To the Editor.—Dr. Norris et al. are to be congratulated for their well-designed clinical trial examining influence of epidural anesthesia and analgesia on outcomes after abdominal aortic surgery.1 A few points of interest deserve more discussion. The authors based their power analysis from a review of 254 previous patients undergoing the same surgery at their institution who required an average postoperative length of stay of 13 days. Although the clinical trial did not observe differences between epidural and nonepidural groups, all study patients experienced a dramatic reduction in length of stay (from 13 to 7 days) for the same surgery at the same institution. This dramatic reduction in length of stay across all groups could easily obscure any potential clinical differences between groups and limits conclusions on effects of epidural anesthesia and analgesia for this patient population undergoing routine clinical care.

Several factors may be involved in this dramatic clinical improvement in all study patients. The study protocol used a defined postoperative clinical pathway, and similar pathways have been shown in other surgical populations to decrease length of stay by 1 to 2 days.2–4 Just as important a factor in this very intensive clinical trial is the high probability of a Hawthorne effect. This is the undesired effect of an intrusive experiment simply by itself. The inherent process of being in a clinical trial or under observation can lead to enhanced efforts and cooperation in the medical staff and can motivate the patient to increased mental and physical well being.5–6 Historically, this effect is named after studies performed at the Western Electric Hawthorne Works in Chicago, where Harvard Business School professor Elton Mayo examined productivity and work conditions. Within the context of intrusive observation, productivity increased (approximately 25%) regardless of manipulation of variables such as rest breaks, work hours, temperature, humidity, and even after return of variables back to prestudy conditions. These improvements have generally been interpreted as being caused by the sheer presence of observation and experimentation regardless of variables being studied. The Hawthorne effect is a potential limitation of all prospective clinical trials where the subjects and caregivers are aware of the presence of a study. The intrusive effect of Norris et al.’s well-designed clinical trial and the use of a clinical pathway could have easily been responsible for the dramatic reduction in length of hospital stay pre- and post-study, and these factors may have overshadowed any effects of epidural anesthesia and analgesia that may exist in the context of ordinary clinical care. Perhaps the most reasonable conclusion from this study is that an intensive, structured, clinical trial can markedly reduce length of stay after abdominal aortic surgery.

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To the Editor:—We read with great interest the report by Norris et al.1 ‘Double-masked randomized trial comparing alternative combinations of intraoperative anesthesia and postoperative analgesia in abdominal aortic surgery.’ Since the landmark reports of Yeager et al.2 and Tuman et al.,3 it appeared that either intraoperative anesthesia or postoperative analgesia may indeed affect postoperative outcome in certain high-risk patients undergoing major operations. However, more recent studies have suffered methodologic deficiencies in trying to confirm or refute these findings. It is therefore quite gratifying to see a large, randomized, blinded clinical trial to determine what effect, if any, intraoperative anesthesia and postoperative analgesia has on outcome and length of stay in these high-risk patients.

However, we do not believe the findings of Norris et al. support the conclusion that intraoperative anesthesia or postoperative analgesia ‘offers no major advantage or disadvantage.’4 Multiple studies consistently demonstrate that postoperative epidural analgesia provides superior pain relief compared with systemic opioids.5–7 However, Norris et al. states ‘there were no differences in VAS pain scores over time among the four treatment groups for VAS-least pain, VAS-now pain, or VAS-cough pain.’8 The mechanism by which previous papers demonstrated improved outcome is unclear.2,9 The working hypothesis is that epidural analgesia blunts the stress response either through improved analgesia or sympatholysis. This stress reduction then attenuates the postoperative hypercoagulable state, thereby improving outcome. If, as in Norris et al.’s, postoperative pain scores are the same in all groups, how would one ever expect to see a difference in outcome? If the patients had received more aggressive dosing regimens and thus produced the expected better pain control in the epidural groups, one might then expect an outcome difference.

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Pain Control and Postoperative Outcome

To the Editor:—The randomized clinical trial by Norris et al.1 comparing the outcome of alternate combinations of intraoperative anesthesia and postoperative analgesia doesn’t support previous evidence2,3,4 and meta-analysis5,6 that documented lower mortality, morbidity, less pain, and better outcomes of combined or pure regional anesthesia techniques with postoperative local anesthetic infusions.

It might hence be widely quoted as the crown witness of regional anesthesia; in our opinion inappropriately so, because inadequate doses, regimen, and concentrations of local anesthetics were used. Indeed, the authors concede this inadequacy. Short of blocking the activation of the hippocampus-pituitary axis and the sympathetic stimulation associated with surgical trauma and insufficient to treat and respond to postoperative pain, we cannot expect an outcome benefit from the addition of a regional technique.

However, with adequate intraoperative concentrations of local anesthetics, we find a third percent of bupivacaine necessary to achieve surgical blockade, the authors might have encountered (and feared) challenging episodes of hypotension secondary to low systemic vascular resistance and attenuation of the thoracic cardiac accelerators during periods of decreased preload from blood loss, third spacing, and

Underdosing the Epidural Invalidates a Good Clinical Trial

To the Editor:—The randomized clinical trial by Norris et al.1 comparing the outcome of alternate combinations of intraoperative anesthesia and postoperative analgesia doesn’t support previous evidence2,3,4 and meta-analysis5,6 that documented lower mortality, morbidity, less pain, and better outcomes of combined or pure regional anesthesia techniques with postoperative local anesthetic infusions.

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However, with adequate intraoperative concentrations of local anesthetics, we find a third percent of bupivacaine necessary to achieve surgical blockade, the authors might have encountered (and feared) challenging episodes of hypotension secondary to low systemic vascular resistance and attenuation of the thoracic cardiac accelerators during periods of decreased preload from blood loss, third spacing, and
vasodilation. Intraoperative use of epidural anesthesia to achieve surgical blockade may therefore not convey the desired outcome benefits for this particular surgical procedure.

When used for postoperative pain control for aortic aneurysm repair however, epidurals will yield outcome benefits, provided that (1) adequate concentrations are used (we recommend the equivalent of an eighth percent of bupivacaine or more), (2) the infusions rates are adjusted swiftly, with boluses where needed, to respond to interpatient variability and changing anioceptorine needs.

We suggest furthermore that a convincing study should document effective treatment, in this case regional anesthesia intraoperatively, either by achieving adequate surgical blockade before induction or afterwards by, for example, pupillometry. In summary, while the work by Norris et al. was flawless in many ways, we feel it lacks validity due to shortcomings of the (regional anesthesia) protocol in several arms of the study.

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To the Editor:—We would like to comment on the study by Norris et al. This study did not show any benefit from the combination of epidural anesthesia and analgesia with general anesthesia and systemic opioid analgesia. We are concerned, however, that the negative findings (broadly stated as thoracic epidural anesthesia–analgesia “offers no major advantages or disadvantages”) may be caused by shortcomings in the study design. Specifically, we question the choice of length of stay as the primary outcome variable on which analyses are based. Length of stay is not very sensitive, and is affected by numerous factors, including surgical practices and established care paths, which may obscure the benefits of epidural analgesia (as measured by more sensitive parameters).

In fact, a growing body of evidence shows that the use of epidural anesthesia and analgesia in the perioperative period is beneficial. Using a rigorous recovery protocol in the context of “multimodal surgical recovery programs,” recent studies have demonstrated clear benefits from epidural anesthesia and analgesia (e.g., reduced hypercoagulability, accelerated return of bowel function, decreased pulmonary complications, and earlier mobilization).

Furthermore, studies demonstrating benefit from regional techniques used in multimodal recovery programs tend to minimize perioperative opioid use. Thus, analgesia is achieved while avoiding opioid-related adverse effects, such as decreased gastrointestinal motility that can delay recovery. Norris et al. chose to administer opioids (fentanyl) to all patients and may have obscured or offset the potential benefit of epidural analgesia—at least in terms of length of stay.

In sum, the conclusions of Norris et al. may be overstated. The lack of a rigorous recovery protocol, use of opioids in all patients, and selection of an insensitive primary outcome measure (length of stay) may have contributed to the negative findings of this study. Therefore, we caution against the more general interpretation that epidural anesthesia–analgesia is not beneficial.

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References


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To the Editor.—Congratulations to the authors for this excellent study. Some comments: The equal analgesic effectiveness in both epidural analgesia (EDA) and intravenous patient-controlled analgesia (PCA) in this study is surprising. Our own and others’ experiences have demonstrated superior dynamic pain relief during EDA versus intravenous PCA, also after abdominal aortic surgery. The authors have improved analgesic effectiveness of intravenous PCA by a background infusion, with an initial dosage of 80 μg/h fentanyl plus 40 μg on demand. Calculations result in a possible cumulative fentanyl consumption of approximately 2 mg/24 h. The intravenous infusion of fentanyl (75 μg/h) induces ventilatory disturbances, and in some patients severe respiratory insufficiency or apnea. The additional use of a background infusion during intravenous PCA increases the risk of respiratory depression about five-fold. Therefore background infusion during intravenous PCA is not recommended for routine postoperative analgesia on the ward, especially in patients with higher risk. Increased dosages of opioids may induce sleep disturbances, fatigue, and disability, which all are undesired side effects after high-risk surgery. These doubts do not refer to special study conditions, but to routine analgesia on the ward.

Two questions: how high was the fentanyl consumption during intravenous PCAs and EDA at days 1, 2, and 3? Did side effects from fentanyl occur?

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To the Editor.—We write to make the case that the practice of providing a priori sample size calculations, recently endorsed in an ANESTHESIOLOGY editorial, is in fact undesirable. Presentation of confidence intervals serves the same purpose, but is superior because it more accurately reflects the actual data, is simpler to present, addresses uncertainty more directly, and encourages more careful interpretation of results. The clinical trial report lauded in the editorial in fact serves to illustrate the drawbacks of sample size calculation as a data analysis tool. The a priori calculation presented is based on assumptions about length of stay (normally distributed with a SD of 4.5 days) that did not hold in the actual data, an analysis (comparison of mean length of stay between two groups by t test) that was not presented, and a sample size that was not attained. It therefore does not help the reader understand the results, which is the proper goal when reporting on a study that has been completed. The post hoc power calculation presented retains most of these deficiencies, and therefore does not help the reader to assess the strength of evidence against a 1.0-day mean advantage for one treatment versus another. In contrast, a confidence interval for the difference in means would directly address this issue. Although the presence of outliers would require a bootstrapping method to obtain a valid confidence interval for a difference in means, this bit of extra effort is certainly worthwhile for the central issue of a study, and in any case, much better than relying on convoluted reasoning with invalid power approximations.

Perhaps the worst aspect of reporting sample size or power calculations is that it encourages interpretation of studies’ results based only on P values, in particular the widespread fallacy of interpreting P > 0.05 as proving the null hypothesis. The other article cited by the editorial provides a glaring example of this type of reasoning, concluding that reporting of sample size calculations did not change over time in any journal but did increase overall (see their fig. 2). Returning to the clinical trial report, consider the statement that death rates “were similar” in the four subgroups. While this is an accurate characterization of what was actually observed, unsophisticated readers are liable to interpret this (contrary to the authors’ intentions) to mean that the study found strong evidence against any substantial difference in death rates. In fact, the exact 95% confidence interval around the odds ratio for death comparing intravenous versus epidural postoperative analgesia goes from 0.36 to 5.4, which is wide enough to make clear to most readers that this study by itself provides only very weak evidence against a clinically important difference in death rates.

We urge reviewers, editors, and quality studies to give authors full credit for providing confidence intervals instead of sample size calculations in reports of completed studies. Indeed, for the reasons illustrated here, it would be best to discourage the practice of using sample size and power calculations as substitutes for more direct assessment of uncertainty using confidence intervals.

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Sample Size Calculations in Clinical Research

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Background Infusion during Intravenous Patient-Controlled Analgesia: The New Routine Analgesia?

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(accepted for publication April 25, 2002)
To the Editor—It would like to commend Norris et al. for performing an elegant and important study. The authors answered the primary question of the study and showed that length of hospital stay (LOS) did not differ among the four treatment arms. The rationale for using LOS as the primary outcome measure was that it is the “variable most directly proportional to an integrated final negative effect of all significant perioperative morbidity.” Although the authors explain in the discussion why they chose not to focus on “relatively rare events (death and myocardial infarction),” they go on to summarize the important findings of the study in the abstract reporting on LOS followed immediately by the statement: “Postoperative outcomes were similar among the four treatment groups with respect to death, myocardial infarction. . .”. The article lacks a clear statement in the abstract or in the limitations section explaining that the study was insufficiently powered to test differences in these outcomes. The message to the reader with respect to cardiovascular outcomes is contradictory, especially in view of two recent publications utilizing pooled analysis of thousands of patients showing that regional techniques reduced the incidence of postoperative myocardial infarction and mortality, respectively. The limitations of meta-analyses are well known, however, in the absence of large prospective trials designed to specifically answer questions on whether regional techniques have an impact on less frequent but more serious postoperative morbidity events, anesthesiologists will be limited to using such data.

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References


In Reply—We thank Dr. Liu for his comments and interest in our clinical trial. We agree that standardization of perioperative care may improve outcome and reduce length of stay (LOS) and we addressed this concept in our manuscript. This outcome benefit has been largely attributed to the reduction in the variation of clinical care. Our explicit and detailed perioperative clinical care protocols unquestionably reduced (and in some instances eliminated) variation in clinical care. However, our primary goal was not to reduce variation in care, but to optimize perioperative care in all treatment groups. Failure to optimize clinical care and postoperative pain relief in all treatment groups has significantly limited interpretation of clinical trials evaluating the role of anesthetic and analgesic techniques on outcome. Aggressive perioperative heart rate and blood pressure control, intensive physician-directed postoperative analgesia, and accelerated postoperative feeding and mobilization are several important aspects of our trial that both standardized and optimized clinical care. These features of our trial may have accelerated recovery and reduced perioperative morbidity, both of which could result in a LOS benefit regardless of anesthetic or analgesic technique. We observed an overall 31% reduction in mean LOS in our trial compared with historical controls at our institution (12.7 vs. 8.8 days). This rather marked reduction in LOS therefore made it unlikely that the hypothesized effect (2.5 day reduction in LOS) would be observed in any treatment group. Although some may argue that this invalidates our trial, we strongly argue to the contrary. If, as others have chosen to do, we proceeded with a similar trial with only an epidural treatment group, one may have concluded (very inappropriately) that epidural anesthesia and analgesia dramatically reduced LOS and perioperative morbidity in patients undergoing aortic surgery. We also agree that the Hawthorne effect is a potential limitation of all prospective clinical trials. It is currently not possible to determine when, and to what extent, this effect impacts a given trial. While it is certainly possible that caregivers and patients may have become more motivated to accelerate some aspects of postoperative recovery due to their awareness of our trial, the impact should have been similar in each of the treatment groups. Masking of both caregiver and patient to treatment assignment helped to insure that any Hawthorne effect, if present, was not treatment group specific. In addition, it is very unlikely that this effect had any significant impact on postoperative morbidity. Of particular note, median LOS for nonconsented (n = 123) and nonrandomized (n = 7) patients surviving to discharge was 8.0 days (range; 3–85) and 6.0 days (range; 6–10), respectively (Norris EJ, et al. unpublished data, 2001). These patients were not subjected to the rigors of our study protocols and epidural techniques were used in only two patients. We stand firmly behind the conclusions of our trial and believe they are both valid and important. We appreciate the comments from Drs. Kehlet and Dahl. We agree that factors other than pain control impact on important perioperative outcomes. Indeed, that concept impacted significantly on the design of our previous clinical trial performed between 1988 and 1991. In that trial we aggressively protocolized and optimized perioperative clinical care in both treatment groups. We introduced the use of rational blood pressure and heart rate control in an effort to reduce perioperative

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Regional Techniques and Length of Hospital Stay after Abdominal Aortic Surgery

To the Editor—We thank Dr. Liu for his comments and interest in our clinical trial. We agree that standardization of perioperative care may improve outcome and reduce length of stay (LOS) and we addressed this concept in our manuscript. This outcome benefit has been largely attributed to the reduction in the variation of clinical care. Our explicit and detailed perioperative clinical care protocols unquestionably reduced (and in some instances eliminated) variation in clinical care. However, our primary goal was not to reduce variation in care, but to optimize perioperative care in all treatment groups. Failure to optimize clinical care and postoperative pain relief in all treatment groups has significantly limited interpretation of clinical trials evaluating the role of anesthetic and analgesic techniques on outcome. Aggressive perioperative heart rate and blood pressure control, intensive physician-directed postoperative analgesia, and accelerated postoperative feeding and mobilization are several important aspects of our trial that both standardized and optimized clinical care. These features of our trial may have accelerated recovery and reduced perioperative morbidity, both of which could result in a LOS benefit regardless of anesthetic or analgesic technique. We observed an overall 31% reduction in mean LOS in our trial compared with historical controls at our institution (12.7 vs. 8.8 days). This rather marked reduction in LOS therefore made it unlikely that the hypothesized effect (2.5 day reduction in LOS) would be observed in any treatment group. Although some may argue that this invalidates our trial, we strongly argue to the contrary. If, as others have chosen to do, we proceeded with a similar trial with only an epidural treatment group, one may have concluded (very inappropriately) that epidural anesthesia and analgesia dramatically reduced LOS and perioperative morbidity in patients undergoing aortic surgery. We also agree that the Hawthorne effect is a potential limitation of all prospective clinical trials. It is currently not possible to determine when, and to what extent, this effect impacts a given trial. While it is certainly possible that caregivers and patients may have become more motivated to accelerate some aspects of postoperative recovery due to their awareness of our trial, the impact should have been similar in each of the treatment groups. Masking of both caregiver and patient to treatment assignment helped to insure that any Hawthorne effect, if present, was not treatment group specific. In addition, it is very unlikely that this effect had any significant impact on postoperative morbidity. Of particular note, median LOS for nonconsented (n = 123) and nonrandomized (n = 7) patients surviving to discharge was 8.0 days (range; 3–85) and 6.0 days (range; 6–10), respectively (Norris EJ, et al. unpublished data, 2001). These patients were not subjected to the rigors of our study protocols and epidural techniques were used in only two patients. We stand firmly behind the conclusions of our trial and believe they are both valid and important. We appreciate the comments from Drs. Kehlet and Dahl. We agree that factors other than pain control impact on important perioperative outcomes. Indeed, that concept impacted significantly on the design of our previous clinical trial performed between 1988 and 1991. In that trial we aggressively protocolized and optimized perioperative clinical care in both treatment groups. We introduced the use of rational blood pressure and heart rate control in an effort to reduce perioperative...
cardiac morbidity. These design features reduced the number of confounding variables and reduced the likelihood of unrevealed aspects of patient management impacting outcome. Subsequent work from our institution has demonstrated that factors such as organizational characteristics of intensive care units and nurse-to-patient ratios are associated with reduced LOS, lower hospital costs, and improved perioperative outcome. We therefore contend that the conclusion of our trial—“in patients undergoing surgery of the abdominal aorta, thoracic epidural analgesia combined with a light general anesthesia, and followed by either intravenous or epidural patient controlled analgesia, offers no major advantage or disadvantage when compared to general anesthesia alone followed by either intravenous or epidural patient controlled analgesia”—is very appropriate in 2001. We must disagree with Andreae that our postoperative feeding and mobilization regimens were vastly accelerated compared with traditional postoperative care prior to the initiation of our trial. Furthermore, we do not believe that aortic surgery should be equated with colonic surgery. The analgesic regimens used in our trial were carefully developed and refined by experts in acute pain management and vascular anesthesia specifically for patients undergoing aortic reconstruction. Our goal was to optimize pain relief and minimize side effects while preserving postoperative masking. We believe that these goals were achieved with remarkable success. Patients randomized to epidural patient-controlled analgesia (PCA) received on average over 50% less opioid than patients randomized to intravenous PCA (Norris EJ, et al. unpublished data, 2001). Plasma fentanyl levels at 6, 24, and 48 h reflected this as well (Norris EJ, et al. unpublished data, 2001). These data are contrary to Kehlet and Dahl’s suggestion that our epidural analgesia “merely reflected an epidural opioid regimen.” Since the conclusion of our trial, we have made continued efforts at our institution to accelerate recovery after aortic surgery. Median LOS for abdominal aortic surgery at our institution over the years 1998–2000 was 5.0 days (Norris EJ, et al. unpublished data, 2001). That LOS has been attained in the virtual absence of epidural techniques.

The comments of Clark et al. are appreciated. They offer the following question: “If postoperative pain scores are the same in all groups, how would one ever expect to see a difference in outcome?” We offer the following question in turn: “If perioperative care and pain relief are optimized and adverse outcomes minimized, is the analgesic technique even relevant?” Clark et al. are making the incorrect assumption that our epidural analgesia regimen resulted in suboptimal pain scores (relief). In our opinion, the more correct assumption is that pain scores were optimized in the intravenous analgesia regimen. Not optimizing pain relief in all treatment groups or comparing an “optimized” epidural regimen to a “suboptimal” opioid regimen are serious deficiencies of design. These deficiencies have plagued many previous studies and are unfortunately present in two recent large-scale, randomized, clinical trials. It is certainly possible that pain scores could have been improved in both our epidural and intranasal analgesic regimens, but not without increased (and unacceptable) side effects.

Dr. Andreae addresses concerns regarding our intraoperative use of “inadequate doses, regimen, and concentrations of local anesthetics.” He suggests that we may have “feared challenging episodes of hypertension,” and as a result reduced our epidural dosing to the extent that it invalidated our trial. As noted above with regard to our postoperative epidural analgesic regimen, our intraoperative epidural regimen was carefully developed and refined by anesthesiologists with extensive experience in aortic reconstruction. Our trial specifically included very high-risk patients requiring complex aortic reconstruction (25%) and high aortic cross-clamping (18%). “Fear” played no role in our study design or treatment protocols. Our intraoperative goals were to optimize all components of anesthesia, maintain appropriate hemodynamics, and preserve masking. This was accomplished with remarkable success. Our intraoperative epidural dosing is well described in our manuscript. To summarize, we used 0.5% bupivacaine as a bolus and followed with a continuous infusion of 0.125% bupivacaine. Adjustments of the epidural infusion were made according to protocol. Of note, nearly two-thirds of patient with intraoperative epidural activation required at least one reduction in the infusion rate and a third of patients required two reductions (Norris EJ, et al. unpublished data, 2001), indicating an adequate level of epidural block. Only 15% of such patients required a single increase in their epidural infusion (Norris EJ, et al. unpublished data, 2001). Testing for adequacy of surgical block—before induction of anesthesia was not planned because of the almost certain unmasking of both patient and treating physician. It has been our experience that if a bilateral (two or more segments) sensory block to pinprick is present after test dose administration via a thoracic epidural, the surgical block will be adequate with bolus dosing of 0.5% bupivacaine. Importantly, there was no evidence of inadequate intraoperative anesthesia in any patient. Finally, it is noteworthy that Andreae seems unconcerned about the adequacy or appropriateness of the “systemic analgesic” regimens used in the meta-analysis trials as reported by W.S. Beattie. Few, if any, of the meta-analysis trials actually used carefully administered intravenous PCA postoperatively. We believe that intravenous PCA is the only legitimate analgesic modality for the control group of any modern-day study evaluating epidural analgesia.

Karanikolas et al. question our choice of LOS as a primary outcome variable. Our rational for using LOS was addressed in our manuscript and we maintain that LOS is a relevant health outcome important to patients, payers, and society. We agree that LOS can be affected by many factors and that is why we rigorously protocolized perioperative medical management, standardized postoperative surgical care, optimized pain relief, and stratified patients by surgeon. We used opioids in our epidural regimens because combination therapy clearly improves pain control and minimizes side effects. A more aggressive multimodal postoperative program may have further reduced LOS, but this would have most likely occurred to a similar extend in all treatment groups. For example, there is little to suggest that the addition of acetaminophen, ibuprofen, and ketorolac to improve postoperative pain would have impacted outcome to a greater extent in one analgesic group over the other.

Karanikolas et al. states that a “growing body of evidence shows that the use of epidural anesthesia and analgesia is beneficial.” Our question is, “compared to what?” The historical studies which form the basis of the recent meta-analysis reviews, as well as those currently being published, have neglected to control, specify, and optimize treatment in the nonepidural wings of their studies. Why is this? Do investigators really think all forms of “parenteral analgesia” are equivalent? Are reimbursement issues at play? Are political or jurisdictional forces preventing proper study design? Are regional enthusiasts with no interest in the nonepidural modalities conducting the studies? The successful prosecution of our study required the cooperation of anesthesiologists, surgeons, internists, ICU nursing, ward nursing, and pain team members. Thus, we were able to institute intravenous PCA in all patients who randomized to that treatment. Investigations will continue to show that epidural techniques outperform: (1) poorly conducted general anesthesia; (2) general anesthesia with higher than normal death or complication rates; and (3) uncontrolled and suboptimal postoperative pain management in the nonepidural wing. Karanikolas et al. conclude with a “caution against the more general interpretation that epidural anesthesia–analgesia is not beneficial.” We agree with that caution, and for the reasons cited above, would add “caution against the more general interpretation that epidural anesthesia–analgesia is beneficial.”

The comments from Drs. Heid and Jage are appreciated. We too were somewhat surprised that our epidural analgesic regimen did not result in superior (dynamic) pain scores. Our intensive, physician-directed, acute pain service’s goal was to optimize pain relief in all patients. This service evaluated patients on arrival to the intensive care unit, at 2 and 6 h after intensive care unit arrival, three times daily for the first 5 postoperative days, and daily through postoperative day 7. The acute pain attending was available for consultation at all times and
a member of the pain service was available on-site for patient eval-
uation 24 h a day. It may therefore not be a complete surprise that both
analogic regimens resulted in good pain control and similar pain
scores. Importantly, optimization of pain control was done in a double-
masked setting, as was the evaluation of pain scores. Investigator bias
has no doubt had a very significant impact on many clinical trials
evaluating analogic techniques. Efforts to eliminate bias and optimize
care are important aspects of our study design that need to be incor-
porated in future trials. Fentanyl consumption in the intravenous PCA
group averaged approximately 75 μg/h for the first 36 h period and
approximately 45 μg/h for the second 56 h period (Norris EJ, et al.
unpublished data, 2001). In the epidural PCA group, consumption was
approximately 35 μg/h and approximately 20 μg/h for the first and
second 36 h periods, respectively (Norris EJ, et al. unpublished data,
2001). Side effects were generally mild and easily managed.

Bacchetti and Leung address concerns regarding the use of sample
size and power calculations and promote the reporting of confidence
intervals. We agree that confidence intervals are useful, and that is why
we presented them for LOS—the design variable (primary outcome)
of our trial.1 Sample size data were presented to indicate the planned
sample size or power calculations is that it encourages interpretation
of results based only on P values, in particular the widespread
fallacy of interpreting P > 0.05 as proving the null hypothesis’ is
absurd. Sample size is sample size. When designing a clinical trial some
goal must guide the study population size. Bacchetti and Leung seem
unaware of that fact. What method to determine sample size would
they suggest? Post hoc power calculations are also important and
should be part of all manuscripts where the observed treatment effect
is small and the authors conclude in favor of the null hypothesis, that
is, no difference among treatment groups. These calculations are fre-
quently helpful to the reader when attempting to determine whether
the presence of outliers would require a bootstrapping method to obtain
a valid confidence interval for a difference in means.

Finally, we thank Dr. Amar for his comments and interest in our
clinical trial.1 He is correct that our study was not powered to detect
differences among or between treatment groups with regard to car-
diovascular outcomes. However, that is not a “limitation” of our trial.
Our study question and design were clearly articulated in our manu-
script. The trial was powered for LOS, not cardiovascular outcomes.

We reported in our Results that “hospital mortality, cardiac death, and
mortality at 12 months were not different among the four treatment
groups,” and with regard to major (cardiac) morbidity, “no significant
difference was observed among the four treatment groups.” These are
an accurate characterization of what was observed in our trial. Al-
though the casual reader of only our abstract may very well misinter-
pret, “postoperative outcomes were similar among the four treatment
groups with respect to death, myocardial infarction,” the conscien-
tious reader of the entire manuscript will not.

In summary, we appreciate the opportunity to respond to all of
these letters and thank all of the contributors for their comments and
interest in our trial.

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(Accepted for publication April 25, 2002.)

In Reply.—Drs. Bacchetti and Leung comment on both the pub-
lished article by Norris et al., and my accompanying editorial. They
specifically argue that a priori sample size calculations are “in fact
undesirable,” and argue that the article by Norris et al. “serves to
illustrate the drawbacks of sample size calculation as a data analysis
tool.” I strongly disagree with the former statement, but appreciate
their arguments regarding the latter. I think that two sources of dis-
agreement involve our differing perspectives and our terminology.
Evaluating Clinical Trials in Anesthesia

To the Editor—ANESTHESIOLOGY recently published an editorial1 and research article2 on the topic of the design of clinical trials. The journal and its editorial board are to be commended for again calling the attention of its readers to the role of appropriate clinical trial design in the ethical and scientific conduct of clinical trials and the meaningful interpretation of their results.

The scientific study was designed to compare the quality of clinical trials among four journals over 20 yr with the aim of improving the quality of future clinical trials in anesthesia through an analysis of the deficiencies of published studies. Unfortunately, the study contains a number of deficiencies in the design and statistical analysis that detract from its message.

Although it was the purpose of the study to compare ten characteristics of quality related to study design among the four journals and between time periods, data from the four journals within each time period were deemed to be “similar” and therefore “pooled” before statistical analysis. Examination of the data in figures 1–4 suggests that the data from the four journals within the various time periods could be shown to be different by standard statistical analysis (this is especially obvious in fig. 4). Even if the data within each period were compared statistically and shown to be “not different,” that would be insufficient justification for “pooling” the data because “not different” is not “the same.”

The authors planned to compare the frequency of reporting each characteristic among journals and between time periods. Had they made all planned statistical comparisons, 280 would have been made. Designating \( p < 0.01 \) as the criterion for rejection of the null hypothesis to account for this number of comparisons is insufficient to avoid a Type I error. Using \( p < 0.01 \) as the criterion for rejection of the null hypothesis is even insufficient to avoid a Type I statistical error if they ultimately made only 15 comparisons.

Although the authors were interested in evaluating the quality of study design during the 20 yr period from 1981–2000, they were only able to compare results from the period 1981–1985 with those from the period 1991–1995. They were unable to include in the statistical analysis the data from the last period in which they were interested, the first 6 months of 2000, because “the numbers were too small.” That is, the study was underpowered to accomplish its aims because of a deficiency in experimental design leading to a Type II statistical error. Nonetheless, this did not prevent the authors from including the data from the first 6 months of 2000 in the table and figures as though they were included in the statistical analysis.

The author’s hypothesis failed to clearly define the primary outcome variable and the magnitude of the change that would be sufficient to conclude that a difference was present. A pilot study of the 10 characteristics of quality related to study design could have provided an estimate of expected scores of studies published at the beginning of the period of interest 1981 and served as the basis of a well-formulated hypothesis and sample size calculation that could have prevented the above statistical errors.

Examination of table 1 suggests that the authors compared the percent of trials for which the criteria were present rather than the frequency of reporting each characteristic. If this was in fact done, it inflates the power of the study because the sample size for each time period is inflated to 100 (because the range would be 0–100) rather than the actual sample size of 80 that the authors studied in the time periods 1981–1985 and 1991–1995. Although the data from the first 6 months of 2000 was not included in the statistical analysis, reporting these data as a percent of the trials misrepresented the sample size of 20 and makes it look equivalent to the sample sizes from the other two periods.

Other problems with the study exist, including the question of the validity of the evaluation instrument and reporting the results as mean scores (fig. 1).

The point of this communication is that, while the authors are to be commended for their efforts to improve the quality of future clinical trials in anesthesia through an analysis of the deficiencies of published studies, their message would have had a greater impact and their study...
In Reply.—We thank Dr. Avram for his comments on our publication and respond to his comments as follows. The aim of this study was to “evaluate the quality of study design in clinical trials published in four leading anesthesia journals between 1981 and 2000.” We did not intend to establish differences among the four journals (and the individual journals were not identified in the paper) and therefore, the data can be legitimately pooled. Even if we had sought to pool the data based on a P value > 0.05, this approach is not novel. After pooling the raw data (and not percentages from the four journals), we compared each criterion in the two time periods. Applying the same criteria for correction of type 1 errors as we used in this study (number of comparisons in excess of 10), we corrected the P value for the 15 comparisons in this study by reducing the P value by 5-fold, resulting in a P < 0.01. It is important to recall that the threshold for correcting for type 1 errors is arbitrary. Indeed, Dr. Avram did not find fault with our threshold for defining type 1 errors in clinical trials. Moreover, as we restrict the P value for type 1 errors, we inversely increase the risk of a Type II error and this relationship should not be overlooked.

To provide an up-to-date snapshot of the quality of clinical trials in anesthesia, we included clinical studies from the year 2000. These studies were selected from a much smaller pool of published studies than those selected in 1981–1985 and 1991–1995, and as stated in the methods, they were not included in the analysis.

The primary outcome variable of this study was the mean analysis score, evaluated between 1981–1985 and 1991–1995. This score increased significantly with a P value that was so small (P < 0.00001) that we had corrected for 5,000 comparisons, it would still have yielded a statistically significant change in the mean analysis score. Comments about insufficient power relate only to negative studies, particularly when ethical, moral, and fiscal issues are not at stake.

Dr. Avram commented on the limitations of the quality criteria that we used. We acknowledged this limitation in our study by stating that we had modified existing quality criteria and made some arbitrary decisions about several criteria to ensure that they were relevant and applicable to anesthesia trials. Unfortunately, the original quality criteria by DerSimonian et al. were not tested for validity. We agree with Dr. Avram that median values may have been more appropriate measures of central tendency of the scores to report rather than mean values, although with normally distributed scores, the difference between mean and median values would have been moot.


References


(Accepted for publication July 1, 2002.)

Harm Associated with Reprogramming Pacemakers for Surgery

To the Editor.—With interest, we read the recent review articles “Cardiac Rhythm Management Devices, Parts 1 and 2” by Atlee and Bernstein. We fully agree with the authors that in a pacemaker-dependent patient the device should be reprogrammed to an asynchronous mode, as stated in the text (page 1505) and in table 8 (page 1504) of the article. However, the paper does not contain a clear statement as to what to do with patients who are not fully pacemaker-dependent, i.e., patients with an intrinsic rhythm who have occasional episodes of bradycardia. In these patients, reprogramming the device in an asynchronous mode can provoke harmful interactions with the patient’s intrinsic rhythm, resulting in R-on-T-phenomenon causing possible ventricular fibrillation. This phenomenon is demonstrated in two examples (fig. 1) of intraoperative Holter recordings in patients with intrinsic rhythm in whom the pacemaker was reprogrammed to an asynchronous mode.

Therefore, we strongly recommend that a pacemaker should not be reprogrammed to an asynchronous mode in patients who have an intrinsic cardiac rhythm with only occasional episodes of bradycardia. To protect the battery, the atrial and ventricular sensing should be programmed, if possible, to a bipolar mode. If an episode of bradycardia, pacemaker-triggered beat; arrow = pacemaker stimulus, double arrow = pacemaker stimulus in the intrinsic T wave)

Fig. 1. Intraoperative Holter recordings of two patients with intrinsic cardiac rhythm in whom the pacemaker was reprogrammed to an asynchronous mode. (* = intrinsic cardiac beat, ** = pacemaker-triggered beat; arrow = pacemaker stimulus, double arrow = pacemaker stimulus in the intrinsic T wave)
In Reply—Drs. Filipovic, Michaux, and Seeberger remark that our two-part review article does not contain a clear statement as to how to manage patients who are not pacemaker-dependent.1,2 They suggest that reprogramming the device to an asynchronous mode could produce harmful interactions with the patient’s intrinsic rhythm, including the R-on-T phenomenon causing ventricular fibrillation (VF). While they illustrate the R-on-T asynchronous pacing in intraoperative Holter recordings from two patients, there is no VF in either recording.

A search of the Ovid Medline database (1966–present) reveals only a single case report describing VF induced by R-on-T ventricular pacing (i.e., stimulation during ventricular repolarization, particularly during the upstroke of the T wave).3 This occurred after coronary angiography in an elderly man who had suffered a recent myocardial infarction (MI) and presented with syncope. A temporary ventricular-inhibited pacemaker had been placed after sinus pause was documented. The R-on-T phenomenon was attributed to sensing failure. Ventricular tachyarrhythmias initiated by R-on-T ventricular extrasystoles have been described both in the setting of thrombolysed acute MI4 and in tachyarrhythmias initiated by R-on-T ventricular extrasystoles have been described both in the setting of thrombolysed acute MI and in patients with acute MI prior to the thrombolytic era.5 At least one report suggests that in the setting of acute MI, R-on-T extrasystoles appear more likely to trigger VF than ventricular tachycardia.6 To our knowledge, there are no reports of R-on-T extrasystoles or asynchronous pacing triggering ventricular tachyarrhythmias in anesthetized patients.

Magnet-induced asynchronous ventricular pacing is used routinely in pacemaker follow-up, both as part of examinations in pacemaker clinics and physicians’ offices and during transtelephonic screening, and asynchronous (“noise mode”) pacing is induced automatically when pacemakers identify persistent electromagnetic interference (EMI), as described below. The induction of VF by ventricular stimuli occurring during ventricular repolarization appears to be so rare that most pacemaker practitioners, even those with many years of experience, have never seen it.

As discussed,2 EMI between 5 and 100 Hz overlaps the frequency range of intracardiac signals, and is not filtered out by the pacemaker’s sensing circuitry. Possible responses to EMI are: (1) inhibition or triggering of stimulation; (2) asynchronous pacing; (3) mode resetting; or (4) damage to the pulse-generator circuitry.7 To protect against inappropriate inhibition of pacing stimuli, some devices may revert to asynchronous pacing at the basic-rate interval when exposed to continuous EMI above a certain frequency.7 In others, repetitive noise detection in the noise-sampling period causes temporary reversion to noise mode.8 At the lowest field strength, there is no effect. But, as the field strength increases, there is a greater tendency to inhibition because the noise may be sensed intermittently. With still higher field strengths, noise is sensed continuously and asynchronous pacing occurs. There can be considerable variation between different pacemakers and their susceptibility to EMI.7,8

We agree with Filipovic et al. that if a patient is pacemaker-dependent and EMI is likely to cause significant interference, a triggered or asynchronous mode should be programmed.5 However, for patients with adequate intrinsic rhythm, we suggest several measures to reduce the likelihood of adverse effects due to surgical EMI.2 Also, if electrocautery must be used in the vicinity of the pulse generator or leads (closer than 15 cm), the pulse generator should be identified and its response to strong, continuous EMI ascertained.2 If electrocautery usage might compromise the patient in any way, a compatible programming device must be available in the operating room, with the pulse generator accessible to the programming head and someone experienced in programming present.

Therefore, based on available evidence and our own experience, we believe that asynchronous pacemaker operation, whether preprogrammed or consequent to sensed strong, continuous EMI (i.e., noise mode), is highly unlikely to trigger ventricular tachyarrhythmias. We suppose this might be possible in patients with acute MI or in patients with severe underlying heart disease and dangerous imbalance (e.g., severe hypokalemia, digitalis, or catecholamine excess).

Finally, Filipovic et al. suggest that to protect the “battery” (we are sure they mean the pulse generator), bipolar atrial and ventricular sensing should be used. If the implanted pacing system has this capability, the bipolar configuration is desirable because it offers superior immunity to far-field sensing and because the very short distance between electrodes minimizes the effective antenna length and thus the susceptibility to radiated electromagnetic interference of the sort commonly encountered.5 However, we disagree with the implication that any pacemaker can always be switched on by placing a magnet over the pulse generator. This will not occur if the magnet response has been programmed off, an option in some pulse generators.7

References


Accepted for publication May 4, 2002.
Vecuronium Sensitivity in Part Due to Acute Use of Phenytoin

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References


To the Editor.—Exaggerated sensitivity to vecuronium in a brain dead woman1 has an additional contributing factor, namely, the acute action of phenytoin. There is a difference in acute or chronic use of phenytoin. It has a weak postjunctional blocking effect that, in the acute phase, causes a partial blockade at the neuromuscular junction.2 This is not generally realized in the awake patient receiving phenytoin, but it contributes to blockade by nondepolarizing muscle relaxants should the patient require anesthesia.3,4

This partial blockade, in time, likely about 10 days to 2 weeks, promotes increased numbers of extra-junctional nicotinic acetylcholine receptors, resulting in resistance to nondepolarizing muscle relaxants (receptor upregulation).5 The woman described in this article was in the acute phase of phenytoin administration, so that potentiation of the effect of vecuronium was due, in part, to residual vecuronium or its metabolite (pharmacokinetics), acute phase phenytoin (pharmacodynamics), steroids, and perhaps her acute central nervous system depression. She had received 1.5 mg/kg vecuronium in more than 15 hours, and recovered normal responses after more than 60 hours.

However, the likely major factor in all this is the overdose of vecuronium, because the lack of neuromuscular monitoring during its administration prevented identification of the time of complete neuromuscular blockade.

In Reply:—We appreciate the opportunity to respond to the excellent comments made about our case report.1 Several studies2–5 have demonstrated that acute administration of phenytoin enhances vecuronium-induced neuromuscular blockade. The possible mechanism is pharmacodynamic interaction between anticonvulsants and nondepolarizing muscle relaxants (receptor upregulation).5 The woman described in this article was in the acute phase of phenytoin administration, so that potentiation of the effect of vecuronium was due, in part, to residual vecuronium or its metabolite (pharmacokinetics), acute phase phenytoin (pharmacodynamics), steroids, and perhaps her acute central nervous system depression. She had received 1.5 mg/kg vecuronium in more than 15 hours, and recovered normal responses after more than 60 hours.

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However, the likely major factor in all this is the overdose of vecuronium, because the lack of neuromuscular monitoring during its administration prevented identification of the time of complete neuromuscular blockade.

The patient in our article received 250 mg/day of intravenous phenytoin twice on the first hospital day. Vecuronium was concomitantly administered at 4 mg/h and lasted for 15 h, 40 min. Her train-of-four ratio (TOF ratio) did not exceed 80% until 64 h passed after discontinuation of vecuronium. As plasma concentration of phenytoin was not measured during this period, we cannot estimate the influence of phenytoin on the value of TOF ratio. Metabolism of phenytoin is by hepatic microsomal enzymes that are susceptible to stimulation or inhibition by other drugs. Below a plasma concentration of 10 μg/ml of phenytoin, its metabolism follows first-order kinetics and the elimination half-time averages 24 h.7 At plasma concentrations of phenytoin above 10 μg/ml, the enzymes necessary for metabolism become saturated and the elimination half-time becomes dose-dependent (zero-order kinetics).7 In this context, we could speculate that the elimination half-time was more than 24 h, although no exact data are available regarding a plasma concentration of phenytoin after its intravenous administration. Therefore, we cannot deny an augmentation of vecuronium-induced neuromuscular block by the acutely administered phenytoin. For all this speculation, TOF ratio observed in this patient could be explained well by blood concentrations of vecuronium and its metabolite, 3-desacetylvecuronium. If we performed neuromuscular monitoring during vecuronium administration or phenytoin administration in this patient, the effect of the latter on the residual neuromuscular blockade could be more detailed as Dr. Gronert pointed out. We thank Dr. Gronert for his interest in our case report and his insightful comments on acute use of phenytoin.

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References


(Accepted for publication May 6, 2002.)
To the Editor:—Dr. Rooke et al. provide much food for thought in their recent editorial. They neatly describe the predicament that we as anesthesiologists face, namely, the challenge of caring for an increasingly aging population. Anesthesiology as a specialty has experienced a significant expansion in the direction of laboratory-based research in the past decade, perhaps sacrificing a more holistic view of the delivery of perioperative care. The older patient is particularly in need of such a multidisciplinary approach. A pertinent example is that of the older patient undergoing ambulatory surgery. Preoperative assessment should include evaluation of social circumstances, not just who is at home, but how many stairs the patient will have to go down to the bathroom.

Cognitive assessment before surgery is vitally important to the issue of valid consent. A Mini Mental State Examination (MMSE) score of 19 infers that the patient is incapable of making safe decisions and transfer of power of attorney may be necessary before proceeding with surgical intervention.

A patient with a MMSE score of 26 may be managing just fine in her own environment, but will become agitated in the alien atmosphere of the hospital facility. This agitation may earn her the administration of further sedation! Further cognitive decline can be anticipated for up to 1 week after surgery and anesthesia. This means we need to know who is going to manage the medications during that important first week. Prescribing optimal analgesia will be futile if our patient does not remember where she left those pills and what time she should take them. Other simple issues, usually beyond our remit, include nutrition and mobility. If the perioperative period encompasses the safe and effective recovery of our patients, then who gets the shopping and cooks the meals is something we should be aware of. So when was the last time we asked any of these questions? Anesthesiology for the older patient is nothing new per se, we have been managing elderly patients in the operating room, postanaesthesia care unit, and intensive care throughout the development of our specialty. What is a challenge is the holistic approach to clinical practice. Whether this means a new subspecialty interest or departmental leaders in the field remains to be seen.

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(Accepted for publication May 21, 2002.)
To the Editor—The case report by Ganapathy et al.\(^1\) of alleged transient neurologic symptoms following intrathecal ropivacaine and their subsequent anatomy-based defense\(^2\) of de Jong's\(^3\) criticism forgets a very important principle: anatomic variation.

Ganapathy et al.\(^1\) state: 'The spinal cord ends at the level of L1, and our spinal puncture was performed at L2-L3.' Maybe yes, maybe no. Hogen\(^4\) in an elegantly simple letter to the editor, cogently cites earlier anatomic studies\(^5\)\(^6\) pointing to the clinical importance of understanding that what lies beneath the lumbar vertebral bodies (via counting palpable bony landmarks relative to Tuffier's Line) may be unreliable and that the conus medullaris may be as low as L3. Nothing in the report by Ganapathy et al.\(^1\) accurately (i.e., radiographically) documents the level of their dural puncture (their experience notwithstanding) and is a major reason why accuracy of ascertaining proper vertebral levels based on surface anatomy may be only 50%.\(^7\) In other words, we probably are not where we think we are more than we realize. Perception of paresthesia may be blunted in the sedated patient and we probably are not where we think we are more than we realize.

Blind faith in normative anatomic relationships as evidenced by Ganapathy et al.\(^1\) does not refute de Jong's\(^3\) excellent criticism of their case report. The time course and constellation of problems Ganapathy et al.\(^1\) present do spinal catheters go? Anesth Analg 1993; 76:1004

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(Received for publication May 21, 2002.)

In Reply—Doctor Appleyard deftly deflects Ganapathy et al.'s\(^1\) inference—x-ray vision in positioning the spinal needle tip away from the conus medullaris—by cautioning practitioners that Tuffier’s intercrestal line is an approximation to the L4-L5 interspace at best, and that the conus medullaris often ends well caudal of the L1 vertebral body. In other words, even in the hands of experienced clinicians, the spinal needle tip as often as not approaches the conus closer than we sometimes appreciate.\(^2\)

The authors\(^3\) may take heart from Reynolds' analysis\(^7\) of 7 instances of conus medullaris injury from spinal needle insertion. As she points out: although the spinal cord is said to terminate at L1, it extends to L2 in nearly one-half (43%) of women; likewise, Tuffier’s intercrestal line is a patently unreliable method of identifying lumbar interspaces, such that "...anaesthesists commonly select a space that is one or more segments higher than they assume."

To be sure, as Ganapathy et al.\(^1\) point out, conus trauma ought to elicit a paresthesia but then, as Doctor Appleyard notes, that response may have been muted by preoperative sedation. Every other symptom and neurologic sign—progressive paraplegia—may be caused by spinal injection of the spinal cord (rather than a spinal rootlet) mechanical injury secondary to lumbar puncture.\(^5\)\(^6\)

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(Received for publication May 21, 2002.)
Amsorb® Causes No Less Carbon Monoxide Formation than Either “New” or “Classic” Sodalime

To the Editor:—In a recent study1 (supported by Abbott—the supplier of Amsorb®) comparing degradation of volatile anesthetics and formation of carbon monoxide (CO), COHB, and compound A in the presence of different carbon dioxide absorbents, Kharasch et al. report that for desflurane the order of CO formation was Baralyme® > “classic” sodalime > “new” sodalime > Amsorb®. The foundation for this statement seems to be lacking. Use of the symbol “>” usually implies statistical significance. However, in this case, the only statistically significant differences are those between Baralyme® and the other three absorbents. In other words, Amsorb®, although causing less CO formation than does Baralyme®, causes no less CO formation than that caused by either “new” or “classic” sodalime.

In addition, the statistical methodology used in this complicated study design is inadequately described. A simple statement that analysis of variance was used is not informative. Which type of analysis of variance was used and which multiple comparison procedures did the authors utilize to support their statements?

Although the flaws described above might seem to be of minor importance, a major objection is that the final statements “in comparison with sodalime and Baralyme®, Amsorb® caused minimal if any CO formation . . .” and “These findings seem relevant to patient safety” can now be used by the study sponsor as evidence of product superiority in fact for the most relevant volatile anesthetic in terms of CO production (desflurane) no difference between Amsorb and sodalime has been demonstrated.

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Reference

(Accepted for publication May 21, 2002.)

Acupuncture for Postoperative Nausea and Vomiting Prophylaxis: Where’s the Point?

To the Editor:—Dr. Rusy et al. are to be congratulated for publishing an article as timely as it is courageous concerning electroacupuncture at P6 (A.K.A. Master of the Heart-6, MH6) for prophylaxis of nausea and emesis in children after tonsillectomy.1 The article is timely in view of the recent FDA “black box” warning concerning droperidol, strongly discouraging its use in view of reports of QT prolongation, torsades, and death. The article is courageous in evaluating a treatment some physicians regard with skepticism. The article concludes electroacupuncture at MH6 reduces the feeling of nausea but that the effect may not be powerful enough to reduce the incidence of vomiting after tonsillectomy. The study found no reduction in the incidence of vomiting or need for rescue medications. In view of these results, the authors do not support the use of acupuncture in lieu of prophylactic intravenous antiemetics. Before condemning a therapy, however, it is essential to scrutinize the methodology employed in its evaluation.

In patients under a general anesthetic, after removal of the second tonsil, acupuncture needles were inserted at the MH6 acupuncture point to a depth of 1 cm in all patients. Aside from the placement

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2 cuns above the wrist crease between the flexi carpi radialis tendon and the tendon of the palmaris longus, no other method was apparently employed to ascertain correct location and depth of placement. Many acupuncture practitioners will slowly advance an acupuncture needle with gentle rotation until a De Qi or “arrival of Qi” sensation is appreciated by a patient as a “muscular ache” and by practitioner as a “needle grab” by muscle. In fact, some authorities feel that a needle must be advanced to a depth where De Qi is experienced for treatment to be effective.1 It was curious whether the investigators employed such a technique to help insure proper needle placement, and how the standard depth of 1 cm was determined. Median nerve discharge is common with needle placement at MH6, and may be extremely uncomfortable in an awake patient.

While the MH6 acupuncture point has been most extensively studied for PONV, it seems odd that a point classically used for cardiac or respiratory disorders that is the special command point for the thorax3 should receive such singular attention in nausea. Certain points along the stomach meridian may hold greater promise in this regard. Stomach-36 (ST-36), for example, is the special command point for the abdomen,4 located 3 cuns distal to the inferior border of the patella and a finger-breadth lateral to the tibial tuberosity is one of the four strongest acupuncture points on the body and may be used to treat nausea. Stomach-43 (ST-43) located on the dorsum of the foot in the second interosseous space is also promising. The combination is likely to be superb. There are, at present, no published reports evaluating the efficacy of these points for PONV.

The investigators may be correct that electroacupuncture at MH6 lacks sufficient potency to prevent postoperative emesis. It is encouraging that the therapy reduces the incidence of nausea. Further study of more potent acupuncture points that are more closely related to the problem at hand may yield more favorable results.

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(Accepted for publication June 22, 2002.)

We do not believe that our report condemns the use of acupuncture for postoperative nausea and vomiting in children after emetogenic procedures. Rather, it does substantiate the notion that there was a treatment effect and that further investigations are needed to attempt to establish a useful role for these techniques. We are optimistic that carefully controlled placebo-controlled trials such as ours will eventually lead to more mainstream adoption of acupuncture in children. Once we can establish strong treatment effects, we will be in a better position to begin to advocate for the use of acupuncture even in nonsedated children.

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Reference


(Accepted for publication June 22, 2002.)

To the Editor.—We read with interest the recent editorial by Gaba1 discussing the application of video and simulation technology as novel approaches to teaching regional anesthesia to our residents, namely the use of the Sony Clie Personal Data Assistants (PDAs) with high-resolution color displays (e.g., PEG-N760C, PEG-T615C) as teaching aids for regional anesthesia (fig. 1).

PDAs are gaining rapid popularity within the medical field because of their ability to store and rapidly retrieve vast amounts of data—both prepackaged and user-customized—in a small, readily-accessible package. PDA applications such as pharmacology references (e.g., Epocrates), electronic handbooks (e.g., Harriet Lane, Five Minute ClinicalConsult), and patient logging programs are already widely utilized. The recent introduction of high-resolution color screens combined with ever-expanding PDA memory capacity now facilitate more dis-

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Use of High-Resolution Color Personal Data Assistants as Regional Anesthesia Teaching Aides for Resident Education

To the Editor.—We read with interest the recent editorial by Gaba1 discussing the application of video and simulation technology as novel approaches to teaching regional anesthesia to our residents, namely the use of the Sony Clie Personal Data Assistants (PDAs) with high-resolution color displays (e.g., PEG-N760C, PEG-T615C) as teaching aids for regional anesthesia (fig. 1).

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play, or visual-based applications. Our PDA-based teaching tools are merely a specific application of the current display capabilities of the newest generation of PDAs.

The color Sony Clies are bundled with PC software (PictureGear Lite) that exports color photographs that can be displayed on the PDA (using PictureGear Pocket). The PDA image can be zoomed in and out, and repositioned both vertically and horizontally. The pictures, a compromise between fine detail and manageable file sizes, are surprisingly detailed and have good clarity. Average high quality pictures consume about 100 Kb of memory. While 128 Mb of Flash Memory (enough to store more than 1,000 pictures) costs about $100, smaller memory cards with more than adequate capability for our purposes are even less expensive.

Our PDA-based regional training aides are largely based on numerous photographs of our regional anesthetic techniques. These digital photographs have been organized by type of block, and loaded onto our PDAs. Typical photographs show proper patient positioning, the relevant anatomical landmarks, pertinent cadaveric dissections, and simplified diagrams. In addition to the visual information presented by digital photographs, considerable text-based information is also available for each block, including indications and contraindications, suggested drugs and dosage, guidance in finding an acceptable needle position with the aide of a nerve stimulator, and clinical “pearls.”

The blocks that we currently have documented include the interscalene, infraclavicular, spinal, epidural, femoral, popliteal, and ankle blocks. Clearly such PDA-based teaching aides can never replace the guidance of an experienced regional anesthesiologist. However, we believe that such tools may substantially speed the training process and serve as readily available reference material for regional anesthesia. The unsurpassed accessibility of PDA-based information serves as a valuable resource for those clinicians who do not perform regional anesthesia on a consistent basis. What remains to be seen is if the use of PDA-based information will in reality affect the learning curve in regional anesthesia for residents in training. This is a basis for future work from this department.

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To the Editor.—In their letter to the editor, Mchaourab and Hamill-Ruth¹ ask, “should imaging studies be routinely performed prior to epidural steroid injections?” The answer is yes, emphatically. The authors describe a patient on long-term steroid therapy for asthma who developed epidural lipomatosis that constricted the lumbar dural sac to the point of producing low back pain. There were no signs of radiculopathy, and although the L5-S1 intervertebral disc was protruding slightly, the indication for epidural steroids was doubtful at best; the MRI demonstrated the imperative need to have a precise and objective diagnosis, before initiating an invasive procedure on the spine.

Other reasons can be named to further support performing imaging studies before any pain-related invasive procedure, in which case if the caudal approach would have been attempted for an epidural steroid injection a dural puncture may have occurred. The list can go on and on.²

Abrams, in an earlier letter,³ raised the issue of cost; this may be answered not only by the fact that a more effective treatment may be attained if an accurate diagnosis is known, but as importantly, by defining the occurrence of surgically-related complications.⁴ A precise diagnosis can prevent a falsely attributed complication to the epidural steroid injection, placing the blame instead, on the spinal operation. An extra safety is the selection of the optimal epidural space for epidural steroid injection treatment.

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Radiological Imaging before Epidural Steroid Injections

Fig. 1. Sony Clie Personal Data Assistant (PDA).
Harlequin Syndrome following Internal Jugular Vein Catheterization in an Adult under General Anesthetic

To the Editor — We would like to report the rare perioperative phenomenon of harlequin syndrome in a patient undergoing incision and drainage of an abdominal abscess under general anesthesia.

A 46-yr-old, 64-kg woman was scheduled for laparotomy and drainage of an intraabdominal fluid collection located in her right lumbar region after leakage of intestinal contents following a transduodenal sphincterotomy. She had been in the hospital for 2 months and had undergone multiple procedures to drain fluid collections around her duodenum. A tunneled Hickman catheter (right internal jugular vein) had been removed 3 weeks before this operation following fever and positive blood cultures. Insertion and removal were unremarkable.

Medical conditions included noninsulin-dependant diabetes mellitus hypertension and depression. Current treatment comprised omeprazole, enoxaparin, temazepam, acetaminophen, and paroxetine.

The patient had a rapid sequence induction of anesthesia with propofol, fentanyl, and succinylcholine. Cricoid pressure was applied. The descriptive term harlequin syndrome probably results from interruption of ipsilateral sympathetic supply to the face resulting, in this case, in an abnormal pale and dry right side, and a normal flushed and sweaty appearance on the left. 5 It has not been described in adult patients undergoing general anesthesia or in association with central venous catheterization.

Although insertion of the right internal jugular triple lumen catheter was unremarkable, we suggest that this case of harlequin syndrome resulted from neuropraxia of the facial sympathetic supply during this procedure. Diabetes mellitus and hypertension may predispose one to this condition. Previous injury to the cervical sympathetic nerves may have occurred during the insertion and removal of the Hickman catheter or while cricoid pressure was applied during the difficult intubation, however facial color change was not observed at these times.

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Fig. 1. Harlequin syndrome following internal jugular vein catheterization in an adult under general anesthetic.
To the Editor:—We would like to report an unusually long-lasting anesthetic after the administration of 7.5 mg of hyperbaric bupivacaine (Astra, Westborough, MA) and 25 μg of fentanyl (Abbott Laboratories, North Chicago, IL). The patient was a 20-yr-old female of average height and weight who was scheduled to have orthopedic hardware removed from her ankle. With the exception of a mild upper respiratory tract infection, she was otherwise healthy and had no significant past medical history. After all anesthetic options were discussed, the patient decided to be anesthetized with a spinal anesthetic. With the patient in the right lateral decubitus position, the spinal needle placement was performed with a 25-gauge pencil point needle (B. Braun Medical, Bethlehem, PA) via a midline approach. The L3–L4 interspace was used. The spinal agent consisted of 7.5 mg of hyperbaric bupivacaine (Astra, Westborough, MA) with 25 μg of fentanyl (Abbott Laboratories, North Chicago, IL). The injection of the spinal agent was uneventful and cerebrospinal fluid was aspirated before and after the injection. The direction and speed of the injection were not noted. The spinal needle and bupivacaine were obtained from an unexpired custom supplied spinal tray (B. Braun Medical, Bethlehem, PA). The fentanyl (Abbott Laboratories, North Chicago, IL) was preservative free and steriley drawn up immediately before placing the block. The patient was positioned supine and the surgery proceeded as anticipated. The final cephalad level was T11 bilaterally. She remained hemodynamically stable throughout the procedure. At 8 h post-placement, the sensory level (to temperature) of the spinal had regressed approximately 3 dermatomal levels. The patient’s condition was otherwise unremarkable; she had no back or lower extremity pain. The decision was made to observe her overnight. The next morning she began to experience pain at her operative site but still remained unable to void (requiring urinary catheterization). At this time (approximately 15 h post-placement) her dermatomal sensory level (to temperature) had only regressed a total of 5 levels. This, coupled with inability to void, made us concerned about the evolution of a serious neuraxial process. We obtained an emergent neurology consultation as well as a gadolinium enhanced MRI of the lumbar–sacral spine. The MRI ruled out an inflammatory process or compression of the spinal cord. During this evaluation, the patient’s dermatomal level regressed another level. In light of these findings and evidence of a progressively resolving spinal, it was decided to continue observation and provide supportive care as needed (i.e., pain medication or catheterization). By approximately 36 h post-placement, the patient was able to void on her own and had resolution of her motor and sensory blockade. She was discharged later that day. No incontinence of stool was noted during this whole event.

It is tempting to classify this case as a presentation of cauda equina syndrome, transient radicular irritation, or anterior artery spinal syndrome.1–4 Although these events are possible with hyperbaric bupivacaine, they are rare.5–6 They also involve higher doses of bupivacaine than the one used in this case.1–6 In addition, no other confounding variable that make cauda equina or transient radicular irritation more likely (such as advanced age, presence of vascular disease, use of epinephrine, use of hyperbaric lidocaine, lithotomy position, or performance of a knee arthroscopy) were present.1–6

Our findings are interesting for at least two reasons. First, the time it took for the spinal to resolve was exceptionally prolonged. We expected the duration of the anesthetic to be 4 ± 2 h. The duration of the spinal anesthetic presented in this case was approximately 36 h. Second, although the spinal lasted an unusual amount of time, there was no convincing evidence indicating a significant neurologic event such as cauda equina syndrome, transient radicular irritation, epidural hematoma or abscess, or anterior spinal artery syndrome.

We speculate that this presentation could have been the result of low cerebrospinal fluid volume. In a small study by Carpenter et al.,6 they demonstrated that low cerebrospinal fluid volume will cause increased sensory blockade. Unfortunately, this correlation was not true for motor blockade. The resolution of our patient’s motor and sensory blockade were parallel throughout her presentation.

In conclusion, this case demonstrates that spinal bupivacaine can have an exceptionally prolonged effect in the absence of other confounding factors.

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