Lithium fingerstick whole blood analysis – results self test at home

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Goal of study

Aim of this study is to examine the capability of the Medimate to measure reliably lithium concentration in fingerstick whole blood at home.

This test is part of the larger validation study conducted at home and at the physician's office. This validation study is approved by the Medical Ethical Committee Twente in the Netherlands with reference number: NL62392.044.17.

Introduction Medimate

The Medimate is primarily intended to assess the lithium concentration in blood. Figure 1 shows how a measurement is performed. Specifications of the Medimate are given in table 1. In addition, the Medimate is able to perform a quality control of the applied blood sample due to its ability to detect hemolysis. If light or severe hemolysis is detected, then respectively a warning or automatic rejection of the measurement will follow.

The physician exclusively reserves the right to modify the lithium dose. The dose should not be changed solely on the outcome of the Multireader.

Table 1: Specifications of Medimate

Medimate	Analytes	Serum	Fingerstick	Users
• Multireader (reusable measurement apparatus) • Lab-chip (disposable cartridge)	• **Lithium** • Creatinine • Potassium	• Yes • Yes • Yes	• Yes • Yes • No	• Healthcare professionals (point-of-care) • Lithium users (self-test)

Study design

Nine subjects were requested to test the performance of the Medimate under home conditions. The test was solely focused on assessing precision. Accuracy has already been tested within other tests, therefore no reference measurements were performed for this test to assess accuracy. In this way non-biased test results were obtained providing optimal performance information without any external disturbances (stress and external influence).

The subjects were requested to perform at home three measurements within an hour for five different (not necessarily consecutive) days. They were also asked to perform measurements at least 10 hours after medication intake to minimize the influence on the measurement results by a changing lithium reference level of the subject. The subject was allowed to use a familiarization period. Furthermore, subjects were requested to write down the results on a form after doing a measurement. The measurement results were also independently stored in the Multireader. After performing measurements data was verified by comparison of both data sets.

Acceptance criteria

Several parties have provided acceptance criteria for the performance of lithium measurements, see table 2. These acceptance criteria are quantified in the Total Error Allowable (TEA). Similar to the CLSI[*1] Evaluation protocols[*2] the TEA is separated into error budgets. Two error budgets are discriminated: the precision budget (one for random error deviation) and the accuracy budget (one for systematic error / bias).

The precision budget to meet the Total Allowable Error is 0,06 mmol/l or 6% with a 95% confidence interval. The standard deviation should be less than half the precision budget (less than 0,03 mmol/l or 3%).

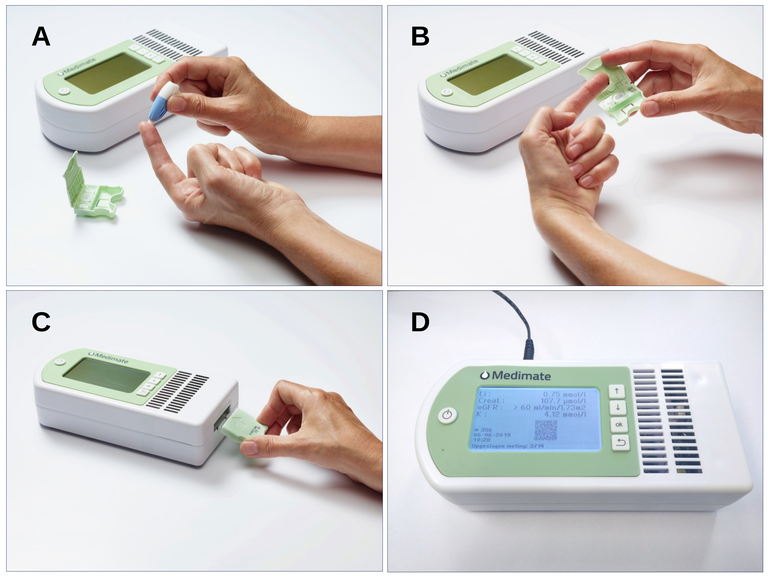

Figure 1: Measurement steps. **A.** Perform fingerstick, **B.** Apply blood droplet on cartridge, **C.** Insert cartridge, **D.** Readout result after 8 minutes

Table 2: Third party performance criteria from the Rhoads Table for the Total Allowable Error

Total Allowable Error	Third party reference	Hometest Lay User
+/- 20% or 0,3 mmol/L	CLIA, WLSH, CAP, AAB	PASS
+/- 15% or 0,3 mmol/L	NYS	PASS
0,2 mmol/L	RCPA	PASS
+/- 10% or 0,10 mmol/L (fingerstick)	Medimate	PASS

Results

The individual test results of eight subjects are shown in Figure 2. One subject did not perform the measurements at any day according to protocol and was later excluded, the reason was that he was recovering from a hypo-manic episode.

In total 122 measurements were performed for this test. Hereby, six times a value was not released by the Medimate (e.g. due to incorrect application of sample or severe hemolysis). Only one measurement result was not within the precision limits, resulting in a test performance of over 99%. Table 3 states the measurement data analysis results where the mean per patient over 5 days is shown as well as the number of measurements and residual evaluation.

Conclusions

Measurements of lithium in fingerstick whole blood show excellent results for home testing by lay users using lithium. The precision budget of the Total Allowable Error is less than 0,06 mmol/l or 6%. Therefore the acceptance criteria are met, see table 2.

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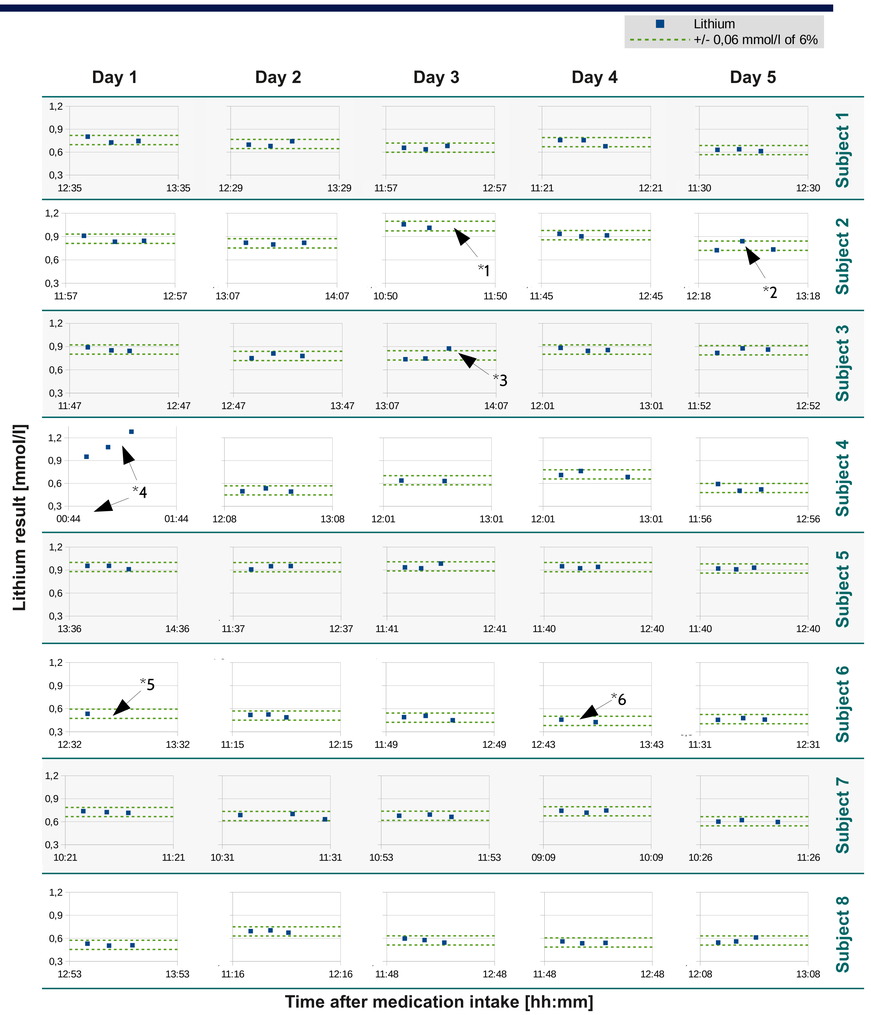

Figure 2: Lithium user test results at home. Eight measurement series are plotted. Each horizontal series is performed by one subject. Three measurement results are plotted for five different days. The measurements are performed after a minimal time interval of 10 hours after medication intake. 95% specification intervals are shown based on own average and specifications of +/- 6% or 0,06 mmol/l.
*1. Severe hemolysis, *2/*3. Elevated outcome with hemolysis indication, *4. Measurements are not performed 10 hours after medication intake and are therefore not stable, *5. Subject measured only once that day, *6. lithium value not released by Medimate for technical reason.

Table 3: Home test lithium analysis results. For every subject the pooled standard deviation is determined. This is the average of the residuals of all five days.

Subject	Mean (mmol/L)	Number of measurements	Measurement not released	Outside specifications (+/- 0,06 mmol/L or 6%)		Pooled stdev (mmol/L)	Pass criteria (mmol/L)	Evaluation
				Hemolysis detected	*No hemolysis detected*			
1	0,70	15	1	0	0	0,028	0,030	PASS
2	0,89	17	2	0	0	0,021	0,030	PASS
3	0,83	15	0	1	0	0,021	0,030	PASS
4	0,71	15	0	0	0	0,028	0,030	PASS
5	0,91	16	2	0	0	0,019	0,030	PASS
6	0,48	13	1	0	0	0,018	0,030	PASS
7	0,68	15	0	0	0	0,017	0,030	PASS
8	0,58	15	0	0	0	0,019	0,030	PASS
Total	**0,73**	**122**	**6**	**1**	**0**	**0,022**	**0,030**	**PASS**

[*1] CLSI = Clinical and Laboratory Standards Institute
[*2] EP21 Evaluation of Total Analytical Error for Quantitative Medical Laboratory Measurement Procedures, Clinical and Laboratory Standards Institute, 2-16