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Letter to the Editor

Ketamine infusions for sedation in ICU

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The recent work of Perbet et al. [1] is one among scarce studies of ketamine administration in intensive care patients. However, ketamine advantages for sedation of critically ill have been pointed out since many years: it favourably preserves gastrointestinal motility [2], respiratory function [3] and lowers the need for vasopressor therapy, including cases of head injury [4].

Unlike Perbet et al. Buchheit et al. recently shown that ketamine initiation was associated with a dramatic lowering of opioid needs in the context of surgical intensive care [5]. One explanation might be that ketamine counteracts the so-called "opioid induced hyperalgesia", only observed when high dosages of opioids have been used. Perbet et al. carefully titrated remifentanil infusions: approximately 8 μg/kg/h, expected to result in average plasmatic concentrations of no more than 4 ng/mL which are rather low compared to concentrations observed during some surgical procedures.

Moreover, this interesting work challenges the disappointing findings of the recent PODCAST trial, that single ketamine boluses of either 0.5 or 1 mg/kg/h are of no value not only for delirium prevention, but also for postoperative analgesia [6]. The fascinating hypothesis that ketamine anti-neuroinflammatory properties might translate into lower delirium rate in ICU patients may arise from the way ketamine was administrated: not as a single bolus like in the PODCAST study, but as a continuous infusion of 0.2 mg/kg/h (and not 2 mg/kg/h as mentioned in the abstract). Indeed, Hovaguimian et al. showed in a recent meta-analysis that ketamine could at least lower postoperative cognitive dysfunction [7].

Finally, Perbet et al. observed that a 2.5 mg/kg ketamine bolus added a supplementary value, with a lower incidence of delirium than in subjects who benefited only from a continuous infusion. This is another interesting finding that could be integrated in a concentration-effect relationship explaining why the PODCAST study exhibited negative results (Fig. 1).

To conclude, perhaps is it time for a reappraisal of ketamine infusions for ICU sedation.

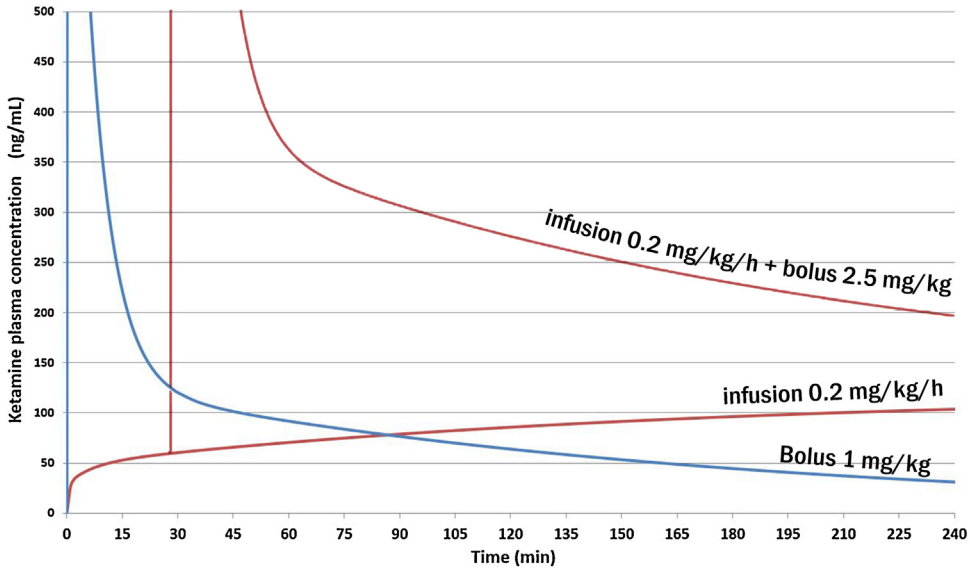

Fig. 1. displays 3 different concentration curves (modelled with Rugloop II© software, Demed, Temse, Belgium). A bolus of 1 mg/kg was the larger dosage in the PODCAST trial. Perbet et al used a continuous infusion of 0.2 mg/Kg/h which is expected to result in a plasmatic concentration of about 100-120 ng/mL. Finally, the upper curve is the combination of a 0.2 mg/kg/h continuous infusion and a random (here at t = 30 min) bolus of 2.5 mg/kg in patients who required a tracheal intubation. The concentration range is obvious, with PODCAST curve << infusion curve < infusion + bolus curve, and may explain the growing efficacy of these growing dosages.

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