Alberta Public Laboratories

Wine coloured samples?

UNIVERSITY OF ALBERTA

Development of laboratory guidelines for hydroxocobalamin interference in patients pulled from housefires

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Abstract

Objectives: OHCob is used for the treatment of cyanide poisoning secondary to smoke inhalation from house fires. OHCob discolors bodily fluids red, potentially interfering with measurements on spectrophotometric-based assays. The objective was to investigate the impact of OHCob interference on chemistry, coagulation, and urinalysis analytes.

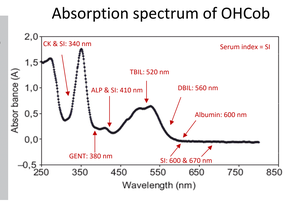
Designs & Methods: Normal and abnormal discard plasma/urine samples were spiked with a high dose (1.5 mg/mL) of OHCob or equivalent diluent volume (control). Samples (n = 5) were run on >40 assays using Beckman Coulter DxC600/Access2/DxH800, STA-Compact STAGO and Siemens Clinitek Atlas analyzers. Dose-response treatments were performed on a subset of assays if interference was >10%. Daily samples obtained from a patient administered OHCob in the emergency department (ED) were analyzed for changes to color and chemistry measurements. **Results**: Spiking studies revealed positive bias (range 26-1298%) to total bilirubin, lactate, magnesium, uric acid, creatinine-enzymatic, prothrombin time, partial prothrombin time, d-dimer and hemoglobin. There was negative interference (range 12-63%) to alanine aminotransferase, aspartate aminotransferase, creatinine-Jaffe and creatine kinase. Urinalysis dipsticks were falsely increased (grades up to 3+) on glucose, ketones, blood, nitrates and leukocytes. Subsequent dose-response treatments showed statistically significant ($p<0.05$) increase/decrease in values. Interference in samples from a patient administered a single dose of OHCob was not detected by hemolysis index (HI), but showed gradual recovery on select chemistry analytes as OHCob was cleared from the body and red colouration faded over time.
Conclusion: Among the assays tested, 16 analytes had varying degrees of interference. These findings will aid in developing reporting procedure to prevent unreliable results from being misinterpreted in the ED. The lack of HI flagging further underscores importance of communication with ED to identify these samples.

Introduction & Objectives

- Cyanokit (hydroxocobalamin, OHCob) is a cyanide poisoning antidote administered to patients rescued from house fires
- Although OHCob has a good safety profile, it turns bodily fluids red. This discoloration can interfere with many assays and produce inaccurate results
- Despite samples appearing like they are hemolyzed, the hemolysis index does not detect them making it challenging to identify these samples

Objectives:

- Investigate the impact of interference on chemistry, coagulation, hematology, urinalysis , and blood gas instruments
- Develop handling and reporting guidelines for samples with OHCob
- Educate the emergency department (ED) about potential interferences and develop a communication plan to identify these samples



Methods

Expired OHCob was obtained from the pharmacy and reconstituted to 30 mg/mL with distilled water (dH_2O)

De-identified normal and abnormal patient plasma, whole blood and urine were split into spiked and control tubes

Spiked: Final concentration of 1.5 mg/mL added to patient samples. Based on literature, this dose reflects maximal concentration found in blood after administration

Control (unspiked): Equal volume of dH_2O added to patient sample

Patient runs (71 analytes, normal & abnormal values)
Instruments: Beckman Coulter DxC600, Beckman Coulter Access II, Beckman Coulter DxH800, Siemens Clinitek Atlas, Stago STA Compact, Radiometer ABL800 Flex, Advanced Osmo1

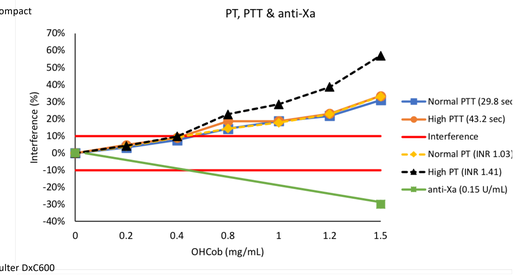
Significant interference defined as >10% as recommended by the Clinical Laboratory Standards Institute EP07
Dose-response treatment performed on analytes with initial interference > 10%

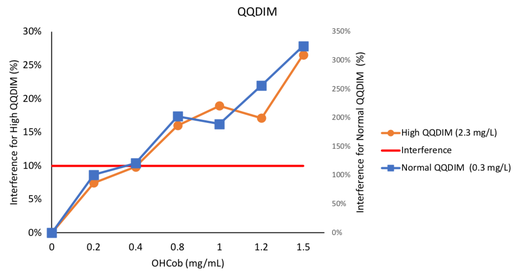
Dose-response treatment: 1.5, 1.2, 1.0, 0.8, 0.4 and 0.2 mg/mL OHCob spiked into a pool of patient sample

Results: Part I

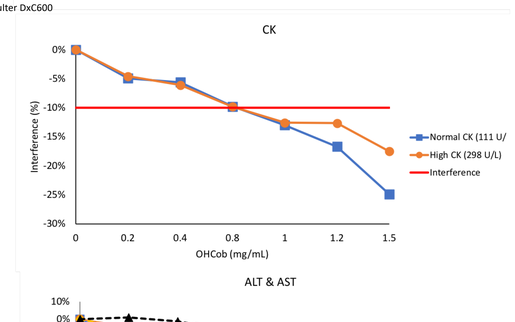
Chemistry, Coagulation, Hematology, Blood Gas and Urinalysis In-vitro Spiking Study – analytes affected by OHCob

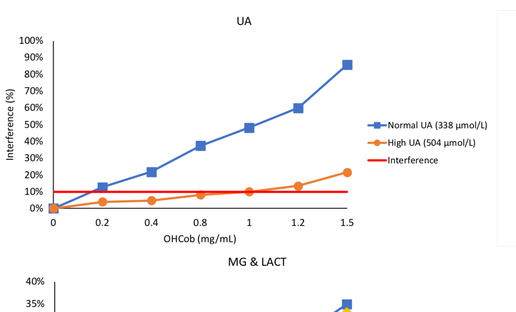
Coagulation: Stago STA Compact

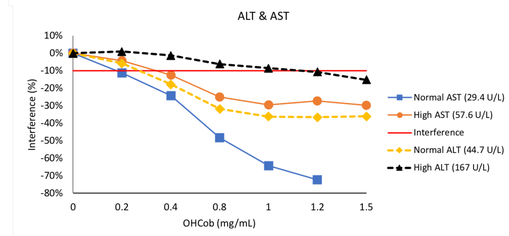


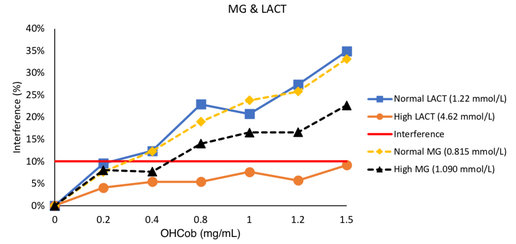


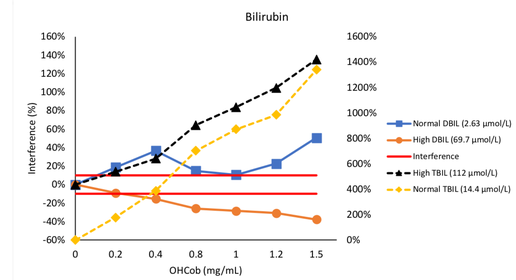
Chemistry: Beckman Coulter DxC600











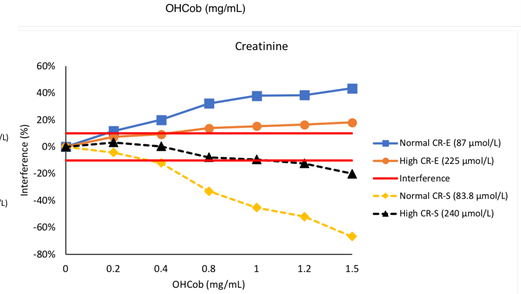


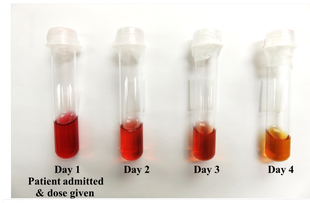
Figure 1: Dose-response treatments were performed on 11 chemistry, 3 coagulation and 7 blood gas analytes. Normal and elevated chemistry and coagulation analytes show either falsely increased or decreased interference as OHCob increases in concentration. Analytes with interference greater than 10% are shown.

Table 1: Interference summary on Beckman Coulter DxH800, Radiometer ABL800 Flex, and Siemens Clinitek Atlas

Instrument type	Wavelength	Impact of interference
Hematology	Hb: 525 nm	Hb variably affected (2-61%) Other CBC differential parameters were unaffected
Blood Gas	478-672 nm	Hb, COHb, HHb, sO2, MetHb, O2Hb, Hct were significantly affected (instrument was unable to produce values)
Urinalysis	Reflectance Photometry Dual readings at reactive and reference wavelengths	Glucose, ketones, blood, nitrates, leukocytes were falsely positive (+1 to +3)

Results: Part II

Patient case, OHCob administered in the ED



Multiple samples received from a patient administered OHCob

Patient was admitted and died shortly after from multi-organ failure

No clear guidelines were available on handling and reporting these samples

Samples were frozen and retrospectively analyzed to determine whether clearance of OHCob over time is associated with recovery of interference on select chemistry assays observed in the in-vitro spiking study

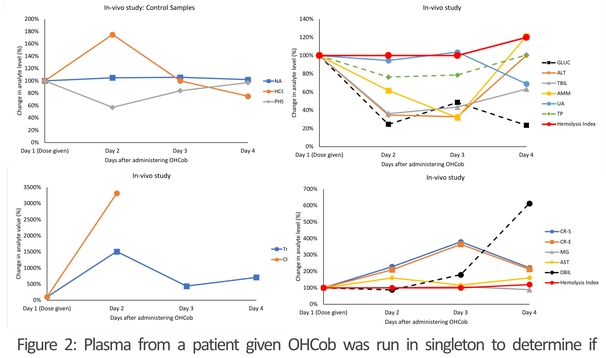


Figure 2: Plasma from a patient given OHCob was run in singleton to determine if recovery of interference occurred as OHCob was eliminated from the body

Conclusions & Recommendations

- 21/71 (30%) of analytes had positive interference, 5/71 (7%) had negative interference and 45/71 (63%) had no interference. 5/71 analytes had borderline interference in the range of 10-20% difference
- Clot-based assays (PT & PTT) were surprisingly affected by OHCob, but the mechanisms remain unclear
- Interference is variable and sometimes unpredictable based on the in-vivo patient case
- Hemolysis index is not flagged, therefore, communication with the emergency department is vital to inform the lab when samples are collected

Table 2: Reporting recommendations

Tests	ALB, CA, ALP, LYTES, CRP, GLUC, LD, LIP, PHS, URE, HCG, FIB,	TnI, ALT, AMM, DBIL, LACT	CBC and diff	AST, CK, CREA, MG, UA, ACET, TDMs, TBIL, Co-oximetry, TP, urinalysis,	PT, PTT, QQDIM, Xa
Reported Out?	Yes Interference <10%	Yes Borderline interference 10-20%	Yes Variable interference for Hb	No Interference >20%	No Interference > 20%
Comment Appended	FIB: "Cyanokit therapy at regular doses does NOT significantly interfere with fibrinogen results" All others: No comment	"Interpreted with caution. Abnormal color caused by Cyanokit"	TBA Further studies on Hb interference is ongoing	"Inaccurate lab results due to abnormal color caused by Cyanokit"	QQDIM/Xa: "Inaccurate lab results due to abnormal color caused by Cyanokit" PT/PTT: "PT and PTT are not reliable in patients treated with Cyanokit, correlate with reflexed fibrinogen testing"

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