## Is it time to cease the single low-dose ketamine injection at induction of anesthesia?

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## Conflict of interest

Pr. Mion has been appointed by Renaudin laboratories (Z.A. Errobi – 64250 ITXASSOU – France), as a ketamine expert, in 2015.

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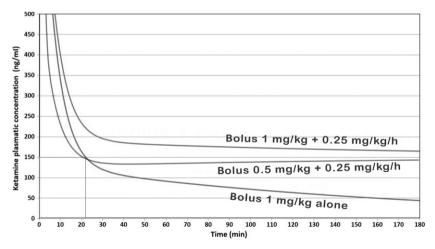
The study from Moro et al. raises interesting questions about the place of ketamine within multimodal analgesia. Previous works demonstrated the failure of small boluses administrated at the induction of anesthesia to lower post-operative pain. Following a 1 mg/kg bolus, concentration falls beneath 150 ng/ml after only 22 min (Fig. 1). This bolus of 1 mg/kg was inefficient in the recent PODCAST trial. On the other hand, when ketamine was shown years ago to prevent chronic post-operative pain, it was administrated as a continuous infusion of 0.25 mg/kg/h<sup>5</sup> or even during the first post-operative days.

Finally, small levels of pain are not expected to be alleviated with small doses of ketamine which is a use-dependent drug: the worst the pain, the more efficient ketamine administration. Ketamine will not block NMDA channels unless they had been opened by intense or repeated noxious stimuli. This 'foot in the door blockade' explains why administration prior to surgical beginning has no peculiar interest. Thus, ketamine failure is not surprising in the context of current multimodal analgesia.

In conclusion, we were told as soon as 2005 that a continuous administration of ketamine was mandatory in front of noxious surgery.<sup>8</sup> It is time to question the widely spread practice of injecting small doses of ketamine at the induction of anesthesia.

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**Fig. 1.** The three concentrations curves have been drawn according to the Domino model (Rugloop II software, Demed, Temse, Belgium). The lower curve shows that ketamine concentration falls below the analgesic threshold (150 ng/ml) 22 min after a single bolus of 1 mg/kg. When a continuous infusion of 0.25 mg/kg is added immediately after a bolus, ketamine concentration curves converge toward the analgesic threshold: for the upper curve, after a 1 mg/kg bolus, and for the intermediate curve, after a 0.5 mg/kg bolus.

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1

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