Clinical Nutrition ESPEN 24 (2018) 14–21

Contents lists available at ScienceDirect

Clinical Nutrition ESPEN

journal homepage: http://www.clinicalnutritionespen.com

Review

# Impact of intermittent fasting on the lipid profile: Assessment associated with diet and weight loss

Heitor O. Santos [a, *], Rodrigo C.O. Macedo [b]

[a] School of Medicine, Federal University of Uberlandia (UFU), Uberlandia, Minas Gerais, Brazil
[b] University of Santa Cruz do Sul (UNISC), Santa Cruz do Sul, Brazil

ARTICLE INFO

*Article history:*
Received 6 January 2018
Accepted 8 January 2018

*Keywords:*
Fasting
Lipids
Clinical analysis
Diet

ABSTRACT

Intermittent fasting, whose proposed benefits include the improvement of lipid profile and the body weight loss, has gained considerable scientific and popular repercussion. This review aimed to consolidate studies that analyzed the lipid profile in humans before and after intermittent fasting period through a detailed review; and to propose the physiological mechanism, considering the diet and the body weight loss. Normocaloric and hypocaloric intermittent fasting may be a dietary method to aid in the improvement of the lipid profile in healthy, obese and dyslipidemic men and women by reducing total cholesterol, LDL, triglycerides and increasing HDL levels. However, the majority of studies that analyze the intermittent fasting impacts on the lipid profile and body weight loss are observational based on Ramadan fasting, which lacks large sample and detailed information about diet. Randomized clinical trials with a larger sample size are needed to evaluate the IF effects mainly in patients with dyslipidemia.



## 1. Introduction

Human fasting is considered as food abstinence and even beverages between 4 h to three weeks [1,2]. Practical application of human fasting encompasses the pre-analytical phase of several laboratory testing, preoperative and postoperative which the discontinue intake is necessary, as gastrointestinal trauma [2–6].

Intermittent fasting (IF) is a restricted feeding period originates in religious and spiritual traditions [7]. The most studied type of IF occurs in the holy month of Ramadan, which is a period that millions of Muslims abstain from caloric and water intake from sunrise to sunset. On average, the Ramadan day is divided in 12 h of fasting and 12 h of non-fasting [7]. Other types of IF are also studied, such as alternate day fasting – e.g., 1 day or more a week fasting – and IF with a longer fasting period during the day, for example, 16 h of fasting for 8 h of non-fasting [1]. These types of IF do not require restriction of water intake because they have no connection with religion [8–10].

IF has gained considerable scientific and popular repercussion, being introduced as a feeding method under certain conditions in the clinical practice. Studies that elaborate pathways created on the basis of the animal experiments may lead to overestimation of IF regarding biochemical markers, such as the traditional lipid profile – including high-density lipoprotein (HDL), low-density lipoprotein (LDL), total cholesterol and triglycerides [11,12].

IF can be considered an energy deficit protocol that leads to lipid profile improve by energy deficit and/or body weight reduction [13]. Hence, the caloric intake and weight loss evaluations are important to investigate the biological effects of IF on lipid profile. This review aimed to consolidate studies that analyzed the effects of IF on lipid profile in humans, emphasizing the physiological mechanisms.

## 2. Methods

A detailed literature research in English was carried with a view to identify relevant studies and to describe and consolidate observational and intervention data that provided parameters of the lipid profile through humans, such as HDL, VLDL, LDL, total cholesterol and triglycerides. In parallel, body weight and dietary information were also considered as data.

In order to improve the evidences regarding biological support, studies that used more detailed markers than the traditional lipid profile were also explored, thus suggesting physiological mechanisms to clarify the improvement of the lipid profile through IF. For this purpose, using the Pubmed, Cochrane and Web of Science databases, the following keywords were used: “Intermittent fasting”, “Ramadan”, “Alternate day fasting”, “lipid profile” and

* Corresponding author. Av. Pará, nº1720 Bloco 2U Campus, Umuarama, 38400-902, Uberlandia, MG, Brazil.
*E-mail address:* heitoroliveirasantos@gmail.com (H.O. Santos).

https://doi.org/10.1016/j.clnesp.2018.01.002
2405-4577/

“intermittent fasting and human metabolic health”. The search for the data involved studies published until October 2, 2017.

## 3. To what extent can intermittent fasting affect the lipid profile in humans?

Intermittent fasting (IF) is a restricted feeding period emerged from religious and spiritual traditions [7]. The most studied type of IF occurs in the holy month of Ramadan. In the meantime, millions of Muslims cease foods and beverages consumption from sunrise to sunset. Overall, Ramadan day consist in 12 h fasting and 12 h feeding [7].

Besides Ramadan, other types of IF are also studied. Alternate day fasting is a broad term so have several definitions. One day or two intervals days a week fasting are most extended examples [1,14,15]. The presence of caloric intake in the fasting day is controversial. Some studies consider high calorie restriction as a fasting day, for example, 25% ingestion of total caloric expenditure in one day, and caloric overcompensation intake on another day – i.e. non-fasting day [8,10]. An interest daily type of IF is 16 h fasting for 8 h feeding [1], however, there can be daily types with more fasting duration, as 16–20 h fasting for 4–8 h feeding. These types of IF do not require restriction of water intake because they have no connection with religion [8–10].

Weight loss methods are important for lipid profile improvement. There is an important link between obesity and dyslipidemia over pro-inflammatory gradient from adipose tissue. The pathophysiology of the typical dyslipidemia observed in obesity is multifactorial, in which overconsumption of calories is crucial [13]. Low-calorie diets can enhance the lipid profile [16]; likewise, IF can leads to lipid profile improve by energy deficit and/or body weight reduction [13].

Lipid profile improvement through IF can occur with or without changes in weight loss (Table 1). Observational studies based on Ramadan are the majority, undoubtedly exhibiting many limitations, such as the lack of food recall from calories to macronutrients (Table 1).

Comparing the pre and post IF period, HDL levels can increase between 1 and 14 mg/dL, LDL levels decrease between 1 and 47 mg/dL, total cholesterol levels decrease between 5 and 88 mg/dL and triglycerides levels decrease between 3 and 64 mg/dL (Table 1).

Although observational studies are the majority of IF research, there are randomized clinical trials showing enhanced lipid profile association with weight loss by virtue of IF program [8,10]. Klempel et al. tested two types of alternate day fasting: 1) High-fat, Low-Carb diet; 2) Low-fat, High-Carb diet. They showed decreased cholesterol, LDL triglycerides and cholesterol, levels and body weight in both groups [8]. Recent study by Trepanowski et al. also tested High-fat, Low-Carb diet and Low-fat, High-Carb diet over alternate day fasting with greater follow-up, corresponding to six months. In contrast to Klempel et al., authors found just improves in HDL levels, while did not decrease LDL, triglycerides and cholesterol levels [10]. Moro et al. found lipid profile improvement in healthy resistance-trained males during two months of normocaloric IF. There was increased HDL and decreased LDL levels in the IF group, whereas normal diet group did not change [9].

## 4. Proposed mechanisms

The increase of tumor necrosis factor alpha (TNF-$\alpha$) and several proinflammatory cytokines are associated with worsening of the lipid profile [17]. In the study by Unalacak et al. interleukin (IL)-2 and IL-8 and TNF-$\alpha$ levels were decreased after the period of Ramadan in eutrophic and obese, however, IL-1 and IL-6 levels weren't decreased. Although there was a decrease in the serum triglycerides of both groups, the other markers of lipid profile did not change, therefore, being inaccurate to affirm that the decrease of TNF-$\alpha$ levels by IF is impacts the improve of the lipid profile [18]. It is known that the antioxidant system is substantial in the lipid profile, thus modulating the lipoproteins [19–21]. However, glutathione, glutathione peroxidase and catalase analyzed in the red blood cells did not improve after Ramadan, according to a study by Ibrahim et al. [22]

IF may increase hepatic production of apolipoprotein A (apo A) and apolipoprotein B (apo B) [23,24]. By means of the apo A production, the serum HDL increases, since apo A is a precursor of HDL. The increase of the PPAR$\alpha$ expression is also responsible for the increase in the serum HDL. Through reducing apo B production the serum levels of VLDL, LDL and small and dense LDL (sdLDL) are decreased [25,26] (Fig. 1). In 1993, Maislos et al. analyzed the apo A – a percussive molecule of HDL, which increased after Ramadan and could be one of the mechanisms that supports the increase of HDL by IF [27]. Five years later, Maislos et al. analyzed the lipoprotein (a) – a harmful lipoprotein to the organism [28], which in turn did not change after Ramadan fasting [29]. In this way, Hammouda et al. also did not find alteration of lipoprotein (a) after Ramadan; in addition, they also did not find alterations of the C-reactive protein [24]. Adlouni et al. and Hammouda et al. found an increase of the Apo AI and a decrease of the apo B after Ramadan, reflecting the HDL increase and LDL reduction [23,24]. Akanji et al. also found an increase of the apo AI after Ramadan, however, it wasn't observed neither increase in HDL nor decrease in apo B in patients with dyslipidemia [30].

Klempel et al. measured LDL subtypes. At the end of two months of alternate day fasting, the diameter of the LDL subtypes increased, whereas there was decrease of the serum levels of sdLDL [8], which is beneficial in the cardiovascular scope, because the lower the LDL, the more susceptible to arterial penetration [21,31].

All things considered, the mechanisms that justify the improvement of the lipid profile through IF are not surprising. Probably the mechanism of IF for the improvement of lipoproteins, cholesterol and serum triglycerides are similar to the classics that occur through fat mass loss (Figs. 1 and 2). Above all, dietary quality should be considered. The type of normocaloric or hypocaloric IF improves lipoproteins by greater efficacy of fatty acid oxidation and modulation of apolipoproteins [8,23,24]. In the liver, the oxidation of fatty acids is increased through higher expression of peroxisome proliferator-activated receptor alpha (PPAR$\alpha$) and peroxisome proliferator-activated receptor-gamma coactivator 1-alpha (PGC-1$\alpha$) in the fasting state [26]. Through increase of fatty acid oxidation in the liver, the accumulation of triglycerides in the hepatocytes decreases, thus decreasing the production of very low density lipoprotein (VLDL). By means of decreasing the VLDL production thus reducing levels of VLDL and TG in the bloodstream, Since apo B composes VLDL, serum apo B levels are also reduced [13,32]. Through reducing these factors that involve VLDL, consequently the LDL and sdLDL are also reduced. In parallel, serum apo B levels are also reduced, for apo B is part of LDL as well as sdLDL and VLDL [21] (Fig. 1).

IF may also decrease the expression of cholesteryl ester transfer protein (CETP) when associated with fat mass loss [33]. The CETP is a protein responsible for transferring cholesterol esters from HDL to VLDL, being responsible for lowering HDL levels and increasing VLDL levels. Therefore, the decrease in CETP through fasting can be another fact that can increase HDL [34,35] (Fig. 1).

Inherent in the improvement of serum cholesterol, the probable mechanism of fasting and cholesterol reduction occurs by means of enzymatic action. Fasting decreases the expression of sterol regulatory element-binding protein 2 (SREPB-2) [36], diminishing the action of several enzymes responsible for cholesterol synthesis [37,38] (Fig. 2).