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Review Article

Influence of Fasting on gut Microbiota

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Abstract:

In addition to providing nutrition to the body, we also nourish microbes present in the gut since their energy metabolism is regulated by the food which is taken by the host. Due to fasting the gut microbiota significantly changes; an increase in beneficial bacteria that produce short-chain fatty acids (SCFAs) and a potential decrease in inflammatory markers. Fasting plans cause the gut microbiota to adapt by utilizing different substrates and altering its composition. Fasting regimens are associated with metabolic benefits such as improved blood sugar control and weight management.

Keywords: energy metabolism; changes in microbiota composition; glucose metabolism; non-communicable diseases

Introduction

To sustain life, in addition to other things such as water, air, temperature, energy source to perform physiological functions, are required. Energy for these functions in the body is generated through the breakdown of food such as carbohydrates, fats, and proteins, which are converted into adenosine triphosphate (ATP) through a process called cellular respiration. This ATP then serves as the readily available energy source for all bodily functions.

Recently it was established that microbiota residing in the gut consists of a complex community of microorganisms, also cooperating with this process [1]. If the amount of nutrients exceeds the amount required for normal growth, development, and metabolism that can lead to obesity, increased risk of chronic diseases like heart disease, type 2 diabetes, certain cancers, and other health complications due to the accumulation of excess body fat and potential imbalances in specific nutrients depending on what is consumed in excess [2]. Consumption of excess nutrition, particularly diets high in saturated fat, sugar, and processed foods, can significantly disrupt the balance of gut microbiota, leading to a condition called "dysbiosis" where the composition of bacteria shifts towards less beneficial species, potentially contributing to metabolic diseases like obesity, diabetes, and cardiovascular issues; this is mainly due to the fact that certain bacteria thrive on these excess nutrients, while beneficial bacteria may decline in abundance [3]. Non-communicable diseases such as obesity, diabetes, cancer and neurological and gastrointestinal inflammatory diseases (NCDs) have been showing promising results by controlled dietary restrictions and/or intermittent or short-term fasting. The gut microbial community is exposed to the fasting gut microenvironment and also changes in the composition and functioning. The behaviour pattern of these organisms during fasting is discussed in this paper.

To some extent every living being is addicted to food. The food is also an epigenetic factor. Epigenetics is the study of inherited changes in phenotype or gene expression, caused by mechanisms other than changes in the underlying DNA sequence. Understanding the mechanism of epigenetic resetting could be exploited to deal with adult diseases such as cancers, or in 'rejuvenating' aged cells, linked with an accumulation of aberrant epigenetic marks [4].

Dietary patterns may impact gene expression through several mechanisms, for example certain dietary compounds bind to transcription factors and regulate their activity such as polyunsaturated fatty acids (PUFA) with peroxisome proliferator-activated receptors [5-6]. Diet, composition of micronutrients alterations, timing of intake and consumption of nondigestible dietary fibers have all been shown to impact the human GI microbiota. This impact has been correlated with fasting, influencing the composition and function of the enterocytes and microbiota. Emerging preclinical research suggests that gut microbes experience diurnal rhythms, and the health effects of eating patterns, including time-restricted feeding and meal frequency, may be related to the GI microbiota.

Gut microbiota is exposed to reshuffling during fasting with the positive influence on hostmetabolism, gut barrier permeability, brain functions, and subsequently, postpone the onset of non- communicable diseases (NCDs) and in prolonging health. The immune response is observed to be weakened by well-fed intestinal microbiota. In addition, the abundance of protective, beneficial microbial families, such as *Bifidobacteriaceae*, *Lactobacillaceae* and *Akkermanisaceae* could be observed as well. Intermittent Fasting might directly affect gut microbial composition, function and interaction with the host. Ongoing research on the health impact of fasting regimens on GM modulation is warranted and some of

its benefits could be mediated by the circadian system. Mohr and his team [7] studied the long- and short-term Fasting effect on the microbiota and has suggested their observation. Prolonged fasting appears to result in the reduction of total bacterial load and is linked with improved gut health and lifespan extension. When 2 fasts per week regime is followed, dramatic shift in the gut microbiome population after fasting for 12- 16-hour mark was observed. Certain beneficial bacteria were found to be super responsive to fasting. In addition, dietary restriction (DR) decreases body weight, improves health, and extended lifespan by influencing energy intake and circadian rhythms. Short-term fasting (14–22 h) resulted in sexually dimorphic metabolic changes, which were more pronounced during prolonged fasting (38–72 h).

Effects of fasting displayed sexual dimorphism. Women metabolize lipids more during fasting, while men have preference of carbohydrate utilization. Plasma glucose concentrations were shown to be lower, while free fatty acids (FFA) and lipolysis were higher in women compared to men after fasting. Mechanisms that can increase lipolytic rates in women include higher total fat mass, enhanced lipolytic sensitivity to epinephrine, and increased activation of β adrenergic receptors [8].

Fasting was found to have a significant alteration in the types of bacteria with a profound roleto play in the health of the gut microbiota. As a sequence to this alterations, short chain fatty acids (SCFAs) production and other metabolites with positive influence of metabolic health in humans. Fasting can alter the types of bacteria in the gut. For example, water-only fasting can reduce the relative abundance of Fusobacterium, which has been closely linked to colorectal cancer. Though fasting can promote microbial fermentation resulting in the production of beneficial metabolites, prolonged length of fasting period affects the gut microbiome [9].

The gut microbiota community is found to get affected by the length of the intermittent fasting period. For example, 16 hours of fasting may increase *Akkermansia* decreases *Alistipes*, though these effects vanish once fasting ends. Blood pressure was found to reduce due to the changes in the gut microbiome during fasting.

Recent studies on the influence of fasting on the gut microbiota suggests that intermittent fasting can alter the composition of the human gut microbiota by increasing taxonomic diversity and promoting microbial remodelling. It is significant to observe that during fasting, a particular family of anaerobic bacteria called *Lachnospiraceae* flourished. Significant changes in the gut microbiota, during intermittent fasting leads to the increase in the production of short-chain fatty acids (SCFAs), decrease the circulating lipopolysaccharides levels, as well as ameliorate obesity and metabolic risks [10-13].

Fast food and microbiome

In the recent realm of microbiota research, significant observations have been made in unravelling the mysteries of our body with intricate microbial communities. Most of the "fast food" is categorised as "Junk food diets", often associated with a reduction in the gut microbiota diversity, an indication of dysbiosis for a healthy gut. This situation implies that there are few types of microorganisms in the gut, which can have a negative impact on overall health [14].

Fasting reset microbiome

Shorter fasting period of around 16–24 hours yield positive changes in the gut microbiota providing digestive benefits without the need for an extended fasting period. Prolonged fasting for 3–5 days aligns with the turnover rate of the gut lining and facilitates cell regeneration.

Fasting affects metabolic health and Improves glucose homeostasis:

Fasting improves Glucose homeostasis (GH), a method body adapts to regulate blood sugar levels within a narrow range. A complex system of hormonal and neural mechanisms synergistically work to ensure that cells have enough glucose to function.

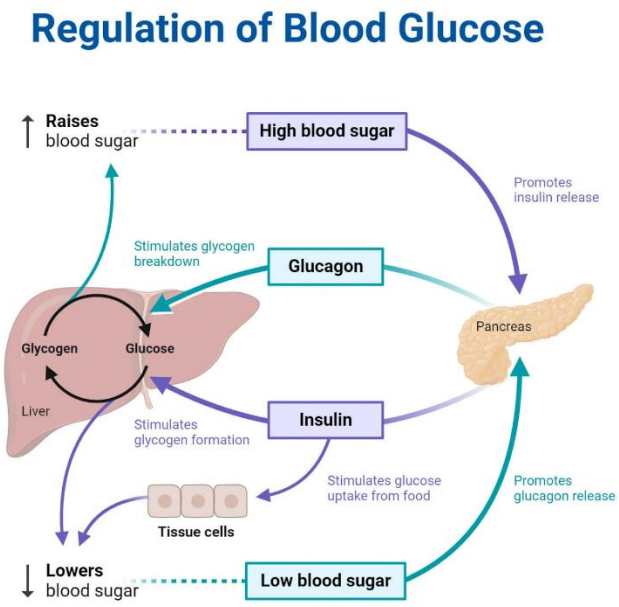

Figure 1: The Glucose Homeostasis.

When blood sugar rises due to a meal (Path 1), the pancreas releases insulin. The interaction of Insulin with liver and muscle tissue, leads to the uptake of glucose from the blood stream into the cell. The excess glucose than what is needed is stored as a type of carbohydrate (glycogen) in the liver capable of bringing back blood glucose levels to normal level. In case of a prolonged gap after eating a mean, blood glucose levels will begin to fall (Path 2). This signals liver cells to breakdown glycogen into glucose monomers to be released back into the bloodstream.

Fasting Reduces inflammation:

It is well known that a diet having a high-calorie for example Western diet – can increase the risk of developing diseases including obesity, type 2 diabetes, heart disease which are closely associated with chronic inflammation in the body. A potential explanation could be given that changing our diet – in particular by fasting – protects us from inflammation, especially the damaging form that underpins many diseases

related to a Western high calorie diet. In turn, it is a hint that high calorie diet might increase the risk of these diseases. (Figure-2). In addition, scientific evidences have shown that some patients taking a high fat diet have increased levels of inflammasome activity.

A recent discovery provides a new way in which fasting helps to reduce inflammation. In a number of chronic diseases, inflammation is due to damaging side-effect of our immune system. Inflammation is under control by increasing the levels of a chemical in the blood known as arachidonic acid a lipid, during fasting but increases after a meal. We are fully aware of the role played by lipids such as storing energy and transmitting information between cells. Researchers were surprised to observe that in cultured immune cells, arachidonic acid turns down the activity of the NLRP3 inflammasome. This observation surprised the team as arachidonic acid was previously thought to be linked with increased levels of inflammation, not decreased. This implies that regular fasting over a long period could help to reduce chronic inflammation, a lucrative idea.

There could be a yin and yang effect (the idea that opposing but complementary forces interact to create a dynamic system. In Chinese philosophy, yin and yang are two forces that are opposite but interconnected, and their balance is essential for harmony and health) [15].

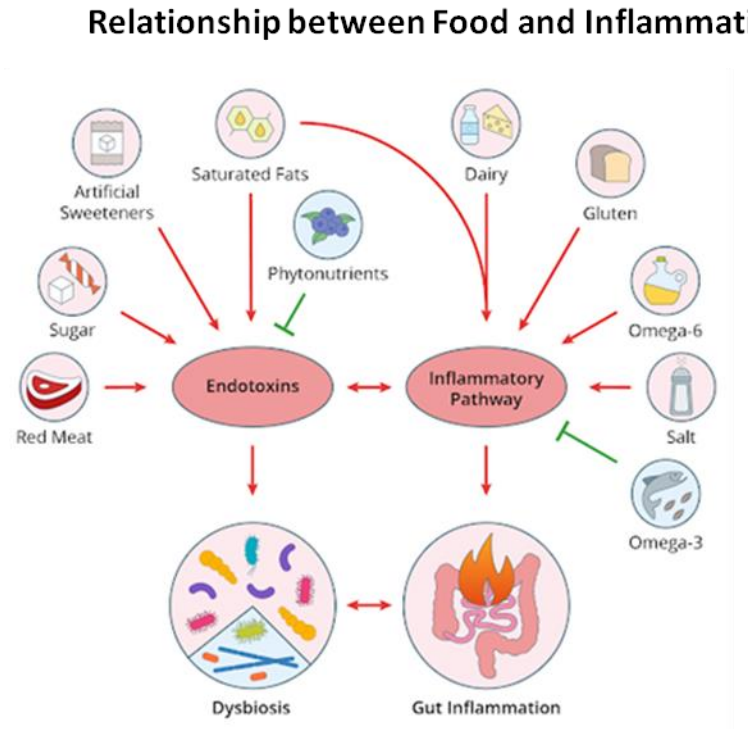

Figure 2: Figure showing the relationship between food we consume as a causal factor for the development of inflammation in the gut due to dysbiosis.

Fasting Improves stress resistance: Fasting has been anticipated to improve stress resistance. As a curative therapy, new pathways such as gut–brain axis has generated a lot of interest with the recent discoveries concerning the microbiota and its role in anxiety and depression management. In the field of psychonutrition the protective role of a healthy/anti-inflammatory diet on depression onset and the effectiveness, omega 3 fatty acids in the treatment of anxiety and depression including other nutrients are identified.

In the 1990s and 2000s, some trials explored the effect of therapeutic fasting (or very low-caloric fasting) on depression and anxiety with inconsistent results and without non-fasting group control. Since fasting interventions are becoming in parallel more and more popular inthe general population, psychological improvement has been reported.

Intermittent fasting is defined as a reduction in the daily duration of diet intake, potential effectiveness.

In addition to weight loss, rodent and human studies have shown that daily intermittent fasting may switch glucose metabolism to ketone metabolism, inducing anti- inflammatory, anti-oxidative and stress resistance effects. Fasting may improve microbiota disturbances and intestinal inflammation through decreased inflammatory foods intake and decreased blood flow dedicated to digestion. To answer the question that intermittent fasting is often combined with caloric restriction, a randomized controlled trial has been carried out comparing caloric restriction with or without 14 h of restricted feeding in type 2 diabetes patients. Both regimens were associated with improved depression, suggesting that caloric restriction should also be studied among fasting interventions [16].

Fasting Reduces blood pressure: In humans, intermittent fasting shows a temporary lowering effect, especially in individuals with high blood pressure, oxidative stress, and the risk of atherosclerosis. One month of alternate-day fasting effectively lowers blood pressure and heart rate in healthy non-obese humans, suggesting that chronic fasting may enhance parasympathetic activity [17].

Regular aerobic exercise results in lowering high blood pressure by about 5 to 8 mm Hg though only regular exercising will be able to prevent blood pressure from rising again. As gold standard at least 30 minutes of moderate physical activity every day is suggested without breakfast or take medicine before measuring your blood pressure as well as to avoid food, caffeine, tobacco and alcohol for 30 minutes before taking a reading.

Research indicates a strong link between the gut microbiota and high blood pressure (hypertension), since, certain chemicals of bacterial origin is capable of altering the blood pressure Due to high blood pressure, alterations in gut bacteria composition can contribute to the development and progression of hypertension by influencing various mechanisms related to blood pressure regulation, including the production of specific metabolites like trimethylamine N-oxide which can have detrimental

effects on blood pressure. Fasting is a promising modality to set it right [18- 20].

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