

Evaluation of lithium determination in three analyzers: flame emission, flame atomic absorption spectroscopy and ion selective electrode

Mehri Aliasgharpour¹, Hamid Hagani²

¹Department of Biochemistry, National Reference Laboratory, Ministry of Health and Medical Education of Iran.

²Department of Statistics, Iran University of Medical School, Tehran, Iran.

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Abstract

Background: Lithium carbonate salt has become an increasingly important substance in the treatment of manic depressive disorders, and its relatively narrow therapeutic range has caused laboratories to monitor the serum concentration carefully. In the present work we evaluated lithium measurement in 3 different analyzers. **Methods & Materials:** Three different analyzers including Flame Emission (FES), Flame Atomic Absorption Spectroscopy (FAAS), and Ion Selective Electrode (ISE) were used. All chemicals had a grade suitable for trace metal analysis. **Results:** Within-day precision of CV was $\leq 1.5\%$ for FES & FAAS, except for ISE (1.9% CV). Between-days precision of CV was less for FES than for FAAS and ISE (1.3% versus 2.2% & 2.3%). The percent recovery of added lithium in pooled patients' serum was higher for ISE than for FAAS and FES (103.4% versus 96.2% and 94.6%). We also obtained a higher average lithium concentration for patients' serum samples (n=16) measured by ISE than for FAAS and FES (0.825 ± 0.30 versus 0.704 ± 0.26 & 0.735 ± 0.19). Paired t-test results revealed a significant difference ($p < 0.001$) for patient sera analyzed with FAAS and ISE. **Conclusion:** We report higher results for ISE than the other two analyzers and conclude that the choice between the two flame methods for patients' serum lithium determination is arbitrary and that FES analyzer is a more attractive routine alternative for lithium determination than FAAS because of its cost and ease of performance. In addition, the results obtained by ISE are precise. However, its accuracy may depend on other interfering factors.

Keywords: Lithium, atomic absorption spectroscopy, ion selective electrodes, flame photometry.

Correspondence to: Mehri Aliasgharpour (MS-ASCP), Department of Biochemistry, National Reference Laboratory, Ministry of Health and Medical Education of Iran, Tehran, Iran. Tel.: (+98) 218889 2070. Email: mehri9@yahoo.com

Introduction

For the effective treatment of manic depressive disorders, administration of lithium salts was approved by the US Food and Drug Administration in 1970 and they have been used widely since then (1). Contrary to the low lithium concentration in normal sera, lithium is toxic in high concentrations and yet is ineffective for treatment if the concentration is too low (2-4). Thus, it is important to maintain the blood serum concentration at relatively narrow therapeutic levels and it is apparent that accurate and precise measurement of lithium in manic patients' sera is vital in order to assure adequate and safe treatment.

Many different methods have been introduced for serum lithium determination. Initially, flame emission spectrometry (FES) and flame atomic absorption spectrometry (FAAS) were used to determine blood serum lithium concentration (5-7). In the late 1980s, ion selective electrodes (ISEs) were developed for lithium (8), and recently a colorimetric method was developed (9). In the present work, we aim to compare and evaluate lithium measurement in 3 different analyzers: FES, FAAS, and ISE.

Materials and Methods

Analyzers and Calibration of the Systems

FAAS: A Varian SpectrAA 20-Plus was used for the analysis. The instrument was calibrated with Li working standards (1, 2, 3, 4 µg/ml) made from Li stock standard solution (1g/L). Manually diluted (1:20) pool control serum samples were then aspirated into the air/acetylene flame where neutral Li atoms absorb light emitted from the Li hollow cathode lamp at 670.8 nm (6). The standard solutions and all the sera dilution were in KCL 2g /L to suppress the interfering substances.

ISE: The AVL model 9180 electrolyte analyzer was used for the analysis. A calibration step was performed for the Li configuration using the manufacturer's suggested procedure. Afterwards, neat pool control serum samples were analyzed.

FES: The (FES) instrument was a CIBA-Corning 480, which was equipped with an automatic diluter. The instrument was calibrated with Multical standard (1.5 mmol/l Li concentration) solution and neat pool control serum samples were introduced to the instrument.

Other necessary chemicals and solutions used in the analysis were of a grade suitable for trace metal analysis and were purchased from Merck Co. De-ionized water (D.I-H₂O) was used for the reagents preparation. The quality control serum material used for the evaluation procedures was Seronorm-Trace Elements serum (Sero AS Asker-Norway).

Precision Studies

We performed within-day and day-to-day precision studies on three analyzers by reconstituting and pooling ten Seronorm Trace Elements Serum vials—quality control material. Within-day precision was determined by analyzing a pool serum over three analytical runs (n=12) on the same working day. Day-to-day precision was determined by analyzing aliquots of pool serum (n=10) on 10 consecutive days.

Recovery Studies

For recovery studies in the three systems, we determined the concentration of the pool patients' serum in triplicates. Then, 200 µL of Li standard solution (2.00 mmol/L) was added to the equal volume of pool serum and percent recovery was calculated.

Table 2 Recovery of lithium added to pool serum

Pool serum (mmol/L) (2mmol/L)	Added Li 200 µl	FAAS	FES	ISE
0.84±0.03	200 µl	Measured* Recovered%	Measured Recovered%	Measured Recovered%
		1.38±0.003 96.2±0.35	1.37±0.01 94.5±0.71	1.45±0.04 103.4±3.04

* n=3

Linearity Studies

The linearity study on each system was determined by assaying the neat pool serum 3 times, performing dilution by a factor of 2, and assaying again. Data was analyzed with linear regression using SPSS software. For the lower detection limit of each system, a sample at the lower concentration was run 20 times, and then mean and ST were calculated.

Patients' Serum Correlation Studies for Lithium

16 patient serum samples, for which Li determination had been requested, were assayed with analyzers. The samples were first analyzed with FAAS, and then underwent further analysis by another two systems on consecutive days. The results were analyzed by paired t-test.

Results

With respect to the precision studies of Seronorm serum control material, the within-day precisions (CV %) were less for FAAS (1.5%) and FES (0.90%) than for ISE (1.9%). The results for between-days precision of CVs were less for FES than for FAAS and ISE (1.3% versus 2.2% & 2.3%), Table 1. Table 2 shows the recovery of added lithium (2.0 mmol/L) for three systems. Table 3 shows the results obtained for linearity and lower limit of detection (LLD) for the analyzers. Analysis of the 16 patients' sera is summarized in tables 4 and 5.

Table 1 Precision assay evaluation for seronorm-trace element control serum

Precision	FAAS	FES	ISE
<i>Within day (36)</i>			
Mean, mmol/L	0.84±0.013	0.83 ±0.008	0.86±0.016
CV% *	1.5	0.90	1.9
<i>Day to day (10)</i>			
Mean, mmol/L	0.83±0.019	0.82 ±0.011	0.87±0.015
CV% *	2.2	1.3	2.3
Dilution	(1:20) ⁺	(1:50) ⁺⁺	neat

*: Obtained CV% is at analytical Li range of 0.82-0.84 mmol/L & target value of 0.83 mmol/L for seronorm-trace element control material.

⁺: Manual dilution; ⁺⁺: Automatic dilution

Table 3 Linear Regression analysis for linearity studies

	FES	ISE
Slope	0.981	0.982
LLD	0.061±0.001	0.095± 0.003
*(mmol/L)/Dilution	/(1:16)	/(1:16)

Dependent variable- AAS; * AAS LDL = 0.00± 0.014/ (1:32)

Table 4 Descriptive analysis for patients' serum

Analyzers	N	Mean
FAAS	16	0.704± 0.26
FES	16	0.735±0.19
ISE	16	0.825±0.30

Table 5 Paired samples statistics for patients' serum lithium

Pairs	95% CI*	t	DF	p
FAAS-FES	-0.083 – 0.021	-1.283	15	0.22
FAAS-ISE	-0.182 -0.061	-4.28	15	0.001

*CI: Confidence Interval; * DF- Degree of freedom

Discussion

Lithium carbonate salts have become an increasingly important substance in the treatment of manic depressive disorders (1-3, 10), and its relatively narrow therapeutic range has caused laboratories to monitor their serum concentration carefully. A variety of techniques are used to determine lithium concentration in patients' serum samples (6, 7). The purpose of the present study was to compare and evaluate lithium measurement in three analyzers: FES, FAAS, and ISE.

Our obtained results indicated lower between-days percentages of CV for FES than for FAAS and ISE (1.3% versus 2.2% and 2.3%) using Seronorm serum control material. The result of within-day precision was higher for ISE than for FES and FAAS as well.

The percent recovery of added lithium for FES and FAAS was satisfactory. However, it was higher for ISE than for FAAS and FES (103.4% vs. 96.2% and 94.6%).

In addition, we obtained a higher average lithium concentration for patients' serum samples (n=16) measured by ISE than for FAAS and FES, and paired t-test results revealed a significant difference ($p < 0.001$) for patient sera analyzed with FAAS and ISE. In summary, our obtained results indicated higher values for ISE than the other two analyzers. These findings are in agreement with those of Serdarevic, who also observed higher results using ISE than AAS and dry-slide technology (11). We conclude that even though ISE determination is precise and easy, its accuracy may depend on other interfering factors such as interfering ions and selectivity of the electrode membrane.

Furthermore, our results are in agreement with Levy and Kate (12), who indicated that the two flame methods—FES and FAAS—compared quite well and were precise. We conclude that the choice between the two flame methods for patients' serum lithium determination is arbitrary and that the FES analyzer is a more attractive alternative for lithium determination than FAAS due to its cost and ease of use.

Conclusions

We report a higher result for ISE than the other two analyzers, and summarize that the choice between the two flame methods for patients' serum lithium determination is arbitrary. The FES analyzer is a more attractive and routine alternative than FAAS due to its cost and ease of use.

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