hydrochloride (10 mg three times a day for as long as 20 days) did not affect values for 17-hydroxycorticosteroids. In vitro data do show that there is a small increase in the apparent value for urinary 17-hydroxycorticosteroids when chlordiazepoxide or its lactam or N-desmethyl metabolite is added to urine. However, this increase does not appear to be large enough to be of significance. The fact that this small increase is not corroborated by the in vivo data may be explained by intrapatient variation from day to day. There was no decrease in the values for 17-ketosteroids either in vivo or in vitro, in contrast to previously reported results.

In serum analyses—including aspartate aminotransferase, alkaline phosphatase, bilirubin, albumin, total protein, and protein electrophoresis—with use of as much as 10-fold the therapeutic blood concentrations of chlordiazepoxide and 200-fold the blood concentrations of the major metabolites, we saw no in vitro effect of the addition of chlordiazepoxide or either of its metabolites. No in vivo data for serum are presented here. These data will be included in a future study on drug interference.

References

Use of Control Sera for Monitoring Temperature Changes during pH and p\text{CO}_2 Measurments

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We evaluated the temperature coefficients from 25 to 38 °C for aqueous calibration materials, serum (protein-based) control material, and patients' samples in blood pH measurements and gas analysis. Whereas the aqueous buffers and calibration gases (used as unknowns) were not affected by changing temperature, the temperature coefficients of patients' samples and protein-based control materials varied similarly to those reported in the literature: 0.011 and 0.014 vs. 0.015 pH/°C, and 1.76 and 1.57 vs. 1.80 mm Hg/°C. We conclude that the periodic use of suitable control materials can assist in the detection of temperature abnormalities.

Temperature is a critical parameter in blood pH measurement and gas analysis. Reported temperature coefficients of patients' blood samples for pH (ΔpH/°C) and p\text{CO}_2 (Δp\text{CO}_2/°C) are, respectively, 0.015 pH unit per degree Celsius and 1.80 mm Hg per degree Celsius. Thus, the blood pH-gas instrument must have a critical temperature-monitoring device to maintain 37 °C and assure accurate data on a patient's acid–base status.

Most blood pH-gas instruments are equilibrated against aqueous buffers. The present study was undertaken to ascertain if the same temperature coefficients listed above apply to aqueous calibration materials and to serum (protein-based) controls.

Materials and Methods

We used a Model 313 (Instrumentation Laboratories Inc., Lexington, Mass. 02173) blood pH–gas analyzer, equilibrated at 25, 36, 37, and 38 °C. When the temperature had stabilized (±0.05 °C), the instrument was standardized
in the usual manner with the calibration buffers (pH 6.841 and 7.383; certified by Instrumentation Laboratories Inc.) and gases (5.0% and 10.2% CO₂; certified by Puritan Bennett, South Hackensack, N. J.). The gases were equivalent to a pCO₂ of 35.2 and 71.8 mm Hg (4.68 and 9.55 kPa), respectively. The calibration values at 37 °C for pH and pCO₂ were then measured for (a) three commercial control sera: Versatol Acid-Base Acidosis, Normal, Alkalosis (General Diagnostics Division, Warner-Lambert Co., Morris Plains, N. J. 07950); (b) three patients' blood samples: a normal, an alkalotic, and an acidotic; and (c) two different calibration gases (35.2 and 71.8 mm Hg) and buffers (pH 6.841 and 7.383). Duplicate determinations were made for both pH and for pCO₂ at 25, 36, 37, and 38 °C.

Results

pH

There was a marked effect of temperature on the samples from patients and the protein-based control materials, whereas the aqueous buffers were essentially unaffected (Figures 1 and 2). The pH of the bloods and control sera decreased with increasing temperature (25 to 38 °C), the respective coefficients being (-) 0.011 and (-) 0.014 pH/°C (Table 1, Figures 1 and 2).

$pCO₂$

The bloods and control sera showed an increased pCO₂ as the temperature was increased from 25 to 38 °C (Figures 3 and 4), the respective temperature coefficients being (+)
For the patients' blood samples: 0.014 vs. 0.011 H/°C and 1.57 vs. 1.76 mm Hg/°C. In contrast, the aqueous calibration buffers and gases, used as unknowns, showed no response to temperature change.

Factors responsible for these observations cannot be determined by this limited investigation, but a number of factors may be influential: (a) The protein-based material contains several buffer systems (bicarbonate, phosphate, and protein), in contrast to the highly purified aqueous standard buffer; (b) the ionization constant for the weak acids constituting the different buffer systems may respond differently to temperature; and (c) the protein present in the protein-based materials may influence the temperature sensitivity of the blood and control samples by changing either the physical properties of the membranes or, by affecting its mobility, the apparent activity of the hydrogen ion.

This difference in behavior of the calibration materials vs. control sera is an important consideration in routine monitoring of instrument operation, specifically in alerting the operator to any abnormal temperature variation in the blood pH-gas analyzer. Changes in temperature would be readily detected by an inability to obtain the expected value for the control materials. Calibration buffers and gases do not respond to temperature changes, and so cannot be used to reveal such changes.

In conclusion, this study demonstrates that the periodic analysis of suitable control materials, as part of a routine quality-control program, can assist in the detection of temperature abnormalities before they become a problem in blood pH-gas analysis.

References