



Association between Dietary Pattern and Insulin Resistance

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

The current evidence supports the fact that obesity is directly involved in a significant correlation with insulin resistance and type 2 diabetes mellitus (T2DM). Many studies have been published to report the role of many micronutrients, including carbohydrate, lipids and proteins which enhance or worsen the sensitivity of insulin. Thus, this literature review aims to assess the potential association between the different dietary components and insulin resistance based on the findings from the current studies in the literature. It has been suggested that replacing the consumption of fructose with other carbohydrates substances as fibers and starch might reduce such events and enhance insulin sensitivity as these substances pass intact through the gastrointestinal tract to the colon

where they begin to be fermented. Additionally, carbohydrates substances reduce the utilization of free fatty acids by enhancing G-coupling through inhibition of the hormone-sensitive lipase, while the effect of overconsumption of glucose and fructose on insulin resistance is still controversial. Moreover, the quality of lipids is far more important than the quantity. Therefore, frequent ingestion of vegetable oils is suggested to enhance the sensitivity. As for proteins, high protein diets have been proposed for their useful effects. However, they should be carefully described to avoid their potential adverse events.

Keywords: Diabetes; insulin resistance; diet; endocrine.

1. INTRODUCTION

Insulin resistance in diabetic patients is significantly associated with increased blood glucose levels, which involved in the pathogenesis of various diabetic complications. The current evidence supports the fact that obesity is directly involved in a significant correlation with insulin resistance and type 2 diabetes mellitus (T2DM). This is mediated by the presence of underlying pro-inflammatory mediators that are variously present in patients with obesity and can strongly affect insulin signaling and sensitivity [1,2]. Accordingly, suggestions were made about the role of dietary patterns on this phenomenon and insulin resistance. In addition, many studies have been published to report the role of many micronutrients, including carbohydrate, lipids, and proteins which enhance or worsen the sensitivity of insulin [3,4]. Therefore, this literature review aims to assess the potential association between the different dietary components and insulin resistance based on the findings from the current studies in the literature.

2. CARBOHYDRATE

It is well-known that carbohydrates (CHO) is directly associated with the levels of blood glucose and can significantly impact it by causing whether hypo or hyperglycemia. Although CHO is composed of many substrates, fructose and glucose remain the most common substrated and are commonly found in many food types and dietary patterns. To affect the levels of blood glucose, many factors have been previously reported to impact the association between CHO and this effect. These include the method by which CHO is prepared, the type of CHO, and the presence of certain events that can significantly impact the digestion and absorption of the ingested CHO. Nevertheless, many previous investigations have pointed out the complications that can be caused by the overconsumption of CHO. For instance, previous

studies have demonstrated that the overconsumption of fructose can be significantly associated with many metabolic adverse events such as metabolic syndrome. Consequently, it can occur through induction of serious metabolic damaging pathways [5-8]. However, it should be noted that such findings should be carefully interpreted until further notice because other adjacent factors to fructose overconsumption might be associated. In this context, other investigations have investigated the effect of pure fructose daily overconsumption and compared it to the consumption of glucose [9-11]. However, such findings should not reflect what naturally happens in humans, which do not usually depend on fructose of glucose alone in their daily dietary patterns [8]. It is well-known the metabolic route of fructose is independent of the presence of insulin. Therefore, it has been suggested that patients with T2DM might replace glucose with fructose in their diet to avoid hyperglycemia. Nonetheless, many previous investigations have reported that doing so was significantly associated with many adverse events, such as hypertension, weight gain, increased triglyceride levels, insulin resistance, dyslipidemia, and decreased levels of plasma high-density lipoprotein [12-14]. Moreover, the effect of fructose on the increased deposition of lipids in many tissues within the body as the liver, endocrine cells, and muscles should also be considered when planning to increase the frequency of fructose consumption in the human diet. These suggestions were indicated by previous animal investigations that reported that rodents that ingested high amounts of fructose-rich diets significantly suffered from insulin resistance and increased lipid deposition within their tissues [15,16]. Although the same effect is poorly reported in humans, a previous investigation showed that the daily consumption of fructose for a short period was significantly associated with increased deposition of fat in the liver and muscles and insulin resistance [17]. Insulin resistance and reduced signaling of the insulin receptors are mainly attributable to the

direct effect of fructose on the hepatocytes and serine phosphorylation pathways [18,19]. Besides, previous investigations have also demonstrated that increased fructose consumption can significantly increase the levels of serum endotoxins [20]. This can lead to the development of increased blood glucose levels which can secondarily leak from the intestine to the blood by inducing pro-inflammatory pathways and subsequent insulin resistance [21]. Accordingly, it has been suggested that replacing the consumption of fructose with other CHO substances as fibers and starch might reduce such events and enhance insulin sensitivity as these substances pass intact through the gastrointestinal tract to the colon where they begin to be fermented, reducing the utilization of free fatty acids by enhancing G-coupling through inhibition of the hormone-sensitive lipase [22,23]. Previous investigations have demonstrated the potential beneficial effect of such dietary patterns and showed that insulin sensitivity increased when 15 g/day of resistant starch were daily ingested [22,23]. Accordingly, patients with T2DM are advised to change their dietary patterns to more frequent ingestion of fibers and resistant starch to enhance insulin sensitivity and reduce blood glucose levels.

3. LIPIDS

The exact mechanism that lipids and fatty acids levels in the blood and the human body are involved in the development of insulin resistance is still not well-understood. Although it has been demonstrated that the high intake of lipids is directly and indirectly associated with the development of T2DM by induction of insulin resistance and weight gain, respectively. Previous studies have demonstrated that lipids and free fatty acids do not have any impact on insulin sensitivity [23]. Additionally, previous investigations have also demonstrated that ectopic fatty acids deposition in the peripheral tissues might occur in some diseases as T2DM and obesity secondary to increased uptake of decreased oxidation of fatty acids [24]. Moreover, it has been indicated that increased lipid deposition in the tissues as the liver and muscles is significantly associated with the development of insulin resistance [25,26]. It is now widely accepted that the prolonged consumption of excess lipids is significantly associated with major dysfunctions of many organs like the liver due to the pathological activation of pro-

inflammatory pathways that can also lead to the development of insulin resistance, which it has been previously called lipotoxicity [27,28]. Moreover, it has been suggested that the accumulation of lipids and fatty acids in areas that are not prepared to store them is only correlated with the initiation of insulin resistance. It cannot be considered a direct etiology for this phenomenon as indicated in athletes that present with abundant amounts of free intramuscular fatty acids as insulin is broadly sensitive in these individuals [29]. The formation of ceramide and diacylglycerol are also direct key factors by which the accumulation of fatty acids might lead to insulin resistance [30]. It was previously indicated that ceramide has a significant role in the development of insulin resistance through its direct inhibitory actions on insulin signaling pathways in tissues that are sensitive to this hormone [30]. It was reported that the presence of oleate in the diet reduces the accumulation of ceramide. Therefore, it reduces the incidence of insulin resistance in the human body [31]. It is worth noting that previous investigations have stressed that the quantity of lipids in the diet is not as important as the quality of these ingested lipids, which indicates the need to increase the consumption of vegetable oils rather than lipids of animal origin [32]. The saturation of fatty acids was also reported to be a significant factor that is associated with insulin resistance. Additionally, previous studies showed that saturated fatty acids as stearic and palmitate are associated with impaired insulin signaling. On the other hand, polyunsaturated or monounsaturated fatty acids are not involved in this correlation, and has been reported to even enhance insulin action [33,34] (Fig. 1). In addition to these effects, previous investigations have demonstrated that the accumulation of fatty acids is directly involved in the activation of many pro-inflammatory pathways and induction of significant innate immunological responses. As previously mentioned, the activation of these pathways is directly involved in reduced serine phosphorylation leading to impaired insulin signaling and reduced sensitivity. Moreover, evidence shows that the presence of unsaturated fatty acids can reduce the effects of the inflammatory pathways and can also reduce the synthesis of ceramides [35]. Although many investigations have reported the beneficial effects of increased consumption of unsaturated fatty acids as omega-3 in reducing cardiovascular diseases, the beneficial effects of

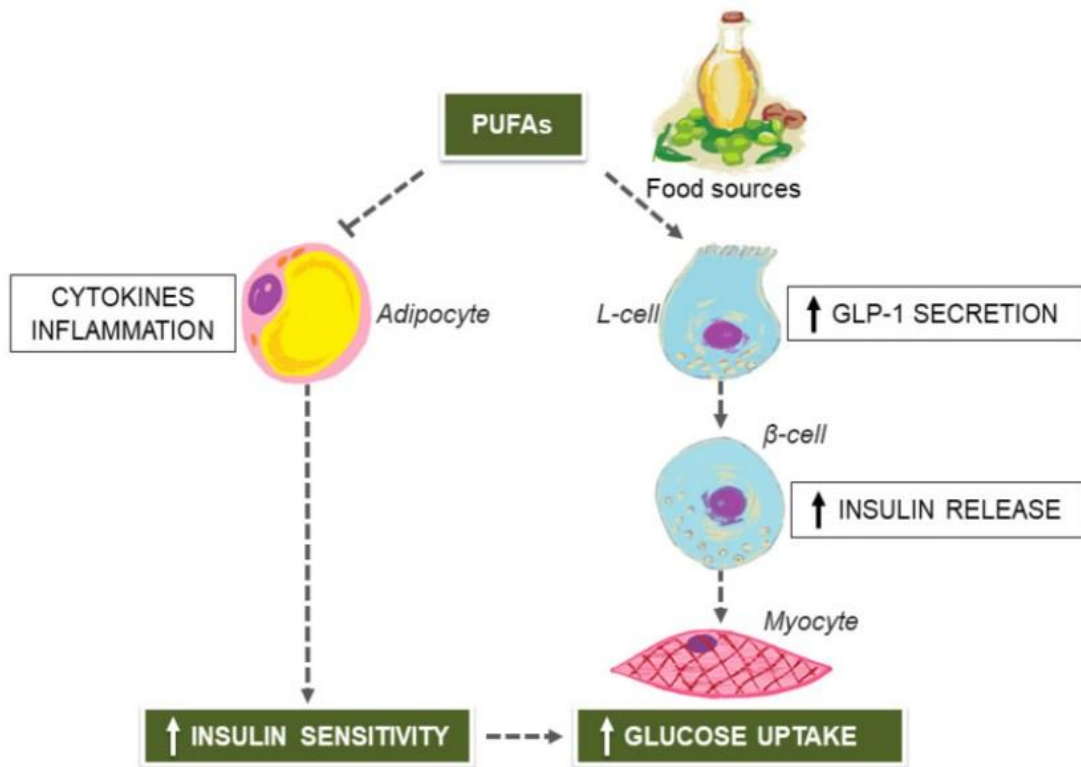


Fig. 1. Effect of polyunsaturated fatty acids (PUFAs) on insulin resistance and glycemic control [38]

these compounds in diabetes and patients with glucose intolerance are still poorly reported [36]. A previous randomized controlled trial reported that the administration of a mediterranean diet was associated with reduced levels of inflammation, enhanced insulin sensitivity, and reduced blood glucose levels [37]. The beneficial effects of the Mediterranean diet were also proved by previous multiple investigations due to the beneficial anti-inflammatory effects of its components and due to increased levels of adiponectin levels which enhances insulin sensitivity.

4. PROTEINS

Evidence from previous studies have shown that the administration of a high protein/low CHO diet is effective in weight loss and associated clinical outcomes [39]. It was previously reported that a high intake of proteins enhances lipid metabolism and reduces glucose hemostasis leading to enhanced outcomes of many diseases as cardiovascular diseases, obesity, and T2DM [39]. Moreover, it is well-known that protein intakes are an effective modulator of the satiety center

and insulin secretion from the pancreas [40]. Previous studies have also demonstrated that protein intake is directly associated with increased release of many mediators as incretins and cholecystokinin. In addition, glucose-dependent insulinotropic polypeptide and glucagon-like peptide 1 are associated with the regulation of food intake and they increase insulin secretion from the pancreas [40,41]. An insulinotropic effect of the dietary proteins was also evidenced, which refers to the ability of lipids to enhance glucose clearance from the blood [42]. It is worth mentioning that some amino acids might adversely modulate the pancreatic cells leading to reduced insulin secretion [42]. Also, it was previously reported that protein intake is associated with sustained insulin secretion that might last for up to five consecutive hours [43]. Evidence from the current studies shows that the impact of a protein-rich diet on insulin resistance is still controversial. Besides, it was previously reported that increased risk of T2DM and cardiovascular diseases might be associated with prolonged intake of non-specific high protein-low CHO dietary patterns [44]. In this context, a previous

trial showed that increased meta-inflammation and reduced insulin sensitivity might be associated with the increased and prolonged intake of proteins [45]. Previous studies showed that protein intake should be moderate and enough to induce weight loss to enhance insulin sensitivity [43]. Previous short-term investigations showed that ingestion of high protein diets was associated with significant improvements in insulin sensitivity, which is probably due to increased weight loss in patients with T2DM or suffer from obesity [43]. On the other hand, other investigations also showed that high protein/low CHO diets are associated with reduced insulin sensitivity [46]. Long-term observational studies reported that insulin resistance was more frequently associated with energy-balanced dietary patterns when compared to high-protein diets. On the other hand, another follow-up for one year investigation reported that the effect of high-protein intake on glycemic control was not significant [46]. Moreover, special considerations should be given to the types of the amino-acids that are present in the ingested proteins. For example, some amino acids as alanine and glutamate might have a useful insulinotropic effect that might lead to increased insulin secretion and enhanced signaling when compared to other amino acids. Besides, it was previously reported that leucine amino acid might be able to increase the post-prandial release of insulin by enhancing glycemic control [40]. Moreover, previous investigations have reported that the increased levels of branched-chain amino acids were significantly associated with enhanced insulin sensitivity in patients with obesity [47,48]. Furthermore, previous studies have demonstrated a potential role between aminoacidemia and hyperinsulinemia that might lead to secondary adverse events on the sensitivity and release of insulin from the islets cells of the pancreas [43,47].

5. CONCLUSION

In this literature review, the discussion was round the association between dietary patterns, including CHO, lipids, and proteins on insulin resistance. As for CHO, the current evidence suggests to reduce intake of fructose, glucose and fibers which might lead to glycemic control and enhance insulin sensitivity. The quality of lipids is far more important than the quantity. Therefore, frequent ingestion of vegetable oils is suggested to enhance the sensitivity. As for proteins, high protein diets have been proposed

for their useful effects. However, it should be carefully described to avoid their potential adverse events.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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