

Perineural vs intravenous administration of dexamethasone: more data are available

Editor—We read with great interest the recent editorial wherein Martinez and Fletcher¹ discussed the analgesic effects of i.v. and perineural administration of dexamethasone, after publication of a single recent trial.² After performing a systematic search in the PUBMED, CENTRAL, Embase, and Google Scholar™ databases without language restriction, we were able to capture two additional trials that specifically investigated this question.^{3–4} Contrary to the paper by Desmet and colleagues,² these investigations provide support in favour of the perineural route of administration.

Kawanishi and colleagues³ injected dexamethasone 4 mg during nerve stimulator-guided interscalene brachial plexus block with 20 ml of ropivacaine 0.75%, while Rahangdale and colleagues⁴ used a dose of 8 mg, combined with a 0.45 ml kg⁻¹ mixture of bupivacaine 0.5% and epinephrine 1:300 000 for ultrasound-guided sciatic nerve block. A meta-analysis on the duration of analgesia performed with Review Manager (RevMan version 5.2; Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration 2012) suggests that, when compared with the i.v. route, the perineural administration of dexamethasone extends duration of analgesia by mean differences (95% confidence interval) of 174 (278; 71) min ($P=0.001$) and 162 (324; -1) min ($P=0.05$) after a fixed- and random-effect model, respectively. Although a definitive conclusion cannot be drawn from a small meta-analysis of only 173 patients, and confirmation by additional randomized controlled trials is warranted, the preliminary data to date favour the perineural route.

Importantly, as Martinez and Fletcher point out, safety data supporting perineural dexamethasone are scarce. In addition to the clinical investigation of 60 patients⁵ and a subgroup analysis on 407 patients⁶ described by Martinez and Fletcher, we draw attention to a series of 2000 intrathecal injections of 8 mg dexamethasone for the treatment of post-traumatic visual disturbance in 200 patients, performed without any neurological sequelae reported.⁷

In conclusion, we thank Martinez and Fletcher for their insightful editorial. Although support for the clinical benefit of perineural dexamethasone exists, we emphasize their conclusion that further clinical investigations should be conducted to confirm these findings and the safety profile of this route of administration. Only then can the widespread use of perineural dexamethasone be recommended.

Declaration of interest

None declared.

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Gastrointestinal morbidity as primary outcome measure in studies comparing crystalloid and colloid within a goal-directed therapy

Editor—We read with interest the article by Yates and colleagues¹ who compared a balanced crystalloid (CRY) and balanced hydroxyethyl starch (HES) solution within a haemodynamic algorithm guided by pulse power wave analysis in patients undergoing elective colorectal surgery. The primary outcome measure was the inability to tolerate a full enteral diet at postoperative day 5 (POD5) either by mouth or via a feeding tube for any reason, including nausea, vomiting, abdominal distension, or ileus.¹ While their results showed no difference between the HES and CRY groups, a total of 31% of the study patients failed to tolerate a full diet on POD5. This result is seriously contrasting with a recently published study by Feldeheiser and colleagues,² also comparing a balanced crystalloid and a balanced colloid solution within a goal-directed haemodynamic algorithm in patients with metastatic ovarian carcinoma undergoing cytoreductive surgery. They reported a lower rate of 18.7% not tolerating a full diet on POD5, despite a substantially higher POSSUM operative score (32 vs 12 points).

Postoperative gastrointestinal (GI) morbidity as primary outcome measure in studies comparing two i.v. solutions seems to be very challenging as this primary endpoint is assumed to be multifactorial and can only be compared appropriately if multiple factors contributing to postoperative ileus

(POI) are controlled within a clinical pathway.³ The major determinants are addressed as items in the guidelines for perioperative care published by the enhanced recovery after surgery (ERAS) group.^{4, 5} Feldheiser and colleagues had a good adherence to the ERAS items related to enhanced recovery from POI, such as intra- and postoperative use of thoracic epidural analgesia (93.8%), avoidance of long-acting opioids for maintaining anaesthesia (83%), postoperative nausea and vomiting prophylaxis (77.1%), goal-directed volume therapy and a restrictive baseline infusion rate (100%), avoidance of nasogastric intubation after surgery (70.8%), early feeding (46% of the patients had oral fluid intake 6 h after surgery), and early mobilization (68.8% of the patients were mobilized on the first postoperative day). Unfortunately, Yates and colleagues did not provide detailed information about their adherence to these ERAS items related to POI, although that seems essential in conducting a study with GI function as primary outcome measure. The authors only stated that the patients have been treated following the ERAS principles; thus, they reported a length of hospital stay of median 8 days in the crystalloid group and 9 days in the HES group which is about 3–4 days longer than in patients undergoing colorectal surgery who were treated strictly following an ERAS protocol.⁶ In addition, ERAS guidelines suggest early feeding⁵ and in this context, a recent study in patients undergoing colorectal surgery who were treated within an enhanced recovery programme showed that all study patients were tolerating a full diet on POD5.⁷ In our opinion, it would have been more appropriate to investigate if there was a difference in tolerating a full diet within the first 3 postoperative days than on POD5 between the HES and CRY groups. Furthermore, according to a consensus statement published by the enhanced partnership, a positive fluid balance >2 litres on the day of surgery is associated with a poorer outcome.⁸ Patients in both groups in the Yates study had a lot of fluid and fall significantly outside of the guidelines in this consensus statement with regard to the fluid balance (3610 and 4226 ml in the HES and CRY groups, respectively). This is of major interest, as each additional litre of fluids given during the day of operation has been shown to increase the risk of delaying postoperative recovery by 16% and the probability of postoperative complications by 32%.⁹ It seems to us that the lower rate of GI morbidity in patients with more extended surgery in the study by Feldheiser and colleagues² arises from treating patients within a clinical pathway with adherence to ERAS recommendations. Consequently, we think that in the study by Yates and colleagues,¹ the primary outcome measure cannot be fully assessed, as other contributing factors to POI are not shown. Owing to the high failure rate of patients not tolerating diet on POD5, other factors seem to have a higher impact on the primary outcome measure than the type of i.v. solution.

Furthermore, the haemodynamic optimization protocol using stroke volume variation (SVV) by pulse power wave analysis (LiDCOrapid™ monitor, LiDCO, Cambridge, UK) during the intraoperative period raises questions. In contrast to an outcome-based algorithm developed for the oesophageal Doppler (ODM),¹⁰ the protocol by Yates and colleagues, which

uses SVV by LiDCOrapid™ monitor has never been shown to improve outcomes. The use of this algorithm resulted in a 25% decrease in stroke volume (SV) after induction of anaesthesia followed by no significant optimization of SV in both groups up to the end of surgery with still about a 20% reduced SV compared with baseline values. Although former studies have reported a high correlation of SVV and change of cardiac output,^{11, 12} Yates and colleagues¹³ previously showed by themselves that SVV obtained by LiDCOrapid™ is a poor parameter to predict a beneficial volume administration with an area under the curve (AUC) of 0.64 (0.52–0.78) in patients undergoing non-cardiac surgery who were ventilated with a tidal volume >8 ml kg⁻¹. This finding is supported by recent studies indicating an intraoperative poor to fair predictive value of SVV obtained by LiDCOrapid™ in colorectal and vascular surgery.^{14, 15} Additionally, a haemodynamic protocol which is based on SVV as single parameter seems to be challenging, as SVV can be affected by vasopressor changes depending on the balance of volume recruitment from unstressed to stressed volume, change in resistance for venous return, and baseline heart function.¹⁶ Furthermore, with respect to about 20% of the study patients who had laparoscopic surgery, the applicability of SVV-guided volume therapy by LiDCOrapid™ during laparoscopic surgery remains unknown, whereas only SVV by ODM has been shown as a reliable indicator of fluid responsiveness with an AUC of 0.92 (0.82–0.98) in patients undergoing laparoscopic surgery with an intra-abdominal pressure <15 mm Hg.¹⁷ Owing to these facts, in our opinion, the study by Yates and colleagues¹³ compared two i.v. solutions within a non-outcome-based intraoperative haemodynamic protocol guided by a dynamic preload parameter obtained from pulse power wave analysis which raises concerns about adequately predicting a beneficial fluid administration during open and laparoscopic non-cardiac surgery.

In summary, due to the limitations regarding the primary outcome measure and the haemodynamic treatment, we think that any conclusion from this study has to be drawn very carefully.

Declaration of interest

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Reliability of the ASA physical status scale in clinical practice: methodological issues

Editor—I was interested to read the paper by Sankar and colleagues¹ published in the September 2014 edition of the *British Journal of Anaesthesia*. The purpose of the authors was to evaluate ASA physical status (ASA-PS) inter-rater reliability and validity in clinical practice. They reported that the ASA-PS score had moderate inter-rater reliability (κ 0.61), with 67.0% of patients being assigned to the same ASA-PS class in the clinic.¹

It is crucial to know that there is no value of κ that can be regarded universally as indication of good agreement. Two important weaknesses of κ value to assess agreement of a qualitative variable are as follow: it depends upon the prevalence in each category which means it can be possible to have different κ value having the same percentage for both concordant and discordant cells. Table 1 shows that in both (a) and (b) situations, the prevalence of concordant cells are 80% and discordant cells are 20%; however, we get different κ value (0.38 and 0.60), respectively. κ value also depends upon the number of categories which means the higher the categories, the lower the amount of κ value.^{2,3}

Based on their results, ASA-PS score had moderate ability to predict in-hospital mortality (receiver-operating characteristic curve area 0.69). For prediction studies, we need two different cohort data sets or at least split one cohort data set to develop our prediction model and then validate it.^{2,3}

As a take-home message, for reliability and validity analysis, appropriate tests should be applied by researchers. Otherwise, misdiagnosis and mismanagement of the patients cannot be avoided.

Table 1 Comparison of two observers' diagnosis with different prevalence in the two categories

(a)	Observer 1		
	Positive	Negative	Total
Observer 2			
Positive	70	10	80
Negative	10	10	20
Total	80	20	100
$\kappa = 0.38$			
(b)	Observer 1		
	Positive	Negative	Total
Observer 2			
Positive	40	10	50
Negative	10	40	50
Total	50	50	100
$\kappa = 0.60$			