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Full Length Research Paper

Comparison of direct assay and friedewald formula for determination of LDL cholesterol

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ABSTRACT

Cardiovascular diseases are a veritable public health problem worldwide. Its diagnosis and monitoring require among other things the determination of serum LDL cholesterol levels. For this, two methods of determination are often used: direct measurement and the Friedewald equation. The Friedewald formula is commonly used especially where the reference method is unavailable for technical and financial reasons. We investigated lipid status in one hundred subjects comparing the enzymatic method and LDL cholesterol estimation using the Friedewald formula. The MultiQC 6.0 software and Student's test were used to analyse the results and P < 0.05 was considered to be statistically significant. Correlation with two methods was satisfactory with only a few discordant results. However, Friedewald equation always keeps its usefulness in our resource limited countries.

Keywords: LDL cholesterol, direct assay, Friedewald Formula

INTRODUCTION

The prevalence of cardiovascular diseases continues to rise around the world. According to WHO estimates, 16.7 million new cases of cardiovascular disease are reported each year worldwide and 29.2 million registered deaths (Heron MP et al, 2009). In 2010, cardiovascular diseases were the first cause of mortality in developing countries. They are quickly becoming a major public health problem especially with the emergence of atherosclerosis and its complications. Senegal is no exception to the rule, where they are the second cause of death after malaria (*OMS*, 2007). Studies have shown the importance of lipids in the management and monitoring of patients with cardiovascular risk (Bayer P et al, 2005). The LDL fraction, more than any other, is reported to correlate with the occurrence of cardiovascular events (Gordon T et al, 1981). Thus, an accurate and precise determination of LDL cholesterol is critical for early identification of patients at risk.

However, the determination of LDL cholesterol by the Friedewald method has its limitations and is variously appreciated since the introduction of method of direct determination, which presently is the standard assay method.

Should we now leave the Friedewald method simply for economic reasons? Only a comparative study of two methods can enlighten us on the validity of the results reported in our daily practice.

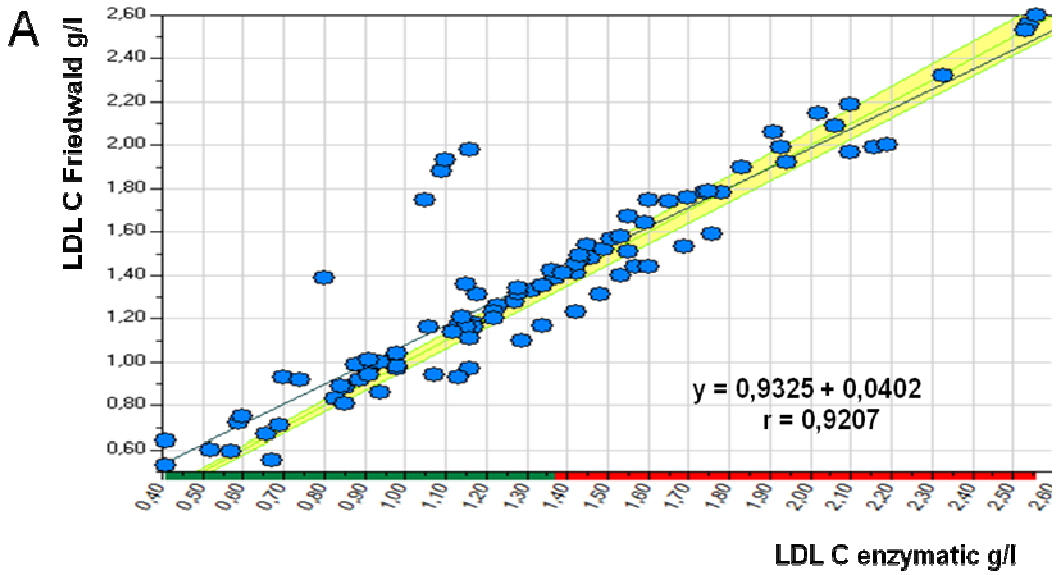
MATERIALS AND METHODS

Population

This is a prospective study conducted at the biochemistry laboratory of Aristide Le Dantec University Hospital in Dakar, Senegal. We randomly selected one hundred patients who came to have lipid profile tests. These patients did not present with dyslipidemia and had serum triglyceride levels of less than 3 g / l.

Table 1: Concentrations biochemistry parameters with LDL c values obtained by two methods. Values are represented by means ± standard deviation. Minimun and maximum values are also represented

	Mean ± SD	Maximun value	Minimun value
LDL c (enzymatic) (g/l)	**1,305 ± 0,4739**	**2,56**	**0,41**
LDL c (Friedwald) (g/l)	**1,356 ± 0,4679**	**2,60**	**0,53**
Total Cholesterol (g/l)	**2,122 ± 0,1131**	**3,2**	**1,03**
HDL Cholesterol (g/l)	**0,530 ± 0,2444**	**0,87**	**0,18**
Triglycerides (g/l)	**1,182 ± 0,7391**	**2,8**	**0,15**



METHODS

The samples were taken from fasting subjects in vacutainer tubes without anticoagulant and centrifuged at 3000 rpm for 5 minutes. The total cholesterol, HDL, LDL and triglycerides were determined by standard enzymatic methods according the instructions on Cobas Integra analyzer 400 (Roche^{R}). The values of total cholesterol, HDL cholesterol and triglycerides were used to calculate LDL using the Friedewald equation which is thus: LDL cholesterol = total cholesterol - (HDL cholesterol + triglycerides / 5). Normal and pathologic controls were used to validate the results.

StatisticaL Analysis

The results were analyzed using a MultiQC 6.0 statistical software for data processing and Student's test. $P < 0.05$ was considered to be statistically significant.

RESULTS

Concentrations values are expressed as mean with standard deviation, but difference between mean LDL cholesterol obtained with the two methods was not significant.

Table 1 summarizes the mean concentrations of the different lipid parameters studied. The correlation of results with two methods obtained was satisfactory with only 5 discordant samples (figure 1 A). However, the different patterns show that 27% of the samples are outside the tolerance zone (green spots) (figure 1 B).

DISCUSSION

Cardiovascular diseases are very common heterogeneous disorders. In addition to genetic factors, environmental and especially nutritional factors influence their occurrence. Total cholesterol and its LDL fraction responsible for the formation of atherosclerotic plaques are very closely associated with increased coronary risk. This association is found to be consistent in many studies where the relative risk is multiplied by 2 when cholesterol increases from 2 to 2.5 g / l, and by 3 with an increase between 2.5 and 3 g / l (Machecourt J et al, 2002).Optimal control of LDL cholesterol allows the reduction of cardiovascular risk by 20 to 30% (Bruckert E et al, 2010). This control requires the determination of

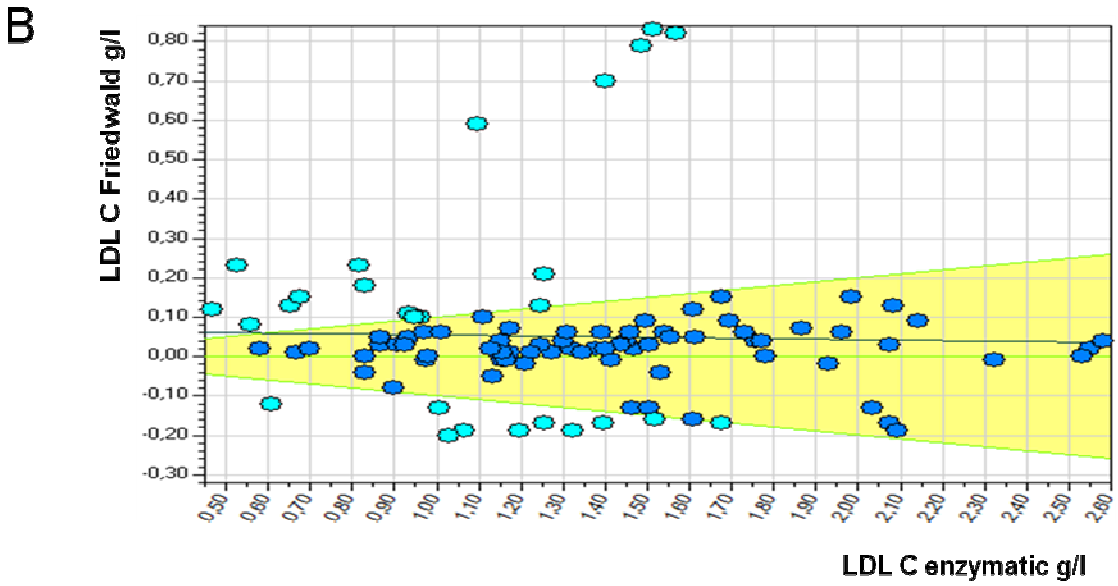


figure 1. Comparison of LDL cholesterol values obtained by two methods

A: Regression line for the LDL c enzymatic and LDL c Friedewald: y = 0.9325 + 0. 0402 (r = 0. 9207). Value is represented by a point. The area switching capability (red line) is between 1.37 and 2.60 g / l and the non switching capability area (green line) between 0.40 and 1.37 g / l.
B: Concentration difference shows that 27% of the samples are out of tolerance. These points are located outside the bisector and are represented by green dots.

LDL cholesterol which can be done directly or by calculation.

The accuracy of the calculation method is highly dependent on the accuracy of the considered parameters such as total cholesterol, triglycerides and HDL cholesterol.

It is the method often used in our health facilities, because it is more readily available and cheaper.

Our study shows that the averages for the two methods as well as standard deviations are not significantly different with a correlation of 0.92 (Table 1).

This correlation between the two methods has been demonstrated by Bayer et al (Bayer P et al, 2005). According to their study, there was no significant difference for LDL cholesterol values. Similarly, the recent study by Can (Can M. et al, 2010) showed a strong and significant correlation ($p < 0.01$) among 1000 patients.

However, the scatter diagram (Figure 1A) shows two concentration levels (between 0.40 and 1.36 g / l and between 1.37 to 2.60 g / l). Commutability area is located between 1.37 and 2.56 g / l for 10% tolerance. They are not strictly equivalent, but they can be exchanged without altering the diagnostic capacity of the patient (Bland JM et al, 1986).

Indeed, the values are close to the regression line and can be concluded that the interchangeability of the two methods only apply for values of LDL cholesterol slightly abnormal. The same findings were reported by Nauck (Nauck M et al, 2000). However, with the direct measurement method, 44% of patients had cholesterol levels greater than 1.30 g / l, while this percentage was 51% with the calculation method.

In this case we can say that the calculation method overestimates the percentage of subjects who had an LDL-cholesterol and therefore risk of heart disease. These results were also confirmed by Sahu et al (Sahu S et al, 2005).

The results showed that 23.5% of patients had cardiac risk using the calculation method and that this percentage was lower with the direct determination (17.5%).

Analysis of the differences diagram (Figure 1B) shows that 73% of the results are in the polygon of tolerance, or where both methods are consistent, there must be at least 90% results in the area of tolerance. These results are obtained with a medical tolerance of ± 10%. Between 0.45 to 1.60 g / l many values are outside the tolerance range.

Until now, there is no study that has shown a perfect concordance between the two methods that we have analyzed. This could be explained by the fact that the estimate always includes errors related to the specificity of the determination of the parameters taken into account.

It should however be emphasized that the study by Edjeme (Edjeme A et al, 2010) proposed that the Friedewald method remains useful in the laboratory,

although it should be alternated with the direct method in some cases of dyslipidemia, as in hypertriglyceridemia.

CONCLUSION

LDL cholesterol is a parameter for diagnosis and monitoring of cardiovascular disease. Direct determination is the method of choice but a remains problem especially in our resource-poor settings. Results confirm that some values are similar for both methods. Thus, the LDL cholesterol by Friedewald formula keeps its place in our healthcare institutions with some caution in case of dyslipidemia.

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