

Adequate Sedation or Deep Sedation? Interpreting Sex-Neutral Dexmedetomidine ED50 Findings in Upper Limb Surgery [Letter]

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Dear editor

Fan et al's study makes a useful contribution to perioperative pharmacology by addressing whether biological sex modifies the median effective dose of dexmedetomidine for preoperative sedation in adults undergoing upper limb surgery under brachial plexus block.¹ Still, two issues deserve further discussion before the conclusion is translated into bedside dosing.

The definition of adequate sedation may have been deeper than many regional anesthesia clinicians would target. Fan et al defined success as a Modified Observer's Assessment of Alertness/Sedation score <3 at 26 min after infusion start. This threshold implies arousal only after loud, repeated verbal stimulation or tactile stimulation. In upper limb surgery under regional anesthesia, the desired state is often different: calm, comfortable, easily rousable, and able to cooperate with positioning, block assessment, and intraoperative communication. The internal inconsistency is notable. After the primary assessment, the intraoperative dexmedetomidine infusion was titrated to maintain a MOAA/S score of 3–4, not <3. Table 4 also shows that the median MOAA/S score at 26 min was 3 in both groups, suggesting that many patients were sitting at the border between the prespecified "success" and a clinically acceptable cooperative sedation state. A recent randomized trial in upper limb surgery under brachial plexus blockade selected recovery to MOAA/S 5, patient and surgeon satisfaction, and recovery time as key outcomes, reflecting how regional anesthesia sedation is judged beyond a single depth threshold.² Likewise, a 2025 meta-analysis of regional anesthesia sedation found that dexmedetomidine was associated with bradycardia in 24.8% of patients compared with 2.7% for remimazolam, while remimazolam reached target sedation about 6 min faster.³ Such data make the clinical depth target central, not merely semantic.

A statistical nuance also matters. "No sex difference" is not synonymous with equivalence. Fan et al reported Dixon ED50 values of 1.26 µg/kg in men and 1.28 µg/kg in women, with overlapping 95% CIs, a P value of 0.804, and similar probit ED50 estimates of 1.31 and 1.32 µg/kg. In the adjusted model, sex was not significant, yet the odds ratio for male versus female was 0.31 with a wide 95% CI of 0.04–2.55. That interval is compatible with materially different effects in either direction. The sample size was chosen to obtain crossover pairs for ED50 estimation, not to test clinical equivalence between sexes. CONSORT guidance is explicit that failure to detect superiority does not demonstrate equivalence; an equivalence or noninferiority margin should be prespecified and interpreted against the effect estimate and its precision.⁴

Fan et al should be commended for advancing sex-aware anesthetic dosing, but the clinical message may be better framed as "no detected ED50 difference under this threshold," rather than "sex-neutral dosing is established."

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