double-blind, randomised clinical trial. *Lancet* 2017;390(10091):267-75.
- [6] Quintard H, L'Her E, Pottecher J, Adnet F, Constantin J-M, De Jong A, et al. Intubation and extubation of the ICU patient. *Anaesth Crit Care Pain Med* 2017;36(5):327-41.

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