

- 4 Steiness J, Hägi-Pedersen D, Lunn TH, *et al.*, RECIPE trial group. Nonopioid analgesic combinations following total hip arthroplasty (RECIPE): a randomised, placebo-controlled, blinded, multicentre trial. *Lancet Rheumatol* 2024; **6**:e205–e215.
- 5 Mulita F, Karpetas G, Liolis E, *et al.* Comparison of analgesic efficacy of acetaminophen monotherapy versus acetaminophen combinations with either pethidine or parecoxib in patients undergoing laparoscopic cholecystectomy: a randomized prospective study. *Med Glas (Zenica)* 2021; **18**:27–32.
- 6 Ögren C, Varkey E, Wolf A, *et al.* High-frequency, high-intensity TENS compared to standard treatment with opioids for postoperative pain relief after laparoscopic cholecystectomy: a multicentre randomized controlled trial. *Eur J Pain* 2024; **28**:1772–1784.

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Hypnotic and antinociceptive contribution of magnesium sulphate during balanced total intravenous anaesthesia in total thyroidectomy: a randomised double-blind clinical trial: reply to van Zuylen

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Editor,

We thank van Zuylen¹ for his thoughtful remarks and for highlighting areas needing clarification.

First, our trial was designed primarily to assess the hypnotic contribution of magnesium sulphate (MS) during total intravenous anaesthesia, rather than its effects on hyperalgesia or postoperative analgesia. We recorded total morphine consumption in the PACU and over the entire postoperative period, expressed as oral morphine equivalents. There was no significant difference in the median [IQR] between the control (CO) and MS groups: Group CO, 6 [0 to 12.75] mg; Group MG, 6 [1.25 to 18.25] mg; $P=0.42$, as detailed in the Appendix.² As this secondary outcome was neither adjusted for multiplicity nor subjected to a formal sensitivity analysis – and given our limited sample size – the risk of a false-negative result (type II error) cannot be excluded.

Second, although we observed higher postoperative pain scores in the MS group, our thyroidectomy cohort – with uniform local anaesthetic infiltration and a multimodal postoperative analgesia protocol – is not predisposed to severe pain,³ and our modest sample size limits statistical precision. Although the median difference in pain scores may appear clinically relevant, it did not reach statistical

significance and could simply reflect random variation rather than a true treatment effect; moreover, as van Zuylen pointed out, no pre-operative pain assessment was performed, and the study was not powered for this specific secondary outcome. These findings must, therefore, be interpreted with caution, and dedicated studies in more painful procedures are warranted.

Third, we agree that chronic alcohol consumption may influence pain perception. We defined alcohol use conservatively and binarily as weekly intake at least 100 g – a low threshold that is likely easily reached in Northern European countries and may, therefore, inflate the classification of ‘at-risk’ consumption.⁴ This definition was applied equally in both groups, with no significant intergroup difference.

In conclusion, we appreciate these insights and trust these clarifications will aid readers in interpreting our findings. We agree that future studies should not only address postoperative pain and the contribution of MS to procedure-specific multimodal analgesia but also target specific populations – such as opioid-experienced patients, those with chronic pain, and individuals with high levels of catastrophising or peri-operative anxiety – to better define the role of magnesium in tailored antinociception.

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Conflicts of interest: MC has received interview and speaker's honoraria from GE Healthcare, Aguettant and Baxter. MC is Associate Editor at the *European Journal of Anaesthesiology*. He is a member of the Belgian Association for Regional Anaesthesia Board and of the Scientific Committee of the European Society of Anaesthesiology and Intensive Care.

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References

- 1 van Zuylen M. Reply to - Hypnotic and antinociceptive contribution of magnesium sulphate during balanced total intravenous anaesthesia in total thyroidectomy: a randomised double-blind clinical trial. *Eur J Anaesthesiol* 2026; **43**:186–187.
- 2 Beck F, Bonhomme VL, Hardy PY, *et al.* Hypnotic and antinociceptive contribution of magnesium sulphate during balanced total intravenous anaesthesia in total thyroidectomy: a randomised double-blind clinical trial. *Eur J Anaesthesiol* 2025; **42**:948–950.
- 3 Gerbershagen HJ, Aduckathil S, van Wijck AJ, *et al.* Pain intensity on the first day after surgery: a prospective cohort study comparing 179 surgical procedures. *Anesthesiology* 2013; **118**:934–944.
- 4 Wood AM, Kaptoge S, Butterworth AS, *et al.* Risk thresholds for alcohol consumption: combined analysis of individual-participant data for 599 912 current drinkers in 83 prospective studies. *Lancet* 2018; **391**:1513–1523.

DOI:10.1097/EJA.0000000000002276

Eur J Anaesthesiol 2026; **43**:159–190