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Evaluation of a Blood Gas and Chemistry Monitor for Use during Surgery

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An observational study was performed to evaluate a new blood gas and chemistry monitor (GEM-6™ Diamond Sensor Systems, Ann Arbor, Michigan) in nine patients during cardiac surgery. Paired blood samples were analyzed by the instrument under test and by standard clinical laboratory instruments. The differences between the measurements of the new and the standard instruments are summarized as follows (mean ± standard deviation, units of measure, number of samples): *p*H (−0.039 ± 0.02, 154); P_{CO_2} (2.63 ± 1.8 mmHg, 154); venous P_{O_2} (−2.0 ± 3.0 mmHg, 72), hematocrit (4.7 ± 2.7%, 98), potassium (0.18 ± 0.13 mmol, 100), and ionized calcium (0.195 ± 0.11 mmol, 100). Because the differences in arterial P_{O_2} measurements were markedly heteroscedastic, a logarithmic transformation was employed, which upon retransformation gave the test instrument's 95% confidence limits as within 5.1% below to 46% above the nominal value on 82 samples. However, on the 14 samples having nominal values below 165 mmHg (the upper limit of the calibrated range of the GEM-6™) the 95% confidence limits were from 5.4% below to 23.6% above the nominal reading. No failures of the test instrument occurred during the evaluation, and quality control standards run before, midway through, and again after sampling from each patient all gave readings within the manufacturer's tolerance. For all variables except hematocrit and ionized calcium, this instrument matches the values from the laboratory well enough over the clinically important range to supplant it for intraoperative monitoring purposes. (Key words: Monitoring: blood gas analysis.)

DURING SURGERY rapid changes often occur in blood gases, acid–base status, potassium, ionized calcium, and hematocrit. Having an instrument that can monitor these variables on site, rather than having to await results from the stat laboratory, may improve patient care.

The GEM-6™ (Diamond Sensor Systems, Ann Arbor, Michigan) is a new analytic system intended to measure these variables in the operating room. It utilizes miniaturized electrodes for blood gas and electrolyte determination and an electrical conductivity method[1,2] to estimate the hematocrit. The electrodes are housed in a disposable pack with two calibrating reagents and a sealed waste disposal receptacle (to minimize biohazard). The instrument can analyze manually introduced discrete blood samples or automatically aspirate arterial and venous blood from a cardiopulmonary bypass machine. Each disposable pack can process 50 samples over an active service time of up to 8 h and, utilizing a standby mode, has a useful lifetime of 36 h. The instrument performs an automatic two-point calibration initially and after every hour of operation. A single-point calibration is done after each measurement. Three types of quality control solutions are provided by the manufacturer for testing the system at the low, middle, and high end of the physiologic range of all variables except hematocrit.§ The required sample volume is 2 ml for all tests, and approximately 130 s are required to process a specimen.

We conducted an observational study comparing GEM-6™ measurements made in the operating room with those made by conventional instruments in the stat laboratory.

Materials and Methods

With institutional approval and individual informed consent we studied nine patients undergoing coronary artery or valvular operations. We received instruction in use of the instrument from the manufacturer's representative and followed the user's manual faithfully throughout the study. Preoperatively, we installed connections into the bypass circuit for automatic blood sampling. To assure that each disposable pack was performing within specifications, we performed a quality control test using the three standard solutions on a rotating basis, before, midway through, and again after sampling from each patient. The instrument was set to display the blood gas data at 37° C.

An adapter was used before and after bypass to allow analysis of specimens in syringes. Paired samples were drawn from the patient's radial arterial catheter and the central venous port of the pulmonary artery catheter into heparin-washed plastic syringes and immediately analyzed by both the the GEM-6™ and our stat laboratory. During bypass the instrument was set to draw samples automatically from the bypass circuit on command approximately every 10 min. Comparison samples were drawn from the arterial and venous perfusion tubing (with a time-offset to compensate for the transport lag through the instrument's sampling tubing) and immediately sent to the stat laboratory for analysis.

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§ Although not used in the current study, the manufacturer now provides two types of vials of cell-free electrolyte solution to test the hematocrit function.

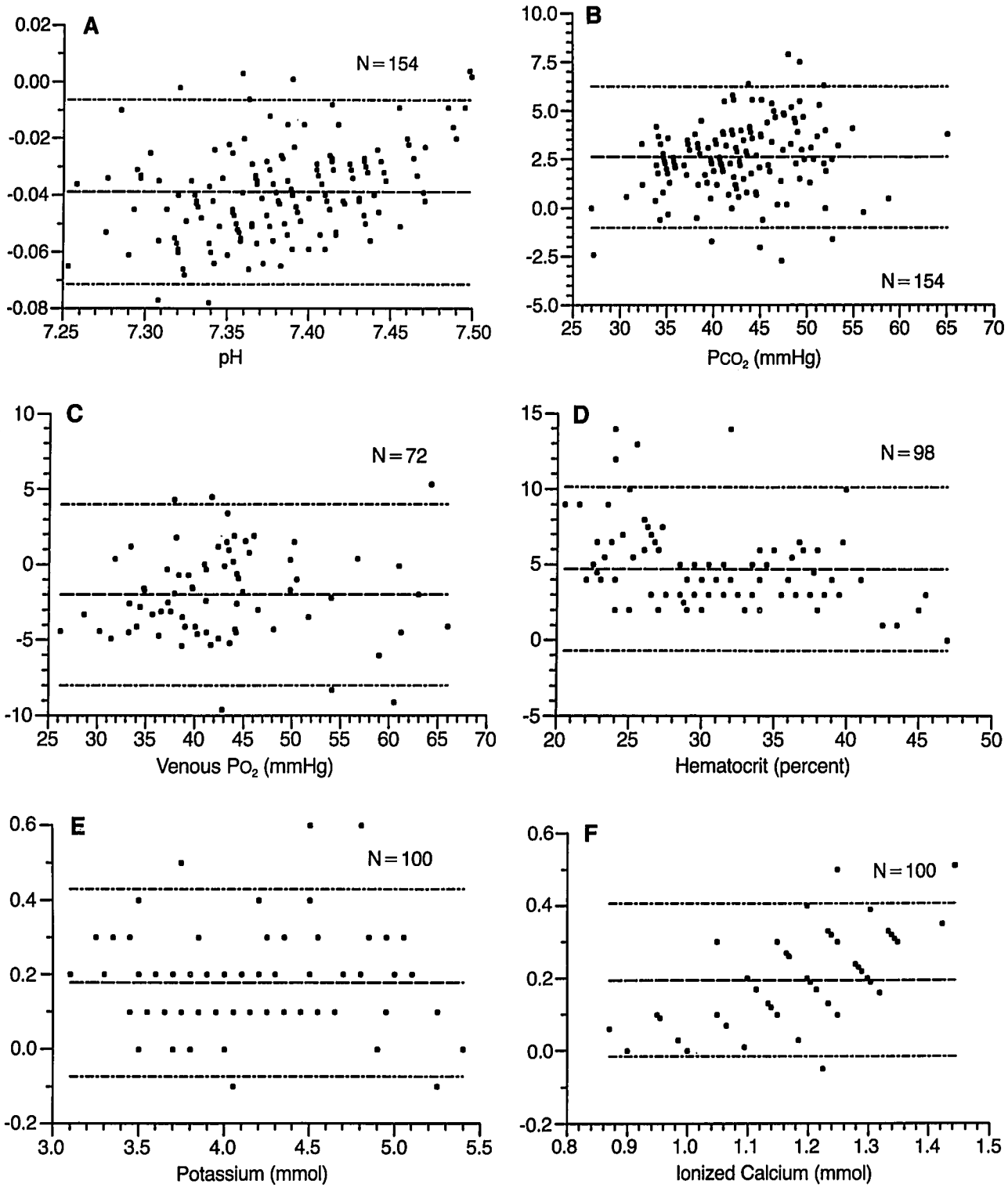

FIG. 1. Scattergrams of the differences between the GEM-6™ and corresponding laboratory measurements. The abscissae give the average of the paired measurements, and the ordinates give the difference between them. The mean of the differences is indicated with a dashed line, and the limit of agreement (an interval of ±2 SD about the mean) is enclosed by the pair of dot-dashed lines. (*A*) the *p*H, (*B*) the P_{CO_2} in mmHg, (*C*) the venous P_{O_2} in mmHg, (*D*) the hematocrit in percent, (*E*) the potassium ion concentration in mmol, and (*F*) the ionized calcium concentration in mmol. The number of data points (N) is given in each graph, and the units indicated apply to both axes.

In the stat laboratory a technician and a separate set of analytic instruments were dedicated solely to this study to assure immediate processing of the specimens for comparison. Stat laboratory measurements were made utilizing a Corning Model 178® *p*H/blood gas analyzer, a Corning Model 902® sodium/potassium analyzer, a Radiometer Model ICA1® ionized calcium analyzer, and a Clay Adams Autocrit Ultra-3, Model 0575® for packed-cell hematocrit determination. The stat laboratory instruments were calibrated according to the recommendations of their respective manufacturers, and the blood gas machine was tested with quality control procedures developed in our institution.[3] Statistical analysis was performed by the method of Altman and Bland[4,5] and by linear regression. For all variables probit plots were constructed of the differences between the GEM-6™ measurements and those of the laboratory instruments.

Results

Four disposable electrode packs were used on two patients each, and one pack was used for a single patient. Four of the packs had a combined active service and standby time of approximately 8 h, and one pack was kept on standby overnight between patients, resulting in a combined active service and standby time of 30 h. The instrument took approximately 48 min for warm-up, 5 min for an initial two-point calibration, and 5 min for the first quality control test of each electrode pack. Four packs had a total of six quality control tests run, and one pack had three. No failures of the instrument or the disposable packs occurred during the study, and the five packs were found to be within manufacturer's tolerance on all quality control tests.

Scattergrams of the difference between the GEM-6™ and the corresponding laboratory measurements are plotted against the average of the paired measurements in figure 1*A* through 1*F*. The means of the differences (shown as a dashed lines) form a measure of the bias between the instruments, and the SD form a measure of their precision.[5] Visual inspection of the probit plots (not shown) revealed that the differences between all of the paired measurements were approximately normally distributed. Thus, 95% of the differences between individual measurements should fall within an interval of ±2 SD from mean difference between the measurements (called the limit of agreement[5] and enclosed by the pairs of dot-dashed lines). As marked, proportional error was present in the P_{O_2} measurements, and the venous and arterial data were separated for analysis to avoid having the large errors in the high P_{O_2} readings obscure the illustration of the smaller errors in the important low P_{O_2} range. These are shown in figures 1*C* and 2, respectively. A logarithmic transformation was necessary to make the arterial P_{O_2} values more nearly homoscedastic.

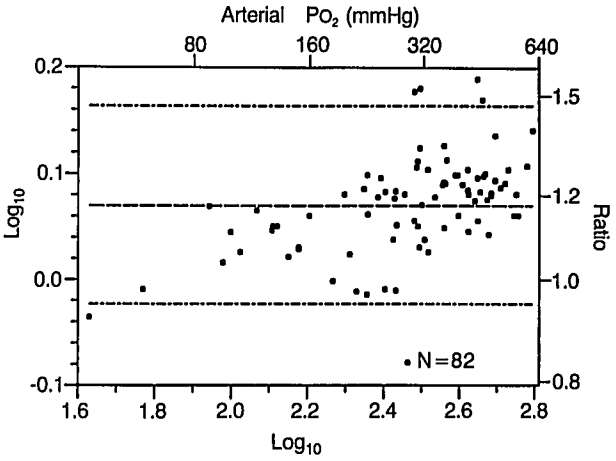

FIG. 2. Scattergram of the difference between the (base 10 logarithmically transformed) arterial P_{O_2} values measured by the GEM-6™ and Corning blood gas machines *versus* the average of their logarithms. The corresponding ratio of the two measurements is shown on the right-hand scale, whereas the geometric means of the measurements (in mmHg) is shown on the top scale. The dashed and dot-dashed lines are as in figure 1.

Linear regressions were calculated for all variables, and plots of the pooled residuals (not shown) were constructed as a function of the measured values, the time interval since the last two-point calibration, and the time-in-service of the electrode packs. Visual inspection revealed no evidence of nonlinearity, drift, or increasing variability in the measurements with time. However, the regression lines for the individual electrode packs were found not to be colinear ($P < 0.05$, F test[6]) for all of the variables except P_{CO_2}. (This is a consequence of the variability between electrode packs producing larger errors than the random measurement errors occurring within a given pack.)

The summary statistics are given in the first five columns of table 1. For comparison, the nominal value and tolerance limits of the appropriate manufacturer's quality control solution are shown in the sixth and seventh columns. Our data are also to be compared to the performance guidelines for stat laboratories promulgated by the American Association for Clinical Chemistry (columns eight through ten).¶

Discussion

Recent advances in techniques of chemical analysis and electronic instrumentation have enabled the introduction of sophisticated and easy-to-use instruments to perform

¶ Guidelines for Providing Quality Stat Laboratory Services. Washington, DC, American Association for Clinical Chemistry Press, 1987.

TABLE 1. Errors of Measurement

Variable Name	GEM-6™ – Stat Lab				Manufacturer's QC Limits		AACC Guidelines			Range Tested	Unit
	N	Mean	SD	Limits of Agreement	Nominal	Range	Nominal	Bias	SD		
*p*H	154	−0.039	0.02	−0.07 to −0.01	7.37	±0.04	7.40	0.03	0.02	7.25–7.50	—
P_{CO_2}	154	2.63	1.8	−1.0 to +6.3	42	±5	40	3	2	27.0–65.1	mmHg
$P\bar{v}_{O_2}$	72	−2.0	3.0	−8.0 to +4.0	70	±12	60	3	2	26.2–66.1	mmHg
Pa_{O_2}	82	0.071*	0.047*	−5.1% to +46%	147	±12	—	—	—	44.4–530.	mmHg
Hct	98	4.7	2.7	−0.7 to +10.1	—	—	40	2	1.5	20–47	%
K^+	100	0.18	0.13	−0.07 to +0.43	3.8	±0.6	3	0.1	0.1	3.1–5.4	mmol
Ca^{++}	100	0.195	0.11	−0.02 to +0.41	1.2	±0.4	1.25	0.04	0.02	0.87–1.45	mmol

QC = quality control; AACC = American Association for Clinical Chemistry.

* The mean and standard deviation are expressed as base 10 logarithms. The limits of agreement have been retransformed and expressed as a percentage of the nominal value.

laboratory tests near the patient. To date, most of these have been intended for physician's office use,[7] but some perform the traditional stat laboratory functions encountered in anesthesia and intensive care. These offer not only faster turnaround than the hospital laboratory, but also the possibility of savings in labor costs.

At least three manufacturers have targeted cardiopulmonary bypass as the initial application for new technology in blood gas analysis because a large number of samples are required and the need for rapid turnaround is particularly acute. Some instruments use sensors located in-line,[8–11] giving the advantage of continuous measurement but at the expense of difficulties in maintaining calibration and performing quality control tests.[8,9] The analytic methods used in-line will soon become available in instruments making direct intravascular measurement,[12–14] while a discrete-sample instrument (similar to the GEM-6™, but requiring a smaller sample volume) is being developed for intensive care use.

Although the GEM-6™ makes discrete, rather than continuous measurements, its analysis time (approximately 2 min) is comparable to the response time of an in-line instrument.[8] The discrete-sample approach offers the important advantage that the instrument (and its cost) can be shared among several patients. Furthermore, in contrast to either in-line or *in vivo* measurement, the sampled technique allows for automatic initial calibration, for automatic recalibration during use, and for quality control tests to be run at will.

A useful criteria for whether a monitoring instrument can substitute for the conventional laboratory is whether the limits of agreement between their measurements is clinically acceptable.[5] This approach to methods comparison is more appropriate than regression analysis for several reasons: 1) Although the manufacturer must construct a regression line to calibrate a newly developed instrument, the user often will not have the resources to first perform a regression and then to transform the instrument's indicated values according to the locally derived calibration line. Rather, the user will want to know the *a priori* relationship between the new and old methods of measurement. 2) Clinical instruments used for making comparative measurements may have considerable error of their own, causing the slope and intercept of the regression line to be underestimated.[9,15,16] 3) Reporting a correlation coefficient near unity may give the false impression of good agreement between methods when the regression line deviates widely from the line of identity. 4) A correlation coefficient near unity can also result when an imprecise instrument is tested over a large range of the independent variable.[17]

The limits of agreement shown in table 1 for *p*H, P_{CO_2}, venous P_{O_2}, and potassium are probably acceptable for most clinical purposes. The means and SD of the difference between measurements fall within the American Association of Clinical Chemistry stat laboratory performance guidelines for P_{CO_2}, and they come close to meeting the guidelines for *p*H, venous P_{O_2}, and potassium. This is without making allowance for the fact that the difference statistics include the error components of the stat laboratory instruments themselves.

For arterial P_{O_2} the logarithmic transformation resulted in a limit of agreement expressed as a percentage error about the nominal reading (−5.1% to +46% after taking antilogarithms). Although this appears to be wide, examination of the scattergram (fig. 2) reveals that large differences between the GEM-6™ and laboratory values occurred only for high oxygen tensions (beyond the calibrated range of either instrument). Reanalysis of the 14 arterial data points having a nominal P_{O_2} of less than 165 mmHg (the upper calibration limit of the GEM-6™) gave a limit of agreement of −5.4–+23.6% of the nominal reading (−0.024 to +0.092 on the log scale). Alternatively, neglecting the heteroscedasticity and analyzing these 14 points without the logarithmic transformation gave a limit of agreement of −4.2 to +24.6 mmHg.

Measurement of blood samples with high P_{O_2} is known to be problematic,[18] and we encountered similar disagreement with high P_{O_2} in evaluating an in-line instrument.[9] The presence of heteroscedasticity means that the instrument will perform better at the low end of its range where accuracy is more important clinically. Unfortunately, most of the values of our arterial samples occurred in the (less important) upper end of the range. However, the limit of agreement for the venous specimens (−8.0 to +4.0 mmHg) and the lower-tension arterial specimens suggests that the accuracy of P_{O_2} measurement by the GEM-6™ is adequate over the clinically important portion its range.

However, the hematocrit measurement deviates unacceptably from packed-cell hematocrit values. Being derived from a measurement of electrical conductivity, it may vary with changes in red cell geometry and plasma ion concentration.[1,2] We understand that the manufacturer is planning to build in a correction for the concentration of sodium, the principal plasma ion. Also, the limit of agreement (and the manufacturer's tolerance range) for ionized calcium are as wide as the entire range of the normal values (1.12–1.23 mmol), making this measurement of little clinical utility.

A decision to have user-operated laboratory instruments in the operating room imposes an additional medical and legal responsibility[7] on the anesthesiologist for the proper functioning and quality control of the new clinical laboratory. One should be aware of guidelines and standards regarding testing in distributed hospital laboratories issued by the Joint Commission on Accreditation of Hospitals, Veterans Administration, and Medicare.[19] The user should also be be aware that instrument performance under operating room conditions may not be as good as it is in the research laboratory.[9] Furthermore, even instruments designed for operation by nonspecialized personnel may suffer a loss of accuracy and fail to meet the manufacturer's specifications when operated by other than qualified laboratory technologists.[20,21] These factors argue for a strong cooperative relationship between laboratory medicine specialists and the clinicians using the instruments.

In conclusion, the GEM-6™ is reliable, convenient to use, and agrees satisfactorily with laboratory blood gas and potassium analyzers over the clinically important range of values to substitute for them in the operating room. However, the hematocrit and ionized calcium measurements are not accurate enough to supplant conventional laboratory measurements.

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