Self-monitoring blood cholesterol (SMBC) testing: within-person day to day variation in a healthy volunteer

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1. Introduction

Currently, Point of care testing (POCT) has revolutionized the self-testing of a number of parameters such as blood pressure, glucose and lipids. Point of care tests provide significant benefits to patients:

• The tests are usually minimally invasive as most of them require only a small amount of blood usually collected from the finger and requires no sample preparation (1).

• The tests are usually completed within 5 minutes, leading to a reduction in the result turnaround time, thereby allowing a quicker decision being made (2,3).

• The patient being involved with their testing improve their compliance, adherence to treatment and therapeutic control (4,5)

• The self-testing also allows the patients to make less visits to the laboratory or GP practice to have their bloods taken (4,5,6)

Well-known examples are the self-testing of blood pressure in patients with hypertension. Studies have shown that self-monitoring results in small, but significant reductions in blood pressure and better adherence to treatment (7). Self-Monitoring of Blood Glucose (SMBG) has been shown to be helpful in 4 distinct ways: First, both patient and clinician are able to ascertain high or low levels of glucose and thereby make the necessary therapeutic adjustments. Second, SMBG provides the patients the chance to detect or confirm whether they have a hyper or hypo incident. Third, the SMBG devices also provide patient education and disease management

information. Fourth, SMBG helps motivate the patients (8)

There are a number of point of care cholesterol measuring systems on the market, such as Accutrend Plus, BeneCheck Plus, CardioChek PA, Cholestech LDX, Veri-Q and 3in1, these measuring devices range from portable handheld lipid blood testing devices to compact desktop analysers 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 use reflectance or biosensor technology with single-use, disposable, dry reagent test strips, rotors or cassettes. The lipid fractions and ratios can be measured individual or as multiple tests: a full lipid profile would consist of total cholesterol, HDL-Cholesterol and triglyceride. In addition, calculated lipid fractions and ratios such as total cholesterol/HDL ratio and calculated LDL-Cholesterol can be estimated with some of the measuring systems (9,10). 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) (9). Lipid and lipoprotein concentrations vary during the normal course of daily activity. Studies have demonstrated that within person variability is sufficient to make an individual move in and out of the pre-defined risk categories defined by the respective lipid guidelines. 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 test 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, this 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 is time that Self-Monitoring of Blood Cholesterol or Lipids (SMBC or SMBL) in the management of hyperlipidaemia, especially during the initiation of therapeutic agents takes its place like SMBG that plays a pivotal role in the management of diabetes. One important factor to take into consideration is the within person day to day variation, especially if these devices are going to be used for helping both the patient and clinician in being able to ascertain lipid levels after initiation of medication at the appropriate time and thereby make the necessary therapeutic adjustments. The ranges of within person biological variability (expressed as the coefficient of variation) that have been described in the literature show the CV% for total cholesterol is 2.5% - 10.9%, for HDL-cholesterol is 3.6% - 12.4%, for LDL-cholesterol 7.8% - 13.6% and for triglyceride 12.9% - 40.8% (11-14) In this case study, we assessed the within person day to day variation of lipids: Total Cholesterol (TC), High Density Lipoprotein Cholesterol (HDL – C), Triglyceride and calculated Low Density Lipoprotein Cholesterol (LDL-C) using the CardioChek PA (Indianapolis, IN) a handheld, battery-powered device that use proprietary test strips and a reflectance photometry processor to perform a wide range of in-office tests on a single fingerstick whole blood sample (15–40 μL).

2. Material & Method

Finger prick (capillary) whole blood was taken from a single subject taking between 7.30 and 10.00 am (fasting) on 12 days in 2 months. TC, HDL - C, Triglyceride, calculated LDL-C and TC/HDL - C ratio on the CardioChek PA

were estimated immediately according to manufacturer's instruction. The mean, Standard Deviation (SD), Coefficient of Variation (CV), Coefficient of Variation Percent (CV%) of the values calculated on the daily estimations taken. The CardioChek PA is a handheld whole blood analyser utilising reflectance photometry. The CardioChek PA is FDA 510(K) declared, Clinical Laboratory Improvement Amendments (CLIA) waived, and European Conformity (CE) labeled and Cholesterol Reference Method Laboratory Network (CRMLN) certified. It measures TC, triglycerides, HDL -C and calculates LDL - C and TC/HDL - C ratio. The vial of test strips contains a MEMo Chip that has information on specific calibration and on how to read the particular test strip. Results are available in 2-5 minutes. The device can be linked to computers, and is compatible with Windows® 7/Vista™/XP operating systems.

3. Results

Figure 1 shows the daily TC concentration ranged between 3.71 – 4.88 mmol/L, with a mean of 4.27 mmol/L, the LDL-C concentration ranged between 1.8 – 2.84 mmol/L, with a mean of 2.4 mmol/L. the HDL-C concentrations ranged between 1.29 – 1.59, with a mean of 1.48 mmol/L, the TC/HDL-C ratio ranged between 2.3 – 3.3 mmol/L, with a mean of 2.90 mmol/L. Triglyceride concentrations ranged between 0.6 – 1.3 mmol/L, with a mean of 0.8 mmol/L.

Table 1 shows, the standard deviations of total cholesterol concentration, LDL-Cl, HDL-C, TC/HDL-C and triglyceride concentrations, were 0.39 mmol/L, 0.33 mmol/L, 0.10 mmol/L, 0.30 mmol/L and 0.18 mmol/L, respectively and the coefficient of variation % (CV%) of TC concentration, LDL-C, HDL-C, TC/HDL-cholesterol and triglyceride concentrations, were 9.3%, 13.7%, 7.0%. 10.5% and 23.1% respectively.
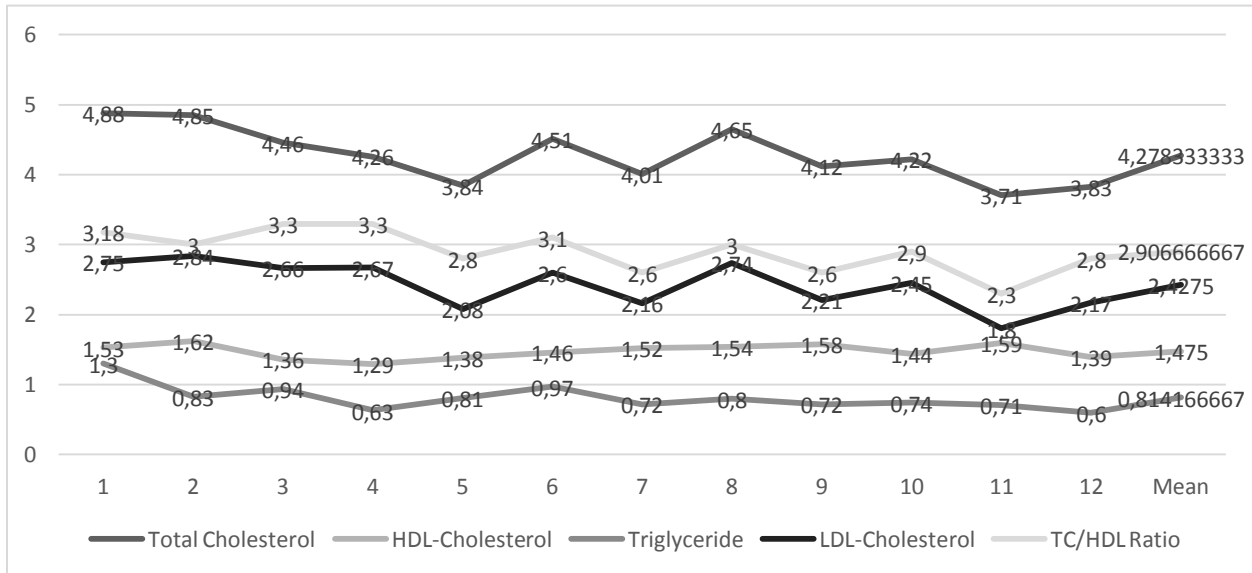

Figure 1: Daily Finger Prick Lipid Measurements with CardioChek PA in healthy Individual (Fasting Sample)

Table 1: Mean, SD and CV% of daily finger prick lipid measurements with CardioChek PA in healthy Individual (Fasting Sample)

	Mean	SD	CV%
Total Cholesterol	4.278333333	0.396641201	9.270927958
HDL-Cholesterol	1.475	0.104315954	7.072268043
Triglyceride	0.814166667	0.188412426	23.14175145
LDL-Cholesterol	2.4275	0.332295734	13.68880468
TC/HDL-Cholesterol Ratio	2.906666667	0.304192921	10.46535279

SD- Standard deviation, CV% - Coefficient of Variation Percent

4. Discussion

Lipid and lipoprotein concentrations vary during the normal course of daily activity. Studies have demonstrated that within person variability is sufficient to make an individual move in and out of the pre-defined risk categories defined by the respective lipid guidelines. More than 60% of the total variation is caused by biological variation and the analytical variation accounts for the remaining (9). The ranges of within person biological variability (expressed as the coefficient of variation) that have been described in the literature show the CV% for total cholesterol is 2.5% - 10.9%, for HDL-cholesterol is 3.6% - 12.4%, for LDL-cholesterol 7.8% - 13.6% and for triglyceride 12.9% - 40.8% (11-14). Comparative studies have shown that the CardioChek PA is fairly accurate when compared with traditional laboratory methods (9), therefore the expected analytical variation from the device is robust. On evaluation of biological variation studied in this healthy volunteer using the CardioCheK PA, the total cholesterol, HDL-cholesterol, LDL-cholesterol and triglycerides estimations taken on 12 separate days within a two-month period fell within the intra-individual variation determined in 53 healthy volunteers over a one-year period (12). This would suggest that the biological variation with the CardioChek PA in the healthy volunteer is as expected and if such devices get approved for patient self-testing or self-monitoring of blood cholesterol (SMBC). There is the potential that such patient self-testing or self-monitoring cholesterol testing devices could be used in helping both patient and clinician ascertain whether the appropriate lipid level targets have been achieved and therefore making it possible to make the necessary therapeutic adjustments. Secondly, SMBC would be able to provide the patients the chance to detect or confirm their lipid levels. Thirdly, the SMBC devices would provide patient education and disease management information. Fourthly, SMBC would help motivate the patients.

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