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Imprecision Evaluation of Self-Monitoring of Blood Cholesterol (SMBC) Handheld Point of Care Testing Devices: Elemark™ and Cardiochek PA

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Abstract

The aim of this study was to determine the imprecision of two cholesterol point of care testing devices, the very established CardioChek PA and recently the Elemark™ which is a mobile blood testing device capable of testing multiple parameters for the management of hypercholesterolaemia undergoing certification. The imprecision study of the Elemark™ and CardioChek PA were performed using blood donations from 3 healthy normal lipidemic subjects. There were 10 repetitions for the within run imprecision and the number of measurement days was 6 for between day imprecision. This study showed comparable within run and between day imprecision between the CardioChek PA and the Elemark™. Based on the imprecision guidelines from the NCEP and CRMLN both devices showed reasonable within run imprecision for their total cholesterol and HDL-cholesterol estimations but not the LDL-cholesterol calculations. The between day imprecision for both devices was reasonably consistent with the published within person biological variability. With more accuracy and imprecision studies being carried out in understanding these cholesterol testing point of care devices, their value, or lack of, in the lipid monitoring would become more apparent.

Keywords: Blood cholesterol; Elemark™; CardioChek PA

Introduction

In the management of hyperlipidaemia, it is expected that after initiating pharmacological interventions such as statins, fibrates, bile acid sequestrants and more recently; PCSK9 inhibitors; the patients are expected to have follow up laboratory tests done at 6 weeks, 3 months, 6 months and yearly. However, the practice is that patients have these blood tests done for their next visit to the outpatient lipid clinic and this usually requires the patients to visit their local hospital laboratory or General Practice (GP) to have their bloods taken and the lipids estimated prior to their visit to the outpatient lipid clinic. It would be an advantage if point of care cholesterol testing devices could be properly evaluated and understood in order to see if they could be used to monitor patients on lipid lowering pharmacological interventions.

There are a number of point of care cholesterol measuring systems on the market, such as Accutrend Plus, BeneCheck Plus, CardioChek PA, Cholestech LDX, these measuring devices range from portable handheld lipid blood testing devices such as the Accutrend Plus, BeneCheck Plus, CardioChek PA to compact desktop analysers such as the Cholestech LDX that can measure a number of lipid fractions and ratios on whole blood; plasma or serum, collected from the finger or venous blood. The method of analysis uses reflectance or biosensor technology with single-use, disposable, dry reagent test strips, rotors or cassettes. The lipid fractions and ratios can be measured individually or as multiple tests: a full lipid profile would consist of total cholesterol, HDL-Cholesterol and triglyceride. Calculated lipid fractions and ratios such as total cholesterol/HDL ratio and calculated LDL-Cholesterol can be estimated with some of the measuring systems [1,2]. Two cholesterol point of care testing devices have been Cholesterol Reference Method Laboratory Network (CRMLN) certified: Cholestech LDX® System (Alere, UK) and Professional CardioChek PA (Polymer Technology Systems Inc, Indiana, US, BHR Pharmaceuticals Ltd., Nuneaton, UK) [1]. The list prices of the devices (excluding VAT): Accutrend Plus, BeneChek PLUS, CardioChek PA and Cholestech LDX are £199, £75, £479 and £950, respectively [2]. Recently, The Elemark™ a smart phone, self-testing cholesterol measuring device for total cholesterol, HDL-cholesterol, LDL-cholesterol and triglycerides, which has connectivity options like Wi-Fi and the 3G HSPA and the data can also be synced with cloud storage. It enables sharing the information with a third party such as the patient's care giver and allows real time monitoring. The Elemark™ device and care system is currently going through CE approval for professional and self-testing this year [3,4].

Lipid concentrations vary within the course of the day and the ranges of within person biological variability (expressed as the coefficient of variation percent) that have been described in the literature for healthy volunteers shows the CV% ranges

for total cholesterol is 2.5% to 10.9%, for HDL-cholesterol is 3.6% to 12.4%, for LDL-cholesterol is 7.8% to 13.6% and for triglyceride 12.9% to 40.8% [5-8]. The within person day to day variation in a healthy volunteer was assessed using one of the cholesterol testing POCT devices, the CardioChek PA and the CV% fell within the expected CV% described in the literature: total cholesterol 9.3%, HDL-cholesterol 7.0%, LDL-cholesterol 13.7% and triglyceride 23.11% [9]. In another study, 2 more point of care cholesterol testing devices, (3 in 1 and Elemark™) were investigated alongside the CardioChek PA and their estimated total cholesterol, HDL-cholesterol, LDL-cholesterol and triglyceride CV%s all fell within the intra-individual variation determined in healthy volunteers [10].

In addition to biological variation, there is also the point of care device's analytical performance. There is very little data on the imprecision of handheld lipid blood testing devices. For the laboratory analytical imprecision measured as coefficient of variation percent (CV%), the Cholesterol Reference Method Laboratory (CRMLN) cholesterol certification criteria for total cholesterol is ≤ 3%, for HDL-cholesterol is ≤ 4% and for LDL-cholesterol ≤ 4% and HDL-cholesterol ≤ 4% [9-11] and the National Cholesterol Education Programme (NCEP) recommended imprecision performance criteria for laboratory total cholesterol ≤ 3% and HDL-cholesterol ≤ 6% [12,13].

The imprecision (within and within-run imprecision) for the CardioCheK PA, was 3.7% for total cholesterol and 6.2% for HDL-cholesterol for level 1 concentration and 3.6% for total cholesterol and 3.5% for HDL-cholesterol for level 2 concentration [14]. In an evaluation by the UK NHS Purchasing and Supply Agency of the CardioChek, it showed, for total cholesterol, a imprecision of 12%, for HDL-cholesterol 22% and for triglyceride 14% [1]. In addition, the inter-assay imprecision of the Multicare Cholesterol system was 4.51% (range, 2.38% to 8.54%) for total cholesterol and 3.29% (range, 1.06% to 7.45%) for triglyceride [15].

The goal of this study was to determine the imprecision of two cholesterol point of care testing devices, the very established CardioChek PA and recently the Elemark™ which is a mobile blood testing device capable of testing multiple parameters for the management of hypercholesterolaemia undergoing certification [3,4].

Materials and Methods

The imprecision study of the Elemark™ and CardioChek PA were performed using blood donations from 3 healthy normal lipidemic subjects attending the Clinical Trials Laboratory Services Limited. Venous whole blood was collected into lithium heparin tubes **(Table 1)**. Samples were then analysed for total Cholesterol, HDL-Cholesterol, LDL-Cholesterol, Triglyceride using the CardioCheK PA device and the Elemark™ device according to the manufacturer's instructions.

Elemark™

The Elemark™ is a smart phone, self-testing cholesterol measuring device for total cholesterol, HDL-cholesterol, LDL-cholesterol and triglycerides using Elemark™ compatible cholesterol test strips. There were 10 repetitions for the within run imprecision for the 3 subjects (Subject 1, 2 and 3). The number of measurement days was 6 for between day analysis for Subject 1. The analytes estimated were: Total Cholesterol, HDL-Cholesterol, LDL-Cholesterol, and Triglyceride. The mean, standard deviation (SD), coefficient of variation percent (CV%) of the total number of estimations was calculated.

Table 1 Showing details of subjects.

Variables	Subject 1	Subject 2	Subject 3
Gender	Female	Male	Female
Age (years)	51	48	43
Fasting	Minimum 4 hours	Minimum 4 hours	Minimum 4 hours
Haemoglobin g/dl	15.1 g/dl	13.7 g/dl	13.1 g/dl
Haematocrit (%)	44%	40%	39%
Drug Free (4 hours)	Nil	Nil	Nil
Smoke and Alcohol free (24 hours)	Nil	Nil	Nil

CardioChek PA

CardioChek PA measures full lipid profile in as little as 90 seconds. It is portable; hand held; battery powered; easy to use with finger stick sample of up to 40 ul. It measures total cholesterol; HDL-cholesterol and triglyceride and calculates LDL-cholesterol and TC/HDL ratio. It is FDA cleared, CE Certified, CLIA waived, CRMLN certified for Cholesterol and HDL-cholesterol strips meet NCEP guidelines for accuracy and imprecision.

There were 10 repetitions for the within run imprecision for the 3 subjects (Subject 1, 2 and 3). The number of measurement days was 6 for between day analysis for Subject 3. The analytes estimated were: Total Cholesterol, HDL-Cholesterol, LDL-Cholesterol, Triglyceride. The mean, standard deviation (SD), coefficient of variation percent (CV%) of the total number of estimations was calculated.

Results

CardioChek PA

Table 2 shows the within-run and between-day imprecision for total cholesterol, triglyceride, HDL-cholesterol and LDL-cholesterol for volunteers 1, 2 and 3 with the CardioChek PA. The within-run for total cholesterol for the subjects 1, 2, and 3 were 5.4%, 8.3% and 7.0%, respectively. The within-run imprecision for triglyceride for volunteers 1, 2 and 3 were 4.0%, 12.1% and 9.4%, respectively. The within-run imprecision for HDL-cholesterol for volunteers 1, 2 and 3 were 5.5%, 3.4% and 3.4%, respectively. The within-run imprecision for LDL-cholesterol for volunteers 1, 2 and 3 were 9.8%, 12.0% and 14.0%, respectively. The between-day imprecision for subject 3 for total cholesterol, triglyceride, HDL-cholesterol

and LDL-cholesterol, were 8.0%, 22.4%, 8.0% and 9.4%, respectively.

Table 2 Imprecision data for the CardioChek PA.

Analytes	Subject	Mean Concentration (mmol/l)	Within-run (n = 10), CV (%)	Mean Concentration (mmol/l)	Between-day (n= 6), CV (%)
Total Cholesterol (mmol/l)	1	5.2	5.4	--	--
	2	5.3	8.3	--	--
	3	4.7	7	4.5	8
HDL-Cholesterol (mmol/)	1	1.8	5.5	--	--
	2	1.7	3.4	--	--
	3	1.9	3.4	1.4	8
LDL-Cholesterol (mmol/l)	1	3.2	12	--	--
	2	2.4	14	--	--
	3	2.6	9.4	2.6	9.4
Triglyceride (mmol/l)	1	1.2	4	--	--
	2	1	12.1	--	--
	3	0.7	9.4	0.9	22.4

Table 3 Imprecision data for the Elemark™

Analytes	Subject	Mean Concentration (mmol/l)	Within-run (n = 10), CV (%)	Mean Concentration (mmol/l)	Between-day (n= 6), CV (%)
Total Cholesterol (mmol/l)	1	5.6	5	5.7	4
	2	5.8	3	--	--
	3	4.8	5.3	--	--
HDL-Cholesterol (mmol/)	1	1.8	4.3	1.8	14
	2	1.6	6.2	--	--
	3	2.1	6	--	--
LDL-Cholesterol (mmol/l)	1	3.1	10	3.4	15.3
	2	3.8	5.5	--	--
	3	2.35	14.4	--	--
Triglyceride (mmol/l)	1	1.5	6.4	1.1	30.3
	2	0.8	5	--	--
	3	0.7	5.6	--	--

Elemark™

Table 3 shows the within-run imprecision for total cholesterol for volunteers 1, 2 and 3 were 4.9%, 2.9% and 5.3%, respectively. The within-run imprecision for triglyceride for volunteers 1, 2 and 3 were 6.4%, 4.9% and 5.6%, respectively. The within-run imprecision for HDL-cholesterol for volunteers 1, 2 and 3 were 4.3%, 6.2% and 6.0%, respectively. The within-run imprecision for LDL-cholesterol for volunteers 1, 2 and 3 were 10.0%, 5.5% and 14.4%, respectively. The between-day imprecision for subject 1 for total cholesterol, triglyceride, HDL-cholesterol and LDL-cholesterol, were 4.0%, 30.3%, 14.0% and 15.3%, respectively.

Discussion

The CRMLN cholesterol certification criteria for total cholesterol ≤ 3%, HDL-cholesterol ≤ 4% and HDL-cholesterol ≤ 4% and LDL-cholesterol ≤ 4% and HDL-cholesterol ≤ 4% [11]. The NCEP recommended imprecision performance criteria for laboratory total cholesterol ≤ 3% and HDL-cholesterol ≤ 6% [12,13].

In this study, the within-run imprecision for the CardioChek PA ranged between 5.4-8.3% for total cholesterol. This was mildly higher than the recommended CV% for total cholesterol provided by both the NCEP and CRMLN guidelines of 3%, including Whitehead et al. findings using the CardioChek PA of 3.6% to 3.7%, but lower than the CV% seen in the UK NHS Purchasing and Supply Agency evaluation of the CardioChek PA of 12%. The within-run imprecision for CardioChek ranged between 3.4% to 5.5% for HDL-cholesterol. This was comparable to the recommended CV% for HDL-cholesterol by the NCEP guidelines of 6% and CRMLN guideline of 4%. This was also consistent with Whitehead et al. findings [12] but lower than the findings in the UK NHS Purchasing and Supply Agency evaluation [1]. The within-run imprecision for CardioChek ranged between 9.4% to 14.0% for LDL-cholesterol, which was higher than the recommended CV% for LDL-cholesterol the CRMLN guideline of 4%. The within-run imprecision for the Elemark™ ranged between 3.0% to 5.3% for total cholesterol. This was reasonably within the recommended CV% for total cholesterol provided by both the NCEP and CRMLN guidelines of 3%. The within-run imprecision for Elemark™ ranged between 4.3% to 6.2% for HDL-cholesterol. This was comparable to the recommended CV% for HDL-cholesterol by the NCEP guidelines of 6% and CRMLN guideline of 4%. The within-run imprecision for Elemark™ ranged between 5.5% to 14.4% for LDL-cholesterol, this was higher than the recommended CV% by the CRMLN guideline of 4%. The within-run imprecision of triglyceride for the CardioChek PA was 4.0% to 12.1% and for the Elemark™ was 5.0% to 6.4%. This within-run imprecision of the CardioChek PA was similar to the CV% for triglyceride observed in the UK NHS Purchasing and Supply Agency evaluation of the CardioChek PA but higher than the Elemark™ imprecision [1]. The within-run imprecision of triglyceride for the Elemark™ was comparable to that observed in other point of care devices such as the MultiCare [15]. The between day imprecision (CV%) of the CardioChek PA was 8% for total cholesterol, 8% for HDL-cholesterol, 9.4% for LDL-cholesterol and 22.4% for triglyceride. Whilst the between day imprecision (CV%) of the Elemark™ was 4% for total cholesterol, 14% for HDL-cholesterol, 15.3% for LDL-cholesterol and 30.3% for triglyceride. These results were reasonably consistent with the within person biological variability (expressed as the coefficient of variation percent) that have been described in the literature for healthy volunteers with CV% ranges for total cholesterol 2.5% to 10.9%, for HDL-cholesterol 3.6% to 12.4%, for LDL-cholesterol 7.8% to 13.6% and for triglyceride 12.9% to 40.8% [5-8].

Conclusion

This study albeit using a small sample size showed comparable imprecision between the FDA cleared, CE marked, CLIA waived and CRMLN certified CardioChek PA and the Elemark™. Based on the imprecision guidelines from the NCEP and CRMLN, both devices showed reasonable imprecision for their total cholesterol and HDL-cholesterol estimations but not the LDL-cholesterol calculations. The Elemark™ is a smart phone *in vitro* diagnostic device that rapidly tests for total cholesterol, triglyceride and HDL-cholesterol on a whole blood sample without centrifugation.

With more accuracy, imprecision and cost effective studies on cholesterol testing point of care devices such as the Elemark™ being carried out, their value or lack of in the lipid monitoring would become more apparent.

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