Procjena analitičkih značajka analizatora GEM Premier 3000

Analytical properties of the GEM premier 3000 analyzer evaluated

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Sažetak

Uvod: Razvoj senzorske tehnologije doveo je do pojave analizatora koji iz uzorka pune krvi brzo i jednostavno određuju koncentracije analita, ne samo u laboratoriju nego i uz bolesnika. Analizatori za pretrage uz bolesnika najčešće se instaliraju u jedinice intenzivne skrbi s ciljem bržeg dobivanja rezultata i ranijeg započinjanja terapije.

Cilj rada: Prije instalacije i puštanja u rad analizatora za pretrage uz bolesnika GEM Premier 3000 u Jedinici intenzivnog liječenja Kirurške klinike učiniti procjenu analitičkih značajka i utvrditi kompatibilnost rezultata s rezultatima analizatora u centralnom laboratoriju.

Materijali i metode: Procjena analitičkih značajka analizatora ispitana je određivanjem analitičke nepreciznosti u seriji, nepreciznosti iz dana u dan, netočnosti i usporednim određivanjem koncentracije analita u uzorcima bolesnika na ispitivanom analizatoru i na analizatorima na kojima se ti analiti određuju u centralnom laboratoriju kao referentnim analizatorima. Ispitivanja su provedena u skladu s preporukama NCCLS.

Rezultati: Dobiveni su zadovoljavajući rezultati ispitivanja nepreciznosti u seriji za sve analite (CV ≤ 3,46%), a rezultati ispitivanja nepreciznosti iz dana u dan bili su zadovoljavajući za sve analite (CV ≤ 4,65%) osim za laktat (2. razina, CV = 9,35%; 3. razina, CV=5,55%). Rezultati ispitivanja netočnosti bili su zadovoljavajući za sve analite (R ≤ 4,53%) osim za laktat (1. razina, R = 13,59%; 2. razina, R = -11,00%; 3. razina, R = 10,00%). Svi izračunati koeficijenti korelacije bili su unutar raspona 0,9727–0,9920, osim za natrij (Pearsonov, r = 0,9207) i pokazuju visok stupanj korelacije rezultata koncentracije analita u uzorcima bolesnika između referentnih analizatora i ispitivanog analizatora za sve analite. Regresijska analiza po Passingu i Babloku također pokazuje vrlo dobru podudarnost usporednih rezultata koncentracije analita u uzorcima bolesnika između ispitivanog analizatora i referentnih analizatora.

Zaključak: Rezultati određivanja koncentracije analita u uzorcima bolesnika dobivenih na ispitivanom analizatoru kompatibilni su s rezultatima dobivenim na referentnim analizatorima u centralnom laboratoriju. Analizator je jednostavan za rad, a automatsko, samostalno provođenje kontrole kavalitete rada poslije svakog uzorka i samostalno otklanjanje grešaka omogućuje siguran rad i pouzdan rezultat.

Ključne riječi: pretrage uz bolesnika, parametri acidobazične ravnoteže, elektroliti, metaboliti

Abstract

Introduction: The development of sensor technology has led to the advent of analyzers for fast and simple determination of analyte concentration in whole blood samples that can be performed in a laboratory and as point of care testing (POCT). POCT analyzers are generally put in at intensive care units to enable rapid test results and earliest possible therapy introduction.

Aim: To evaluate analytical properties of the GEM Premier 3000 analyzer and compatibility of the results obtained by use of this analyzer with those reported from analyzers used in central laboratory before the GEM Premier 3000 POCT analyzer fitting and placing in operation at Intensive Care Unit, University Department of Surgery.

Material and methods: Analytical properties of the analyzer were evaluated by determination of within-run imprecision, between-run imprecision, inaccuracy, and comparative determination of analyte concentrations in patient samples on the study analyzer and the analyzers used for the respective analytes at central laboratory as reference analyzers. The study was performed in accordance with ECCLS recommendations.

Results: Satisfactory results were recorded on within-run imprecision for all study analytes (CV ≤ 3.46%), and on between-run imprecision for all analytes (CV ≤ 4.65%) except for lactate (Level 2, CV = 9.35%; Level 3, CV =5.55%). Inaccuracy evaluation yielded satisfactory results for all study analytes (R ≤ 4.53%) except for lactate (Level 1, R = 13.59%; Level 2, R = -11.00%; Level 3, R = 10.00%). Correlation coefficients were within range 0.9727–0.9920, except for sodium (r = 0.9207) and showed high correlation of all analyte concentrations determined in patient samples on the study analyzer and reference analyzers. Passing Bablok regression analysis also indicated a very high compatibility of analyte concentrations measured in patient samples by use of the study analyzer and reference analyzers.

Conclusion: Results of analyte concentration determination in patient samples obtained by use of the study analyzer were compatible with those produced by reference analyzers at central laboratory. The GEM Premier 3000 analyzer has proved to be simple to operate, while automated and independent quality control performed after each individual sample and automated error elimination ensures safe work and reliable test results.

Key words: point of care testing, acid-base balance parameters, electrolytes, metabolites

Pristiglo: 16. ožujka 2007. *Received: March 16, 2007*

Prihvaćeno: 11. rujna 2007. *Accepted: September 11, 2007*

Uvod

Poremećaji acidobazične ravnoteže i elektrolita fiziološki i klinički su povezani i česti su u kliničkoj praksi. Brza i točna dijagnoza, te odgovarajuće liječenje takvih poremećaja od velike su važnosti (1,2). Razvoj tehnologije, naročito senzorske tehnologije, doveo je do pojave analizatora koji iz uzorka pune krvi brzo i jednostavno određuju spomenute analite, ne samo u laboratoriju, nego i uz bolesnika (engl. *point of care testing*, POCT) (3). Elektrokemijski senzori našli su svoje mjesto u kliničkoj kemiji zahvaljujući jednostavnosti, minimalnom održavanju i sposobnosti mjerenja klinički važnih analita u uzorku pune krvi u širokom koncentracijskom rasponu. Evoluciju POCT analizatora omogućili su razvoj minijaturnih senzora i njihova integracija u male sofisticirane analizatore koji su vratili testove ka bolesniku s ciljem bržeg dobivanja rezultata, ranijeg započinjanja terapije i time poboljšane skrbi bolesnika (3). Pretrage uz bolesnike tako postaju pristupačne bolnicama kao alternativa centralnom laboratoriju, prvenstveno u jedinicama intenzivne skrbi gdje učinkovito liječenje bolesnika zahtijeva redovito praćenje parametara acidobazične ravnoteže i elektrolita, ali i na drugim lokacijama za praćenje akutnih i kroničnih stanja (3). Spektar pretraga analizatora smještenih neposredno uz bolesnika sve se više širi u cilju što brže i detaljnije obrade i zbrinjavanja bolesnika, što unaprjeđuje kako klinički tako i ekonomski aspekt liječenja.

GEM Premier 3000

Ispitivani analizator GEM Premier 3000 je prijenosni analizator za brzu analizu uzoraka pune krvi uz bolesničku postelju. Proizvođač analizatora je tvrtka Instrumentation Laboratory Company, Lexington, MA, USA. Analizator simultano određuje vrijednosti: pH, pCO_2, pO_2, Na^+, K^+, Ca^{++}, glukoze, laktata i hematokrita. Mjerenje koncentracije analita temelji se na potenciometriji (pH, pCO_2, Na^+, K^+, Ca^{++}), amperometriji (pO_2, glukoza, laktat) i konduktometriji (hematokrit). Namijenjen je zdravstvenom stručnom osoblju na bilo kojoj bolničkoj lokaciji i u skladu je s europskim standardima.

Analizator ima dvije sastavnice: instrument i zamjenjivi umetak koji je primarna sastavnica. Zamjenjivi umetak je potpuno zatvoren sustav koji sadrži sve sastavnice potrebne za analizu uzorka: iglu za uzimanje uzorka, senzorsku karticu, kalibracijske/kontrolne otopine, cjevčice, ventile, crpke i posudu za otpad.

Kada se umetak stavi u analizator provodi se automatska kalibracija senzora. Nakon automatski provedene kalibracije, a prije analize uzoraka bolesnika slijedi vanjska provjera kalibracije i ispravnosti umetka pomoću komercijalnih uzoraka. Slijedeće kalibracije se izvode automatski u određenim vremenskim razmacima kako bi se omogućila neprekidna točnost analizatora. Analizator automatski provodi tri vrste kalibracija: kalibraciju u jednoj točki, ka-

Introduction

Acid-base balance and electrolyte impairments are physiologically and clinically related, and are frequently encountered in clinical practice. A rapid and accurate diagnosis, and appropriate management of these impairments are of utmost importance (1,2).

Technological advances, sensor technology in particular, have resulted in the development of analyzers that provide fast and simple determination of these analytes both in laboratory setting and as point of care testing (POCT) (3,4). Electrochemical sensors have found application in clinical chemistry because of their simple use, minimal maintenance required, and ability to measure clinically relevant analytes in whole blood samples across a wide concentration range. The development of miniature sensors and their integration in small sophisticated analyzers have enabled evolution of POCT analyzers, thus bringing test analyses close to the patient in order to obtain test results within the shortest possible time, ensuring early therapy initiation and improved patient care in general (3). POCT has become available in hospitals as an alternative to central laboratory. This refers to intensive care units (ICU) in particular, where efficacious patient management requires regular monitoring of the acid-base balance parameters and electrolytes, as well as to other hospital settings requiring close monitoring of acute and chronic states (3,4). The spectrum of POCT analyzers has been continuously expanding towards ever faster and thorough patient care and examination, thus improving both clinical and economic aspects of treatment (4).

GEM Premier 3000

The GEM Premier 3000 analyzer evaluated in the present study is a portable analyzer for rapid POCT analysis of whole blood samples, manufactured by Instrumentation Laboratory Company, Lexington, MA, USA. This POCT analyzer provides simultaneous determination of the following analytes: pH, pCO_2, pO_2, Na^+, K^+, Ca^{++}, glucose, lactate, and hematocrit. Determination of analyte concentration is based on potentiometry (pH, pCO_2, Na^+, K^+ and Ca^{++}), amperometry (pO_2, glucose and lactate), and conductometry (hematocrit). The analyzer is intended for use by health professionals in any type of hospital setting and is designed in concordance with European standards.

The analyzer consists of two components, i.e. the instrument and the replaceable cartridge as a primary component. The replaceable cartridge is a closed system that contains all components needed for sample analysis, i.e. the needle for sampling, sensor card, calibration/control solutions, lines, valves, pumps, and waste container. Cartridge insertion in the analyzer is followed by automated sensor calibration. External validation of the calibration and cartridge accuracy is performed by original samples

libraciju u dvije točke i kalibraciju kisika. Kalibracija u jednoj točki se provodi automatski i poslije svakog uzorka.
Kao ekskluzivitet proizvođač navodi program aktivne automatske kontrole kvalitete rada, tzv. iQM™ (engl. *Intelligent Quality Management*). Program iQM™ zamjenjuje konvencionalnu unutarnju kontrolu kvalitete rada koja je ovdje sastavni dio operativnog sustava i provodi kontrolu svih mjernih parametara nakon svakog uzorka bez intervencije korisnika. Program iQM™ počinje s radom automatski nakon uspješno provedene validacije automatske kalibracije instaliranog umetka. Neprekidno prati izvođenje cijelog procesa analize uzorka (uključujući senzore, otopine i elektroniku), omogućava trenutno otkrivanje greške i automatski izvodi korektivne akcije radi otklanjanja greške.
Drugi, također ekskluzivni program, je program FPRC (engl. *Failure Pattern Recognition Checks*) koji pomaže u identifikaciji mikro ugrušaka, nekih grešaka u radu senzora i identifikaciji nekih interferencija. Analizator GEM Premier 3000 za vrijeme analize uzorka automatski provjerava prisutnost mikro ugrušaka i interferencija.
Postoji nekoliko vrsta umetaka koji se razlikuju po konfiguraciji analita (pH, plinovi u krvi/hematokrit/elektroliti/metaboliti), broju testova (75–600, neovisno o broju kalibracija i kontrola) i vremenu trajanja umetka (2 ili 3 tjedna). Uzorak za analizu može biti arterijska, kapilarna ili venska krv, a jedini prihvatljivi antikoagulansi su Li–/ Na-heparin u konačnoj koncentraciji od 25 IU/mL. Ostali antikoagulansi (EDTA, citrat, oksalat, NaF) mogu štetno djelovati na senzore i ne prepuručuju se. Volumen krvi potreban za analizu je 135–150 μL, a vrijeme analize uzorka je 85 sekundi.
U procjeni analitičkih značajka ispitivanog aparata rabili smo slijedeće analizatore centralnog laboratorija: Ciba Corning 865, Vitros 250 i Olympus AU 640.

Analizator Ciba Corning 865

To je biokemijski analizator za određivanje vrijednosti parametara acido-bazične ravnoteže, elektrolita, metabolita, hemoglobina i derivata hemoglobina. U ovom je ispitivanju to bio referentni analizator za usporedna određivanja vrijednosti pH, pCO_2, pO_2, K^+, Na^+ i Ca^{++} u uzorcima bolesnika. Mjerna tehnologija ispitivanih analita temelji se na elektrokemijskom fenomenu (tehnologija ISE, amperometrija i potenciometrija). Hematokrit nije moguće odrediti na ovom analizatoru, pa taj analit nije podvrgnut analitičkoj procjeni. Proizvođač analizatora je Ciba Corning Diagnostics Corporation, MA, SAD.

Analizator Vitros 250

To je diskretni biokemijski analizator koji radi na načelu suhe kemije. U ovom ispitivanju to je bio referentni analizator za usporedna određivanja koncentracije laktata. Koncentracija laktata u plazmi određuje se spektrofoto-

upon automated calibration and before patient sample analysis. Subsequent calibrations are performed automatically at preset time intervals in order to ensure constant accuracy of the analyzer performance. Three types of calibration are automatically performed, i.e. single-point calibration, double-point calibration, and oxygen calibration. Single-point calibration is performed automatically following each individual sample.
The manufacturer points to the exclusive program of active automated performance quality control termed Intelligent Quality Management (iQM™). The iQM™ program has replaced conventional internal performance quality control, which has now become an integral part of the operating system, performing control of all measured parameters after each individual sample without user's intervention. The iQM™ program is started automatically upon properly performed validation of automated cartridge calibration. The program continually controls the entire process of sample analysis (including sensors, solutions and electronics), enables instantaneous error detection, and performs corrective actions for error elimination.
Another exclusive program is Failure Pattern Recognition Checks (FPRC), which helps in the identification of microthrombi, some errors in sensor performance, and interferences. During sample analysis, the GEM Premier 3000 analyzer performs automated control of microthrombi and interferences.
There are various types of cartridges that differ in analyte configuration (pH, blood gases/hematocrit/electrolytes/metabolites), number of tests (75–600, irrespective of the number of calibrations and controls), and duration (2 or 3 weeks). The sample to analyze can be arterial, capillary or venous blood, and Li–/Na-heparin in final concentration of 25 IU/mL is the only anticoagulant acceptable. Other anticoagulants such as EDTA, citrate, oxalate and NaF may cause damage to the sensors and are not recommended for use. The blood volume for analysis is 135–150 μL, and the time of sample analysis is 85 seconds.
The following analyzers fitted at central laboratory were used in the assessment of clinical characteristics of the study analyzer: Ciba Corning 865, Vitros 250, and Olympus AU 640.

Ciba Corning 865 analyzer

This analyzer is intended for determination of acid-base balance parameters, electrolytes, metabolites, hemoglobin and hemoglobin derivatives. In the present study, Ciba Corning 865 analyzer served as a reference analyzer for comparison determination of pH, pCO_2, pO_2, K^+, Na^+ and Ca^{++} in patient samples. The measurement technology for study analytes is based on electrochemical phenomenon (ISE technology, amperometry and potentiometry). Hematocrit cannot be determined on this analyzer, therefore this analyte was not submitted to analytical eva-

metrijski. Proizvođač aparata je Ortho Clinical Diagnostics, NY, SAD.

Analizator Olympus AU 640

To je otvoreni, diskretni, višekanalni biokemijski analizator (proizvođač je tvrtka Olympus Optical Co., Ltd., Tokyo, Japan) na kojem su, kao referentnom analizatoru, rađena usporedna određivanja koncentracije glukoze u uzorcima bolesnika. Metoda određivanja koncentracije glukoze je enzimatski UV test (metoda heksokinaza).

Na analizatorima se redovito provodi kontrola kvalitete rada (unutarnja i vanjska), kao i postupci održavanja prema preporukama proizvođača.

Cilj rada

Cilj rada bio je prije instalacije i puštanja u rad analizatora za pretrage uz bolesnika GEM Premier 3000 u Jedinici intenzivnog liječenja Kirurške klinike, učiniti procjenu analizatora u centralnom laboratoriju, kako bi se ispitale njegove analitičke i tehničke značajke i utvrdila kompatibilnost rezultata s rezultatima analizatora u centralnom laboratoriju, s obzirom na predviđenu radnu lokaciju i činjenicu da će na njemu raditi nelaboratorijsko osoblje.

Analitička procjena učinjena je određivanjem nepreciznosti u seriji, nepreciznosti iz dana u dan, netočnosti i usporednim određivanjem koncentracije analita u uzorcima bolesnika na ispitivanom analizatoru i na analizatorima na kojima se koncentracija tih analita određuje u centralnom laboratoriju kao referentnim aparatima koji su uključeni u program vanjske kontrole kvalitete rada. Ispitivanja su provedena u skladu s preporukama NCCLS (engl. *National Committee for Clinical Laboratory Standards*, dokument EP09-A2) (4). Budući da pretrage uz bolesnike zauzimaju sve važnije mjesto u kliničko laboratorijskoj dijagnostici i tehnologijski se najbrže razvijaju, za očekivati je da će ispitivani analizator u nekim značajkama nadmašiti klasične laboratorijske analizatore.

Materijali i metode

Analizatori

Gem Premier 3000

Nakon stavljanja umetka u analizator provodi se automatska kalibracija senzora. Nakon automatski provedene kalibracije, a prije analize uzoraka bolesnika slijedi vanjska provjera kalibracije i ispravnosti umetka pomoću komercijalnih uzoraka za validaciju (Calibration Validation Products, CVP, Instrumentation Laboratory Company, Lexington, MA, SAD). Slijedeće kalibracije se izvode automatski u određenim vremenskim razmacima.

Kontrolu kvalitete rada nakon uspješno provedene validacije automatske kalibracije instaliranog umetka automatluation. The analyzer is manufactured by Ciba Corning Diagnostics Corporation, MA, USA.

Vitros 250 analyzer

It is a discrete biochemistry analyzer operating on the dry chemistry principle. In the present study, Vitros 250 analyzer served as a reference analyzer for comparison determination of lactate concentration. Plasma lactate concentration is determined by spectrophotometry. The analyzer is manufactured by Ortho Clinical Diagnostics, NY, USA.

Olympus AU 640 analyzer

It is an open, discrete, multi-channel biochemistry analyzer manufactured by Olympus Optical Co., Ltd., Tokyo, Japan, which served as a reference analyzer for comparison determination of glucose concentration in patient samples. Glucose concentration is determined by the method of enzymatic UV assay (hexokinase method).

All three analyzers are regularly submitted to performance quality control (internal and external) and maintenance procedures in line with the manufacturers' instructions.

Aim

The aim of the study was to evaluate analytical properties and technical characteristics of the GEM Premier 3000 analyzer before its fitting and performance at University Department of Surgery ICU, and to determine the level of compatibility between the results obtained on this analyzer and those produced by the analyzers used at central laboratory, with due consideration of the specific clinical setting and analyzer utilization by non-laboratory personnel.

Analytical evaluation was performed by determination of within-run imprecision, between-run imprecision, inaccuracy, and concurrent determination of analyte concentrations in patient samples on the study analyzer and reference analyzers used for the respective analyte at central laboratory, included in the program of external quality control. All tests were performed according to recommendations issued by the National Committee for Clinical Laboratory Standards (NCCLS), Document EP09-A2 (4). As POCT has been gaining importance in clinical laboratory diagnosis and undergoes fastest technological advances, the study analyzer is expected to prove superior to classic laboratory analyzers according to some of its characteristics.

Material and methods

Analyzers

GEM Premier 3000

Cartridge insertion is followed by automated sensor calibration. Upon automated calibration and before sample analysis, external validation of the calibration and cartrid-

ski preuzima program iQM™ pomoću kontrolnih otopina sadržanih u umetku.

Analizator Ciba Corning 865

Za kalibraciju se rabe izvorne kalibracijske otopine (Buffer 6,838 i Buffer 7,3/COox Zero; Bayer HealthCare LLC, MA, SAD), a za kontrolu kvalitete rada izvorni kontrolni uzorci proizvođača koji sadrže tri razine vrijednosti analita (Rapid QC Complete Level 1, 2 i 3; Bayer HealthCare LLC, MA, SAD).

Analizator Vitros 250

Za određivanje koncentracije laktata u plazmi korišten je višeslojni film (Vitros Lac Slide). Za kalibraciju se rabi izvorni kalibrator (Calibrator kit 1), a za kontrolu kvalitete rada kontrolni uzorci Performance Verifier I i II. Proizvođač filmova, kalibracijskih i kontrolnih otopina je Ortho Clinical Diagnostics, NY, SAD.

Analizator Olympus AU 640

Za određivanje glukoze korišten je reagens Glucose, za kalibraciju System Calibrator, a za unutarnju kontrolu kvalitete rada Olympus Control Level 1 i 2. Proizvođač reagensa, kalibratora i kontrolnih uzoraka je Olympus Life and Material Science Europa GmbH, Hamburg, Njemačka.

Procjena analitičkih značajka analizatora GEM Premier 3000

Ispitivanje nepreciznosti unutar serije

Provedeno je višekratnim (20 puta) mjerenjem koncentracije slijedećih analita: pH, pCO_2, pO_2, Na^+, K^+, Ca^{++}, glukoze i laktata u uzorcima kontrolnih otopina Critical Care QC Contril 9 Multipak koji sadrži tri razine vrijednosti analita (Level 1, 2 i 3; Instrumentation Laboratory).

Ispitivanje nepreciznost iz dana u dan

Provedeno je određivanjem koncentracije istih analita tijekom 20 dana u uzorcima kontrolnih otopina Rapid QC Complete 1, 2 i 3 (Bayer HealthCare) koji sadrže tri razine vrijednosti analita.

Ispitivanje netočnosti

Provedeno je određivanjem koncentracije analita: pH, pCO_2, pO_2, Na^+, K^+, Ca^{++}, glukoze i laktata u 20 uzoraka kontrolnih otopina Critical Care QC Contril 9 Multipak koje sadrže tri razine vrijednosti analita (Level 1, 2 i 3; Instrumentation Laboratory).

Usporedna određivanja pokazatelja acidobazične ravnoteže i koncentracije elektrolita

Analizirano je 160 uzoraka pune krvi (arterijska, venska, miješana krv) na analizatoru Ciba Corning 865 (analiti: pH, pCO_2, pO_2, K^+, Na^{++}, Ca^{++}) kao referentnom analizatoru i na ispitivanom analizatoru GEM Premier 3000.

ge is performed by use of original samples, Calibration Validation Products (CVP, Instrumentation Laboratory Company, Lexington, MA, USA). Subsequent calibrations are performed automatically at certain time intervals. Upon proper validation of automated calibration of the cartridge inserted, performance quality control is automatically taken over by iQM™ program using control solutions contained in the cartridge.

Ciba Corning 865 analyzer

Original calibration solutions (Buffer 6.838 and Buffer 7.3/COox Zero) are used for calibration, and original control samples Rapid QC Complete Level 1, 2 and 3 employed for performance quality control. The calibration and control solutions are manufactured by Bayer HealthCare LLC, MA, USA.

Vitros 250 analyzer

A multilayer film (Vitros Lac Slide) was used to determine lactate concentration in plasma; original calibrator (Calibrator kit 1) was used on calibration; and control samples Performance Verifier I and II were used on performance quality control. The films, calibration and control solutions are manufactured by Ortho Clinical Diagnostics, NY, USA.

Olympus AU 640 analyzer

Glucose reagent was used on glucose determination, System Calibrator was used on calibration, and control samples Olympus Control Level 1 and 2 were used on internal quality control. The reagent, calibrator and control samples are manufactured by Olympus Life and Material Science Europe GmbH, Hamburg, Germany.

Evaluation of analytical characteristics of the GEM Premier 3000 analyzer

Within-run imprecision study

Within-run imprecision was assessed by multiple (20 times) concentration determination of the pH, pCO_2, pO_2, K^+, Na^+ and Ca^{++}, glucose and lactate analytes in samples of the Critical Care QC Contril 9 Multipak control solutions containing three levels (Level 1, 2 and 3; Instrumentation Laboratory Company, Lexington, MA, USA).

Between-run imprecision study

Between-run imprecision was assessed by determination of the same analyte concentrations for 20 days in samples of the control solutions Rapid QC Complete Level 1, 2 and 3; Bayer HealthCare LLC, MA, USA.

Inaccuracy study

Testing for inaccuracy was performed by determination of the pH, pCO_2, pO_2, K^+, Na^+ and Ca^{++}, glucose and lactate analytes in samples of the Critical Care QC Contril 9 Multipak control solutions containing three levels (Level 1, 2

Nije bilo posebnih vađenja krvi za potrebe ovoga ispitivanja, nego su se rabili uzorci krvi bolesnika kojima je zatraženo određivanje plinova u krvi i pH. Uzorci krvi su se vadili u heparinizirane štrcaljke i analizirali istodobno na oba analizatora odmah nakon primitka kako bi se izbjegle promjene u koncentraciji plinova koje bi mogle nastati dužim stajanjem uzoraka.

Usporedna određivanja koncentracije glukoze i laktata

Analizirano je 50 uzoraka plazme bolesnika (Li-heparin): za glukozu na analizatoru Olympus AU 640, a za laktat na analizatoru Vitros 250 kao referentnim analizatorima i ispitivanom analizatoru GEM Premier 3000. Nije bilo posebnih vađenja krvi za potrebe ovoga ispitivanja, nego su se rabili uzorci krvi bolesnika kojima je traženo određivanje glukoze i laktata u plazmi.

Statistička analiza

Statistička obrada rezultata napravljena je pomoću programa MedCalc (verzija 9.0.1.1; Frank Schoonjans, Belgium). U svrhu procjene nepreciznosti izračunati su srednja vrijednost ($\bar{x}$), standardna devijacija (SD) i koeficijent varijacije (CV, %), a u svrhu procjene netočnosti izračunat je postotak odstupanja srednje izmjerene vrijednosti od srednje deklarirane vrijednosti (R, %) (5). Stupanj povezanosti rezultata prikazan je pomoću Pearsonova koeficijenta korelacije (r) s izračunatim (95%) intervalima pouzdanosti (CI) za svaki ispitivani analit. Regresijskom analizom rezultata po Passingu i Babloku izračunati su jednadžba pravca i intervali pouzdanosti (95% CI) za nagib pravca (b) i odsječak na osi y (a) za svaki ispitivani analit. Kriteriji prihvatljivosti rezultata bili su slijedeći:

1. Za procjenu nepreciznosti, vrijednost koeficijenta varijacije manja od 5,00%,
2. Za procjenu netočnosti, odstupanje srednje izmjerene vrijednosti od srednje deklarirane vrijednosti manje od 5,00%,
3. Za procjenu stupnja povezanosti rezultata, koeficijent korelacije veći od 0,9500.

Rezultati

Rezultati ispitivanja nepreciznosti u seriji (srednja vrijednost, standardna devijacija, koeficijent varijacije; N = 20, kontrolni uzorak Critical Care QC Contril 9 Multipak: razine 1, 2 i 3) prikazani su u tablici 1.
Rezultati ispitivanja nepreciznosti u seriji zadovoljavajući su za sve analite (CV ≤ 3,46%).
Rezultati ispitivanja nepreciznosti iz dana u dan (srednja vrijednost, standardna devijacija, koeficijent varijacije; N = 20, kontrolni uzorak Rapid QC Complete: razine 1, 2 i 3) prikazani su u tablici 2.

and 3; Instrumentation Laboratory Company, Lexington, MA, USA).
Concurrent determination of acid-base balance parameters and electrolyte concentration
A total of 160 whole blood (arterial, venous and mixed blood) samples were analyzed on the GEM Premier 3000 analyzer and Ciba Corning 865 (analytes: pH, pCO_2, pO_2, K^+, Na^+ and Ca^{++}) as a reference analyzer. Blood samples collected from patients where determination of blood gases and pH was requested were used in the study, thus requiring no additional blood sampling. Blood samples were collected in heparinized syringes and analyzed simultaneously on both analyzers immediately upon receipt, in order to avoid changes in gas concentrations that may occur on sample storage.

Concurrent determination of glucose and lactate concentration

Fifty patient plasma samples (Li-heparin) were analyzed on the Olympus AU 640 (for glucose) and Vitros 250 analyzer (for lactate) as reference analyzers and on GEM Premier 3000. Blood samples collected from patients where determination of plasma glucose and lactate were requested were used in the study, thus requiring no additional blood sampling.

Statistical analysis

Statistical analysis of the results was performed by use of MedCalc Version 9.0.1.1 (Frank Schoonjans, Belgium) software. The mean ($\bar{x}$), standard deviation (SD) and coefficient of variation (CV%) were calculated for assessment of imprecision. Percentage of the mean measured value deviation from the mean declared value (R%) was calculated for assessment of inaccuracy (5). The level of result correlation was expressed by Pearson's correlation coefficient (r) with calculation (95%) of confidence intervals (CI) for each of the study analytes. Passing Bablok regression analysis of results was used to calculate the equation of direction and 95% CI for the slope (b) and y-axis intercept (a) for each of the study analytes. The criteria for the results to be considered acceptable were as follows:

1 for imprecision assessment, CV lower than 5.00%;
2 for inaccuracy assessment, deviation of the mean measured value from the mean declared value lower than 5.00%; and
3 for assessment of the level of result correlation, correlation coefficient greater than 0.9500.

Results

Results of the within-run imprecision study (mean, SD, CV; N = 20; Critical Care QC Contril 9 Multipak control sample Level 1, 2 and 3) are shown in Table 1. Results of the

Tablica 1. Rezultati ispitivanja nepreciznosti u seriji

Table 1. Results of within-run imprecision testing

Analyte	Level 1		Level 2		Level 3	
	$\bar{x} \pm SD$	CV (%)	$\bar{x} \pm SD$	CV (%)	$\bar{x} \pm SD$	CV (%)
pH	7.121 ± 0.002	0.03	7.390 ± 0.000	0.00	7.62 ± 0.000	0.00
pCO_2 (kPa)	9.585 ± 0.067	0.70	5.040 ± 0.094	1.87	2.495 ± 0.022	0.90
pO_2 (kPa)	8.950 ± 0.221	2.47	13.130 ± 0.172	1.31	20.025 ± 0.171	0.86
Na^+ (mmol/L)	161.950 ± 1.664	1.01	133.800 ± 0.616	0.46	117.050 ± 0.394	0.34
K^+ (mmol/L)	5.970 ± 0.057	0.96	3.715 ± 0.037	0.99	2.570 ± 0.047	1.83
Ca^{++} (mmol/L)	1.482 ± 0.016	1.09	1.022 ± 0.008	0.75	0.617 ± 0.005	0.76
Glucose (mmol/L)	16.155 ± 0.146	0.89	5.090 ± 0.055	1.09	3.195 ± 0.060	1.89
Lactate (mmol/L)	6.020 ± 0.083	1.39	0.890 ± 0.031	3.46	2.640 ± 0.050	1.90

Tablica 2. Rezultati ispitivanja nepreciznosti iz dana u dan

Table 2. Results of between-run imprecision testing

Analyte	Level 1		Level 2		Level 3	
	$\bar{x} \pm SD$	CV (%)	$\bar{x} \pm SD$	CV (%)	$\bar{x} \pm SD$	CV (%)
pH	7.115 ± 0.005	0.07	7.347 ± 0.005	0.06	7.558 ± 0.005	0.07
pCO_2 (kPa)	9.635 ± 0.300	3.11	5.290 ± 0.102	1.93	2.970 ± 0.113	3.80
pO_2 (kPa)	19.640 ± 0.344	1.75	13.570 ± 0.230	1.69	5.145 ± 0.239	4.65
Na^+ (mmol/L)	117.850 ± 0.366	0.31	136.600 ± 0.681	0.50	157.750 ± 0.851	0.54
K^+ (mmol/L)	3.000 ± 0.000	0.00	4.800 ± 0.000	0.00	6.570 ± 0.047	0.72
Ca^{++} (mmol/L)	1.748 ± 0.009	0.51	1.414 ± 0.011	0.77	0.847 ± 0.009	1.03
Glucose (mmol/L)	11.275 ± 0.148	1.32	5.255 ± 0.076	1.45	2.550 ± 0.069	2.70
Lactate (mmol/L)	8.925 ± 0.301	3.37	0.475 ± 0.044	9.35	2.44 ± 0.135	5.55

Tablica 3. Rezultati ispitivanja netočnosti

Table 3. Results of inaccuracy testing

Analyte	Mean declared value			Mean measured value			% deviation, R		
	Level 1	Level 2	Level 3	Level 1	Level 2	Level 3	Level 1	Level 2	Level 3
pH	7.13	7.40	7.62	7.121	7.390	7.620	-0.13	-0.14	0.00
pCO_2 (kPa)	9.20	4.90	2.40	9.585	5.040	2.495	4.19	2.86	3.96
pO_2 (kPa)	9.30	13.70	20.80	8.950	13.130	20.025	-3.76	-4.16	-3.73
Na^+ (mmol/L)	6.00	3.80	2.60	5.970	3.715	2.570	-0.50	-2.24	-1.15
K^+ (mmol/L)	161	134	117	161.9	133.8	117.1	0.59	-0.15	0.04
Ca^{++} (mmol/L)	1.14	1.01	0.62	1.482	1.022	0.617	2.92	1.19	-0.48
Glucose (mmol/L)	15.80	5.00	3.30	16.515	5.090	3.196	4.53	1.80	-3.18
Lactate (mmol/L)	5.30	1.00	2.40	6.020	0.890	2.640	13.59	-11.0	10.00

Nepreciznost iz dana u dan bila je zadovoljavajuća za sve analite (CV ≤ 4,65%) osim za laktat (2. razina, CV = 9,35%; 3. razina, CV = 5,55%).
Rezultati ispitivanja netočnosti (srednja deklarirana vrijednost, srednja izmjerena vrijednost, R; N = 20, kontrolni uzorak Critical Care QC Contril 9 Multipak: razine 1, 2 i 3) prikazani su u tablici 3.
Rezultati ispitivanja netočnosti bili su zadovoljavajući za sve analite (R ≤ 4,53%) osim za laktat (1. razina, R = 13,59%; 2. razina, R = -11,00%; 3. razina, R = 10,00%).
Rezultati usporednih određivanja koncentracije analita u uzorcima bolesnika na referentnim analizatorima i ispitivanom analizatoru GEM Premier 3000 (srednja vrijednost, standardna devijacija) i izračunati Pearsonov koeficijent korelacije (r) prikazani su u tablici 4.
Dobiveni koeficijenti korelacije pokazuju visok stupanj korelacije za sve analite osim za natrij.
Rezultati usporednih određivanja koncentracije analita u uzorcima bolesnika obrađeni regresijskom analizom po Passingu i Babloku prikazani su u tablici 5.
Rezultati pokazuju vrlo dobru podudarnost rezultata između ispitivanog analizatora i referentnih analizatora.

Rasprava

Rezultati procjene ispitivanog analizatora GEM Premier 3000 pokazali su da nepreciznost u seriji, nepreciznost iz dana u dan i netočnost za većinu analita zadovoljavaju unaprijed utvrđene kriterije prihvatljivosti (CV < 5,00%; R < 5,00%) za sve tri ispitivane koncentracijske razine analita. Korelacija rezultata između ispitivanog analizatora i referentnih analizatora također zadovoljava kriterij prihvatljivosti kod većine analita (r > 0,95).
Kriterije prihvatljivosti nisu zadovoljili rezultati ispitivanja nepreciznosti iz dana u dan za laktat (2. razina i 3. razina),

within-run imprecision study were satisfactory for all the analytes investigated (CV ≤ 3.46%).
Results of the between-run imprecision study (mean, SD, CV; N = 20; Rapid QC Complete control sample Level 1, 2 and 3) are shown in Table 2. Between-run imprecision was satisfactory for all the analytes investigated (CV ≤ 4.65%) with the exception of lactate (Level 2, CV = 9.35%; Level 3, CV = 5.55%).
Results of the inaccuracy study (mean declared value, mean measured value, R; N = 20; Critical Care QC Contril 9 Multipak control sample Level 1, 2 and 3) are shown in Table 3. Results of the inaccuracy study were satisfactory for all the analytes investigated (R ≤ 4.53%) with the exception of lactate (Level 1, R = 13.59%; Level 2, R = -11.00%; Level 3, R = 10.00%).
Results of concurrent determination of study analyte concentrations in patient samples on the GEM Premier 3000 analyzer and reference analyzers (mean, SD) as well as the calculated Pearson's coefficients of correlation (r) are shown in Table 4. The coefficients of correlation obtained showed high correlation for all analytes except sodium.
Results of concurrent determination of analyte concentrations in patient samples processed by Passing Bablok regression analysis are presented in Table 5. The results showed high compatibility between the study analyzer and reference analyzers.

Discussion

Assessment of the study analyzer GEM Premier 3000 revealed the within-run imprecision, between-run imprecision and inaccuracy to meet the preset criteria of acceptability for the majority of analytes (CV < 5.00%; R < 5.00%) at all the three analyte concentration levels evaluated. Correlation of the results obtained on the study analyzer and

Tablica 4. Rezultati usporednih određivanja koncentracije analita u uzorcima bolesnika i koeficijenti korelacije

Table 4. Results of concurrent determination of analyte concentrations in patient samples and coefficients of correlation

Analyte	Reference anayzer $\bar{x} \pm SD$	Study analyzer GEM Premier 3000 $\bar{x} \pm SD$	Pearson's correlation coefficient (r) 95% CI
pH	7.319 ± 0.093	7.327 ± 0.097	0.9909 (0.9876–0.9934)
pCO_2 (kPa)	5.626 ± 1.281	5.440 ± 1.321	0.9852 (0.9798–0.9891)
pO_2 (kPa)	15.277 ± 6.041	15.539 ± 6.390	0.9876 (0.9831–0.9909)
Na^+ (mmol/L)	3.633 ± 0.580	3.525 ± 0.622	0.9915 (0.9884–0.9938)
K^+ (mmol/L)	140.369 ± 5.509	137.55 ± 5.647	0.9207 (0.8931–0.9414)
Ca^{++} (mmol/L)	0.814 ± 0.188	0.826 ± 0.219	0.9727 (0.9629–0.9800)
Glucose (mmol/L)	7.680 ± 3.566	8.152 ± 3.838	0.9920 (0.9859–0.9955)
Lactate (mmol/L)	2.508 ± 1.364	2.602 ± 1.348	0.9914 (0.9848–0.9951)

Tablica 5. Rezultati regresijske analize po Passingu i Babloku

Table 5. Results of Passing-Bablok regression analysis

Analyte	Direction equation	b, slope 95% CI	a, y-axis intercept 95% CI
pH	y = 0.0100 + 1.0000 x	1.0000–1.0357	-0.2529–0.0100
pCO_2 (kPa)	y = -0.3891 + 1.0326 x	1.0084–1.0582	-0.5238–(-0.2513)
pO_2 (kPa)	y = -0.6160 + 1.0564 x	1.0428–1.0699	-0.7955–(-0.4295)
Na^+ (mmol/L)	y = -0.1000 + 1.0000 x	1.0000–1.0769	-0.3769–(-0.1000)
K^+ (mmol/L)	y = -3.0000 + 1.0000 x	1.0000–1.1111	-18.000–(-3.0000)
Ca^{++} (mmol/L)	y = -0.1167 + 1.1667 x	1.1250–1.2105	-0.1526–(-0.0825)
Glucose (mmol/L)	y = -0.0231 + 1.0795 x	1.0392–1.1500	-0.7100–0.0618
Lactate (mmol/L)	y = -0.0132 + 1.0377 x	0.9962–1.0949	-0.1387–0.0795

rezultati ispitivanja netočnosti za laktat (sve tri razine) te koeficijent korelacije za natrij.

Ograničenja ove procjene su činjenice što su se u vrijeme kad se provodila procjena (2006. g.) kao referentni aparati upotrebljavali analizatori Ciba Corning 865 (godina proizvodnje 1996.) i Vitros 250 (godina proizvodnje 1998.). To su mogući razlozi neprihvatljivosti nekih rezultata (natrij, laktat).

Procjenu analitičkih značajka analizatora GEM Premier 3000 ispitivali su i drugi autori.

Beneteau-Burnat i sur. uspoređivali su analizator GEM Premier 3000 i Radiometer® ABL 725 (6). Za ispitivanje nepreciznosti rabili su vodene kontrolne uzorke (ContrIL 9 Multipak, proizvođač Instrumentation Laboratory). Rezultati ispitivanja nepreciznosti u seriji i nepreciznosti iz dana u dan dali su zadovoljavajuće vrijednosti koeficijenata varijacije za sve analite (rezultati za glukozu i laktat su bili granični za pojedine razine). Koeficijenti korelacije dobiveni usporednim određivanjem uzoraka bolesnika na oba aparata (N = 110) su bili u rasponu od 0,91–0,99 (za natrij r = 0,94, za ionizirani kalcij r = 0,91), a regresijska analiza također nije pokazala razliku rezultata između dvaju analizatora.

Steinfelder-Visscher i sur. uspoređivali su analitičke značajke analizatora GEM Premier 3000 i analizatora Ciba Corning 865. Usporedbom rezultata 127 uzoraka pune krvi bolesnika autori su za sve analite osim kalija (r = 0,79) dobili zadovoljavajuće rezultate (7).

Analizator je jednostavan za rukovanje. Kako je bio na ispitivanju u kliničkom laboratoriju, bila je potrebna minimalna izobrazba osoblja. Za vrijeme ispitivanja nije bilo potrebe za intervencijom servisera, jer nema potrošnih dijelova. Postupci održavanja su minimalni. Zamjenjivi umetak je zatvoren sustav i on se jedini povremeno mijenja (ovisno o broju testova/vremenu trajanja umetka). Otpadna posuda ugrađena u umetak povećava biološku sigurnost operatera, jer na najmanju mjeru svodi kontakt operatera

reference analyzers also satisfied the criteria of acceptability for most of the analytes evaluated (r>0.95).

The preset criteria of acceptability were not met in the study of between-run imprecision for lactate (Level 2 and 3), of inaccuracy for lactate (all three levels) and of coefficient of correlation for sodium.

A limitation of the present assessment was the fact that at the time of assessment (2006), the Ciba Corning 865 (manufactured in 1996) and Vitros 250 (manufactured in 1998) analyzers were used as reference analyzers. This may have been the reason for some of the results being found unacceptable (sodium and lactate).

Analytical characteristics of the GEM Premier 3000 analyzer have also been investigated by other authors. Beneteau-Burnat *et al*. (6) compared GEM Premier 3000 and Radiometer®ABL 725 analyzers. They assessed imprecision using aqueous control samples (ContrIL 9 Multipak manufactured by Instrumentation Laboratory Company, Lexington, MA, USA). Testing for within-run imprecision and between-run imprecision produced satisfactory coefficients of variation for all study analytes (borderline results were obtained for glucose and lactate at particular levels). Coefficients of variation obtained by comparison determination of patient samples on both instruments (N = 110) ranged from 0.91 to 0.99 (sodium r = 0.94 and ionized calcium r = 0.91). Regression analysis showed no result differences between the two analyzers either (6).

Steinfelder-Visscher *et al*. compared analytical characteristics of the GEM Premier 3000 and Ciba Corning 865 analyzers. Comparison of the results obtained in 127 patient whole blood samples yielded satisfactory results for all study analytes except for potassium (r = 0.79) (7).

The GEM Premier 3000 analyzer is simple to use. As the analyzer testing was performed at a clinical laboratory, the study required minimal training of the personnel. During the study, there was no need of service intervention, as there are no consumable parts, and the device requires minimal maintenance procedures. The exchangeable car-

s uzorkom krvi. Različite konfiguracije umetka (različit izbor testova, broj testova i trajanje umetka) omogućavaju korisniku fleksibilnost i ekonomičnost.
Aktivna automatska kontrola rada (poslije svakog uzorka bez sudjelovanja korisnika) omogućava znatno brže otkrivanje grešaka (najduže u roku od 30 minuta), što je znatna prednost u odnosu na klasične aparate gdje se kontrola kvalitete rada provodi svakih osam sati. Nakon otkrivanja greške slijedi samostalno otklanjanje greške i dokumentacija korektivne akcije ili isključivanje iz radnog procesa senzora koji nije prošao kontrolu do otklanjanja greške. Ova neprekidna automatska kontrola omogućuje siguran rad i pouzdane rezultate u svako doba.
Kvaliteta pretraga učinjenih uz bolesnika ovisi o predanalitičkim, analitičkim i poslijeanalitičkim čimbenicima. Problemi u radu s aparatima najčešće su uzrokovani predanalitičkim greškama. Suradnja laboratorijskog i kliničkog osoblja i izobrazba osoblja koje radi na aparatu uz bolesnika o mogućim predanalitičkim pogreškama neophodna je za pouzdan i kvalitetan rezultat.
Analizator ne zahtijeva posebne uvjete okoline (radna temperatura 15–35 °C, relativna vlažnost 5–90%), a promjene barometarskog tlaka ne utječu na rad aparata.
Računalo omogućava povezivanje analizatora s postojećim laboratorijskim informatičkim sustavom i prijenos rezultata. Analizator se može povezati s modulom za koksimetriju i modulom za koagulaciju. Uz uporabu uređaja UPS aparat može raditi do sat vremena bez napajanja električnom strujom.

Zaključak

Visoka povezanost rezultata (osim natrija), preciznost i točnost (osim laktata) ispitivanog analizatora kompatibilni su s analizatorima centralnog laboratorija. Operativni proces koji ne zahtijeva izučenog laboratorijskog radnika, samostalno, automatsko provođenje kalibracija, kontrola i otklanjanje grešaka te minimalno održavanje čine ga prikladnim za rad u jedinicama intenzivnog liječenja.

Zahvala

Ova procjena financirana je sredstvima tvrtke MD Lab d.o.o., zastupnikom tvrtke Instrumentation Laboratory i Kliničkog zavoda za kemiju KB "Sestre milosrdnice", Zagreb.

tridge is a closed system that is periodically replaced (depending on the number of analyses/cartridge duration). The waste container is an integral part of the cartridge, thus contributing to the biological safety of the operator by minimizing the operator's contact with blood samples. Different cartridge configurations (different test choice, number of tests and cartridge duration) add to the user's flexibility and cost effectiveness.
The active automated performance quality control (calibration and control after each individual sample requiring no user's manipulation) provides considerably faster error detection (within 30 minutes at the latest), which is a significant advantage over classic devices where the performance quality control is carried out every eight hours. Error detection is followed by independent error elimination and documentation of the corrective action or disconnection from performance of the sensor that has not undergone control before error elimination. This continuous automated control ensures safe performance and reliable results at any time.
The quality of POCT depends on preanalytical, analytica and postanalytical factors. The problems encountered on device operation are mostly caused by preanalytical errors. Close collaboration between laboratory and clinical personnel, and proper education of the staff performing POCT on the potential preanalytical errors are necessary for reliable and quality results.
The GEM Premier 3000 analyzer requires no specific setting conditions (work temperature 15–35 °C, relative humidity 5%–90%); barometer pressure variation has no impact on the device performance.
The computer enables connection of the analyzer to the existing laboratory information system and transfer of results. The analyzer can be connected to the oximetry module and coagulation module. By use of UPS device, the analyzer can operate for up to one hour without electricity supply.

Conclusion

The high correlation of the results (except for sodium), and precision and accuracy (except for lactate) obtained on the GEM Premier 3000 analyzer indicated full compatibility with the analyzers used at central laboratory. Simple operation that does not require specially trained laboratory personnel, the independent and automated calibration, performance control and error elimination, and minimal maintenance make the GEM Premier 3000 analyzer suitable for work at ICUs.

Acknowledgment

This assessment study was supported by the MD Lab Co., representative of the Instrumentation Laboratory, and University Department of Chemistry, Sestre milosrdnice University Hospital, Zagreb.

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