GREAT ORMOND STREET HOSPITAL

NHS

University College London Hospitals

NHS Foundation Trust

Prospective pilot study of a novel, reusable, pocket size Point of Care device that could be used to measure ionized calcium in patients undergoing thyroid and parathyroid surgery

V. Rozalén-García, M. C. de Jong, T Ezzat Abdel-Aziz, C.Soromani, F. Lam, J. Honour, T. R. Kurzawinski

Centre for Innovative Endocrine Surgery, UCLH and GOSH, London, UK

INTRODUCTION

- Approximately 20 % of patients who undergo thyroid or parathyroid surgery develop hypocalcaemia.
- Diagnosis and treatment is currently guided by total adjusted calcium (tCa), although ionized calcium(iCa) is thought to be the physiologically active component.
- Measuring tCa is laboratory based, slow and requires large blood samples. This usually delays treatment adjustments and discharge and patients cannot do it at home.
- There is an urgent need to develop and test a simple point of care device which would enable easy, fast and cost effective measuring of iCa in small blood samples.
- We therefore aimed to assess the equivalence of tCa and iCa in a prospective pilot study and to analyse the performance of a new prototype point-of-care device to measure iCa.

Cobas Calcium Gen2

iSTAT

LAQUA

METHODS

Phase 1: Assessing equivalence between tCa and iCa

21 peripheral venous blood tests were performed on 14 patients undergoing thyroid and parathyroid surgery on the first day after the operation. Patient characteristics are described in table 1.
tCa was measured in the main laboratory following routine clinical practice guidelines using Cobas Calcium Gen.2. iCa was also measured on the same venous sample in the ward using iSTAT from Abbott. iCa values were converted to tCa using normal values ratio (tCa 2.2-2.6 mmol/L; iCa 1.12-1.32; averaged ratio 1.97). Paired t-test was used to compare groups. Bland-Altman plot and correlation graphic and Pearson R were used to create graphics.

Table 1

Patient Characteristics		
Age (mean, range)		48 y (22-65)
Gender (n, %)	Female	11 (78,6%)
	Male	3 (21,4%)
Indication for surgery	Thyroid cancer	5 (35,7%)
	Multinodular goitre	6 (42,8%)
	Thyrotoxicosis	2 (14,3%)
	Hyperparathyroidism	1 (7,1%)
Type of surgery	Total thyroidectomy	9 (64,2%)
	Completion thyroidectomy	4 (28,6%)
	Parathyroidectomy	1 (7,1%)

Phase 2: Assessing performance of LAQUA prototype

LAQUA is a quick, easy to use, cost effective, point of care (PoC) device designed to test iCa in different samples for environmental purposes. It is a device based on flat sensor technology, which can measure iCa from just a few drops of a sample. A prototype specially adapted to test iCa in blood was assessed.
iCa measurements were repeatedly performed with 4 prototypes on solutions with different known calcium concentrations manufactured in the laboratory: 0.5, 1 , 1.5, 2 mmol/L. Calibration of the devices was performed as recommended by manufacturer.
Accuracy of the prototypes was assessed by comparing the readings each of them presented with the previously known calcium concentration of the solutions. Statistical test: paired Student t-test.
Precision was assessed by comparing multiple measurements of the same solution, tested with the same prototype. Coefficient of variation was calculated (CV= SD/mean).

A

B

Figure 3
A. Picture of LAQUA Calcium measuring device. Measures are 15x3x2 cm.
B. Calcium solutions prepared in the laboratory used to test performance of LAQUA.

Phase 3: Assesing the performance of the PoC prototype when measuring iCa in blood

Peripheral venous blood was collected from 6 healthy volunteers. iCa was measured using both iSTAT from Abbott and the novel prototype. Results were compared using paired Student t-test.

A

B

Figure 5
A. Picture of LAQUA Calcium prototype optimized for calcium measurements in blood. B. Picture of iSTAT from Abbott. Both devices are hand-held for size reference.

RESULTS

tCa measured by Cobas Calcium Gen 2 and iCa measured by iSTAT were comparable after conversion (Δmean = 0,02 mmol/L ; *p*=0.4).

tCa mean: 2,34 mmol/L (SD 0,18)
iCa mean: 1,18 mmol/L (SD 0,09)
iCa converted to tCa: 2.32 mmol/L (SD 0,17)

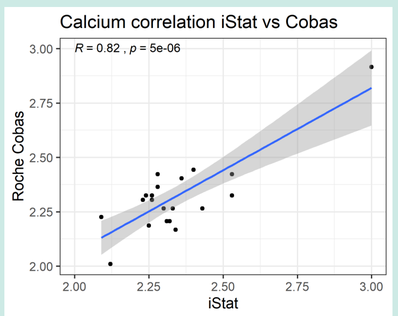

Figure 1
Plot showing tCa values measured by Cobas Calcium Gen 2 (y axis) against converted tCa measured by iSTAT (x axis) in mmol/L. Blue line shows linear model fitting and confidence interval. Pearson R= 0.82. p <0.0001.

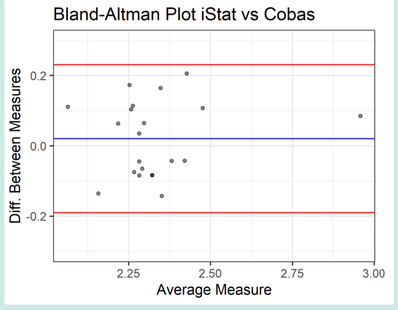

Figure 2
Bland-Altman plot showing difference between measurements by Cobas Calcium Gen 2 and iSTAT in mmol/L. Blue line shows mean difference, red lines show 95% confidence interval (CI). All data points are comprised inside of the CI.

Measuring iCa standardized solutions with novel device showed good accuracy (Δmean vs reference value = 0.09 ; *p* = 0.33).

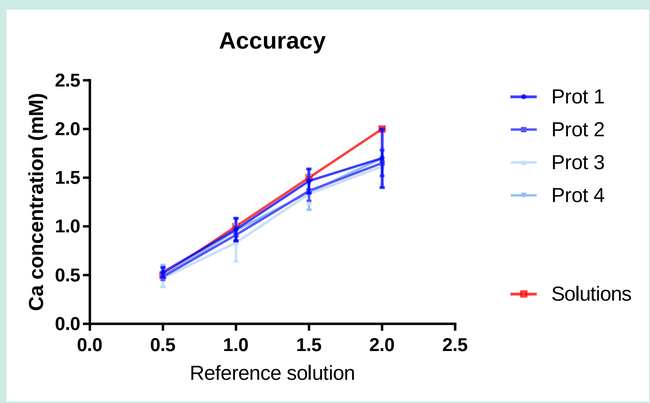

Figure 4

Plot showing mean of three measurements of solutions with known calcium concentration using 4 different LAQUA prototypes. In red, theoretical line showing 100% concordance.

Measuring iCa standardized solutions with novel device showed good precision (CV 3.41%), which is similar to Cobas Calcium Gen 2 (CV of 2.5 %).

Measurements of blood iCa from volunteers by novel device and iSTAT (mean 1.17; SD±0.09 vs. 1.21; SD±0.04) were not equivalent (p<0.03) but difference between them was only 4.5%, which is well within the 10% margin recommended for PoC devices.

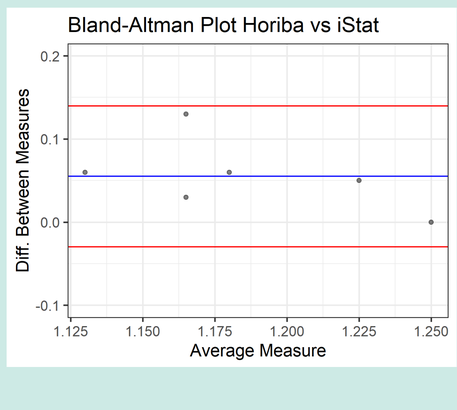

Figure 6
Bland-Altman plot showing difference between measurements by LAQUA prototype and iSTAT in mmol/L. Blue line shows mean difference, red lines show 95% CI.

CONCLUSION

- Our results suggest that iCa can be used instead of tCa to diagnose hypocalcaemia in patients undergoing thyroid and parathyroid surgery.
- LAQUA prototype is a novel PoC device, precise and accurate which offers an exciting opportunity to measure iCa within seconds in small blood samples at hospital bedside and by patients at home.
- When compared to current devices able to measure calcium in blood, LAQUA prototype is portable, cost effective and easy to handle.
- Further testing is required to validate its use for clinical practice. We are currently awaiting approval to run a clinical trial to test the performance of LAQUA prototype when measuring iCa in patients undergoing thyroid and parathyroid surgery.

ACKNOWLEDGEMENTS

We are grateful to SHIRE/TAKEDA for supporting our research with a non competitive grant and to HORIBA for providing us with the LAQUA prototypes optimized to measure iCa in blood.

virginiarozalen.garcia@nhs.net