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Up–Down Sequential Allocation Technique to Investigate the Influence of Opioids on the Efficacy of Epidural Local Anesthetics in Labor Pain

To the Editor:—Congratulations to Linda Polley and her colleagues on their investigation into the reduction of the minimum local anesthetic concentration of epidural bupivacaine by sufentanil in labor.[1] They provide not only scientifically, but also clinically useful information.

Nevertheless, I am somewhat puzzled by their latest results: the minimum local anesthetic concentration in their recent control group (plain bupivacaine) was 0.104% (confidence interval 0.09–0.117). This is a surprise, because two previous studies coauthored by one of the present authors calculated this concentration to be 0.069%,[2] or 0.065%[3] respectively, a value definitely outside their current confidence interval. This represents a significant increase in the minimum local anesthetic concentration of plain bupivacaine, a significant decrease in pain threshold of parturients over the years, or another significant transatlantic difference of 50%. This magnitude of a difference the authors claim they would not like to miss in the comparison to bupivacaine plus sufentanil according to their sample size calculation.[1] Because the authors do not discuss this striking discrepancy, the reader would be eager to know whether this is a side effect of keeping the sample size low by using their method of an up–down sequential allocation technique?

Further confusion is raised by mixing up minimum (table 4) and median (fig. 1) concentration. Of course, one could argue whether the term "minimum local analgesic concentration" (MLAC) is appropriate at all. The authors injected a fixed volume of the local anesthetic solution, 20 ml epidurally, and varied the concentration. This implements a change in dose accordingly. Because it is well known that the dose is at least as important as the concentration, it should better read "minimum local analgesic dose (MLAD)," anyhow.

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In Reply:—We thank Dr. Wulf[1] for his interest in our epidural minimum local analgesic concentration (MLAC) studies[2] and welcome the opportunity to comment further.

Regarding his comments on differences in MLAC estimates, these are neither surprising nor new. I (M.O.C.) have previously presented to the Society of Obstetric Anesthesiology and Perinatology (SOAP)[3,4] an overview of the first seven MLAC bupivacaine studies that were conducted in the United Kingdom, the United States, France, and Italy. There was significant heterogeneity ($P < 0.0001$) in the MLAC estimates. The most significant factor affecting MLAC was, not surprisingly, cervical dilatation. Indeed, within the same institution, Capogna *et al.*[4] have shown an almost threefold increase in MLAC as labor progresses. Other significant factors included are initial pain score, gestation, and use of oxytocin. Also, as the studies have evolved, it can be noticed that the methodology has been further simplified to include subjects with "missed segments" as having ineffective analgesia to reduce the number of repeat tests. This also will tend to increase MLAC. It is of course possible that there are institutional, ethnic, or racial demographic factors involved; hence, the simplicity of the model encourages it to be used by any interested practitioner in many clinical settings.

I agree with his comments regarding terminology, I prefer *median* to *minimum*. However, because the model is analogous to the minimum alveolar concentration (MAC) or minimum infusion rate (MIR) for inhalation and intravenous anesthetics, the convention was continued. The fixed 20-ml volume does, of course, imply variations in dose, and I refer Dr. Wulf to previous comments,

where I question the "pivotal" role of dose and discuss in detail the possibility of concentration-dependent pharmacodynamics for epidural local anesthetics.[5] Incidentally his suggestion of the acronym "MLAD," I understand is already in use for similar intrathecal studies!

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Patient Selection and Presentation of Antiemetic Outcome Variables

To the Editor:—We appreciated the article by Song *et al.*[1] who assessed the potential benefit of subhypnotic propofol dosages applied at the end of anesthesia to reduce postoperative nausea and vomiting (PONV) after maintenance with sevoflurane or desflurane. Although the study was not double-blinded, we would like to express our respect for the nice study design, including the power analysis, with a sufficient number of patients and the consequent stratification and randomization.

However, we see problems with some studies focusing on PONV, and we would like to take this article as an opportunity to raise two questions.

First, we agree that it is reasonable to select "high-risk patients" for antiemetic trials. However, a selection of females or a specific type of operation, or both, can be questioned. Recent studies identifying the clinically most significant factors[2,3] and developing a risk score for the prediction of PONV or postoperative vomiting only (PV)[4,5] were able to show that the incidence of PONV or PV after inhalational anesthesia is mainly related to the patient specific characteristics: female gender, nonsmoking history, history of motion sickness or PONV, young age, and the duration of anesthesia.[6] Furthermore, there is some evidence that a score to predict PV is applicable to other types of surgery because incidences of PV in various types of surgery were mainly related to the distribution of individual risk factors.[7] Thus, it is not surprising that females undergoing laparoscopic cholecystectomies had a PONV incidence of approximately 60%. Thus, bearing the importance of individual risk factors in mind, it is difficult to understand why especially patients with a previous history of motion sickness or PONV were excluded from this study.[1]

Second, data presentation are usually not standardized so that studies cannot be compared or used for meta-analyses.[8] We therefore would like to suggest a minimal standard for outcome presentation for nausea, vomiting, PONV, and rescue treatment for the time intervals of 0-2, 2-6, 6-24 and 0-24 h postoperatively. In contrast, the reported 12-h assessment appears quite artificial and clinically of little relevance, because this would often require disturbances during the night or inaccurate time scaling in the data acquisition. An informative adjunct are Kaplan-Meyer curves that, in contrast to this paper, are not used very often. Again, it would be nice to have them separately for nausea, vomiting, PONV, and rescue treatment.

All in all, we do not intend to criticize this specific article because it bears interesting aspects, but to raise an awareness of difficulties concerning patient selection and data presentation in PONV studies. A more standardized presentation might facilitate future quantitative systematic reviews.

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