Improved Statistical Methods for Quantal Assay

To the Editor.—This letter will argue that a recent report in Anesthesiology would have been improved by different statistical methods; this letter is not a criticism of other research methods in the report. Ginosar et al.1 reported a dose–response study of intrathecal hyperbaric bupivacaine (with intradural opioid) administered for cesarean delivery in patients having a combined spinal–epidural technique. Seven groups of parturients—six patients per group—were randomly assigned to linearly spaced doses of bupivacaine (6, 7, 8, 9, 10, 11, or 12 mg). Success of the block (binary yes/no) was declared at 10 min after administration if a bilateral T6 pinprick sensory level existed (successinduction); successoperation was recorded if surgery proceeded without administration of any supplemental epidural local anesthetics. The observed response rates with increasing dose were successinduction (5/6, 2/6, 6/6, 6/6, 6/6, 6/6) and successoperation (5/6, 2/6, 4/6, 3/6, 6/6, 6/6, 6/6). Ginosar et al. used a version of the Hill equation (also known as the quantal sigmoid Emax model) to relate probability of success to dose of bupivacaine with two parameters, γ and dose50:

\[
\text{Probability(success } = \text{ yes)} = \frac{\text{dose}^\gamma}{\text{dose}^{\gamma} + \text{dose}^\gamma}.
\]

This was further described as logistic regression analysis of naive-pooled data (one observation per patient) using Laplacian estimation routines of NONMEM (version V) statistical software (NONMEM Project Group, University of California, San Francisco, CA). Estimates of ED50 with SEs were reported for successinduction (6.7 ± 0.6 mg) and successoperation (7.6 ± 0.4 mg); point estimates of ED50 without standard errors were also reported (11.0 and 11.2 mg, respectively).

The community of statisticians has produced an extensive repertory of methods for the analysis of quantal response data.2 It is usually assumed that each individual of the relevant population has a dose tolerance or threshold for the particular substance being tested; a descriptive model characterizes the distribution of tolerances. It is possible, but not necessary, to use a logarithmic dose transformation. Assuming large sample properties, sigmoidicity, symmetry, and homoscedasticity, the most common simple model is called the logit or logistic regression:

\[
\text{Probability(success } = \text{ yes)} = \frac{1}{\exp(\alpha + \beta \ln(\text{dose}) + 1) + 1} \Rightarrow \gamma
\]

where α and β are location and scale parameters. Further, assuming a logistic probability density function, maximum likelihood estimation routines for α and β by iteratively reweighted linear regression are available in most statistical software packages; using the δ method, EDx with standard errors may be estimated for any x (0 < x < 100). The ED50 represents the median value of the distribution of tolerances in the population. Counts for success and failure being available in their figure 1, the data of Ginosar et al.1 can be reanalyzed assuming linear spacing of doses. Using the open software R statistical computing and graphics package4 (version 1.8.1) with the base and MASS libraries, the estimates for successinduction are ED50 (6.5 ± 0.4 mg) and ED50 (8.6 ± 0.7 mg); the estimates for successoperation are ED50 (7.7 ± 0.4 mg) and ED50 (10.6 ± 0.9 mg). The poor precision of the ED50 estimates is apparent; the 95% confidence interval for successinduction is 7.2–10.0 mg and for successoperation is 8.8–12.4 mg.

Objections to the statistical methods can be briefly summarized. First, the Hill equation originated in studies of multiple ligand binding to allosteric proteins, in particular hemoglobin, the exponent γ (a slope parameter) being interpreted in a mechanistic way to reflect the cooperativity (interaction of ligands) in binding. In quantal assay, the γ parameter is sometimes described as the steepness of the probability of effect curve for an individual patient.3 The complexity of general and spinal anesthesia allow considerable skepticism that the single parameter γ can have any deterministic/mechanistic interpretation. The more conservative approach is to consider any slope estimate of the doseresponse curve as purely descriptive of the distribution of thresholds in the population.

Second, as an extension of concepts developed in the mixed effects modeling of population pharmacokinetic data (multiple observations per subject), it has been argued that mixed effects modeling can be used on single response data to estimate an intraindividual and an interindividual variance.4 However, a fundamental flaw was demonstrated in assumptions for such methods5: Data with only one observation per subject cannot be used to estimate an intraindividual variance. Thus, the nomenclature “naive-pooled data,” commonly used in population pharmacokinetic modeling, is an incorrect description of the data structure in this experiment.

Third, the NONMEM statistical package is one of the prominent software tools developed for mixed effects modeling. Mathematical calculations within NONMEM such as Laplacian estimation are extremely complex, involving many assumptions and approximations; there is no consensus about the optimal estimation routines for mixed effects software.6 Standard logistic regression software uses commonly accepted routines that allow the estimation of confidence intervals for arbitrary EDx, missing in the NONMEM output. It should be emphasized that even standard logistic regression analysis gives less precision for EDx values at the upper and lower edges of the sigmoid curve.

Fourth, simple algebraic manipulation shows that the quantal sigmoid Emax model can be rewritten in a logistic format:

\[
\text{Probability(success } = \text{ yes)} = \frac{1}{\exp(-\gamma \ln(\text{dose}) + \gamma) + 1} \Rightarrow \gamma
\]

\[
= \beta; \ln(\text{dose}) = -\frac{\alpha}{\beta}
\]

This restatement reveals that the quantal sigmoid Emax model enforces a logarithmic transformation of dose. Such a transformation may or may not be desirable. The standard logistic model leaves this choice to the modeler. In this experiment, bupivacaine doses were linearly spaced, and a logarithmic transform seems unnecessary. However, using a logarithmic dose transformation, the logistic regression estimates (with 95% confidence intervals) are ED50 (6.5 [5.8–7.3] mg) and ED50 (8.7 [7.1–10.5] mg) for successinduction and ED50 (7.6 [6.8–8.5] mg) and ED50 (11.0 [8.8–13.6] mg) for successoperation. The NONMEM estimate for the ED50 of successinduction is 11.0 mg, a value extremely discordant with the observed response rates (fig. 1, Ginosar et al.7); standard logistic regression gives estimates (linear dose, 8.6 mg; logarithmic dose, 8.7 mg) consistent with the observed response rate. The observed response rates for this experiment were nonmonotonic, decreasing at some intermediate doses. This creates difficulty in reliable statistical estimation. Nonparametric methods of obtaining doses for EDx are available and could have been considered.2 If a simple parametric model were desired, standard logistic regression analysis would have been preferred.


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1. Ginosar et al. 2. Standard logistic regression gives estimates (linear dose, 8.6 mg; logarithmic dose, 8.7 mg) consistent with the observed response rate. The observed response rates for this experiment were nonmonotonic, decreasing at some intermediate doses. This creates difficulty in reliable statistical estimation. Nonparametric methods of obtaining doses for EDx are available and could have been considered. If a simple parametric model were desired, standard logistic regression analysis would have been preferred.2

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"The poor precision of the ED50 estimates is apparent; the 95% confidence interval for successinduction is 7.2–10.0 mg and for successoperation is 8.8–12.4 mg."
In Reply—We appreciate Dr. Pace’s taking the trouble to examine our data on spinal bupivacaine for cesarian delivery. Dr. Pace obtains results nearly identical to ours for successful operation but different results for successful induction, particularly the estimate of ED50. Dr. Pace graciously attributes these differences to our use of NONMEM (NONMEM Project Group, University of California, San Francisco, CA), and raises several important questions about using NONMEM for binary data.

Unfortunately, the explanation for the difference is more prosaic. On reexamining our analysis, we discovered an error in our data files analyzed by NONMEM. Dr. Pace correctly inferred our success/failure data from figure 1 of the article. We reft the data using both NONMEM and Excel (Microsoft, Redmond, WA), obtaining results identical to those of Dr. Pace (table 1).

Believing that the differences in results were related to the use of NONMEM, Dr. Pace raised four objections to our modeling approach. His objections raise several important considerations about logistic regression analysis to which we wish to respond.

First, Dr. Pace observes that the steepness parameter γ has no mechanistic interpretation. It simply describes the shape of the distribution.

Second, Dr. Pace points out that estimating interindividual variability with only a single observation in each individual is highly suspect. We agree, which is why we did not estimate interindividual variability in our analysis. As pointed out by Dr. Pace, this has already been addressed in Anesthesiology. “Naive pooled data” is the correct description of the approach taken when data from multiple patients is fit while ignoring intersubject variability, as was done in this article.

Third, NONMEM and Rplus are performing identical calculations, and obtain nearly identical results. We also repeated the analysis with Excel, with assistance from Steven L. Shafer, M.D. (Professor, Anesthesiology Service, Palo Alto Veterans Affair System, Palo Alto, California) and obtained identical estimates to those from NONMEM. We are puzzled at Dr. Pace’s concerns about “extremely complex [calculations], involving many assumptions.” The objective function for logistic regression is simply the calculation of a probability. The probability of multiple observations is the product of the probability of each individual observation, a readily computed number. Finding the parameters of the model that maximize probability of the observations with a naive pooled data approach requires virtually no assumptions at all, which is why a simple Excel spreadsheet and NONMEM generate identical results. We do observe, though, that it is not appropriate to use the Laplacian transformation when estimating single-subject data.

More generally, if one wishes to estimate EDx, the effective dose associated with probability x, the formula is simply

\[ P = \frac{D_x}{D_{\text{ED}_x} + D} \]

These formulas can be used in NONMEM, Excel, or any other estimation tool. The point estimates from such an estimation should be identical with those derived by calculating ED50 from ED95 and γ, but if the program can generate SEs, confidence intervals can be constructed from the SE estimates. This is the only real advantage of estimating ED95 directly, but confidence bounds about the ED95 estimate may be clinically important. Again, whether one uses NONMEM or another tool is irrelevant; all should return nearly identical answers, provided they maximize likelihood.

Fourth, we agree that the standard quantal sigmoid Emax model enforces a logarithmic dose transformation. Fortunately, drugs tend to work on a more or less logarithmic scale, and we think about drugs on a log scale (e.g., a typical clinical guideline is “the correct dose is half to twice the nominal dose,” which reflects log spacing of dose). It is nonsensical to say “the standard model enforces X, Y, or Z” because, by definition, the standard is what it is. The users of the model are free to change it any way they desire, but of course, the changed model is then no longer the “standard” model. In this case, the user is free to substitute log dose, Exp(dose), or any desired transformation of dose into the “standard quantal sigmoid Emax” model if the user believes that is a better reflection of either the data or the underlying biology. Of course, the result is no longer the standard model but a nonstandard model, and the use of a nonstandard model would have to be justified based on pharmacology, biology, or goodness of fit to the data. However, that is only a modest hurdle for the modeler. Dr. Pace notes that the observations were evenly spaced doses, suggesting a logarithmic

### Table 1. Successful Anesthesia at Different Doses of Intrathecal Bupivacaine: ED50 and ED95 for Successinduction and Successoperation

<table>
<thead>
<tr>
<th></th>
<th>ED50 ± SE</th>
<th>γ ± SE</th>
<th>ED95 ± SE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Successinduction</td>
<td>6.50 ± 0.44</td>
<td>10.3 ± 2.8</td>
<td>8.65 ± 0.46</td>
</tr>
<tr>
<td>Successoperation</td>
<td>7.64 ± 0.45</td>
<td>8.16 ± 2.1</td>
<td>11.0 ± 0.95</td>
</tr>
</tbody>
</table>

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transformation seemed unnecessary. The spacing of the doses has little
to do with the preferred model, because it is the response to the dose,
not the spacing of the doses, that determines the shape of the curve.
We agree that, in general, if ED_{95} is of clinical interest, an ED_{95}
calculated from all the data (i.e., reestimating the model parameterized
in terms of ED_{95} and γ), rather than calculated from the ED_{95} and γ, is
probably the optimal method of analysis. The point estimate will be the
same, but the SEs will be estimated about the parameter of clinical
interest. However, using NONMEM or any other estimation tool should
give essentially identical results for this simple problem. The standard
quantal sigmoid E_{max} model, mathematically modified as shown
above, is perfectly appropriate to calculate ED_{95} or any other clinically
relevant dosage.

Even though the results changed slightly with the corrected data
analysis, the conclusion remains unchanged. The data strongly support
using doses of 11–12 mg bupivacaine for single-shot spinal anesthesia
for cesarean delivery. The use of smaller doses increases the likelihood
of inadequate neuraxial anesthesia.

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Edward T. Riley, M.D., Steven Shafer, M.D. * Hadassah Hebrew
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Anesthesiology 2005; 102:479

In Reply:—We are grateful to Dr. Marret et al. for their constructive comments. We agree with their comment that “although the distribution of radiographic spread is well correlated with the spread of analgesic block, this does not mean that [epidurography] is a reliable technique and that the two methods agree.” We do also agree that the Bland and Altman method is proper to confirm whether the two different methods agree.

However, we have not shown the agreement of the two methods; we have rather shown the correlation. In our article, we confirmed that the distribution of radiographic spread correlates well with the spread of analgesic spread. Dr. Marret et al. have noted this correlation in their figure 1 (Y = 0.80X + 0.48; r = 0.95, P < 0.0001). This is what we intended to mention in our manuscript. We have not mentioned that the distribution of radiographic spread agrees with the spread of analgesia completely. Dr. Marret et al. point out that the radiographic spread overestimated the analgesic spread in all cases. However, we have neither overestimated nor underestimated those values. We have investigated the correlation between those values, and we got the relation expression: the analgesic spread = 0.8 × the radiographic spread. This means that, for example, if the radiographic spread is 10 segments, the analgesic spread would be approximately eight dermatomes in many cases.

We understand the comments regarding the bias and limits of agreement. However, we believe that this method is very useful to predict the dermatomal distribution of analgesic block because it is impossible to predict the cephalad and caudal spread of anesthetic, whether it will spread unilaterally and the general pattern of spread without epidurography. Thus, we concluded that epidurography could help to predict the dermatomal distribution of analgesic block.

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Water versus Air Warmers

To the Editor—Taguchi et al.1 stress the essential role of skin temperature and Newton’s Second Law of Thermodynamics in increasing core temperature (Tc) with skin warming systems, but they do not demonstrate this role and they confuse other issues.

To increase Tc directly, the Second Law requires that the warming system’s average cover temperature (Tcvr) > the mean skin temperature of multiple skin sites (Tmsk) > Tc. To demonstrate this, figure 1 shows that in 12 post aortocoronary bypass patients rewarmed for 2 h under a 1.8 m² radiant ceiling, the change in Tc (ΔTc) occurred only when (Tmsk - Tc) > 0°C. If the temperature gradient is Tcvr > Tc, then heat passes from the cover to the skin but not to the core, and the warmer acts as an insulator, increasing Tc indirectly by retaining metabolic heat in the core.

Instead of Tmsk the authors derive the peripheral temperature of the limbs (Tperif). If Tperif represents the buffer between Tcvr and Tc, then Tc did not increase directly because Tperif < Tc. Nor did Tc increase indirectly, for metabolic heat production was similar in both groups but ΔTc was not. What clinically relevant and measurable temperature gradient explains the increase in Tc?

Heat content differences between periphery and core do not reflect tissue insulation. The units of insulation (i.e., thermal resistance) are temperature gradient/heat transfer rate (°C/kCal/h or °C/W), not heat content (kCal or kf). Tissue insulation is proportional to the temperature gradient required to cause heat transfer and increase Tc, which, in fig. 1, required a (Tmsk - Tc) of 1 ± 0.8°C (n = 94). In the authors’ study Tperif represented a heat sink and heat transfer to the core was “constrained” by the lack of an appropriate temperature gradient rather than by tissue insulation.

Peripheral heat content increased 2.1-2.5 times more than core because initially Tperif < Tc (water, -2.6°C; air, -2.1°C) and, therefore, exposed to the same Tcvr, the periphery warmed preferentially. Calculated from the change in heat content at the end of warming (ΔQ), their fig. 4, ΔTc = +2.9°C (water) and +1.7°C (air), as shown in their figure 3. Similarly, ΔTperif = +5.8°C (water) and +4°C (air). Therefore, their data implies a final (Tperif - Tc) of +0.3°C (water) and +0.2°C (air), which is more consistent with the Second Law and the observed increase in Tc than the “±0.8°C” shown in their figure 5.

At the end of warming the change in heat content per unit area warmed was 1.25 times larger for water (185 kCal/m²) than for air (148 kCal/m²). Yet the authors write “... heat transfer rate (rate) per unit anterior area” was similar. This inconsistency results from the measurement method. Heat content is derived from temperature. Heat transfer rate per unit area, or “heat flux” (q*), is directly measured by heat flux transducers. Heat flux, q* = ΔT·h, where ΔT is the cover to skin temperature gradient across the heat flux transducers and h, from Newton’s Law of Cooling, is the heat transfer coefficient (i.e., the efficiency) of that particular system, usually expressed in W/m²·°C. For one conventional water mattress2 (and three others, including a suit

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similar to this study) $b$ was 1.5 times larger than that for four air warmers: $3 - 40 \text{ W/m}^2\cdot\text{°C}$ versus $26 \text{ W/m}^2\cdot\text{°C}$. The larger $b$ of water means that the same $q'$ will produce a smaller $\Delta T$ than with air and, therefore, at the same time $T_{cvr}$, $T_{msk}$ will be higher with water than with air—and heat content is derived from $T_{msk}$. Although $T_{cvr}$ was not measured, $T_{msk}$ was, and it would be instructive to know the $T_{msk}$ difference between the systems.

The change in heat content/warmed area for water was 1.25 times that of air, not 1.5 times, as the ratio of their $b$ values suggests, because $\Delta T$ differed. The air warmer was set to $43\text{°C}$. The low heat capacity of air and environmental heat loss would degrade $T_{cvr}$ to a relatively constant $T_{cvr} < 43\text{°C}$. The water system was set to a target $T_c$ of $37\text{°C}$. The high heat capacity and mass flow rate of water would prevent $T_{cvr}$ environmental degradation. But the system’s servocontrol algorithms would produce a variable $T_{cvr}$: initially high ($40\text{°C}$) but decreasing as $T_c$ increased. As $T_{cvr}$ decreased, $(T_{cvr} - T_{msk})$ also decreased until, finally, the water heat transfer rate equaled that of air (their fig. 1). Had $\Delta T$ been the same, the difference between the systems would have been greater.

It is improbable that an air warmer above the body and water mattress below would match the heat transfer of a water suit because above the body, the change in heat content/warmed area was less with air than with water and below the body, a contour-conforming water suit gives better skin contact, which is essential for conductive heat transfer, than a flat mattress.

This was a sophisticated study of thermoregulatory physiology rather than heat transfer physics. It did not report those fundamental differences in the heat transfer characteristics (i.e., $T_{cvr}$, $T_{msk}$, and $b$) that must be known to safely and effectively exploit the full potential of any skin-warming system. The heat transfer rate, in isolation, is a description of what happened in a specific application. It is not an explanation for why it happened, nor is it suitable for universal application in any clinical situation—those answers lie in the system’s heat transfer characteristics.

Although anesthesiologists believe that air is a more effective heat exchanger than water, in lethal thermal environments (space and diving) water, not air, is used to maintain life because of its better thermal properties. This article and another will encourage further clinical evaluations of water-conditioned heat transfer systems. Those evaluations should be based on the physical principles that determine heat transfer and not on the limitations of current clinical practice.

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In Reply—It is well established that peripheral tissues act as insulators and that the efficacy of this insulation is a strong function of vasomotor status. For example, surface warming is more effective when humans are vasodilated because vasodilation allows facile flow of heat from the skin surface through peripheral tissues to the core. Our article again illustrates this well-established phenomenon and is probably the mechanism by which our volunteers were kept anesthetized throughout the protocol specified.

We do not understand how Dr. English estimates the core-to-peripheral vascular heat transfer characteristics and therefore varies markedly over time. Actual heat transfer rates, the clinically relevant measures of heater efficacy, differ less than might be expected based on $b$.

We are mystified by Dr. English’s assertion that ‘the change in heat content/warmed area for water was 1.25 times that of air, not 1.5 times, as the ratio of their $b$ values suggests.’ We did not report $b$ or the results that would be necessary to calculate this value. Unlike forced-air warming, the circulating-water system we tested includes a servocontrol algorithm. Because the system was set to $37\text{°C}$, heating intensity presumably decreased as core temperature approached $37\text{°C}$. Initial warming rates are thus a better indicator of system capability than rewarming rates near normothermia.

We appreciate Dr. English’s assessment that our investigation was a sophisticated study of thermoregulatory physiology. We note, however, that our volunteers were kept anesthetized throughout the protocol specifically to minimize thermoregulatory responses and allow us to isolate heat transfer characteristics that must be known to safely and effectively exploit the full potential of skin-warming systems. Specifically, we evaluated and reported cutaneous heat transfer, regional body heat content, and core rewarming rates—the clinically relevant system characteristics.
Propofol and Sleep: An Attractive Connection

To the Editor—My 25-yr personal experience considering the choice of drugs for self-administration by physicians, excepting the standbys alcohol, opioids, and stimulants, has usually generated fairly predictable questions. One common query is “why in the world would anyone abuse that” at some time during the evaluation. In fact, the first published report of propofol abuse more than 10 yr ago generated exactly this question. Often, even after time in an established recovery, a satisfactory response to this query is not forthcoming.

The recent paper by Tung et al.1 may represent a unique clear historical hint in the form of case, and sometimes coroner, reports, that uncontrolled research on this subject has been underway for more than a decade? If indeed propofol immediately induces sleep that mimics the best properties of non–drug-assisted rest, including deprivation recovery, then the attraction can become, for a few, overwhelming, despite constant personal danger. For someone with a long-standing concern with physician well being and chemical dependency, the response to the titles alone, of the paper and editorial, prompted the response “so that’s it.”

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Anesthesia Service Medical Group, San Diego, California. cward2@san.rr.com

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Use of the Laryngeal Tube-S™ for Airway Management and Prevention of Aspiration after a Failed Tracheal Intubation in a Parturient

THE laryngeal tube-S™ (LTS™; VBM Medizintechnik, Sulz, Germany) is a new supraglottic airway-management device introduced into the European market in 2002 (fig. 1). It is a newer generation of laryngeal tube which is fitted with a second lumen serving for suctioning, and free gastric drainage. This case report describes the use of the LTS™ for emergency airway management of a parturient after failed attempted tracheal intubation.

A 27-yr-old parturient was brought to the operating theatre for urgent Cesarean section due to prolonged rupture of the amniotic membrane. Her medical history was unremarkable. She had eaten nothing for about 12 h and didn’t have any symptoms of gastroesophageal reflux. Upper-airway examination revealed score II of Mallampati,1 an interincisor gap of about 4 cm, and a thyromental distance of about 2.5 finger breadths. She had limited (less than 30°) extension of the neck. General anesthesia was chosen due to the patient’s refusal of regional anesthesia. After preoxygenation, the patient was anesthetized with a rapid sequence induction: using 450 mg of sodium thiopental and 120 mg of succinylcholine. The Sellick maneuver was applied as recommended by an assistant. A grade III view of the larynx was obtained using a size-3 blade McIntosh laryngoscope. Two attempts at intubation, at the optimal sniffing position by the clinical-anesthesia 3-yr resident, without and with a stylet, failed. Release of cricoid pressure didn’t improve the view, and the pressure was applied again. A senior anesthetist was called. The oxygen saturation decreased to less than 50%. Two-person manual bag and mask ventilation with 100% oxygen was difficult and resulted in only a modest increase in oxygen saturation (60–70%). A size-4 LTS™ was blindly inserted about 5 min after induction, and its cuff inflated with about 80 ml of air. The patient could be ventilated easily and the oxygen saturation increased to 97% using manual ventilation with 100% oxygen. The patient regained consciousness and as she started breathing she began to move her eyelids. Regurgitation of yellowish stomach contents began with the LTS™ in place but it was drained by the suctioning lumen of the LTS™ and no change in oxygen saturation was detected. A nasogastric tube was inserted and about 30 ml of fluid drained from the stomach.

Support was provided solely from institutional and/or departmental sources. The authors thank Homan Yarmohammadi, M.D., the editorial advisor of the Office for Development of Clinical Researches of Namazi Hospital, Shiraz, Iran, for his editorial assistance.

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Use of the Laryngeal Tube-S™ for Airway Management and Prevention of Aspiration after a Failed Tracheal Intubation in a Parturient

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At this time the patient was alert and cooperative. She was reassured and the LTS™ was removed in the presence of the consultant anesthesiologist. Examination of its cuff showed no blood traces. The obstetrician was asked if it was possible to administer regional anesthesia and she agreed after she assessed the fetal heart sound with a sonicaid. Afterwards, there was no evidence of aspiration at any stage of the procedure. Spinal anesthesia was administered and a healthy girl was delivered (weight, 3900 g; APGAR scores 9 and 10 after 1 and 5 min, respectively). A full explanation of the events was given to the patient and her husband. The patient and her baby were discharged from the hospital in good condition 2 and 4 days later, respectively.

Discussion

Difficult or failed tracheal intubation is an important cause of anesthetic-related maternal morbidity and mortality.2 Regurgitation is a rare but significant cause of morbidity and mortality after failed tracheal intubation.3

Considering our management the following should be noted.

1. Omission of antacid premedication was an error.
2. The selected dose of succinylcholine was relatively high.4
3. Release of the Sellick maneuver after failed intubation and difficult ventilation are controversial and not routinely recommended.5
4. It was quite possible that the patient could have been intubated successfully, if another size or type of laryngoscope blade had been used. However, these issues are not the focus of this case report.

Although the Laryngeal Mask Airway™ (LMA™; Laryngeal Mask Company Limited, San Diego, CA) has been successfully used and promoted for management of failed obstetric intubations6–8 it is not effective in all patients.9 The LMA™ may yield in unsuccessful ventilation and gastric inflation due to low median airway-seal pressure and it does not reliably protect against aspiration of regurgitated stomach contents.10 A recent case report regarding the use of the ProSeal™ laryngeal mask airway (PLMA™; Laryngeal Mask Company Limited) for emergency airway management after failed tracheal intubation during Cesarean section has been published.11 Also there are a few reports describing prevention of aspiration of gastric contents with the PLMA™ in situ.12–15 These reports suggest the effectiveness of the PLMA™ to maintain the airway and prevent aspiration in elective and emergency situations. However, in our case a PLMA™ was not ready to use.

The LTS™ may be a good choice for emergency airway management.16–18 It may provide a higher airway seal than the LMA™: an airway pressure as high as 40 cm of H2O would be achievable without gastric inflation and its insertion time is also comparable with that of the LMA™.19,20 Appropriate positioning of the LTS™ has been verified with fiberoptic endoscopy in all patients.20

In contrast to the combitube, the LTS™ has only one adapter that may be connected with a ventilation device, whereas the remaining connector can only be connected to a suction adapter. This may provide additional patient safety in order to prevent an inexperienced user inadvertently attaching the Y-piece to the esophageal tubing.

The LTS™ has encountered some minor problems, so that some may consider it a suboptimal device. Firstly, there are few controlled trials comparing the LTS™ with other similar supraglottic devices such as the PLMA™, LMA™, and combitube. Secondly, it has never been tested in hypoxic and/or hypercarbic patients, as in our presented case. Thirdly, there may be concerns, although unlikely, that the LTS™ may induce dangerous effects like the esophageal obturator. Fourthly, there may be dangerously high cuff pressures when the device is used in an emergency situation to secure the patient’s airway. This is not a major problem, since the cuff pressure of the LTS™ (80 cm of H2O) has been reported to be much lower than that of the combitube (80–300 cm of H2O) and the LMA™ (100–250 cm of H2O).20,21

In conclusion, in the future, the LTS™ may have a role in emergency obstetric airway management.

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References


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To the Editor—Almost everyone has had the hiccups at one time or another. These involuntary contractions of the diaphragm and respiratory muscles that terminate with abrupt closure of the glottis—or ‘hiccups’—are usually transient and do not herald any serious pathology. Occasionally, hiccups persist, lasting hours, days, or weeks. Hicups lasting longer than 48 h are termed ‘persistent’ and those lasting longer than a month are termed ‘intractable.’ Persistent or intractable hiccups may be the presenting symptom of serious pathology.

Despite the varied possible etiologies, in the majority of cases no organic cause can be identified and a diagnosis of idiopathic chronic hiccups is made. As expansive as the potential causes is the list of potential cures. Home remedies such as breath holding, a glass of water, and even a scare to evoke a startle reflex have been tried. Pharmacologic interventions are just as varied. Indeed, several agents traditionally have been suspected as causative agents. Having exhausted pharmacologic remedies, some have tried more invasive techniques such as diaphragmatic pacing probe to alleviate his persistent hiccups after revision of a right hip prosthesis.

The patient was a 76-yr-old man with a history of osteoarthritis and right total hip arthroplasty, who returned to the operating room for revision of a painful loose acetabular implant. Preoperatively, the patient had had an epidural placed for postoperative pain control. In addition, our patient had received midazolam as the initial treatment for patients with persistent hiccups. However, the results of transesophageal atrial pacing probe pacing the diaphragm produced rapid and complete relief. Treatment parameters of frequency and duration were estimates based on clinical experience and patient comfort. Amplitude and probe position was assessed objectively by successful diaphragmatic pacing as determined by changes in respiratory pattern.

It should be noted, however, that the transesophageal atrial pacing probe is not an entirely benign intervention. Future applications of transesophageal atrial pacing probe placement for diaphragmatic pacing should include standard monitors (blood pressure, electrocardiogram, and pulse oximetry) to insure patient safety. In our case, the transesophageal atrial pacing probe for the resolution of persistent hiccups worked; however, a randomized prospective study is warranted to more fully evaluate the efficacy and safety of this treatment modality.

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To the Editor:—Moderate intravenous sedation is routinely administered for diagnostic and interventional procedures to alleviate patient discomfort and anxiety. Oxygen desaturation is a common problem for anesthesiologists providing moderate sedation to patients undergoing upper endoscopy (esophagogastroduodenoscopy, endoscopic retrograde cholangiopancreatography, or bronchoscopy). During these procedures, patients typically receive intravenous propofol for sedation while supplemental oxygen is administered via nasal cannulae. The nasal cannula often becomes an ineffective tool for providing supplemental oxygen when the patient’s mouth is open and the endoscopy probe is in place. We would like to report a technique that is simple and effective for increasing oxygenation in patients receiving moderate intravenous sedation as described above.

After the patient assumes the lateral decubitus or prone position, we place a clear plastic sheet over the patient’s face and tape it to the patient’s head (fig. 1). The nasal cannula is thus effectively converted into a face tent. This technique creates an oxygen reservoir that provides an inspiratory fraction of oxygen of 40–60% with oxygen flows of 4 l/min. After preoxygenation using this technique for a few minutes, we usually titrate intravenous propofol to achieve moderate-to-deep sedation while maintaining spontaneous respiration without oxygen desaturation. We monitor the patient’s respirations with capnography or a pediatric precordial stethoscope placed over the trachea. If the patient becomes apneic because of airway obstruction or oversedation, we still have an average of 2 to 3 min to manipulate the airway before oxygen desaturation occurs.

We make a 12” × 12” or larger plastic sheet using any clean, clear plastic bag (nasal cannula bags, specimen bags, or breathing circuit bags) or the plastic cover from the upper body warming blanket kit. After explaining to the patient that by applying this plastic sheet we will be increasing their oxygen supply, even the most anxious patients are receptive. One concern is that a plastic sheet could increase ‘dead space’ resulting in rebreathing of carbon dioxide and hypercarbia. We routinely monitor rebreathing of carbon dioxide using capnography for prolonged cases or whenever it is available. By maintaining the plastic sheet in a tent-like position covering only the upper two thirds of the head or using oxygen flow greater than 4 l/min, we can avoid rebreathing of carbon dioxide and hypercarbia. There is minimal (0–3 mmHg) carbon dioxide rebreathing with this face tent. During manipulation of the endoscopy probe, we lift the plastic sheet slightly to avoid dragging it into the mouth.

Although there are commercially available masks for bronchoscopy, this technique uses plastic sheets that are ubiquitous and available at no additional cost. We also use this technique for patients undergoing colonoscopy in the lateral decubitus position, rectal procedures in the jackknife position or pain management procedures in the prone position.

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