To the Editor— I have spent some time considering the conclusions reached by Aubrun et al. in their study investigating the relationship between the pain visual analogue scale (VAS) and morphine requirements in the postanesthesia care unit. They demonstrated that the Hill equation could be used to derive a sigmoid relationship between the pain VAS and morphine dosage, and concluded that this relationship is not linear. In their discussion, they referred to an earlier study in which I and colleagues had found a linear relationship between pain intensity and the pain VAS and they seemed to suggest that their study contradicted our earlier results.

The results of the Aubrun et al. study could have been readily predicted from their methodology, in that the Hill equation is a standard approach used to generate a sigmoid curve using population pharmacokinetics. This approach generates a typical dose-response curve. Such a curve could be derived for the dose of a hypotensive drug and blood pressure, or the dose of a sedative drug and hypnotic state. Yet, the effect of interest—be it blood pressure, hypnotic state, or pain intensity—can still be linear phenomena. The results of the study analyzed by the authors do not preclude the possibility that the pain VAS has ratio scale properties and is linear. In fact, if the pain VAS is linear then it would have a sigmoid relationship with morphine dosage.

I have one other concern regarding the conclusions drawn by the authors. In their Methods, they arbitrarily defined “severe pain” as when the patient received a total dose of intravenous morphine greater than 0.15 mg/kg. Because they found an association between an initial VAS score of 70 or greater (VAS70) and morphine dosage greater than 0.15 mg/kg, they concluded that VAS70 was indicative of severe pain. But VAS70 itself may not signify severe pain. Opioid dose-response has substantial interindividual variability, with a five- to tenfold range in requirements. Patients may fail to respond to a specific dose not because they have greater pain intensity but because they have had a lesser response to that dose.

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References


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Although our European counterparts have reported better success with larger doses, even these doses may not be sufficiently large. Evaluation of higher doses (i.e., 5 mg) at 5- to 5-min intervals may demonstrate a better relief profile in most patients. The frequency of adverse events should increase with dose; the anticipated occurrence of these side effects, however, may be exaggerated because of our lack of experience. Clinicians are often too concerned about the respiratory effect of rather small doses of morphine (1–2 mg). In some of our patients undergoing abdominal procedures, tachypnea may have represented intentional defense against pain (to avoid deep breaths). We have noticed a significant drop in respiratory rate to a more normal range after relief of pain in some of these patients.

We continue to believe that postoperative pain is undertreated because of the caregiver’s fear and lack of experience. It has been known for quite some time that a VAS of 70 or 80 should be considered severe pain, and that severe pain requires more morphine for treatment than mild or moderate pain. Although postoperative treatment should be individualized, the safety and efficacy of higher doses of morphine must be determined prospectively in patients with moderate-to-severe postoperative pain.

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References

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In Reply:—We thank our colleagues for their comments and criticisms of our study,1 and we wish to offer the following responses.

First, it is not hard to measure respiratory rate, oxygen saturation, and arterial blood pressure during morphine titration because monitors perform those functions well. Moreover, determination of Ramsay score is also very rapid, because an awake patient who is able to rate his or her visual analog scale (VAS) can be easily quoted 1 on the Ramsay score. Concerning the verbal and subjective behavioral scale used by our nurses, the reader could refer to our recent published study.2 The definition of inadequate analgesia requiring rescue was subjective: the anesthesiologist decided to stop morphine titration and use another analgesic technique, usually when more than 10–15 bolus of morphine were administered.

We do not accept the term “retrospective” used by Larijani and Goldberg. Indeed, the design of our study was clearly defined after a pilot study,3 a special data sheet was implemented (although this data sheet is now that used in routine practice in our unit), and all consecutive patients who fulfilled the criteria for inclusion and did not fulfill the criteria of exclusion were included. Thus, we think that this study was prospective.

We agree with Larijani and Goldberg that we need more information on the relationship between morphine requirement and the type of surgery. The influence of gender is real, but its magnitude seems not to be very important. Last, we previously demonstrated that age does not modify morphine requirement during intravenous morphine titration,4,5 whereas subcutaneous morphine requirement during the initial 24 h is significantly decreased in elderly patients.6 Larijani and Goldberg suggest that higher-bolus doses could be more rapidly efficient. We agree with this hypothesis, but the incidence of adverse outcomes may also increase. Only a randomized study could provide the response, and we have begun such a study.

Larijani and Goldberg report that their patients who had abdominal hysterectomy required a higher dose of morphine. In our study, 35 women underwent abdominal hysterectomy and they actually required 14 ± 8 mg (0.23 ± 0.14 mg/kg) morphine during intravenous titration, indicating that this surgery induced severe postoperative pain requiring a greater dose of morphine. However, comparison of the morphine doses during postoperative intravenous titration must be done cautiously, because the anesthetic regimen during the preoperative period, including the type and dose of opioids administered, may markedly interfere with that dose. The interest of our study is only to provide data from a large population to help to recognize some important relationships between the measurement of pain using VAS and morphine requirements. Further studies are required to precise the

References

(Accepted for publication November 20, 2003.)
Is Overestimation of Bispectral Index in Sedated Intensive Care Unit Patients Only Related to Electromyographic Activity?

To the Editor:—Based on previous research reporting that electromyographic activity has been shown to elevate the bispectral index (BIS) in patients not receiving neuromuscular blockade, Vivien et al. investigated the magnitude of the decrease in BIS value following administration of neuromuscular blocking drugs (NMB) in sedated intensive care unit patients. They concluded that BIS might be lower with paralysis for an equivalent degree of sedation because of high muscular activity. Therefore, Vivien et al. ascribe the BIS value modification only to suppression of muscular activity due to the use of NMB. Nevertheless, the effect of administration of a neuromuscular blocker on BIS and electromyographic activity was highly variable among the 45 patients studied, and in 13 of the 45 patients there was no change in BIS range assessment. These considerations could support the hypothesis that BIS modification may be related not only to muscular activity suppression but also to NMB properties.

NMB are reported to potentiate the effects of anesthetics. Despite the emphasis that all NMB are completely devoid of analgesic properties, some elicit analgesia. Laudanosine, the atracurium and cisatracurium metabolite, elicits dose-dependent analgesia in the mouse, attenuated by coadministration of μ1- and μ2-selective antagonists, indicating a μ-related mechanism for analgesic properties of laudanosine. A cross-tolerance between laudanosine and morphine has also been observed. Moreover, at clinical concentrations reported in cerebrospinal fluid, atracurium and laudanosine are able to activate the central α2β2 nicotinic acetylcholine subtype receptors. Agonists for these receptors showed analgesic activity. Epibatidine, a potent ligand identified at the α2β2 nicotinic acetylcholine receptor subtype, displayed a potent nicotinic activity and a strong nicotinic analgesic effect. Taken together, these data indicate that the coadministration of the NMB atracurium or cisatracurium in sedated patients could potentiate the effects of midazolam and sufentanil sedation, and therefore decrease BIS value. This hypothesis is also consistent with a study reporting that mivacurium, a NMB without analgesic properties, does not alter hypnotic level during propofol anesthesia.

Nevertheless, it is not possible to support or deny the suggested hypothesis; interestingly, the NMB used in the study of Vivien et al. were not reported. A list of NMB administered to the patients could maybe offer an aid, pro or contra.

The clinical relevance is that the modification of BIS detected by Vivien et al. in sedated intensive care unit patients after administration of NMB may be related not only to muscular activity block, as masterfully demonstrated, but also to other cofactors related to NMB or their metabolites’ properties.

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References


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In Reply:—We appreciate the interest of Drs. Fodale and Santamaria in our article examining the decrease in bispectral index (BIS) following the administration of a neuromuscular blocker and would like to reply to their comments. Above all, we must correct a mistake in the letter: The neuromuscular blocker used in our study was clearly reported as 0.5 mg/kg atracurium in every patient studied. Otherwise, we think that the analysis of the authors is simply invalid for several reasons.

First, Peat et al. reported that the prolonged use of atracurium is not associated with excessive accumulation of laudanosine, so long as the renal and hepatic functions are normal. On the other hand, Grigore et al. also reported that laudanosine accumulation may occur in patients with both fulminating hepatic and renal failures, but it is not associated with any measurable central neurologic effect. In our study, we investigated either a single standard dose of atracurium or the beginning of a longterm administration. Therefore, we do not think that we could have observed central neurologic effects due to high concentrations of laudanosine in our patients.

Second, an analgesia-mediated property was described experimentally for laudanosine through a μ1 mechanism and stimulation of the central α2β2 nicotinic acetylcholine receptor. However, BIS is less influenced by analgesic than by sedative drugs, and consecutive BIS change because of laudanosine should have been very limited.

Third, the authors reported in a recent review that data about the evidence of the depressive effects of laudanosine on the central nervous system in humans are not yet available. They also reported that the laudanosine administration would either stimulate the central nervous system or have convulsive effects. Such effects would logically and expectedly result in an increase in BIS values, in contrast to that suggested in the letter from the authors.

Finally, even if a BIS decrease following atracurium administration would have been due to the sedative effect of laudanosine produced after atracurium administration, it seems unlikely that BIS recovery after laudanosine elimination would have been exactly parallel to electromyographic activity recovery after atracurium elimination, as observed in our patients.

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References

Management of Patient Body Temperature Is Challenging

To the Editor.—We thank Gali et al. for their description of what they consider to be a pressure/burn injury following the use of the Allon thermoregulation system.1 Management of patient body temperature and successful maintenance of normothermia in such a procedure is challenging and, as noted by the authors themselves, the patient maintained normothermia and her temperature at the end of the procedure was 36.3°C.

The incidence of pressure ulcers during surgery is well documented in the literature. Overall incidence is around 8%, depending on type of surgical procedure and length of surgery. The incidence rate is positively correlated to the length of the procedure and exceed 13% in procedures lasting longer than 7 h.2–5

As Gali et al. state, this patient had numerous risk factors that predisposed her to pressure-related injury during the operative procedure, including prolonged surgery (6.5 h), advanced age, severe muscle wasting, poor nutritional status, end-stage liver disease, and intraoperative hypotension. We therefore beg to differ with the authors favoring the injury as being primarily due to a burn. This interpretation is based on the surgeon’s impression and on the patient’s postoperative complaint of a burning sensation in the affected area.

It is nearly impossible to differentiate by observation alone whether a skin lesion is due to pressure or a burn, whereas a burning sensation is certainly not specific to burns and can be caused by different kinds of lesions. Moreover, water temperature in the garment is limited to maximum of 40.8°C, so a contact burn due to overheating is virtually impossible.6–7 The Allon system itself was checked and found to be functioning properly.

In anticipated long-duration procedures and in chronically ill, high-risk patients, the usual precautions of meticulous attention to adequate relief of pressure points should be followed. MTRE’s user’s manual and leaflet guidelines specifically recommend the use of protective means for pressure sores between the operating table and the ThermoWrap. Furthermore, using ThermoWrap reduces the risk of developing such skin lesions because the Allon system is equipped with a unique pressure relief algorithm, the purpose of which is to address the known phenomena of intraoperative pressure ulcers.

MTRE’s main goal is to provide normothermia in anesthetized patients with maximal patient safety. Despite our excellent track record (< 0.5% reported skin injury out of ≥ 10,000 procedures), MTRE is continuously looking into new concepts, materials, and wraps that will improve patient safety even more.

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References

7. Stewart TP, Magnano SJ: Burns or pressure ulcers in the surgical patient? Decubitus 1988; 1:36–40

In Reply.—A 13% incidence of pressure sores quoted by Dr. Sharon is much higher than we see in our liver transplant population. In the past 8 yr, this is the only case of skin injury documented in our liver transplant patients. The skin injury that our patient developed had the imprint of the water-warming device on it, removing any doubt that the warmer was involved in the injury. The occurrence of this injury despite proper placement and functioning of the device suggests that adjustments to the Allon system may be necessary.

It is true that our patient had risk factors predisposing her to skin injury, but we were concerned about temperature maintenance because of these factors. If she had been healthy and well nourished, she would have been less likely to need a device to help maintain her body temperature. With regard to the pressure relief algorithm, the only information that we could find is one unpublished trial of three patients, which revealed pressures of up to 200 mmHg (measurement limited because of 200 mmHg as the maximum range of calibration).

Although the Allon system may help maintain normothermia, it may do so at some risk to patient well-being.


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The Perioperative Use of Cyclooxygenase-2 Selective Nonsteroidal Antiinflammatory Drugs May Offer a Safer Alternative

To the Editor—We read with interest the excellent review article of randomized, controlled trials involving the effects of nonsteroidal antiinflammatory drugs (NSAIDs) on bleeding after tonsillectomy. Although the results of this meta-analysis suggest that the use of NSAID therapy after tonsillectomy should be abandoned both at the hospital and at home, we must remind the readers that the perioperative use of cyclooxygenase (COX)-2 selective NSAIDs may offer a safer alternative in the management of posttonsillectomy pain. Previous data have suggested that celecoxib, rofecoxib, and valdecoxib have analgesic effects similar to conventional NSAIDs when used for acute pain. Further, because platelets express only COX-1 and are incapable of expressing COX-2, selective COX-2 inhibitors do not inhibit platelet function. We have found that the perioperative administration of rofecoxib possesses a more favorable pharmacokinetic profile than the other COX-2 selective NSAIDs in the management of pediatric tonsillectomy pain. Rofecoxib provides onset of clinical analgesia within 27 min and has an elimination half-life of 17.5 h; therefore, it can be administered once daily. Rofecoxib is available as a strawberry-flavored oral suspension (containing 12.5 mg or 25 mg of rofecoxib per 5-ml solution), which makes pediatric dose titration easy to accomplish.

We recently evaluated the analgesic efficacy and safety of administering rofecoxib (1 mg/kg) prior to pediatric tonsillectomy. This study revealed no significant increase in measured intraoperative surgical bleeding or in the likelihood of reoperation for bleeding. Furthermore, the perioperative administration of rofecoxib resulted in a significant decrease in postoperative pain and more than a threefold reduction in the incidence of postoperative nausea and vomiting. The reduction in postoperative nausea and vomiting may be attributable to either the improved analgesic efficacy of rofecoxib or to its centrally mediated action. It has been demonstrated in an animal model that activation of the medullary vomiting center involves prostaglandins, and the preemptive administration of COX inhibitors significantly decreased lipopolysaccharide-induced emesis. NSAIDs with significant penetration into the central nervous system may be advantageous in reducing postoperative nausea and vomiting. Previous studies in rats have revealed that 35% of rofecoxib plasma concentrations penetrated into the cerebrospinal fluid; this relative penetration into the central nervous system was independent of dose (< 150 mg/day).

Therefore, we believe the perioperative administration of rofecoxib, a selective COX-2 inhibitor, may offer significant advantages over conventional NSAIDs in the management of tonsillectomy pain.

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References

Effects of Postoperative Nonsteroidal Antiinflammatory Drugs on Bleeding Risk after Tonsillectomy

To the Editor—As stated by Marret et al., posttonsillectomy hemorrhage (PTh) can be life-threatening, and an incidence of perhaps 4.5% per year in the United States with a reoperation rate of 1–5.5% is not insignificant, particularly when associated with concerns surrounding the administration of general anesthesia under such circumstances. Nonsteroidal antiinflammatory drugs (NSAIDs) are, however, now widely used not only in the operating room and ward but also at home, and they are widely believed to be safe and effective. Unfortunately, Marret et al. considered just seven investigations that satisfied their chosen criteria, none of which in fact reported a significant difference between the groups studied. Simply combining the results of these into a single analysis to create the reported result does not provide an adequate answer to the concerns expressed. In addition, anesthesiologists are aware that the chosen operative technique, together with the skill and experience of the operating surgeon, can be of significant importance. The total number of patients in the seven studies is small, but there is marked variability, including the NSAID chosen, the number of doses administered, the surgery undertaken, and whether a primary or secondary hemorrhage occurred. An additional qualifying study was not included.

In 1984, Carrick reported the potential adverse consequence of increased risk by salicylate administration on platelet function when PTh occurred in 1 of 350 patients versus just 1 of 355 patients receiving acetaminophen. NSAIDs, including aspirin (acetylsalicylic acid), inhibit platelet cyclooxygenase and prolong bleeding time by preventing the biosynthesis of thromboxane A₂, leading to reduced platelet aggregation. NSAIDs are very widely used, and because they are available without prescription many patients take them perioperatively. To overcome this problem, the New York Eye and Ear Infirmary has instructed patients not to use aspirin or products containing aspirin, as well as other NSAIDs, for at least 7 to 10 days before and after surgery. This, as well as the standard of specialist medical care, is...
To the Editor:—Marret et al. provided a meta-analysis of nonsteroidal antiinflammatory drugs (NSAIDs) and bleeding risk after tonsillectomy using return to the operating room as their primary endpoint.1 The authors carefully reviewed the literature and selected seven articles for inclusion.2-8 We are concerned that the conclusions reached are invalid and that the wording in the current Marret et al. article1 provides fodder for lawyers without adequate scientific knowledge to support these admonitions.

The authors have combined repeated single-dose intramuscular administration, continuous infusion, and chronic administration of

### Table 1. Patients Undergoing Tonsillectomy at Glan Clwyd Hospital

<table>
<thead>
<tr>
<th>Year</th>
<th>Patients (No.)</th>
<th>PTH</th>
<th>NSAID</th>
<th>Senior Surgeon (%)</th>
<th>Senior Anesthetist (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1991</td>
<td>596</td>
<td>0</td>
<td>0</td>
<td>91</td>
<td>28.5</td>
</tr>
<tr>
<td>1992</td>
<td>637</td>
<td>4</td>
<td>0.6</td>
<td>136</td>
<td>38.8</td>
</tr>
<tr>
<td>1993</td>
<td>510</td>
<td>4</td>
<td>0.8</td>
<td>92</td>
<td>32.4</td>
</tr>
<tr>
<td>1994</td>
<td>545</td>
<td>2</td>
<td>0.4</td>
<td>97</td>
<td>21.5</td>
</tr>
<tr>
<td>1995</td>
<td>573</td>
<td>2</td>
<td>0.4</td>
<td>143</td>
<td>17.1</td>
</tr>
<tr>
<td>1996</td>
<td>572</td>
<td>6</td>
<td>1.0</td>
<td>104</td>
<td>22.7</td>
</tr>
<tr>
<td>1997</td>
<td>519</td>
<td>5</td>
<td>1.0</td>
<td>166</td>
<td>19.1</td>
</tr>
<tr>
<td>1998</td>
<td>526</td>
<td>2</td>
<td>0.4</td>
<td>221</td>
<td>17.7</td>
</tr>
<tr>
<td>1999</td>
<td>456</td>
<td>5</td>
<td>1.1</td>
<td>384</td>
<td>40.1</td>
</tr>
<tr>
<td>2000</td>
<td>451</td>
<td>5</td>
<td>1.1</td>
<td>262</td>
<td>54.7</td>
</tr>
<tr>
<td>2001</td>
<td>313</td>
<td>9</td>
<td>2.9</td>
<td>181</td>
<td>28.8</td>
</tr>
<tr>
<td>2002</td>
<td>151</td>
<td>2</td>
<td>1.3</td>
<td>110</td>
<td>41.1</td>
</tr>
</tbody>
</table>

Senior surgeon and senior anesthetist are trained and experienced specialists. NSAID = nonsteroidal antiinflammatory drug administered intraoperatively; PTH = posttonsillectomy hemorrhage requiring reoperation.
Table 1. Bleeding Leading to Reoperation

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Bleeding Control</th>
<th>&lt; 24 h NSAIDs</th>
<th>Bleeding Control</th>
<th>&gt; 24 h NSAIDs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bailey3</td>
<td>Ketonolac IM × 24 h (adults)</td>
<td>0/43</td>
<td>0/37</td>
<td>1/43</td>
</tr>
<tr>
<td>Gunter5</td>
<td>Ketonolac IV × 1 dose</td>
<td>0/47</td>
<td>1/49</td>
<td>0/47</td>
</tr>
<tr>
<td>Harley8</td>
<td>Ibuprofen × 2 wk</td>
<td>0/11</td>
<td>0/16</td>
<td>0/11</td>
</tr>
<tr>
<td>Ramsing4</td>
<td>Ketonolac IV × 1 dose</td>
<td>0/15</td>
<td>1/15†</td>
<td>Unknown</td>
</tr>
<tr>
<td>St. Charles7</td>
<td>Ibuprofen × 2 wk</td>
<td>0/55</td>
<td>1/55†</td>
<td>Unknown</td>
</tr>
<tr>
<td>Solanen14</td>
<td>Ketonolac × 24 h; infusion × 24 h (adults)</td>
<td>0/25</td>
<td>1/40</td>
<td>Unknown</td>
</tr>
<tr>
<td>Sutters6</td>
<td>Ketonolac IM × 1 dose</td>
<td>0/42</td>
<td>0/45</td>
<td>0/42</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>0/198</td>
<td>4/257§</td>
<td>1/198</td>
</tr>
</tbody>
</table>

Date are expressed as numbers.

* Time not described: the first 15 patients were not included because five hemorrhages were attributed to poor surgical technique. † Patient returned to the operating room because of lack of cooperation. ‡ Likely that bleeding occurred more than 24 h after surgery. § chi-square $\chi^2 = 0.209$ (underpowered with $\alpha < 0.8$).

IM = intramuscularly; IV = intravenously; NSAID = nonsteroidal antiinflammatory drug.

NSAIDs. Unlike aspirin, the effects of most NSAIDs on platelet function are very short-lived. For pediatric patients, the half-lives of ketorolac and ibuprofen are approximately 2 h and 1.5 h, respectively.6,10

Because significant effects on platelet function are reversible and related in part to a blood concentration of NSAIDs, virtually no antiplatelet effect would be present after 5 to 6 drug half-lives. Therefore, any bleeding attributable to single doses of these medications would have to occur in the immediate postoperative period, and certainly within the first 24 h.11,12

Hemorrhage that occurs after 24 h is unlikely to be caused by these medications unless they are administered after hospital discharge; we do not know if this is different with infusions or intramuscular administration.

When examining the duration of treatment (table 1 of the Marret et al. review), studies by St. Charles7 and Harley and Dattolo8 involved patients who received treatment for 2 weeks. Both patients who had bleeding in the Harley and Dattolo study did so 2 to 7 days after the operation, so it is possible that their bleeding could be attributed either to the continued use of the NSAIDs or to the loss of eschar (table 1); clearly, there are insufficient numbers for analysis. Regarding single-dose administration of ketorolac, in our experience, a single dose after the operation is completed and after hemostasis is obtained has not been associated with an increased incidence of bleeding.6,13,14

Marret et al. mentioned our article to describe the general incidence of bleeding, but they did not comment on the fact that the incidence of bleeding in our retrospective review of more than 300 children having a tonsillectomy did not reveal a higher incidence of hemorrhage, even though they had received ketorolac. In the Marret et al. analysis, the incidence of bleeding within the first 24 h after a single dose of ketorolac was 2 of 109 patients receiving ketorolac versus 0 of 104 controls (table 1). Again, this cohort is too small for adequate analysis.

The risk of 1 in 29 patients having hemorrhage after NSAIDs therapy as described by Marret et al. is a gross overstatement. At least two bleeding events were attributed to surgical technique, whereas five others occurred at a time well after the drug had been eliminated from the body. Therefore, antiplatelet effect caused by that NSAID drug was no longer present. Using the data presented comparing 0 of 198 controls versus 4 of 257 patients receiving NSAIDs with bleeding less than 24 h after surgery, including one patient who returned to the operating room because of lack of cooperation, the rate of bleeding is statistically insignificant ($\chi^2 = 0.209$ chi-square). A crude power analysis suggests that to demonstrate a difference with these frequencies, more than 4,000 patients would need to be studied ($\alpha = 0.05$, with power of 0.8) to demonstrate a difference in treatment groups.

We suggest that Marret et al. reexamine their data, taking into consideration the effect of the drug’s half-life on platelet function. Elimination of cases in which the hemorrhage occurred beyond the period when the drug could have had antiplatelet effects, in which patients returned to the operating room because of poor surgical technique or lack of cooperation, and in which patients received the ibuprofen chronically (their bleeding could be attributable to either loss of eschar or antiplatelet effects), would allow the authors to make more accurate recommendations. We certainly acknowledge that ketorolac can cause hemorrhage if administered preoperatively or intraoperatively before hemostasis is completed, but we believe that it is a very safe analgesic when administered as a single dose after hemostasis is obtained.

Anesthesiology. V 100, No 3, Mar 2004
References

In Reply.—We appreciate the three comments concerning our meta-analysis on the risk of nonsteroidal antiinflammatory drugs (NSAIDs) after tonsillectomy. Drs. Dsida and Coté suggest excluding patients who had bleeding 24 h after tonsillectomy and who received NSAIDs for less than 24 h, or patients with bleeding induced by lack of cooperation and poor surgical technique. Under these criteria, more than half of the cases of reinvention published in the original articles would be excluded. Moreover, Dsida and Coté cite one controlled, double-blind, randomized trial that studied NSAIDs given within 24 h postoperatively. This study reports two children in the postoperative ketoprofen group (n = 42) who required electrocautery to stop their bleeding. In contrast, none of children in the placebo group (n = 20) returned to the operating room. Including this study in the analysis proposed by Dsida and Coté (table 1) leads to a statistically significant risk of primary hemorrhage (0 of 218 in the control group vs. 6 of 299 in the NSAIDs group; P = 0.04, Fisher exact test). We performed an intention-to-treat analysis based on the original data. Consequently, all patients included in the study were analyzed according to the groups to which they were originally randomly assigned, whatever the duration of treatment or the cooperation of the patient or surgeon. The intention-to-treat approach maintains a comparable distribution of established groups of patients that are similar apart from the randomized factor. Excluding randomized patients after their inclusion in the trial may lead to bias due to a modification of allocation. All of the trials included in our meta-analysis were randomized. Therefore, in our meta-analysis the distribution of patients was similar between the different groups except for the use of NSAIDs. When Drs. Dsida and Coté claim that NSAIDs have no effect, it means that the risk of bleeding should be similar whatever the NSAID dose, duration of treatment, or name of the surgeon. Moreover, they cannot deny that short-term administration of NSAIDs may have long-term consequences. NSAIDs inhibit cyclooxygenase, resulting in an inhibition of platelet aggregation. Thus, NSAIDs given immediately in the postoperative period may increase the importance of hemosta induced by the tonsil dissection. The eschar situated in the soft tissue near the tonsillar bed may be more important with the use of NSAIDs than with a control treatment and may explain secondary bleeding related to the loss of eschar of tonsillar fossa. The postoperative administration of NSAIDs, whatever the duration of treatment, may consequently increase the risk of early and late reoperation. Excluding patients who had later bleeding after a single dose of NSAIDs may underestimate the effect of NSAIDs on bleeding in the final analysis. In one of the studies, Dsida and Coté also suggested the exclusion patients who were operated on by the same surgeon and who were especially at risk for complications. However, the same surgeon also operated on other randomized patients. This seems to be an unacceptable handling of the data that may introduce some bias into the analysis. Excluding cases is contrary to the principle of intention-to-treat. The exclusion of patients in randomized controlled trials has been recognized as an overestimation of the benefit of treatment in comparison with the intention-to-treat analysis, based on the submitted data. Similarly, the exclusion of patients who experienced adverse effects such as hemorrhage may underestimate the risk of NSAIDs use after a tonsillectomy.

Drs. Lake and Khater report a retrospective cohort of patients scheduled for tonsillectomy at Glan Clwyd Hospital between 1991 and 2002. Interestingly, their data document a clear increase in the incidence of reoperation after tonsillectomy related to the increased number of patient who used NSAIDs. When NSAIDs were administrated to less than half of the patients (from 1991 to 1998), the incidence of reoperation was less than 1%. In contrast, the incidence was greater than 1% during the past 4 yr, and as high as 2.9% in 2001 when NSAIDs were used in more than 50% of the patients. Lake and Khater also advocated that NSAIDs decrease the incidence of postoperative nausea and vomiting. Although this is a reasonable assertion, alternative treatments devoid of effect on hemostasis may be more appropriate in this setting. In fact, other treatments such as ondansetron or dexamethasone reduce postoperative nausea and vomiting and postoperative pain. Physicians also have cyclooxygenase-2 inhibitors to relieve postoperative pain and prevent postoperative nausea and vomiting, as suggested by Joshi et al. We agree that selective inhibitors of cyclooxygenase could be an interesting alternative because of their lack of effect on platelet aggregation. In contrast, anesthesiologists do not have such pharmacologic alternatives to stop bleeding after a tonsillectomy.

Dsida and Coté and Lake and Khater point out a randomized, double-blind, controlled trial that compared postoperative NSAIDs analgesia with preoperative NSAIDs or placebo, published in 2002 after the completion of our own research in 2001. In this trial, two children in the postoperative NSAIDs group returned to the operating room because of postoperative bleeding. We updated our meta-analysis to include the result of this last study. A significant increase in reoperation
To the Editor.—Boyce and Peters1 describe the interesting case of complete vasomotor collapse during resection of a recurrent right carotid body tumor involving the right carotid bifurcation requiring excision and autologous vein grafting. The authors suggest mechanical or electrical stimulation of the right carotid sinus nerve as the initiating event leading to vasomotor collapse. Rarely, however, does a significant increase in afferent activity from a single baroreceptor site result in the described persistent profound hypotension because of compensation from other baroreceptor sites, even in the absence of a right vagus nerve.

Alternatively, if in this patient the tumor had infiltrated the right carotid sinus wall such that no deformation (strain) of the baroreceptors could take place as can occur in severe carotid atherosclerosis, then there would be no afferent neural input to the hindbrain from this site. Under these circumstances, the vasomotor integration centers in the hindbrain would not recognize zero input from the right carotid sinus as a legitimate null signal, particularly in the presence of normal afferent signals from other baroreceptor sites. Subsequently, sudden significant afferent activity in the right carotid sinus nerve, either from exogenous deformation of the sinus wall or direct stimulation, would probably be interpreted as a very significant signal by the hindbrain because of the neural history from this site, resulting in the reported dramatic decrease in blood pressure. A similar phenomenon is occasionally seen during carotid endarterectomy when severe atherosclerotic plaque is suddenly removed from the carotid sinus area.2,3

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References


( Accepted for publication September 23, 2003.)
To the Editor—Most of the preventable incidents in anesthesia practice involve human error, with breathing circuit disconnections featuring prominently. Overt equipment failures constitute a small proportion of preventable incidents, but equipment design is contributory in many categories of human error.1-4 We herein report a case of a breathing circuit obstruction resulting from failure to completely remove the transparent packaging.

A 36-yr-old, 185-cm, 86-kg healthy man with no history of previous anesthesia underwent uneventful induction of general anesthesia for endoscopic sinus surgery conducted in a standard manner with midazolam, fentanyl, propofol, and vecuronium. Tracheal intubation was accomplished with an 8.0-mm-ID oral cuffed endotracheal tube. Proper endotracheal tube placement was confirmed by auscultation of bilateral breath sounds and end-tidal carbon dioxide. Endotracheal tube depth was confirmed and secured. At the request of the surgeon, the breathing circuit was briefly disconnected and the table was rotated 180 degrees. The existing 90-degree gas sampling connector was removed, and a straight gas sampling connector (SIMS Portex, Inc., Fort Myers, FL) was removed from its plastic packaging and placed in-line. Chest excursion immediately ceased and the ventilator failed to cycle. Hand ventilation with the anesthesia machine was attempted and failed. An Oxygen E-Cylinder with a Mapleson circuit (Vital Signs, Totowa, NJ) was used to ventilate the patient without difficulty with intravenous propofol infusion to maintain anesthesia. Auscultation of the chest revealed normal breath sounds. Careful inspection of the breathing circuit revealed a taut, transparent diaphragm of plastic packaging obstructing the straight connector at its interface with the breathing circuit (fig. 1). The clinician's thumb had inadvertently retained this transparent obstruction on removal from its packaging. Following removal of the obstruction, the circuit was reconnected and the case proceeded uneventfully.

In summary, we suggest that as an additional measure of safety, packaging for airway components be considered both for its visibility and potential for airway circuit obstruction (fig. 2). We contacted the manufacturer (Portex, Inc., Keene, NH) and MEDWATCH (the U.S. Food and Drug Administration Safety Information and Adverse Event Reporting Program) to alert them of our experience.

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References

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Fig. 1. Straight gas sampling connector (SIMS Portex) with plastic packaging forming an obstructive membrane.

Fig. 2. Straight gas sampling connector (SIMS Portex) in its original plastic packaging.
Revenue Gain for Academic Anesthesiology Departments if the Centers for Medicare and Medicaid Services Provide Full Reimbursement to Teaching Physicians

Table 1. Impact of Teaching Rules on Academic Anesthesiology Departments

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases (No.)</td>
<td>2,549</td>
<td>7,096</td>
</tr>
<tr>
<td>Total ASA units billed (No.)</td>
<td>40,600</td>
<td>124,100</td>
</tr>
<tr>
<td>Total allowable</td>
<td>$700,000</td>
<td>$2,140,000</td>
</tr>
<tr>
<td>50% not paid because of faculty supervision of resident care at 1:2 ratio</td>
<td>$350,000</td>
<td>$1,070,000</td>
</tr>
<tr>
<td>Revenue lost per case</td>
<td>$137</td>
<td>$151</td>
</tr>
</tbody>
</table>

Medicare cases billed in 1996 by two different academic anesthesiology departments; allowable calculated using the 2003 Galveston, Texas, conversion factor ($17.23). Estimates are based on the assumption that all cases would be performed using the staffing model of one teaching anesthesiologist to two residents. This information is based on data from a previous study by Abouleish et al.²

ASA = American Society of Anesthesiologists.

References

To the Editor: —Following the 1996 publication of new rules regarding payment to teaching physicians, the Centers for Medicare and Medicaid Services (then known as the Health Care Financing Administration) reduced by 50% the payments made to teaching anesthesiologists for medical direction of residents at a ratio of one faculty member to two residents. After 1996, the Centers for Medicare and Medicaid Services paid 100% of allowable charges to a teaching anesthesiologist only when the physician either personally performed the care or medically directed only one resident. Because resident care could not be billed to the Centers for Medicare and Medicaid Services, this change in the teaching rules resulted in a significant reduction in payments to academic anesthesiology groups.¹ Recently, the Centers for Medicare and Medicaid Services were asked to reexamine these teaching rules by both anesthesiology societies and Senator Hillary Clinton (written communication to Mr. Thomas Scully, April 2003).

Using data from a previously published study,² we examined the potential financial impact that a change to full reimbursement would have on two of the four academic anesthesiology groups examined in that investigation (the database for the other two groups did not identify Medicare and other payers). Groups A and D (as designated in the previous study) provided care to 2,549 and 7,096 Medicare beneficiaries undergoing surgery during the 1-yr study period. For purposes of analysis, we used the conversion factor for the Galveston, Texas, area ($17.23) and assumed that all anesthetic procedures were performed by anesthesiologists supervising residents at a 1:2 ratio.³ We calculated that the annual revenue lost by the current rules, versus the pre-1996 rules, was $550,000 for group A and $1,070,000 for group D (table 1). The estimated lost revenue per case was similar between the two groups ($157 and $150 for groups A and D, respectively).

If the previous rules for full payment (which are similar to the current rules applied to other medical specialties) were applied, the increase in revenue would help academic anesthesiology departments successfully meet their economic challenges.

Support was provided solely from institutional and/or departmental sources.

Deviation of the Cauda Equina by Changing Position

To the Editor:—We have obtained interesting information about spinal puncture using magnetic resonance imaging. It is important to understand the anatomy of the cauda equina when performing spinal anesthesia. Previous studies using computed tomography or magnetic resonance imaging have shown that in the supine position, the cauda equina lies symmetrically in the dorsal subarachnoid space.¹—³ However, a patient is usually placed in the lateral decubitus position during spinal puncture. Thus, it is necessary to obtain detailed anatomic information about the cauda equina in the lateral decubitus position. Magnetic resonance imaging reveals interesting and important information about the anatomy of the cauda equina. In seven healthy volunteers, axial views of magnetic resonance imaging of the cauda equina during both the supine and left lateral decubitus positions were obtained and compared. In all subjects, a movement of the cauda equina was observed by changing position. The cauda equina lay symmetrically at the dorsal side of the subarachnoid space when the patient is in the supine position (fig. 1A). However, it moved to the left side of the subarachnoid space when the patient was placed in the left lateral decubitus position (fig. 1B). Our observations are similar to those that Fink et al. reported in an abstract at the 1993 Annual Meeting of the American Society of Anesthesiologists (published in ANESTHESIOLOGY 1993; 79:A288). These results suggest that the cauda equina has considerable mobility in the cerebrospinal fluid. During the lateral decubitus position, it may dynamically move to the gravity-dependent side. This phenomenon may alter our thought on spinal anesthesia. First, we should care about cauda equina syndrome. If a spinal needle is inserted downward in the lateral decubitus position, it may increase the possibility of injury to the cauda equina. Second, it is necessary to consider the specific gravity of local anesthetics for spinal anesthesia. Differences in anesthetic effects between hyperbaric and
To the Editor—New anesthesia machines incorporate novel designs of familiar components to provide additional functionality. The current literature and the U.S. Food and Drug Administration’s MAUDE database* contain periodic reports of difficulties in operating this modern equipment.1,2 The onus is on anesthesiologists to remain vigilant to possible new problems with this equipment and to new manifestations of old problems.3 We recently experienced a condition in which the design of the Drager Fabius GS (Draeger Medical Inc., Telford, PA) anesthesia machine’s breathing circuit exposed a loss of redundancy that was heretofore present in anesthesia machines.

After induction of anesthesia, mechanical ventilation and 2% desflurane in nitrous oxide/oxygen were provided with a Drager Fabius GS anesthesia machine. Set gas flows were 2 l/min of nitrous oxide and 1 l/min of oxygen. The anesthesia machine had been completely checked according to the manufacturer’s directions immediately before the case. This included leak tests of the circuit, breathing bag, and ventilator, all of which showed satisfactory results. Immediately after induction, we realized that the patient was latex-allergic and replaced the anesthesia machine with a nonlatex bag. A few minutes later, we noted that the breathing circuit was empty. This is never a normal condition with the Fabius GS, as this machine has a piston ventilator and uses the breathing bag as the gas reservoir during mechanical ventilation.3 A scan of the monitors revealed that the circuit gas sampled by the gas analyzer at the Y piece contained 23% oxygen, 52% nitrous oxide, and 1.3% desflurane, all lower than the machine was set to deliver (fig. 1). The oxygen sensor on the machine also showed that less oxygen was being delivered than the machine was set for. We inferred that the machine was entraining room air, as it is designed to do under conditions of insufficient fresh gas flow, but this appeared to be inconsistent with the Y flows set on the machine, and we immediately suspected a breathing circuit leak. We disconnected the patient from the anesthesia machine, switched to manual ventilation mode, closed the adjustable pressure-limiting valve, and attempted to pressurize the circuit. This revealed a large hole hidden in the folds of the nonlatex breathing bag. The breathing bag was quickly replaced, the circuit was successfully pressure-tested, and mechanical ventilation and delivery of anesthetics were resumed. Thereafter, gas monitor values were consistent with machine settings. Afterwards, the patient denied recall of intraoperative events.

This is not the first report of a sudden inability to pressurize the breathing circuit of the Fabius GS. In 2002, several reports were made to the Food and Drug Administration of an inability to pressurize the breathing circuit, sometimes after successfully completing a leak test. This problem was traced by Drager’s engineers to a small change in a proven design, and the problem has been definitively addressed.

The Drager Fabius GS uses a piston-driven ventilator, and the piston is not the breathing circuit gas reservoir. Instead, the breathing bag


References

Fig. 1. Anesthesia machine settings during the event described. Inset shows contemporaneous gas analyzer readings. The difference was due to room air entrained through a large hole in the breathing bag.
serves as the reservoir during both mechanical and manual ventilation. Breathing bag failure compromised the function of our anesthesia machine in both ventilation modes: the inability to pressurize the circuit in manual mode and decreased oxygen and anesthetic concentrations in mechanical mode.

Our failure was not so catastrophic that the patient could not be ventilated (at least mechanically), and it had nothing to do with the anesthesia machine itself. Adequate mechanical ventilation continued throughout the event. However, the anesthesia machine entrained room air presumably freely through the hole in the breathing bag. This path of air entrainment explains another important feature of this event: no alarms sounded to alert clinicians of the failure.

The Fabius GS has a ‘low fresh gas flow’ alarm to alert users that insufficient gas is entering the circuit to make up for removal due to uptake and leaks. With inadequate fresh gas flow, the piston empties the breathing bag and then room air is entrained into the piston chamber so that the ventilator delivers the set tidal volume. A small negative pressure is generated when the ventilator attempts to draw from an empty breathing bag, triggering the alarm. In our case, the circuit was always in continuity with the atmosphere because of the large hole in the breathing bag, no negative pressure was developed, and no alarms sounded, but room air was entrained. Instead, we detected and corrected a massive circuit leak (induced after machine checkout) by observation of a constellation of inconsistencies. Despite improved alarm systems, previously secondary monitors such as agent analyzers are sometimes the only alerts to impending failures (in this case, awareness).4

Relative to older designs, subtle changes in the external operation of the Fabius GS conceal radical internal changes that both add functionality and completely alter its response to failure conditions. The use of a piston ventilator with room air entrainment as a backup gas source is safe because it ensures adequate ventilation. However, this design could lead to awareness5 without the use of agent analysis or some measure of anesthetic depth, and is also of concern when considering the use of the machine to care for patients on high inspired oxygen concentrations.

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References

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In Reply—The letter by Sandberg and Kaiser describes the entrainment of room air through a hole in a reservoir bag placed on a Fabius GS anesthesia machine (Draeger Medical Inc., Telford, PA) after the machine check had been completed. Before any adverse event could occur, the problem was identified by noting that the reservoir bag was not filling with gas during mechanical ventilation and that the concentrations of oxygen and anesthetic in the circuit were less than the concentrations set to be delivered by the machine. This report underscores several important issues concerning the safe use of not only a new design of an anesthesia machine like that of the Fabius GS but also of all anesthesia machines.

Machine checkout is a fundamental aspect of the strategy to use any anesthesia machine safely. Having confirmed proper functioning of the anesthesia machine prior to induction, Sandberg and Kaiser made an appropriate decision to avoid exposing the latexallergic patient to latex by changing to a bag that did not contain latex. Because the procedure was already under way when the bag was changed, they did not have an opportunity to repeat the machine checkout, which would have identified a leak in the system. Once the preuse checkout is completed, changing or disconnecting any components of the circuit should be avoided unless the checkout can be repeated prior to use.

Another important point is the value of training users to understand the proper functioning of the anesthesia machine. The Fabius GS is designed with the reservoir bag as part of the circuit during mechanical ventilation so that fresh gas can accumulate in the bag during inspiration. The intent of this design is to improve the accuracy and consistency of tidal volume delivery by eliminating the interaction between fresh gas flow and tidal volume characteristic of a traditional anesthesia machine design. The authors had been trained to understand that the reservoir bag on the Fabius GS is an indicator of adequate fresh gas flow, just as the bellows is on a traditional anesthesia machine. After the reservoir bag was changed they continued with mechanical ventilation, but they quickly recognized that a problem existed when the reservoir bag did not fill. User training has become especially important with the development of new anesthesia machine designs, because indicators of proper functioning are different from traditional machine technology.

The importance of monitoring technology to patient safety has been emphasized repeatedly in the literature, and this report is just one more example. Indeed, observation of oxygen and anesthetic vapor concentrations led Sandberg and Kaiser to suspect that air was entering the breathing circuit. No matter how advanced anesthesia delivery systems become, monitoring the concentration of gases and vapors delivered to the patient will remain fundamental to confirming that the patient is receiving what the anesthesia provider intends to deliver.

To understand how the Fabius GS design facilitated the identification of the hole in the reservoir bag, it is useful to speculate about the implications of a similar situation when using a traditional anesthesia machine design. On a traditional anesthesia machine, the reservoir bag is excluded from the breathing circuit during mechanical ventilation. Had the bag been changed after induction and the start of mechanical ventilation on a traditional anesthesia machine, the hole in the bag might not have been recognized until the end of the procedure, when manual positive pressure ventilation was needed to facilitate emergence. The Fabius GS design likely led to an earlier recognition of the problem, because the bag did not fill with gas as expected immediately after it was changed.


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