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Pitfalls with mass spectrometry in clinical anesthesia

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Abstract

Mass spectrometry of respired gases puts a powerful analytic tool into the hand of the clinician. However, serious misinterpretations may result if the principle of operation and certain weaknesses of spectrometry are not appreciated. The potential pitfalls of clinical mass spectrometry are related to the need to have one unit serve many patients and to the design of the spectrometer and its algorithms.

Introduction

For many years the continuous measurement of inspired and expired carbon dioxide (CO_2) during anesthesia has been recommended not only to assess the adequacy of the patient's ventilation, but also to help in detecting air embolism and decreased cardiac output. The infrared capnographs that have been on the market for many years have served this function well. They respond rapidly, are calibrated easily, and are rugged, precise, and reasonably accurate as long as nitrous oxide is not used or the error it introduces is taken into consideration. More recently, oximetry, particularly of inspired gases, has been promoted as a safeguard against the inadvertent administration of anesthetic gases dangerously low in oxygen. These oximeters are usually of the fuel-cell or polarographic type. Compared with the infrared CO_2 analyzers, oximeters perform much less reliably, require more maintenance, and are slower to respond to changes in oxygen concentration (8).

Once it was possible to measure two gases combining the measurements and including those of other respired gases became desirable. This hope has been fulfilled with the clinical mass spectrometer. Mass spectrometers manufactured by Perkin-Elmer and Chemetron are now being introduced into operating rooms and are hailed as units that typically measure and report not only inspiratory and expiratory CO_2 and oxygen but also nitrogen, nitrous oxide, enflurane, halothane, and isoflurane. Fig. 1 shows a typical readout of a Perkin-Elmer mass spectrometer that presents data from a patient under isoflurane anesthesia with nitrous oxide and oxygen. On the bottom the capnogram is displayed and the table gives data on both inspired as well as expired values, here reported in mmHg, of the different gases. From the capnogram the unit also calculates an inspiratory-to-expiratory ratio and a respiratory rate.

The advantages of the mass spectrometer in an operating room have been described (3, 14, 17, 19). However, this very expensive instrument also has its pitfalls, which must be known to the user in order to avoid serious mistakes. Some of these pitfalls can be appreciated by understanding the underlying algorithms. The sampling site and the

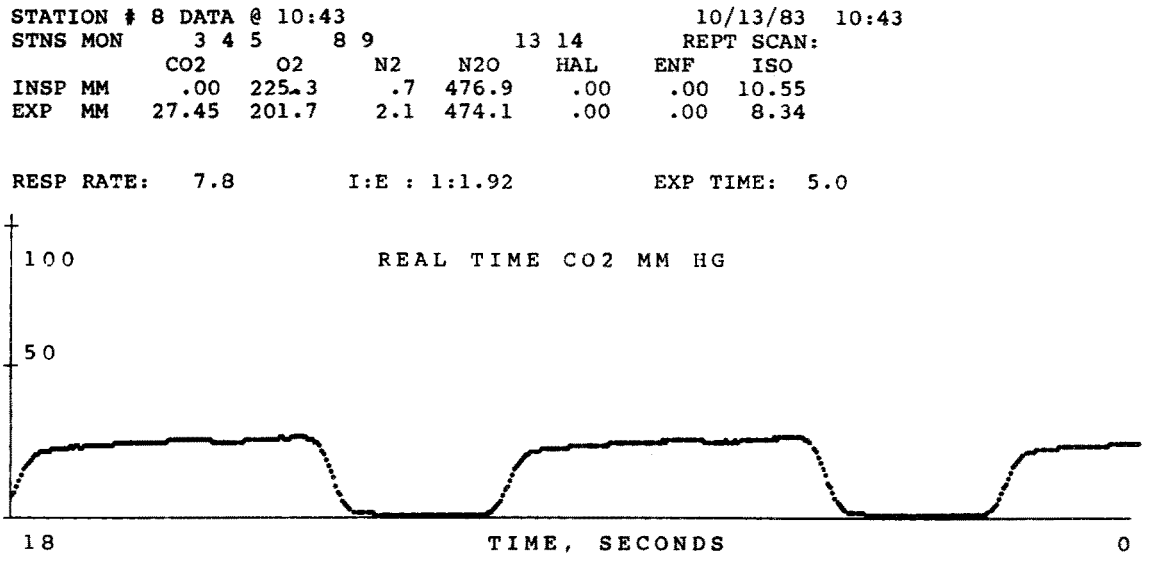

Fig. 1. Printout from a Perkin-Elmer mass spectrometer. The first line identifies the station, date, and time and the second line the other stations being sampled. If one station asks for repeated sampling (every other time), the station is identified. The third line identifies the gases analyzed. Argon is also analyzed but not reported. The remaining information is self explanatory.

anesthesia circuit can affect the data. The unpredictable relationship between end-expired CO_2 and arterial P_{CO_2}, the delay between sampling and analysis, the interpretation of data presented as units of pressure or percentage, and possible errors introduced by water vapor as well as other gases in the mixture such as helium or a propellant all require attention. For analysis, the mass spectrometer removes gas from the circuit, the volume of which is of particular interest to those who use low-flow or pediatric systems. The question whether the gas is removed by continuous or intermittent pumping also affects the interpretation of results. Finally, the alarms deserve comment.

Time factors

Even though an analysis of a gas is rapidly completed once it reaches the ionizing chamber of the mass spectrometer, long delays can confront the clinician before the system updates the data. Three factors are responsible for this.

Multiple user. Because mass spectrometers are so expensive, one analyzer often serves up to 12 or even 16 stations in sequence. Thus, if gas analysis of a few breaths per patient takes only 20 s, and individual patient will be served only every 200 s if 10 stations are in use and correspondingly longer if more stations. In addition, commercial mass spectrometers allow a clinician to change the sequence in which stations are served. The ability to dedicate the system for a fixed time to a single station also engenders delays. While this feature is advantageous to the individual exercising such an option, it may reduce the frequency of analyses for the other stations to less than once every three minutes. This time limit is generally accepted as the longest tolerable because a cardiac arrest or hypoxia longer than three minutes can cause irreversible damage. A desirable frequency of measurement would be less than once a minute (19).

Transit time. Because mass spectrometers typically serve multiple stations, these monitors must be centrally located and gas samples from the various operating rooms must be transported to the mass spectrometer through capillary tubes. The transit time, depending on the distance between station and analyzer and the sampling flow rate, may amount to 15 s.

Number of breaths. The system identifies the capnogram and, depending on its algorithm, selects data suitable for analysis. Thus, one or two breaths may pass before the analyzer locks in on a breath and completes and reports its analysis. Typically two breaths are analyzed, but the number of breaths varies among systems. A fixed sample interval can be selected on some machines, but one has to compromise to avoid excessive delays on the one hand and sample times too short for proper analysis of all capnograms on the other. In case more than two breaths are selected for analysis the required additional time will hardly affect the total time for the analysis with high respiratory rates. However, with low rates of 6 to 10 breaths per minute, the analysis per patient is significantly longer.

Selecting only one or two breaths for analysis may result in errors due to artifacts introduced by the spectrometer when it switches from room to room.

Continuous vs. intermittent sampling

It is possible to aspirate gases continuously from every station instead of only when the mass spectrometer is switched to a station (17). With continuous sampling, gas flows from all stations through all capillary tubings all the time so that a sample is always ready for analysis by the mass spectrometer. This reduces the delay caused by flushing out old gas and transporting new gas through the capillary tube; yet the gas analyzed is still older than a current breath. Data shown on a screen in an operating room may become invalid long before the spectrometer can analyze the next sample from that operating room. Oxygen tensions in inspired and expired gas and, consequently, in arterial blood may plummet to unacceptable levels in far less than three minutes.

The effect of mass spectrometric sampling as a sink for gases

High gas flows are customarily used with semi-closed anesthesia systems; continuously sampling gas at about 200 ml per minute for the mass spectrometer is of no great consequence in such systems. However, during closed circuit anesthesia, this sampling rate, approximately equal to the oxygen consumption of the patient, will equal 50% of the fresh gas flow into the system. This makes an analysis of oxygen and nitrous oxide uptake more difficult. From such analysis, the 'unit doses' can be calculated (11). The proponents of closed circuit anesthesia emphasize the advantage of calculating the uptake of drug by the body and they stress that the uptake of nitrous oxide can guide the calculation of the uptake of other inhalation anesthetics. Yet, when the mass spectrometer is sampling gas, which is analagous to a leak in the system, these calculations become complex.

Instead of continuously aspirating gas samples, samples can be taken at often irregular intervals. This compounds the difficulties in calculating oxygen consumption and anesthetic uptake.

The effect of anesthetic breathing systems

When the mass spectrometer is used intraoperatively, the sampling site may influence the data displayed. The two most commonly used breathing systems in the operating room are the circle and the Bain systems. The sampling site should be as near the endotracheal tube or face as possible, which is accomplished by using an elbow adapter with a sampling probe inserted between endotracheal tube and breathing circuit. While this is straightforward with a circle system, problems arise with the modified Mapleson-D (Bain) system.

In this valveless system fresh gas flows continuously close to the endotracheal tube where it can dilute the end-tidal CO_2 and thus also distort the measurement of other gases to values lying between end-tidal and fresh gas. The higher the fresh gas flow, the greater this problem; also, the closer the sampling site to the fresh gas outlet, the greater the dilution and the higher the sampling flow, the more pronounced the mixing. This problem of fresh gas mixing at the usual elbow sampling site with the Bain circuit has been examined in some

detail both in our laboratory and with patients at our institution (unpublished data). When we sampled gas from the endotracheal tube connector or lower, end-tidal and fresh gases did not mix at fresh gas flow rates as high as 15 l per minute and expiratory flow rates as low as 1 l per minute.

In a series of patients for whom the Bain circuit was used we sampled end-tidal gases at the tip of the endotracheal tube and at a mid-endotracheal port. These were compared with samples obtained from the standard elbow sampling site. The peak expired CO_2 values were the same at all three locations although the CO_2 waveforms obtained at the middle and the end of the endotracheal tube more closely resembled square waves. It should be noted that our series included no pediatric patients.

The carbon dioxide waveform

Not all mass spectrometers display a CO_2 waveform. Display of the waveform is an important clinical aid because capnograms with brisk up and down slopes and a smooth plateau add confidence to the data and aid in distinguishing poor samples. In addition, it has been observed that certain capnographic waveforms are diagnostic. An extensive list of examples has been published (18).

Signals measured by the mass spectrometer are processed by a computer that is an integral part of the system. The CO_2 signal can be used to identify inspiration and expiration and thus can serve as the reference for all calculations. The computer software detects maximal and minimal values for the end-tidal and inspired concentrations of CO_2 as well as the transients. These are used for calculating inspiratory and expiratory values of all gases as well as respiratory rate and inspiratory to expiratory ratios.

One approach is based on level-crossing techniques. During an initial learning period maximal and minimal CO_2 concentrations are derived from the CO_2 waveform and the distance between the maximal and the minimal value is calculated. Two levels are then arbitrarily set, for example 25% and 75% of this difference above the minimal value. A measured concentration of CO_2 falling below the 75% level is then diagnosed as 'inspiration' and a concentration below the 25% level followed by a rise above this level as 'expiration'. During subsequent breaths new maximal and minimal values will be identified and new thresholds calculated and used. The crossing of these levels can be used to trigger the system to perform specific actions such as updating the screen, checking alarm limits, or calculating respiratory rate and inspiratory to expiratory (I:E) ratio. Two approaches in determining inspiratory and end tidal values can be used.

1. At the moment the CO_2 signal reaches its minimum or maximum, alle other signals are sampled and the results are stored.
2. A minimum or maximum for all signals can be determined independently during the course of inspiration or expiration.

The advantage of the first method is that the sum of all measured signals will total 100% of all gases detected by the mass spectrometer; for the second method this may not be true because peak values may not coincide. Note that the first method assumes that all gases reach their minimal and maximal values at the same time; this may not be true as the waveform of different gases may be affected differently by the long capillary tubes (7, 9, 14).

If calculations and decisions are based on the CO_2 waveform, the quality of the capnogram must not be jeopardized. Safeguards against errors must be and have been incorporated into the software. For instance, within a programmed time frame, excursions extending above or below a threshold should be detected; excursions of CO_2 tensions should occur within a physiological range and consecutive end tidal maxima should not vary excessively. These safeguards cannot be taken for granted and the user of mass spectrometers should find out where his mass spectrometer falls short.

For example, we have seen an instance with a mass spectrometer system, where all built-in safeguards failed to detect and report elevated CO_2 levels. This system stores in memory the latest calculated threshold levels for each patient. It uses these in the next sample period, thus decreasing the time necessary for gas analysis at that station.

While the system was sampling 10 other stations, hypoventilation caused the CO_2 values in the patient to rise above the thresholds which the system had calculated. New tresholds were calculated after a delay of about 15 s; however, because the patient was ventilated at a rate of 8 breath/min^{-1}, it took an additional 10 to 15 s to determine the new thresholds. This allowed detection of a breath, so that the 'no breath' alarm was not triggered. Before the system could complete the analysis of the elevated CO_2 and give an alarm, a master overrun switch on this system (set at 40 s), forced the system on to the next station.

Displaying the CO_2 waveform is important because errors in the analysis can result from the dynamics of the operating room, e.g., sampling while ventilator settings are being changed, hiccoughing, suctioning, or surgical motion. Even when capnograms without these artifacts are obtained, the analysis may contain errors due to improper flow rates in the long capillary lines, which may distort the gas fronts particularly during rapid breathing (7, 14). These fronts may then lose their proper square-wave appearance and instead show long slopes.

If water gets into the sampling lines, it can also interfere by hindering flow. This is minimized by avoiding dependent positioning of the sampling site and by using small filters at the sampling site.

The I:E ratio may not be reported correctly when it is based on the capnogram. The beginning of expiration consists of exhaled gas that contains no CO_2. Thus, the capnogram lags behind the actual expiration. If there is an expiratory pause during which the spectrometer samples gas, fresh gas will be entrained from the inspiratory limb of a circle system or from the fresh gas of a Bain circuit. This fresh gas contains no CO_2 and the capnogram descends as though inspiration were occurring. Both mechanisms will make the expiratory time appear briefer than it is, thus the I:E ratio appears increased. Without a direct measurement of flow, an exact measurement of the I:E ratio is not possible. Patients breathing spontaneously under anesthesia have respiratory patterns that introduce new complexities that may not have been considered by the software of the mass spectrometer (4). Since the respiratory rate is calculated from the capnogram, it is useful to check the rate reported by the mass spectrometer: when the rate is obviously wrong (see Fig. 2) all other data reported by the unit are unreliable.

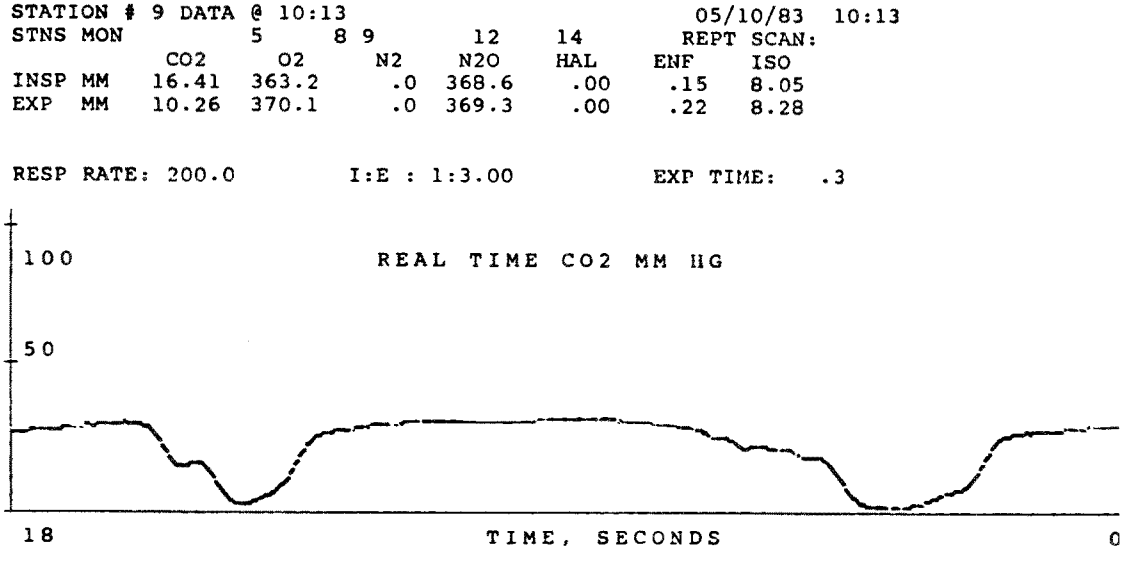

Fig. 2. Mass spectrometer read out with erroneous data. Observe the excessive respiratory rate, indicative of a failed analysis of Co_2 data.

Helium and propellants

Introduction of a gas undetectable by a spectrometer can distort data. Assume for instance that during laser surgery of the airway or ventilation of a patient's lungs with tracheal stenosis, helium is employed but that the mass spectrometer has no specific collector plate for this noble gas. The spectrometer will calculate the partial pressures of the measured gases as if they alone made up the total local barometric pressure and thus will artificially increase the partial pressures of the measured gases. This is a dangerous situation if the mass spectrometer is accepted as a reliable oximeter because it would calculate and display erroneously high oxygen concentrations.

In mass spectrometers equipped for helium analysis another problem arises. Some spectrometers with ion pumps cannot evacuate the noble gas quickly from the high vacuum chamber of the analyzer. Therefore, after correctly analyzing a gas mixture containing helium, the spectrometer will switch to the next station before all the helium has been evacuated from the chamber and, thus, the partial pressures of the sample from that station (not using helium) will be read erroneously low.

Other gases as well can be added during anesthesia. A patient who becomes bronchospastic, for example, and is treated with a metered bronchodilator such as Ventilin®, Alupent®, Isuprel®, or Norisodrine® receives not only the incorporated bronchodilator drug but also the gaseous propellant. We have noted that some spectrometers (Perkin-Elmer MGA 1100 but not Chemetron) confuse the propellant with isoflurane. Spectrometers ionize the propellants, which are mixtures of fluorinated hydrocarbons such as dichlorodi- and dichlorotetrafluoromethane; they are well ionized and are cleared from the system promptly. The propellants have spectral peak components that overlap those of isoflurane but not those of its isomer enflurane or any of the other measured gases. The propellants easily saturate the isoflurane collector in the Perkin-Elmer system (it may read 70 mmHg isoflurane) and, in so doing, cause the sum of partial pressures to exceed local barometric pressure. This generates a twofold problem. First, if a propellant is introduced into this system while the spectrometer is sampling (which is easily avoidable), it will seem as if excessive isoflurane had been administered. Secondly, the validity of the other gas values is put into question by an incorrect sum of the partial pressures. Fortunately, this effect is quite transient and does not affect a subsequent sample from either that station or another. Continued experience may reveal more substances that deceive the spectrometer.

Water vapor

During anesthesia, inhaled gases are typically quite dry, whereas exhaled gases are saturated with water vapor. At 37°, the alveolar vapor pressure of water is 47 mmHg (10). This may present a difficulty when a mass spectrometer is used because water vapor does not register on a collector plate and varies during the respiratory cycle. Several approaches deal with this (1, 16). When the various gases are analyzed, the sum of their fractions should equal one, or the sum of all partial pressures should equal local barometric pressure. This will yield accurate values for dry gases. However inspired gases are humidified on their way to the alveoli and their partial pressures in the lung will be lower than indicated as a result of the unmeasured water vapor. Exhaled gases are saturated with water vapor when they leave the alveoli but are desaturated by the time they arrive at the ionization chamber of the spectrometer. So again, one is measuring gases that differ from those at the alveolar level. At one atmosphere barometric pressure (760 mmHg) saturated water vapor (47 mmHg) constitutes 6% of the total pressure. If this is not taken into consideration, the values of all the measured expired gases will be increased artificially by 6%. This error then distorts derived values such as alveolar-arterial CO_2 gradients.

The barometric pressure of an analyzer can be adjusted to total local barometric pressure minus the saturated water vapor pressure (e.g., 760 − 47 = 713), which will reflect the composition of inspiratory and expiratory gases at the alveolar

level as long as the patient's alveolar temperature remains 37 °C.

The concern about water vapor can be sidestepped by reporting all gases in percentages of dry gas. However, when one wishes to correlate the alveolar percentages of oxygen or CO_2 to partial pressures in blood, cumbersome calculations become necessary.

mmHg or percent

Inspired oxygen is usually reported in either percent or flow rate, arterial oxygen in torr or mmHg, and anesthetic concentration in percent. We find this practice confusing. We know the sum of the inspired as well as the expired gases must equal either 100% or the ambient barometric pressure minus water vapor pressure. Using mixed units (% and mmHg) precludes adding inspired and expired partial pressures to make certain they equal the expected level. Therefore, we use only one unit – mm Hg. This not only allows summing the partial pressures but also facilitates correlation with blood gas levels – also reported in mmHg.

Alarms

The primary purpose of mass spectrometry in the operating room is to enhance the safety of the patient. In our institution we use the alarm thresholds shown in Table 1. Although one may debate each limit, we have found these levels to be clinically useful. They do not cause many false alarms that lead users to deactivate them, a dangerous but common step.

Table 1. Alarm limits on mass spectrometer used at the University of Florida.

	Expiratory		Inspiratory	
	High	Low	High	Low
CO_2	55	no	10	no
O_2	no	100	no	140
N_2	610	no	610	no
N_2O	610	no	610	no
Halothane	40	40	40	40
Enflurane	40	40	40	40
Isoflurane	40	40	40	40

Alveolar-arterial gradient

Another consideration of monitoring respiratory gas deals with the alveolar-arterial (A-a) gradients, which is well described for oxygen (3), carbon dioxide (12), and anesthetic agents (6, 20). Oxygen A-a gradients are affected by many variables including cardiac output, closing volume, and inspired oxygen concentration (5).

Carbon dioxide, one of the more frequently monitored end tidal gases, also has a typical A-a gradient of 4 to 5 mmHg in anesthetized man (13). In a series of 29 healthy elective surgical patients in whom we monitored arterial blood gases and simultaneously sampled end tidal gases, we found A-a CO_2 gradients of at least 10 mmHg in three patients. In addition one patient had a small negative A-a gradient. Though negative A-a gradients have been investigated in great detail, it is still unclear whether they are real or artifactual; there are proponents of both views (2, 9, 15). Thus, while analysis of end tidal gases by mass spectrometer or capnograph provides vital information on gas composition and ventilation, it does not portray blood gases reliably. This is usually of little significance but may become important in some circumstances. For instance, when careful control of arterial CO_2 is intended to influence brain blood flow and hence brain volume during a craniotomy, an error of 10 mmHg will have important clinical consequences.

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