

Ramadan Intermittent Fasting: A Potential Modulatory Approach to Gut Microbiota and Metabolic Disturbances?

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Gut microbiota plays a critical role in the maintenance of metabolic homeostasis [1, 2], and manipulating the microbiome is a promising therapeutic strategy to oppose the increasing incidence rate of metabolic disorders as overweight, obesity, type 2 diabetes, metabolic syndrome [3] and metabolic dysfunction-associated steatotic liver disease (MASLD) [4, 5].

Overweight and obesity, in particular, have been associated with specific shifts in microbiota composition, with several genera predisposing to obesity or, conversely, to metabolically healthy phenotypes [6].

Besides the use of prebiotics, probiotics, drugs and microbiota transplantation, interesting perspectives originate from positive modulation of the gut microbiota secondary to lifestyle changes, in terms of dietary habits and increased physical activity [3].

Intermittent fasting, in particular, is emerging as an effective strategy for treating metabolic disorders, since reduces weight, improves cardiovascular diseases, and decreases the ongoing metabolic dysfunction-associated oxidative stress [7]. Recent evidence suggests that the positive metabolic effects recorded following intermittent fasting can be mediated, at least in part, by changes in gut microbiota [8]. However, the picture is controversial, since confounding

effects include variations of energy and nutrient intake, as well as type and intensity of physical activity. A recent study in women with obesity on intermittent fasting showed a positive effect of physical activity on fecal acetate concentrations but no change in gut microbiota composition [9]. In addition, different types of intermittent fasting have been proposed (i.e., complete alternate-day fasting [10], alternate-day fasting [11], time-restricted feeding [12]), and a comprehensive validation of each subtype of fasting still needs an ultimate assessment.

In this respect, among possible subtypes of intermittent fasting, Ramadan intermittent fasting (RIF) is emerging as a further, challenging model of intermittent fasting, as also recently reported by our research [13].

In this issue of the Journal of Gastrointestinal and Liver Diseases, Selen et al. [14] reported interesting, albeit preliminary results in 10 male volunteers, 6 mildly obese and 4 obese, who fasted for an average of 14-15 hours continuously from dawn to sunset during the 29-day Ramadan month between 23 March - 20 April 2023. In subjects with obesity undergoing RIF, beneficial variations in gut microbiota were observed, with increased alpha and beta diversity and a decrease in Firmicutes / Bacteroidetes ratio, a relevant marker of gut dysbiosis [15]. Changes were paralleled by decreased anthropometric indices but were not secondary to variations in energy and nutrient intake, nor in level of physical activity. Additional beneficial effects were recorded in terms of increased serum HDL cholesterol and decreased serum triglycerides. Although the study is exploratory and results are preliminary due to the scant number of enrolled subjects, findings from Selen et al. [14] add interesting clues to the identification of possible pathways linking gut microbiota, RIF and metabolic homeostasis, pointing to RIF as an independent modulator of gut microbiota.

Further element of interest in this study is the nonsignificant trend towards decreased levels of fatty acid binding protein 4 (FABP4) following RIF. We urge to confirm this finding in larger studies, since RIF might emerge as an innovative preventive and therapeutic tool in a number of noncommunicable diseases, including cardiovascular diseases, atherosclerosis [16, 17], insulin resistance [18], MASLD [19], and increased cancer risk in people with obesity [20, 21].

Future studies must compare changes in microbiota composition during different subtypes of intermittent fasting pointing not only to the long-term management of obesity but

also to systemic pathways linking gut microbiota, metabolic homeostasis and noncommunicable diseases. This approach will contribute to provide low-cost innovative therapeutic tools but also efficient strategies oriented to primary and secondary prevention [22, 23].

Conflicts of interest: None to declare.

Authors' contribution: P.P. conceived the study. A.D.C. and M.H. collected data and drafted the manuscript. P.P. revised the paper. All the authors read and approved the final version of the manuscript.

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