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REVIEW ARTICLE

Fast Interference in Lipid Profile: A Systematic Review

Interferência do Jejum no Perfil Lipídico: Uma Revisão Sistemática

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ABSTRACT

Objective: To critically evaluate, through a careful review of the scientific literature, whether there are significant differences in the lipid profile dosage in fasted and non-fasting blood samples. **Methods:** Studies originally published in the English language and indexed in the last 5 years were analyzed. The inclusion and exclusion criteria were applied freely and independently by a reviewer, who judged the selected studies from the points raised in each item exposed (Table 1). **Results:** The scope of this review included 5 studies that met the selection criteria. The studies used were analyzed for the values of total cholesterol, high density lipoproteins (HDL), low density lipoproteins (LDL) and triglycerides dosed in the fasting and non-fasting states. In the studies analyzed, HDL and total cholesterol remained constant, LDL decreased in concentration and triglycerides increased in concentration between fasting and non-fasting state. **Conclusions:** This review confirms the premise presented by recent worldwide guidelines and consensus on the fact that fasting is not mandatory for the lipid profile, considering that no significant differences were found between fasting and non-fasting dosages, and even for the parameters that presented some divergence, it does not imply relevant clinical alterations, being necessary only to make a small adjustment in the reference values for the state without fasting.
Keywords: Fasting, Lipoproteins, Cholesterol.

RESUMO

Objetivo: Avaliar criticamente, através de uma cuidadosa revisão da literatura cientifica, se existem diferenças significativas na dosagem do perfil lipídico em amostras de sangue coletadas com e sem jejum. **Métodos:** Foram analisados estudos publicados originalmente na língua inglesa e indexados nos últimos 5 anos. Os critérios de inclusão e exclusão foram aplicados livre e independentemente por um revisor, que julgou os estudos selecionados a partir dos pontos levantados em cada item exposto. **Resultados:** Fizeram parte do escopo desta revisão 5 estudos, que preencheram os critérios de seleção. Os estudos utilizados foram analisados quanto aos valores de colesterol total, lipoproteínas de alta densidade (HDL), lipoproteínas de baixa densidade (LDL) e triglicerídeos dosados nos estados de jejum e sem jejum. Nos estudos analisados o HDL e colesterol total mantiveram-se constantes, o LDL apresentou diminuição na concentração e os triglicerídeos apresentou aumento na concentração entre o estado de jejum e o estado sem jejum. **Conclusão:** Esta revisão confirma a premissa apresentada por diretrizes e consensos mundiais recentes sobre a não obrigatoriedade do jejum para a realização do perfil lipídico, tendo em vista que não foram encontradas diferenças significativas entre as dosagens realizadas com jejum e sem jejum, e mesmo para os parâmetros que apresentaram alguma divergência, esta não implica em alterações clínicas relevantes, sendo necessário apenas realizar um pequeno ajuste nos valores de referência para o estado sem jejum.
Palavras-chave: Jejum, Lipoproteínas, Colesterol.

INTRODUCTION

The standard lipid profile consists of the serum determination of total cholesterol, high density lipoproteins (HDL), low-density lipoproteins (LDL), non-high-density lipoproteins (non-HDL), very low-density lipoproteins (VLDL) and triglycerides[1,2]. These parameters are used in clinics to assess the risk of atherosclerotic coronary disease and dyslipidemia[1, 3, 4].

For many years, the literature and the current technical norms established that the measurement of the lipid profile should be performed on blood samples collected during a 12-hour fast[1, 5, 6]. Recent studies show that the non-fasting dosage of the lipid profile portrays more effectively the potential cardiovascular risk, since the patient is in the fed state most of the day[7, 8].

The Danish Society for Clinical Biochemistry (2009), the United Kingdom's National Institute of Clinical Excellence (2014), the European Society for Atherosclerosis and the European Federation of Clinical Chemistry and Laboratory Medicine (2016), recommend that fasting is not mandatory for the dosage of the lipid profile[2,9,10,11]. However, the American College of Cardiology/American Heart Association (ACC/AHA) released a guideline in 2013, showing a preference for using fasting samples for dosing the lipid profile[12, 13].

In December 2016, the Brazilian Society of Clinical Pathology (SBPC), the Department of Atherosclerosis of the Brazilian Society of Cardiology (SBC/DA), the Brazilian Society of Clinical Analyzes (SBAC), the Brazilian Diabetes Society (SBD) and the Brazilian Society of Endocrinology and Metabology (SBEM) prepared the "Brazilian Consensus for the Standardization of the Laboratory Determination of the Lipid Profile", which addresses the flexibility of fasting to assess the lipid profile, whose main advantages and motivations aim at the collection practicality for the patient; safe collection, especially for diabetics on insulin therapy, pregnant women, children, and the elderly; a greater range of times for blood collection, which reduces congestion in the morning in laboratories[7].

Due to controversies on the subject, the present study aims to critically assess, through a careful review of the scientific literature, whether there are significant differences in the dosage of the lipid profile in blood samples collected with and without fasting.

METHODS

The present study is a systematic review whose research was performed in the Medline database. Studies originally published in the English language and indexed in the last 5 years were analyzed. The search strategy used the combination of the descriptors Fasting, Fasting Time, Lipoproteins. To identify the designs of the studies, the terms randomized controlled trial, observational study, and clinical trial were used.

The inclusion and exclusion criteria were applied freely and independently by a reviewer, who judged the selected studies from the points raised in each exposed item (Figure 1).

RESULTS

34 studies involving fasting times and lipoproteins were identified, however only 5 were part of the scope of this review.

Figure 1 shows the flowchart used to select the articles analyzed.

The studies used were analyzed for the values of total cholesterol, HDL, LDL and triglycerides dosed in fasting and non-fasting states and the values found by the authors were organized in Table 2.

In the studies analyzed, HDL and total cholesterol remained constant or had very small variations, LDL showed a decrease in concentration and triglycerides showed an increase in concentration between the fasting state and the non-fasting state.

DISCUSSION

The results confirm the premise, presented by world guidelines, that the measurement of the lipid profile without fasting can be used for evaluation and clinical decision-making, since there are no significant differences in the measurements of fasting and non-fasting parameters[14, 15, 16, 7].

The studies analyzed found very similar variations between the fasting and non-fasting states for the tests that constitute the lipid profile. The parameters of HDL and total cholesterol remained constant or had very small variations between the two fasting states[2,14,16,17,18]. In contrast, LDL and triglycerides showed, respectively, a decrease and an increase in fasting and non-fasting state concentration[14,17, 16, 17, 18].

Most studies used adult and apparently healthy patients[16, 17, 18]. However, the same variations were observed in patients hospitalized after acute coronary syndrome (ACS), a fact evidenced by Steen et al.,(2017) who researched the impact of fasting on the evaluation of patients after hospitalization for ACS. This study proved that although fasting affects the measurements of lipid parameters, the variation is small and clinically insignificant, both after ACS and during the follow-up of these patients[14]. The same was observed in diabetic patients, for whom the lipid parameters showed the same pattern of change after ingestion. Although diabetic patients have higher levels of triglycerides and LDL than healthy patients, the variation found between fasting and non-fasting states was very similar in both groups[16]. These data support the recent guidelines and consensus that standardize the flexibility of the lipid profile even in patients with ACS and in diabetic patients[7].

Table 1. Inclusion and exclusion criteria for articles

Inclusion criteria	Exclusion Criteria
Observational studies (cross-sectional, case-control and cohort)	Literature review
Published in the last 5 years	Intervention studies
In English	
Patients who were evaluated for total cholesterol, HDL, LDL and triglycerides in fasting and non-fasting states	

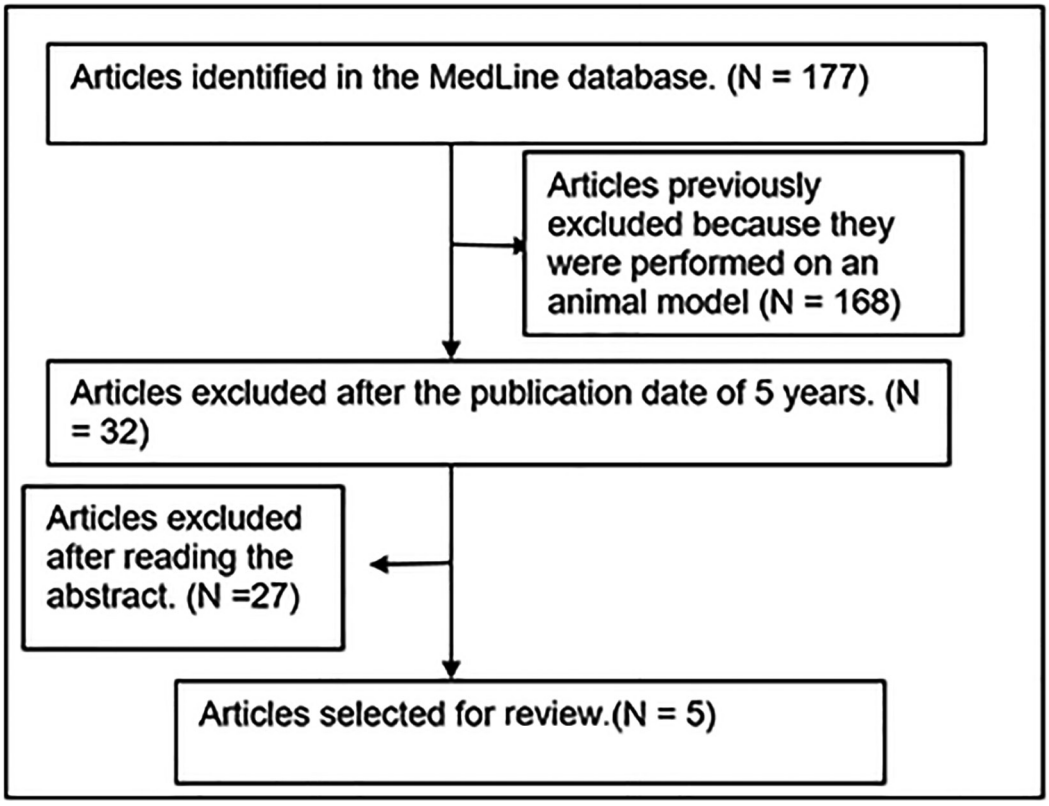

Figure 1. Flowchart of the study selection process

One of the motivations for making the fasting more flexible in order to determine the lipid profile is to increase children's adherence to this test, since applying the fasting requirement in children is more difficult than in adults, due to the majority not being in fasting before a routine visit to the doctor, being necessary to schedule the exam for another day[7, 19]. The study performed by Szternel L et al., (2018), showed that there were no significant differences between the concentrations of most lipid parameters in children, in both fasting states, except for triglycerides and LDL. Even for these parameters, the changes were clinically insignificant and would not impact clinical decision-making[7]. Some similar studies emphasize the importance of determining more accurate reference values for children in order to reduce false-positive and negative results in children[7, 19].

The 2016 Brazilian Consensus for the Standardization of Laboratory Determination of the Lipid Profile stipulates that LDL can be dosed directly or calculated using Friedewald or Martin formulas. However, limitations on the use of Friedewald's formula, such as fasting dosages and triglycerides below 400mg/dL, must be taken into account. For dosages performed without fasting, direct LDL dosing or estimation using the Martin formula is recommended[7, 20]. Most studies analyzed showed only one LDL result per patient that was directly dosed or estimated using the Friedewald formula, except for Sathiyakumar et al., (2018), who made a comparison between the LDL dosed directly and the estimated by the Friedewald and Martin formulas. The authors proved that the LDL estimate by the Friedewald formula in samples without fasting leads to greater errors in the LDL estimate and in the patient's classification regarding cardiovascular risk compared to fasting samples, and they conclude that the LDL estimation by the new method, the Martin's formula, leads to greater precision in the result both in fasting and non-fasting samples[15].

Most of the studies analyzed had the limitation of being performed in a cross-sectional way, that is, they used dosage data

Table 2. Comparisons of concentrations of triglycerides, LDL, HDL and total cholesterol among several studies.

Studies	Patients	Interventions and Methods	Comparação entre as concentrações em jejum e não jejum				Resultados
			LDL Colesterol	HDL Colesterol	Triglicerídeos	Colesterol total	
Steen et al. (2017)[14]	4,177 study patients of PROVE IT-TIMI 22 study.	Of these, 1938 patients of were not fasting and 2199 patients were fasting.	111.4 (30.4) mg/dL x 106.8 (28.6) mg/dL	39.8 (10,7) mg/dL x 40.3 (11,1) mg/dL	167.2 (92.4) mg/dL x 186.4 (113.2) mg/dL	183.1 (34.6) mg/dL x 182.2 (34.4) mg/dL	Significant differences were found for LDL and triglycerides. Levels were 4.6 mg/dL (p <0.001) higher for LDL and 19.2 mg/dL (p <0.001) lower for triglycerides. Fasting levels were 4.3% higher for LDL and 10.3% lower for triglycerides. Fasting did not alter total cholesterol and HDL.
Sathiyakumar et al. (2018)[15]	1,545,634 patients from the second harvest of the Very Large Database of Lipids study.	959,153 fasting patients (≥10-12 hours); 586,481 non-fasting patients.	116 (91–143) mg/dL x 115 (91–142) mg/dL	51 (42–63) mg/dL x 51 (42–63) mg/dL	110 (73–143) mg/dL x 125 (87–182) mg/dL	195 (165–226) mg/dL x 195 (166–226) mg/dL	The measured lipid values were almost identical between the 2 groups, except for a 15 mg/dL increase in the mean triglyceride level in non-fasting patients.
Cartier et al. (2018)[16]	1.093 adult outpatients.	The time elapsed between the fasting test and the non-fasting test was 3.2 days (SD 2.0) and, on average, blood collection was performed 1.6 (SD 1.0) hours after the first meal of the day.	2.57 (1.08) mmol/L x 2.41 (1.04) mmol/L	1.15 (0.34) mmol/L x 1.14 (0.34) mmol/L	2.38 (1.51) mmol/L x 2.66 (1.79) mmol/L	4.75 (1.30) mmol/L x 4.66 (1.28) mmol/L	There was a statistically significant difference (p <0.001) in all studied lipid parameters: total cholesterol (-1.7%), HDL-C (-0.8%), TG increased by 0.28 mmol/L (17%) and LDL-C decreased by 0.16 mmol/L (-6.6%).
Özbek İpteç B et al. (2018)[17]	194 apparently healthy participants.	Fastig blood samples (overnight fasting from 8 to 12hrs) and without fasting (2hrs after the meal) were collected on the same day.	3.24 ± 0.87 mmol/L x 3.01 ± 0.78 mmol/L	0.98 ± 0.33 mmol/L x 0.90 ± 0.30 mmol/L	3.47 ± 2.39 mmol/L x 3.88 ± 2.38 mmol/L	5.46 ± 1.13 mmol/L x 5.17 ± 1.01 mmol/L	There were statistically significant differences for all parameters analyzed when comparing fasting and non-fasting concentrations. With the exception of triglycerides, non-fasting concentrations were lower than fasting for all measured parameters.
Szternel L et al. (2018)[18]	289 presumably healthy children aged 9 to 11 years.	The minimum time interval between the first and second blood samples was 2 days.	98.8 (82.9–117.7) mg/dL x 95.3 (79.7–110) mg/dL	58.4 (50.8–66.8) mg/dL x 57.1 (48.9–64.9) mg/dL	70.8 (53.5–96.2) mg/dL x 91.5 (68.8–132.7) mg/dL	170.0 (149.6–188.2) mg/dL x 170.3 (151–187) mg/dL	Significant differences for the concentration of lipid parameters in the fasting and non-fasting states were observed for: triglycerides (p <0.001), HDL (p=0.002) and LDL (p<0.001), while total cholesterol did not differ significantly in fasting and non-fasting state.

Abbreviations: HDL Cholesterol, high-density lipoproteins; LDL Cholesterol, low-density lipoproteins. Legend: Medium (SD)

from different patients to compare the dosages of the lipid profile in fasting and non-fasting samples. When using the average dosage of the analyzed parameters, variations that occur in the population as a whole are observed, and it is not possible to evidence specific changes that may occur in more specific clinical situations. It is possible to emphasize the need for further studies to more accurately determine a new reference value for the non-fasting state.

CONCLUSION

This review confirms the premise presented by recent worldwide guidelines and consensus on the non-mandatory fasting for the realization of the lipid profile, considering that no significant differences were found between the dosages performed with and without fasting, and even for the parameters that presented some

divergence, this does not imply relevant clinical changes, requiring only a small adjustment in the reference values for the non-fasting state. Therefore, dosages without prior fasting can be used by doctors for clinical decision-making.

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