TOTAL CARBON DIOXIDE/ (TCO_2)

Intended Use

The test for TCO_2, as part of the i-STAT System, is intended for use in the *in vitro* quantification of total carbon dioxide in arterial, venous, or capillary whole blood.

Carbon dioxide is used in the diagnosis, monitoring, and treatment of numerous potentially serious disorders associated with changes in body acid-base balance.

Method Explanation

The measured TCO_2 test method is calibrated to the International Federation of Clinical Chemistry (IFCC) TCO_2 reference method[1] with an algorithm, based on the Henderson-Hasselbalch equation, which uses pH, $\boldsymbol{P}CO_2$, and ionic strength (Na) measurements.

Contents

Each i-STAT cartridge contains one reference electrode (when potentiometric sensors are included in the cartridge configuration), sensors for the measurement of specific analytes, and a buffered aqueous calibration solution that contains known concentrations of analytes and preservatives. For cartridges that contains sensors for the measurement of TCO_2, a list of reactive ingredients is indicated below:

Reactive Ingredient	Minimum Quantity
Carbon Dioxide (CO_2)	25.2 mmHg

Metrological Traceability

The i-STAT System test for total carbon dioxide (TCO_2) measures the amount-of-substance total concentration of all forms of carbon dioxide in the plasma fraction of arterial, venous, or capillary whole blood (dimension mmol L^{-1}) for *in vitro* diagnostic use. TCO_2 values assigned to i-STAT System controls and calibration verification materials are traceable to the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) Reference Measurement Procedure for Substance Concentration Determination for Total Carbon Dioxide in Blood, Plasma or Serum.[1] i-STAT System controls and calibration verification materials are validated for use only with the i-STAT System and assigned values may not be commutable with other methods. Further information regarding metrological traceability is available from Abbott Point of Care Inc..

Expected Values

TEST	UNITS	REPORTABLE RANGE	REFERENCE RANGE	
			(arterial)	*(venous)*
Total Carbon Dioxide/TCO_2	mmol/L	5 – 50	23 – 27*	24 – 29*

*Calculated from Siggard-Andersen nomogram.[2]

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The reference ranges programmed into the analyzer and shown above are intended to be used as guides for the interpretation of results. Since reference ranges may vary with demographic factors such as age, gender, and heritage, it is recommended that reference ranges be determined for the population being tested.

Clinical Significance

TCO_2 is a measure of carbon dioxide which exists in several states: CO_2 in physical solution or loosely bound to proteins, bicarbonate (HCO_3) or carbonate (CO_3) anions, and carbonic acid (H_2CO_3). Measurement of TCO_2 as part of an electrolyte profile is useful chiefly to evaluate HCO_3 concentration. TCO_2 and HCO_3 are useful in the assessment of acid-base imbalance (along with pH and $\boldsymbol{P}CO_2$) and electrolyte imbalance.

Calculated and Measured (Traceable) TCO_2

The calculated TCO_2 provided by the i-STAT System is determined from the measured and reported values of pH and $\boldsymbol{P}CO_2$ according to a simplified and standardized form of the Henderson-Hasselbalch equation.[3]

$$TCO_2 = HCO_3 + 0.03\ \boldsymbol{P}CO_2$$

This calculated TCO_2 measurement is metrologically traceable to the i-STAT pH and $\boldsymbol{P}CO_2$ measurements, which are in turn traceable to primary standard reference materials for pH and $\boldsymbol{P}CO_2$. Like all calculated parameters reported by the i-STAT System, the user can independently determine TCO_2 values from the reported pH and $\boldsymbol{P}CO_2$ measurements using a combination of the equation for HCO_3 given in the $\boldsymbol{P}CO_2$ Cartridge and Test Information (CTI) sheet, and the equation for TCO_2 above.

On the CHEM8+ cartridge, TCO_2 is metrologically traceable to the IFCC TCO_2 reference method. The implication of direct traceability to this TCO_2 reference method – and not to pH and $\boldsymbol{P}CO_2$ standard reference materials – is subtle but significant: the CHEM8+ is independent of the pH and $\boldsymbol{P}CO_2$ traceability. Given the metrological traceability of the CHEM8+ TCO_2 measurement, the traceable TCO_2 is considered to be a measured analyte

Performance Characteristics

Precision data were collected in multiple sites following the protocol recommended by Abbott Point of Care. The means, SDs and CVs from 20 replicates at each site were averaged. The average statistics are presented below.

Method comparison data were collected using CLSI guideline EP9-A[4]. Venous blood samples were collected in lithium heparin evacuated tubes from hospital patients. The whole blood samples were run in duplicate on the i-STAT System. The samples were then centrifuged to obtain plasma and analyzed in duplicate on the comparative instrument. All samples were analyzed on both methods within 15 minutes of each other.

Deming regression analysis[5] was performed on the first replicate of each sample. In the method comparison table, n is the number of specimens in the first data set. Sxx and Syy refer to the estimates of imprecision based on the duplicates of the comparative and the i-STAT methods respectively. Sy.x is the standard error of the estimate, and r is the correlation coefficient.*

Method comparisons may vary from site to site due to differences in sample handling, comparative method calibration and other site specific variables. For TCO_2, values measured on serum or plasma by chemistry analyzers may be slightly lower than TCO_2 calculated from pH and $\boldsymbol{P}CO_2$ due to loss of CO_2 during non-anaerobic handling.[6] Up to 6 mmol/L CO_2 can be lost per hour by exposure of the sample to air.[7]

*The usual warning relating to the use of regression analysis is summarized here as a reminder. For any analyte, "if the data is a narrow range, the estimate of the regression parameters are relatively imprecise and may be biased. Therefore, predictions made from estimates may be invalid",[4] The correlation coefficient, r, can be used as a guide to assess the adequacy of the comparative method ranges in overcoming the problem. As a guide, the range of data can be considered adequate if r>0.975.

Precision Data (mmol/L)

Aqueous Control	Mean	SD	%CV
Level 1	17.4	0.62	3.6
Level 3	34.6	0.62	1.8

Method Comparison (mmol/L)

	TCO_2 **(Calculated) IL BGE**	TCO_2 **(Calculated) Beckman Coulter CX®3**	TCO_2 **(Measured) Beckman Coulter LX®20**
n	62	51	35
Sxx	0.40	0.55	0.48
Syy	0.84	0.55	0.60
Slope	1.136	1.155	1.152
Int't	-4.1	-2.6	-1.5
Sy.x	1.38	1.56	0.96
Xmin	19.3	18.3	21
Xmax	43.9	36.1	35
r	0.965	0.935	0.943

Cartridge Comparison

Performance characteristics for TCO_2 are equivalent in all cartridge configurations. System difference analysis was performed on 40 patient samples using the i-STAT CHEM8+ and i-STAT EC8+ cartridges. In the 14-30 mmol/L range, the average difference was -0.7 mmol/L.

Factors Affecting Results*

Exposing the sample to air allows CO_2 to escape which causes TCO_2 to be under-estimated. The use of partial draw tubes (evacuated tubes that are adjusted to draw less than the tube volume, e.g. a 5 mL tube with enough vacuum to draw only 3 mL) is not recommended for use with the i-STAT System because of the potential for decreased TCO_2 values. Under-filling blood collection tubes may also cause decreased TCO_2 results. Care must also be taken to eliminate "bubbling" of the sample with a pipette when filling a cartridge to avoid the loss of CO_2 in the blood.

Allowing blood samples to stand (without exposure to air) before testing allows TCO_2 to be over-estimated, due to metabolic processes.

*It is possible that other interfering substances may be encountered.

References

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3. CLSI. *Blood Gas and pH Analysis and Related Measurements; Approved Guideline*. CLSI document C46-A [ISBN 1-56238-444-9]. CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898, USA 2001.
4. CLSI. *Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline*. CLSI document EP9-A [ISBN 1-56238-283-7]. CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898, USA 1995.
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7. M.G. Scott, J. Heusel, V.A. LeGrys, and O. Siggard-Andersen, Electrolytes and Blood Gases, in Tietz Textbook of Clinical Chemistry, Third Edition, ed. C.A. Burtis and E.R. Ashwood. (Philadelphia: W.B. Saunders Company, 1999).

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