Mirror-mirror on the wall, anesthesia is a balancing act after all!

Dear Editor,

The article by Siddiqui et al. [1] published in the recent issue of the Journal of Anaesthesiology Clinical Pharmacology is pertinent to the times where intraoperative opioid elimination is being popularized in the name of speculated superiority of opioid-free anesthesia (OFA). [2-5] Interestingly, the index small sample-sized randomized controlled single-centre study fails to suggest OFA superiority over an opioid-based total intravenous anesthesia technique in patients undergoing laparoscopic cholecystectomy. [1] Adding to the thought-provoking findings of the former research group, the multicentric literature accumulating in this rapidly evolving field mandates elucidation. [3-5]

Understandably, the present-day motivation towards OFA is largely driven by the ardent debates on the opioid use-abuse, and is supported by the escalating opioid-sparing potential owing to an enhanced perioperative incorporation of non-opioid analgesics (non-steroidal anti-inflammatory drugs, dexmedetomidine, ketamine, lignocaine, magnesium, dexamethasone, gabapentin, etc.) and the embracement of safer regional techniques such as fascial plane blocks. [2] Despite the sheer novelty of the concept, replacing intraoperative opioids can only be an evidence-based staged process. While the idea of the use of polypharmacy to achieve OFA may simply fall short of impressing a section of the fraternity, a much larger question surrounding the overall safety of OFA remains.

In this context, the premature termination of the postoperative and opioid-free anesthesia (POFA), the largest available OFA randomized clinical trial (RCT) in the light of cases of severe bradycardia in the dexmedetomidine group, highlights the possibility of serious adverse events while contemplating OFA. [3] Albeit the lack of any statistically significant heartrate alterations reported by Siddiqui et al. [1] in their OFA patients receiving dexmedetomidine, the safety of novel OFA regimens is rather under-evaluated in small studies with a carefully chosen patient cohort. [4] It is equally noteworthy that the primary-outcome under evaluation (postoperative hypoxemia, cognitive dysfunction, and ileus) was more common amongst participants receiving OFA in the POFA trial. [3]

Amidst an emerging skepticism around the OFA risk-benefit balance, the lack of any meaningful benefits attributable to OFA in terms of postoperative pain and opioid use, described in the recent systematic review and meta-analysis of 33 RCTs, captivates attention. [4] While this research group led by Salomé *et al.* [4] (akin to Siddiqui *et al.* [1]) proposes a clear-cut advantage of OFA with regards to postoperative nausea and vomiting (PONV) reduction, it simultaneously advises caution in formulating highly motivated OFA protocols in the absence of evidence-based conclusions on its efficacy and safety.

Envisaging OFA as a continuum of the traditional multimodal anesthesia, one may actually be intrigued by the "one drug as an opioid-replacement" concept in the study by Siddiqui *et al.*^[1,2,5] However, the study manages to adequately highlight that OFA, in its present form, materializes as a neoteric research perspective wherein the speculation-evidence inconsistencies need to be closely monitored.^[2,5] Till the date we cannot provide evidence to support benefits of routine opioid-exclusion over and above opioid-sparing, it would continue to be about how we rationally use the opioids in the tightrope walk of delivering a "balanced anesthesia".

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Conflicts of interest

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