Comparison of use of an infrared anesthetic gas monitor and refractometry for measurement of anesthetic agent concentrations

Tamas D. Ambrisko, DVM, PhD, and Alan M. Klide, VMD

Objective—To assess agreement between anesthetic agent concentrations measured by use of an infrared anesthetic gas monitor (IAGM) and refractometry.

Sample—4 IAGMs of the same type and 1 refractometer.

Procedures—Mixtures of oxygen and isoflurane, sevoflurane, desflurane, or N₂O were used. Agent volume percent was measured simultaneously with 4 IAGMs and a refractometer at the common gas outlet. Measurements obtained with each of the 4 IAGMs were compared with the corresponding refractometer measurements via the Bland-Altman method. Similarly, Bland-Altman plots were also created with either IAGM or refractometer measurements and desflurane vaporizer dial settings.

Results—Bias ± 2 SD for comparisons of IAGM and refractometer measurements was as follows: isoflurane, –0.03 ± 0.18 volume percent; sevoflurane, –0.19 ± 0.23 volume percent; desflurane, 0.43 ± 1.22 volume percent; and N₂O, –0.21 ± 1.88 volume percent. Bland-Altman plots comparing IAGM and refractometer measurements revealed nonlinear relationships for sevoflurane, desflurane, and N₂O. Desflurane measurements were notably affected; bias ± limits of agreement (2 SD) were small (0.1 ± 0.22 volume percent) at <12 volume percent, but both bias and limits of agreement increased at higher concentrations. Because IAGM measurements did not but refractometer measurements did agree with the desflurane vaporizer dial settings, infrared measurement technology was a suspected cause of the nonlinear relationships.

Conclusions and Clinical Relevance—Given that the assumption of linearity is a cornerstone of anesthetic monitor calibration, this assumption should be confirmed before anesthetic monitors are used in experiments. (Am J Vet Res 2011;72:1299–1304)
3 and 20 μm to identify and quantify as many as 5 halogenated anesthetic agents (isoflurane, halothane, enflurane, desflurane, and sevoflurane). Carbon dioxide and N₂O are also measured by use of the principles of IR absorption spectroscopy but with a single wavelength. The IAGMs were calibrated by hospital staff every month using the calibration gas supplied by the manufacturer. The monitors were also regularly inspected and maintained by a professional service to ensure that they were in good condition. The manufacturer’s original 2.4-m-long polyvinyl chloride sampling tubes and water traps were used in the study. Before measurements were obtained, the IAGMs were allowed a period of at least 10 minutes, which is more than the recommended minimal warming up time (90 seconds), to reach full specifications. Anesthetic gas sampling rate was set at 0.15 L/min. The measurement results were displayed on the monitors’ screens at a resolution of 0.1 volume percent for the halogenated agents and 1 volume percent for N₂O.

Refractometry—The measurements obtained by use of the IAGMs were compared with those from a handheld refractometer. This was a Jamin-type refractometer that used a double optical path. The scale in this refractometer unit allowed direct reading of desflurane from 0 to 20 volume percent. The concentration of other agents can also be measured with this refractometer if appropriate conversion factors are applied (agent volume percent = desflurane volume percent reading × conversion factor). The following conversion factors were used in this study: 0.78 for isoflurane, 0.81 for sevoflurane, and 4.29 for N₂O. The scale of this refractometer was suitable for measuring agent concentrations across the clinically applicable ranges: isoflurane, 0 to 13 volume percent; sevoflurane, 0 to 16 volume percent; and N₂O, 0 to 85 volume percent. The refractometer was calibrated before each experiment by use of 100% oxygen and air. Both gases have an indicated pressure of approximately 765 mm Hg.

Results

For isoflurane, sevoflurane, desflurane, and N₂O concentrations, measurements were obtained by use of the single type of IAGM and refractometer (Table 1). Agent volume percent data were analyzed by use of the Bland–Altman method (Figure 1), and scatterplots of the original measurements were created (Figure 2). For sevoflurane, desflurane, and N₂O nonlinear relationships between concentrations determined by use of the 2 devices were evident on the scatterplots. The bias of isoflurane measurements was near zero, and the limits of agreement (plus or minus) were < 0.2 volume percent. Most of the sevoflurane measurements obtained by use of the IAGMs were lower than the measurements obtained by use of the refractometer, but the limits of agreement were narrow, similar to those for the isoflurane measurements. However, the limits of agreement for desflurane and
N₂O measurements were much wider. The difference-versus-mean plots for IAGM and refractometer measurements revealed nonlinear relationships for sevoflurane, desflurane, and N₂O. When desflurane measurements were much wider. The difference-versus-mean plots for IAGM and refractometer measurements revealed nonlinear relationships for sevoflurane, desflurane, and N₂O. When desflurane measurements were much wider. The difference-versus-mean plots for IAGM and refractometer measurements revealed nonlinear relationships for sevoflurane, desflurane, and N₂O. When desflurane measurements were much wider. The difference-versus-mean plots for IAGM and refractometer measurements revealed nonlinear relationships for sevoflurane, desflurane, and N₂O.

Table 1—Descriptive statistical data of isoflurane, sevoflurane, desflurane, and N₂O concentration measurements (volume percent) determined by use of a single type of IAGM and a refractometer.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Isoflurane</th>
<th>Sevoflurane</th>
<th>Desflurane</th>
<th>N₂O</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Refractometer (n = 6)</td>
<td>IAGM (n = 24)</td>
<td>Refractometer (n = 9)</td>
<td>IAGM (n = 36)</td>
</tr>
<tr>
<td>Mean</td>
<td>2.9</td>
<td>2.9</td>
<td>4.2</td>
<td>4.0</td>
</tr>
<tr>
<td>SD</td>
<td>1.9</td>
<td>1.8</td>
<td>2.7</td>
<td>2.5</td>
</tr>
<tr>
<td>Minimum</td>
<td>0.7</td>
<td>0.6</td>
<td>0.5</td>
<td>0.4</td>
</tr>
<tr>
<td>Maximum</td>
<td>5.6</td>
<td>5.6</td>
<td>8.3</td>
<td>8.3</td>
</tr>
</tbody>
</table>

Commercially available anesthetic vaporizers were used to deliver halogenated anesthetic agents at various dial settings. Five measurements (4 obtained by use of 4 IAGMs and 1 obtained by use of a refractometer) were obtained for each gas mixture. Each of the 4 IAGM measurements and the corresponding refractometer measurement were subsequently compared and analyzed for each gas mixture.

Figure 1—Plots of differences between concentration measurements obtained by use of a single type of IAGM and a refractometer versus the mean value of those measurements for isoflurane (A), sevoflurane (B), desflurane (C), and N₂O (D). Five measurements (4 obtained by use of 4 IAGMs and 1 obtained by use of a refractometer) were obtained for each gas mixture. Long-dashed lines indicate the bias (mean difference between device measurements), and short-dashed lines indicate the limits of agreement (mean ± 2 SD). Nonlinear relationships are evident for sevoflurane, desflurane, and N₂O.
surements of 0.5 to 12 volume percent were analyzed separately, the agreement between the devices was good (bias ± limits of agreement, 0.1 ± 0.22 volume percent) and there was no correlation between differences and means of the 2 device measurements (data not shown). However, at higher desflurane concentrations, the differences between IAGM and refractometer measurements increased in a nonlinear pattern and the variance of the differences also increased. The IAGMs were unable to measure N₂O at < 10 volume percent because they displayed a zero value in situations when the refractometer measurements and the settings of the flow meters suggested that N₂O concentrations were between 0 and 10 volume percent. These N₂O data were excluded from Bland-Altman analysis and not otherwise reported.

Desflurane measurements obtained with the refractometer agreed with the vaporizer dial settings (0.06 ± 0.29 volume percent), and correlation between differences in values and means of the values derived via the device and the dial settings could not be observed (Figure 3). However, desflurane measurements obtained with IAGMs did not agree with the dial settings (0.49 ± 1.18 volume percent) and there was a nonlinear relationship between differences and means. The agreement between IAGM measurements and dial settings for desflurane was better at < 12 volume percent desflurane, and correlation could not be identified within this range.

Figure 2—Scatterplots of concentration measurements (volume percent) obtained by use of a single type of IAGM and a refractometer for isoflurane (A), sevoflurane (B), desflurane (C), and N₂O (D). Five measurements (4 obtained by use of 4 IAGMs and 1 obtained by use of a refractometer) were obtained for each gas mixture. Solid lines indicate the line of ideal agreement (y = x). Nonlinear relationships between measurements are evident for sevoflurane, desflurane, and N₂O.
The primary aim of the present study was to compare the use of a certain type of IAGM with refractometry for measurement of commonly used anesthetic agent concentrations. Surprisingly, Bland-Altman plots of the differences between means of IAGM and refractometer measurements revealed nonlinear relationships for sevoflurane, desflurane, and N₂O. Nonlinear response is an undesirable quality for any measurement device, and in this instance, it could have been attributed to either the IAGM or the refractometer or to both devices. The relevance of these nonlinear responses depends on whether the limits of agreements are considered important for a certain clinical or research purpose. With regard to isoflurane measurements, this type of IAGM is suitable, when this range of error is acceptable, for clinical monitoring of isoflurane concentrations and for research purposes. The agreement between devices was similar for sevoflurane, but the IAGM generally underestimated the refractometer measurements. This may lead to the delivery of slightly higher sevoflurane concentrations to patients when anesthetic agent dosing relies on this IAGM, and it is also undesirable for research purposes. The most important finding of the present study concerned desflurane measurements; at < 12 volume percent, the agreement between devices was good within narrow limits; however, at higher concentrations, IAGM measurements overestimated refractometer measurements. This type of IAGM monitor can be useful for measuring desflurane concentrations between 0 and 12 volume percent, which is the range of concentrations most often used in clinically and in research studies. Although it is not common practice, higher desflurane concentrations are sometimes used in research, such as in animal experiments, in vitro studies, and studies involving children. If the IAGM was the source of poor agreement in the present study, this monitor would not be able to accurately measure such high desflurane concentrations. The pattern of N₂O measurements was also nonlinear, but this is probably less important because the bias was close to zero and the limits of agreement were narrow, compared with the high minimum alveolar concentration of N₂O in animals.

One of the limitations of the present study was that the accuracy of the refractometer was not verified with self-made calibration standards. Two-point calibration of the refractometer was undertaken (by use of 100% oxygen and air), but both points were low on the desflurane measurement scale (< 3 volume percent) and accuracy and linearity at higher concentrations (up to 20 volume percent) had not been evaluated by the authors. In this regard, the authors relied on the calibration of the refractometer by the manufacturer and the established physical principles of refractometry. Theoretically, inaccuracy of conversion factors might have caused some bias when different agents (other than desflurane) were measured with the refractometer, but it did not influence linearity of measurements because the use of conversion factors implies linear function (measurement = scale reading X conversion factor). Nevertheless, the accuracy of correction factors is independent of possible errors of the particular refractometer unit because they are defined by the refractive indices of desflurane and the other agents in question. The fact that the refractometer measurements agreed with desflurane vaporizer dial settings but the IAGM measurements did not reinforce the assumption that the IAGM was responsible for the nonlinearity observed in this study. Theoretically, refractometry uses a straightforward physical principle and its measurements change strictly linearly with concentrations of each component of a binary gas mixture when the temperature and pressure are constant, as in the present study.

Discussion

The primary aim of the present study was to compare the use of a certain type of IAGM with refractometry for measurement of commonly used anesthetic agent concentrations. Surprisingly, Bland-Altman plots of the differences between means of IAGM and refractometer measurements revealed nonlinear relationships for sevoflurane, desflurane, and N₂O. Nonlinear response is an undesirable quality for any measurement device, and in this instance, it could have been attributed to either the IAGM or the refractometer or to both devices. The relevance of these nonlinear responses depends on whether the limits of agreements are considered important for a certain clinical or research purpose. With regard to isoflurane measurements, this type of IAGM is suitable, when this range of error is acceptable, for clinical monitoring of isoflurane concentrations and for research purposes. The agreement between devices was similar for sevoflurane, but the IAGM generally underestimated the refractometer measurements. This may lead to the delivery of slightly higher sevoflurane concentrations to patients when anesthetic agent dosing relies on this IAGM, and it is also undesirable for research purposes. The most important finding of the present study concerned desflurane measurements; at < 12 volume percent, the agreement between devices was good within narrow limits; however, at higher concentrations, IAGM measurements overestimated refractometer measurements. This type of IAGM monitor can be useful for measuring desflurane concentrations between 0 and 12 volume percent, which is the range of concentrations most often used in clinically and in research studies. Although it is not common practice, higher desflurane concentrations are sometimes used in research, such as in animal experiments, in vitro studies, and studies involving children. If the IAGM was the source of poor agreement in the present study, this monitor would not be able to accurately measure such high desflurane concentrations. The pattern of N₂O measurements was also nonlinear, but this is probably less important because the bias was close to zero and the limits of agreement were narrow, compared with the high minimum alveolar concentration of N₂O in animals.

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ent study. On the other hand, IR spectroscopy is based on the Beer-Lambert law, which is subject to many assumptions, some of which may not always be fulfilled, and is influenced by interactions between molecules and therefore may provide nonlinear responses.

Another limitation of the study was that only a single anesthesia machine was used for generating gas mixtures with each agent. Theoretically, the characteristics of this machine might have influenced the results of the study. However, it is unlikely because the anesthesia machine was only used to generate a stable flow of gas mixtures and the measurement processes occurred entirely within the IAGMs and the refractometer. This situation is different from that in which clinical measurements are obtained; clinical measurements are also influenced by the subjects in which the assessment is performed.

The main finding of the present study was that the IAGM tested did not respond linearly. It is possible that the nonlinearity was caused by the inherent properties of IR absorption technology used in this unit; therefore, other anesthetic agent monitors that function with similar technology may also be affected. The assumption of linearity is important because manufacturers typically recommend a 2-point calibration, including 0 and (usually) a fairly low agent concentration, and they assume linearity at higher (and lower) agent concentrations. This mode of calibration is commonly used in clinical and sometimes in laboratory studies. The results of the present study have indicated that this method may not always be acceptable for anesthetic agent concentrations higher than the calibration points. Based on the findings of this study, it may be prudent to confirm the assumption of linearity before use of IAGMs in research studies. The best policy for use of IAGMs in research would be to calibrate them against known standards or against a reference measurement method involving multiple agent concentrations and encompassing the concentration range of interest.

References