THE EVALUATION OF A NEW INTRAVASCULAR BLOOD GAS MONITORING SYSTEM IN THE PIG

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ABSTRACT. Objective. Our objective was to investigate the accuracy of a new intravascular blood gas sensor, the Paratrend 7 (P7) (Biomedical Sensors Ltd, Pfizer Hospital Products Group, High Wycombe, England) in a porcine model. **Methods.** A total of 12 sensors were inserted into 10 animals under total intravenous anesthesia. Changes in blood gas chemistry were produced over a wide range by manipulating the inspired oxygen and carbon dioxide concentrations and by adjustments in minute ventilation. Blood gas samples (BGA) were taken and analyzed during periods of stability; the results obtained were compared with the readings from the intravascular sensor. **Results.** A total of 292 blood gas samples were taken and analyzed for pHa, $Paco_2$, and Po_2; the results were compared with the readings from the intravascular sensor. Correlation coefficients of $r = 0.98$ for Pco_2 and $r = 0.99$ for Po_2 were obtained. Analysis of bias and precision as mean ± SD of the difference (P7 − BGA) gave the following results: pH bias = −0.03, precision = ±0.04; Pco_2 bias = 0.65 mm Hg, precision = ±3.1 mm Hg; and Po_2 bias = −6.50 mm Hg, precision = ± 0.6 mm Hg. No problems with clot formation on the sensor were seen, and the sensors did not appear to show the "wall effect" seen with other systems. **Conclusions.** The results obtained were well within the requirements for a clinically useful blood gas monitoring system.

KEY WORDS. Equipment: intravascular sensors. Monitoring: blood gas analysis.

INTRODUCTION

The continuous measurement of arterial blood gases with sufficient accuracy and reliability to be clinically useful has been an elusive goal. In general, previously described systems have suffered from a number of problems, including a (1) a large sensor size [1]; (2) the use of abnormally large arterial cannulae; (3) unnacceptable arterial waveform damping and sampling difficulties with conventional cannulae; (4) excessive drift in the accuracy of the sensors used [2]; (5) clot formation on the sensor; and (6) in the case of tip-located sensing elements, excessive "wall effects" as the sensor lies along the arterial wall [3]. This paper describes the results of a study designed to measure the accuracy of a new intravascular sensor inserted into the carotid artery of the juvenile pig.

METHODS AND MATERIALS

Experimental Animals

A total of 10 juvenile pigs (8 to 10 weeks of age), weighing between 17 and 32 kg (mean weight, 18.8 ± 1.5 [SD] kg) were anesthetized with 10 mg/kg of

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ketamine (intramuscularly), followed by the inhalation of isoflurane in oxygen-enriched air at an F_{IO_2} of 0.6. The animals were intubated with a cuffed endotracheal tube and intravenous access was established via a suitable ear vein.

Subsequent total intravenous anesthesia was commenced using bolus doses of midazolam (0.5 mg/kg), fentanyl citrate (100 μg/kg), fluanisone (3 mg/kg), and alcuronium (0.3 mg/kg).

The animals' lungs were ventilated using air/oxygen mixtures from a modified volume preset ventilator (B.O.C., Pneumotron). Initial settings were: tidal volume 10, ml/kg; respiratory rate, 10 breaths/min; and F_{IO_2}, 0.4, subsequently adjusted according to the experimental protocol. Anesthesia was maintained using continuous infusions of midazolam at 1 mg/kg/hr, fentanyl at 200 μg/kg/hr, fluanisone at 6 mg/kg/hr, and alcuronium at 0.3 mg/kg/hr.

Throughout the procedure, heart rate, intraarterial blood pressure, inspired oxygen concentrations, and end-tidal CO_2 concentrations were continuously monitored with intermittent measurements of neuromuscular blockade from a femoral nerve stimulator. The research was carried out under home office personal and project licenses for scientific procedures in animals.

Intravascular Blood Gas Sensor

The intravascular sensor (Paratrend 7, Biomedical Sensors Ltd, Pfizer Hospital Products Group, High Wycombe, England) is a miniaturized, four-component sensor incorporating an amperometric oxygen electrode, proprietary fiberoptic pH and P_{CO_2} electrodes, and a thermocouple for temperature measurement and compensation.

The components are housed in a thin polyethylene tubing (0.45 mm outside diameter) that is permeable to the analytes to be measured and coated in covalently bound heparin (Carmeda AB, Stockholm, Sweden) to reduce fibrin deposition and clot formation. The sensors were calibrated using microprocessor-controlled calibration routines incorporated into the monitoring system. Three tonometered calibration solutions were used, providing a single-point calibration for the P_{O_2} electrode and three-point calibrations for the pH and P_{CO_2} electrodes. Data were collected from the monitor at 3-sec intervals from its RS-232 serial port and were transferred directly into an IBM-compatible personal computer.

Experimental Design

Having established stable total intravenous anesthesia, we exposed and cannulated bilateral carotid and femoral arteries with 18-gauge cannulae (Medicut, Argyle). All four arterial catheters were flushed continuously with a solution of normal saline containing heparin 2 U/ml at a rate of 3 ml/hr from a pressurized flush bag maintained at 300 mm Hg. Arterial pressures were transduced from all the catheters with disposable transducers (Uniflow 43-600F, Baxter Healthcare Corporation, Deerfield, IL), so as to confirm continued cannula patency. Two monitors (Model 78353B, Hewlett-Packard) with analog outputs to a channel chart recorder (Gould 4) were used to display the signals. One ($n = 8$) or two ($n = 2$) intravascular blood gas sensors were inserted via the carotid cannulae so that 10 cm of the sensor was in the artery. One of the femoral catheters was used for monitoring blood pressure and for taking intraarterial blood gas samples. The sensor introducers had a side arm for the connection of the heparin flush solutions and for arterial pressure monitoring.

At each measurement point, arterial blood gas samples were withdrawn anaerobically into 2-ml heparinized syringes and were analyzed immediately on a conventional blood gas machine calibrated and maintained according to the manufacturer's instructions (Model 170, Corning Scientific). The following data were collected and stored for subsequent analysis: intravascular pH (pHi), intravascular P_{O_2} (P_{IO_2}), intravascular P_{CO_2} ($PiCO_2$), intravascular temperature, arterial blood gases (pHa, Pa_{O_2}, Pa_{CO_2}), rectal temperature, arterial blood pressure, respiratory rate, tidal volume, end-tidal CO_2, and F_{IO_2}.

After insertion of the intravascular sensors, baseline blood gas readings were adjusted by manipulation of the ventilatory parameters to achieve nominal starting values of 7.40 pHa, 50 mm Hg Pa_{CO_2}, and 100 mm Hg Pa_{O_2}, as indicated on the intravascular sensor. Rectal temperatures were maintained at 38 ± 1°C (normothermia) with a heated pad. After a 15-min stabilization period, two consecutive blood gas samples were analyzed at 5-min intervals to ensure that a stable baseline state had been achieved. Each of the animals was then subjected to a program of the ventilatory manipulations to produce a range of pH, Pa_{O_2} and Pa_{CO_2} values (Table 1). At each stage, two sets of data were recorded at 5-min intervals after a stabilization period of 15 min.

The intravascular sensors remained in the animal for approximately 8 hr. When the study program had been completed, the animals were given a lethal intravenous injection of pentobarbital. The carotid arteries containing the sensors were further dissected out and opened to expose the sensor–cannula combination. The arterial lumen and sensors were carefully examined for clot formation; the sensors were then inspected again, after careful removal from the cannulae.

Table 1. Program of Ventilatory Manipulations

Stage	Manipulation	Nominal Values
Hyperoxia + hypocarbia	Increased F_{IO_2} + increased ventilation	Pa_{O_2} 150, 250, 500 mm Hg Pa_{CO_2} 40, 30, 20 mm Hg
Baseline	Normal ventilation	Pa_{O_2} 100 mm Hg Pa_{CO_2} 50 mm Hg pHa 7.4
Hypoxia + hypercarbia	Reduced F_{IO} + reduced ventilation	Pa_{O_2} 80, 60 mm Hg Pa_{CO_2} 80, 60 mm Hg
Baseline	Normal ventilation	Pa_{O_2} 100 mm Hg Pa_{CO_2} 50 mm Hg pHa 7.4
Acidosis	F_{IO_2} = 0.4 + added CO_2	pHa 7.0, 6.8
Baseline	Normal ventilation	Pa_{O_2} 100 mm Hg Pa_{CO_2} 50 mm Hg pHa 7.4
Hypoxia	Reduced F_{IO_2}	Pa_{O_2} 40, 25 mm Hg

Table 2. Results of Comparisons between the Intravascular Blood Gas Readings and Those from a Standard Blood Gas Analyzer

	n	r	Bias	% Bias	Precision	% Precision	Drift In vivo (mean ± SD)
pH	292	na[a]	−0.03	na[a]	0.04	na[a]	−0.002 (± 0.005)hr^{-1}
P_{CO_2}	239	0.98	0.65 mm Hg	2.1%	3.1 mm Hg	7.2%	0.42 (± 0.61)%hr^{-1}
P_{O_2}	254	0.99	−4.90 mm Hg	−3.8%	8.7 mm Hg	5.8%	−0.59 (± 1.52)%hr^{-1}

[a]Due to the logarithmic scale of pH measurements, linear regression and percentage values are not presented.

Data Analysis

The comparisons of the intravascular blood gas readings with the blood gas analyzer readings were performed by least squares linear regression and correlation analysis for the P_{CO_2} and P_{O_2}. The bias and precision for all three variables were calculated using the modified Bland and Altman [4] analysis, in which bias is calculated as the mean of the differences (P7 − BGA) and the precision as the SD of these differences.

The in vivo drift was calculated as (final bias − starting bias)/time and is expressed as percentage drift per hour for P_{O_2} and P_{CO_2}.

RESULTS

The results are presented in Table 2 and in Figures 1 through 3. Despite very careful maintenance, calibration, and quality control checks between each group of blood gas analysis samples, there were 11 occasions (4%) in which P_{O_2} comparisons could not be made and 52 occasions (18%) in which P_{CO_2} comparisons could not be made due to calibration failures by the blood gas analyzer. The electrodes function independently in the blood gas analyzer we used, and failure of one does not affect the other two.

DISCUSSION

The intravascular sensors were all inserted without difficulty and reached steady readings within 2 min. The results show that the system was able to measure arterial pH, P_{CO_2}, and P_{O_2} continuously with acceptable accuracy, and precision with minimal drift over a wide range of values. The results compare favorably with

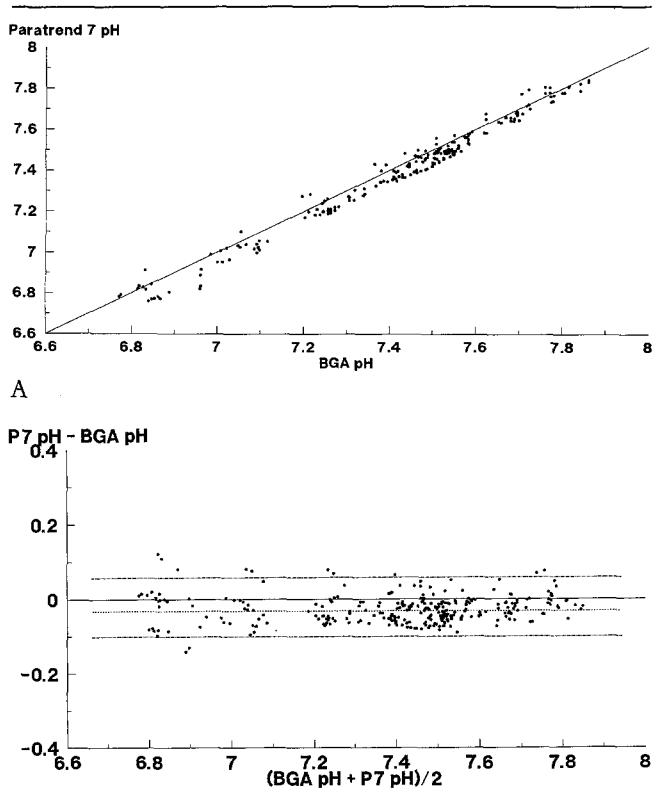

Fig 1. (A) pH values obtained by the intravascular sensor (Paratrend 7) compared with those obtained with a conventional blood gas analyzer (BGA); n = 292, y = 0.009 + 1.00X. (B) Intravascular sensor (P7) pH difference plot; ------ = bias, ·····-····· = ± 1.96X precision.

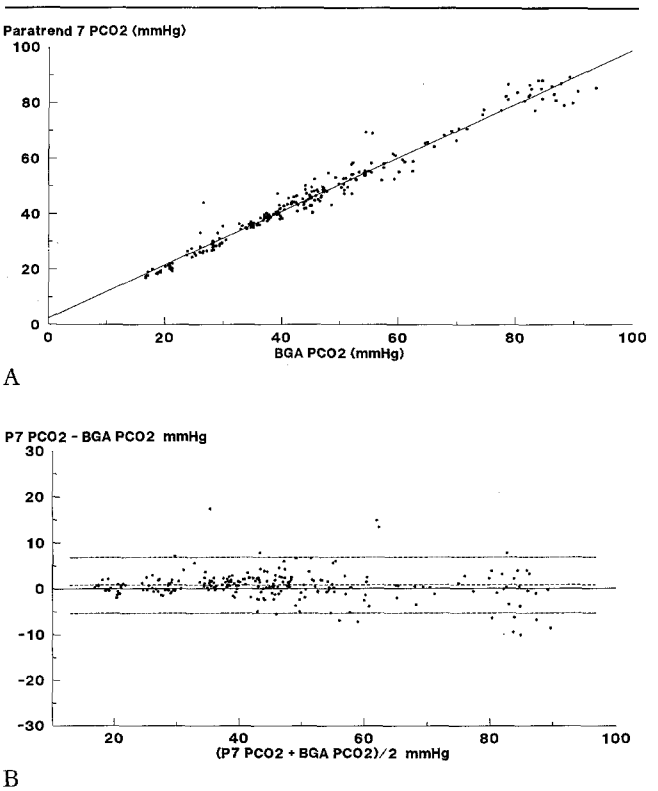

Fig 2. (A)P_{CO_2} values obtained by the intravascular sensor (Paratrend 7) compared with those obtained with a conventional blood gas analyzer (BGA); n = 239, y = 2.40 + 0.96X, _____ = line of regression. (B) Intravascular sensor (P7) P_{CO_2} difference plot; ------- = bias, ·····-····· = ± 1.96X precision.

other animal trials of intravascular sensors [5] and, to our knowledge, this is the smallest combined intravascular sensor so far described.

The bias and precision values calculated are dependent not only on the accuracy of the intravascular sensor, but also on the accuracy of the blood gas analyzer used for the reference values. High levels of bias in the blood gas analyzer could either reduce or exacerbate the apparent bias in the sensor readings, depending on the direction of the analyzer bias; but, poor precision in the analyzer would almost certainly result in poorer precision values being calculated for the sensor. Elser and Hess [6] investigated duplicate blood gas measurements performed on two independently calibrated analyzers (Corning Model 178). The same sample (n = 1,590) was introduced into both analyzers. The bias (precision) for pH, P_{CO_2}, and P_{O_2} were 0.005 (0.009), −0.4 (1.3) mm Hg, and 0.89 (3.29) percent, respectively. Hansen [7] evaluated the bias and precision of a proficiency testing material sent to 400 laboratories. The results represent 13 different analyzer models and 583 instruments. The following results are given as "bias (precision)" and represent the two analyzer models for each parameter with the greatest bias values (based on the means for all instruments): pH −0.016 (0.009) to +0.005 (0.012); P_{CO_2} −2.8 (2.34) to +1.6 (1.10) mm Hg; and P_{O_2} −4.2 (3.00) to +9.05 (5.76) percent. This gives maximum differences of 0.021 pH units, 4.1 mm Hg P_{CO_2}, and 13.2% P_{O_2}.

The CLIA [8] lists criteria for the acceptable performance of blood gas analysis as follows:

pH: Target value ± 0.04
P_{CO_2}: Target value ± 5 mm Hg or ± 8%
P_{O_2}: Target value ± 3 SD

In the study by Hansen et al [7], the most precise analyzer had a precision (1 SD) of 1.62% for P_{O_2}, and the least precise analyzer had a precision of 6.62%. Applying these values to the CLIA criteria above, the three SD values range from 4.87% to 19.87%. It is apparent that even assuming the worst possible case,

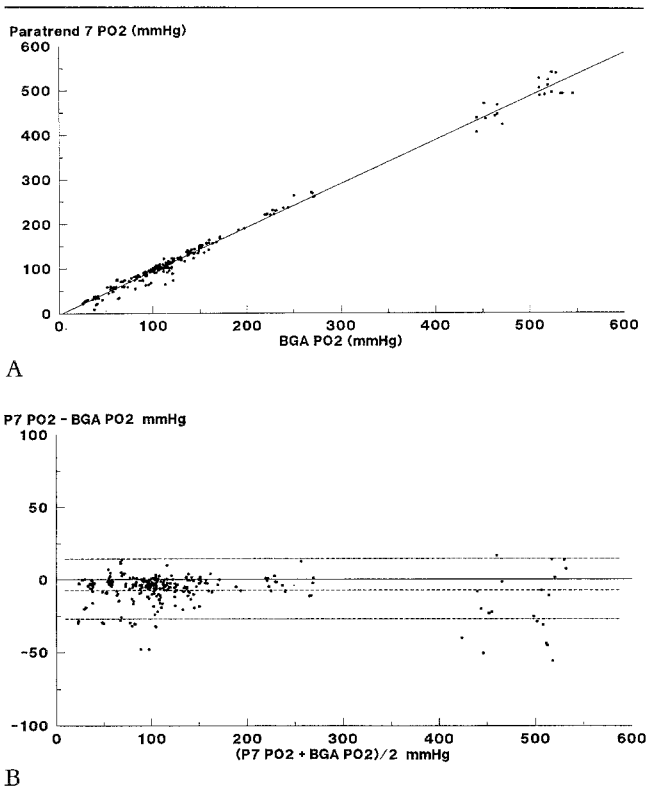

Fig 3. (A) Po_2 values obtained by the intravascular sensor (Paratrend 7) compared with those obtained with a conventional blood gas analyzer (BGA); n = 254, r = 0.99, y = −3.0 + 0.97X; _____ = line of regression. (B) Intravascular sensor (P7) Po_2 difference plot; ------ = bias, ·····- = ± 1.96X precision.

i.e., that all of the errors in measurement come from the intravascular sensor, the results we obtained are well within these recommendations.

The lack of Po_2 readings between 300 and 400 mm Hg is a result of the study design: In order not to prolong the experiment excessively, intermediate readings for Po_2 were not investigated. It is clear from the regression plot that the relationship between the intravascular Po_2 reading and the BGA reading remains linear over the entire range. The absolute precision values at high Po_2 levels are greater, as expected, although the percentage precision values remain small.

The sensors did not demonstrate problems related to fibrin deposition or the "wall effect" described by other investigators, although this clearly needs further investigation during future clinical trials.

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