

Before Dexmedetomidine Can Be Recommended for Treating Agitation on the ICU, Appropriately Designed Studies Must Confirm its Efficacy

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LETTER TO THE EDITOR

We were pleased to read the article by Neto, *et al.* on a retrospective outcome study designed to test the hypothesis that early use of dexmedetomidine would accelerate the resolution of agitation in the ICU [Serpa Neto, A. *et al.*, 2025]. Clinical records in an electronic medical record system were analyzed with natural language processing to identify patients with agitation [Serpa Neto, A. *et al.*, 2025]. Of the 7525 patients studied, 314 were treated with dexmedetomidine and achieved faster resolution of agitation in the ICU than those who did not receive it [Serpa Neto, A. *et al.*, 2025]. Early initiation of treatment with dexmedetomidine accelerated the resolution of agitation [Serpa Neto, A. *et al.*, 2025]. The study is noteworthy, but several points should be discussed.

The first point is that the condition “agitation” was not clearly defined [Serpa Neto, A. *et al.*, 2025]. Agitation was hypothesized when a retrospective electronic text analysis identified the terms “agitation”, “agitated”, “combative”, “restrained”, “aggressive” and others in the electronic records [Serpa Neto, A. *et al.*, 2025]. Of course, this type of analysis carries the risk of bias, as everyone may understand these terms differently. In order to conduct a study on the effect of dexmedetomidine on arousal, a commonly accepted definition of “arousal” must be used, and clear inclusion and exclusion criteria must be applied.

The second point is that it is a retrospective design [Serpa Neto, A. *et al.*, 2025]. Retrospective designs have several disadvantages [Talari, K. *et al.*, 2020]. A retrospective design allows only limited control over the sampling of the population and only limited control over the type and quality

of the predictor variables. In addition, the relevant predictors may not have been recorded in the medical record, and it may be difficult or impossible to establish confounding variables and causality. In addition, some information may be missing because the data are based on the review of medical records that were not originally intended for the collection of data for research purposes. Selection and recall errors also affect the results, and the reasons for differences in the number of lost to follow-ups often cannot be determined, which can lead to bias [2]. The therapeutic benefit or inefficacy of a drug can only be reliably determined with a prospective, randomized, controlled and cross-over design [Selker, H. P. *et al.*, 2019].

The third point is that the effect of concomitant medications was not included in the analysis [Serpa Neto, A. *et al.*, 2025]. Since ICU patients usually receive numerous drugs at different doses, it cannot be excluded that these other drugs interfere with the metabolism and excretion of dexmedetomidine metabolites. Due to this interference with other drugs and metabolites, the effect of dexmedetomidine may vary from patient to patient.

The fourth point is that the effect of dexmedetomidine may also depend on concomitant diseases. Patients with brain diseases may react differently than patients with myocardial infarction. Therefore, it would be important to know with which medical problem the included patients were admitted to the ICU and what was the cause of the agitation.

The fifth point relates to the discrepancy between the title, which states that dexmedetomidine was

used to treat agitation, and the method section, which states that dexmedetomidine was used “only to treat agitation delirium” [Serpa Neto, A. *et al.*, 2025]. Although agitation can be a feature of delirium, agitation can also occur without delirium [Chevrolet, J. C. *et al.*, 2007]. Therefore, it should be clarified whether the included patients all had agitated delirium, only agitation, or whether patients with both pure agitation and agitated delirium were included. This is important because dexmedetomidine may have a different effect on pure arousal than on arousal delirium [Ng, K. T. *et al.*, 2019].

In summary, before concluding that dexmedetomidine has a beneficial effect on agitation in ICU patients, appropriately designed studies need to be conducted to confirm this conclusion.

REFERENCES

1. Serpa Neto, A., Young, M., Phongphithakchai, A., Maeda, A., Hikasa, Y., Pattamin, N., Kitisin, N., Premaratne, G., Chan, G., Furler, J., Stevens, M., Pandey, D., Jahanabadi, H., Shehabi, Y. & Bellomo, R. "A target trial emulation of dexmedetomidine to treat agitation in the intensive care unit." *Critical Care Science*, 37 (2025): e20250010.
2. Talari, K. & Goyal, M. "Retrospective studies – Utility and caveats." *Journal of the Royal College of Physicians of Edinburgh*, 50.4 (2020): 398–402.
3. Selker, H. P., Eichler, H. G., Stockbridge, N. L., McElwee, N. E., Dere, W. H., Cohen, T., Erban, J. K., Seyfert-Margolis, V. L., Honig, P. K., Kaitin, K. I., Oye, K. A. & D'Agostino, R. B. Sr. "Efficacy and Effectiveness Too Trials: Clinical trial designs to generate evidence on efficacy and on effectiveness in wide practice." *Clinical Pharmacology & Therapeutics*, 105.4 (2019): 857–866.
4. Chevrolet, J. C. & Joliet, P. "Clinical review: Agitation and delirium in the critically ill—Significance and management." *Critical Care*, 11.3 (2007): 214.
5. Ng, K. T., Shubash, C. J. & Chong, J. S. "The effect of dexmedetomidine on delirium and agitation in patients in intensive care: Systematic review and meta-analysis with trial sequential analysis." *Anaesthesia*, 74.3 (2019): 380–392.

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