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THE POTENTIAL WAYS FOR PREVENTING POSTPRANDIAL INFLAMMATION – A REVIEW

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ABSTRACT: ***The approaches to alleviate low-grade systemic inflammation during postprandial period are still controversial at present. The aims of this article were to review the possible negative effects of postprandial inflammation and to provide potential way to prevent the risks to health during postprandial period through understanding the possible mechanism. Postprandial inflammation may lead to chronic low-grade systemic inflammation. Previous evidence showed that consumption of saturated fats, the elevation of circulating free fatty acids and high levels of blood glucose may lead to increased postprandial inflammation via activated NF-κB pathway, whereas, dietary with low GI, low saturated fats, and fiber-rich appeared to attenuate the postprandial inflammatory responses via down-regulating the NF-κB pathway. Furthermore, it has been suggested that weight loss may successfully lead to a significant reduction in postprandial inflammatory responses. Many studies indicated that exercise served as anti-inflammatory, however no sufficient and convincing evidence proves that exercise alleviated the subsequent postprandial inflammatory responses to date. Therefore, more studies are warranted to investigate the possible mechanisms of how different exercises and diet/meal/nutrients affect low-grade systemic inflammation.***

KEY WORDS: High fat meal, NF-κB, Postprandial inflammation

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INTRODUCTION

Long-term exposure in postprandial state may lead to a low-grade systemic inflammation. Recently, numbers of evidence suggested that chronic low-grade systemic inflammation was associated with metabolic syndromes (Alvarez et al., 2009; Duncan et al., 2003; Kolb et al., 2010) and some cancers (Garcia-Rio et al., 2010). Chronic low-grade systemic inflammation was characterized by abnormal rises in pro-inflammatory cytokines, such as interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α) and C-reactive protein (CRP). These three pro-inflammatory cytokines are the major components in increased risks of developing atherosclerosis, insulin resistance and other metabolic syndromes (Eisenhardt et al., 2009; Fernandez-Real et al., 2003; Tam et al., 2010). These pro-inflammatory cytokines are principally secreted from adipocytes (Federico et al., 2010; Ikeoka et al., 2010) and/or the macrophages which are infiltrated into adipose tissue (Hirai et al., 2010). Furthermore, some studies also noted that postprandial lipemia may result in the increases of pro-inflammatory cytokines (Ceriello et al., 2004), which may provide a pro-inflammatory environment(Harrison et al., 2009; MacEneaney et al., 2009; Oller do Nascimento et al., 2009) and concomitantly influence individual's health. People spend most of time in postprandial state during daytime. Therefore, to reduce the postprandial low-grade inflammation through understanding the possible mechanism may lower subsequent incidences of metabolic syndromes and cancers.

The approaches to alleviate the negative effects during postprandial period are still controversial at present. The aims of this article are to review the responses of postprandial inflammation and the evidence of their possible negative effects, and to propose how to lower the risks of low-grade inflammation during postprandial period.

Postprandial responses of inflammation

The findings of previous studies indicated that the ingestion of either high fat meal or high carbohydrate meal led to the increases of inflammatory markers (Harrison, et al., 2009; MacEneaney, et al., 2009; O'Keefe et al., 2008). The elevations of inflammatory markers may be attributed to a pro-inflammatory environment. Three major cytokines have been suggested the main attributors of the low-grade systemic inflammation after a meal, which were IL-6, TNF-α, and CRP (Eisenhardt, et al., 2009; Fernandez-Real, et al., 2003). These inflammatory markers have been indicated to be involved in the development of atherosclerosis (Takahashi, 2011), insulin resistance (Shoelson et al., 2007; Tam, et al., 2010), coronary heart disease (Espinola-Klein et al., 2011), and other metabolic syndromes(Eisenhardt, et al., 2009).

It has been suggested that nuclear factor kappa B (NF-κB) pathway directly induced inflammatory responses (Dasu et al., 2011). The NF-κB pathway could be activated by toll-like receptors (TLR) and reactive oxygen species (ROS), which might modulate the inflammatory up-regulation. After consuming a meal, the elevated levels of circulating free fatty acids (FFA) (Boston et al., 2008; Hirai, et al., 2010; Suganami et al., 2007) and/or glucose(Dasu et al., 2008) may stimulate TLR expressions (Dasu, et al., 2011; Shi et al., 2006) in macrophages and/or monocytes (Dasu, et al., 2011; Hirai, et al., 2010), resulting in the up-regulated NF-κB activity, subsequently to exacerbate the postprandial inflammatory responses (Dasu, et al., 2011). Another possible mechanism of postprandial inflammatory responses was ROS, known to up-regulate NF-κB mediated inflammation (Mohanty et al., 2002). Ingestion of saturated fats and high blood glucose concentrations has been demonstrated to increase ROS and subsequently extend the postprandial inflammatory response (Fig 1) (Dasu, et al., 2011; Dhindsa et al., 2004; Mohanty, et al., 2002).

Therefore, it is proposed to attenuate the postprandial inflammatory responses via down-regulating the NF-κB pathway.

Dietary composition

The postprandial inflammatory responses may be remarkably increased by ingestion of the foods, and the phenomena may be due to the decreased signals of NF-κB mediated inflammatory responses (Ghanim et al., 2010; Hirai, et al., 2010). It has been suggested that high glycemic index (GI) meal and high in saturated fats meal could result in increased postprandial inflammatory responses. A high GI meal leads to a remarkable increase of blood glucose level, and it may act as an activator of TLR gene expression (Dasu, et al., 2008). Furthermore, consumption of excess saturated fats might induce the elevations of circulating free fatty acids and ROS (Mohanty, et al., 2002). The high concentration of FFA may stimulate TLR gene expression, and ROS may increase the signals of NF-κB mediated inflammation independently. As a result, the ingestion of low GI and high in unsaturated fatty acids diet, instead of high GI and high in saturated fats diet, may be beneficial to alleviate the postprandial inflammatory responses.

Previous studies have suggested that high GI diet was implicated in exacerbating postprandial inflammatory responses (Dhindsa, et al., 2004; Dickinson et al., 2008). Conversely, low GI diet could decrease the negative effects on postprandial inflammatory responses when compared with high GI diet (Du et al., 2008). A high GI diet could result in an environment of high blood glucose concentrations and accordingly increase the NF-κB mediated inflammatory responses. In the circumstances of impaired insulin sensitivity, the high circulating blood glucose concentration extends the duration during postprandial period, which may amplify the inflammatory. Dickinson, et al. (2008) examined the effects of NF-κB activation on different GI of carbohydrate. Subjects were randomly separated to consume glucose (50g), bread (GI=70) and pasta (GI=35), which contained the same amount of micronutrients and carbohydrate. The results showed that NF-κB activation was significantly higher in glucose and bread than pasta (low GI diet). The postprandial NF-κB responses

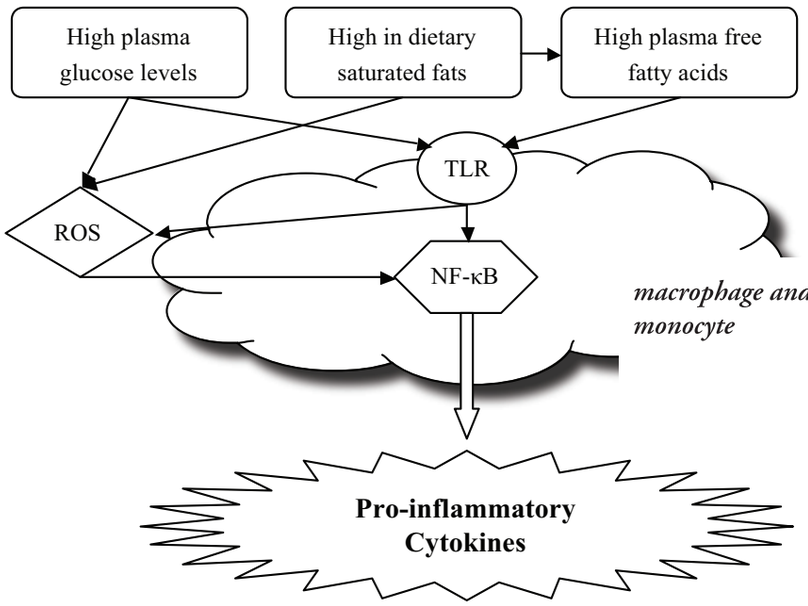

FIGURE 1. Inflammations mediated via the NF-κB pathway. High plasma glucose levels, high in dietary saturated fats and high plasma free fatty acids may lead to postprandial inflammation through increasing TLR and ROS, subsequently activated NF-κB pathway. TLR: toll-like receptors. ROS: reactive oxygen species. NF-κB: nuclear factor kappa B.

in low GI diet in this study were shown very low and might be negligible (Dickinson, et al., 2008). The results provide strong evidence that consumption of a low GI diet could mitigate the postprandial inflammatory responses via decreased NF-κB activity.

The consumption of meal with high saturated fat may result in increased plasma FFA and ROS responses, which consequently may up-regulate inflammatory responses. Previous studies have demonstrated that ingestion of the saturated fat was strongly associated with postprandial NF-κB responses (Ajuwon et al., 2005; Dasu, et al., 2011; Dhindsa, et al., 2004). In contrast, it has been widely suggested that the phospholipid polyunsaturated fatty acid (PUFA), n-3 fatty acid and α-linolenic acid were inversely associated with postprandial inflammatory responses via decreasing NF-κB activity (Hirai, et al., 2010; O'Keefe, et al., 2008). Hence, the consumption of unsaturated fat rich meal in place of saturated fat rich meal may lead to decreased postprandial inflammatory responses (Reynolds et al., 2010; Wall et al., 2010). A review paper published in the *Journal of the American College of Cardiology* suggested that nuts, olive oil, and fish oil were associated with anti-inflammation during either normal or postprandial periods, which provided a practical approach (O'Keefe, et al., 2008).

Plenty of other nutrients play anti-inflammatory roles during postprandial period. Fibers mainly exist in fruits, vegetables and whole grains, and play an important role in healthy diet. It has been suggested that a fiber-rich meal may dramatically decrease inflammatory responses in both nondiabetic and diabetic patients (Esposito et al., 2003). In addition to fiber, herbs and some functional foods (Hirai, et al., 2010; O'Keefe, et al., 2008) may also play the anti-inflammatory properties, which have been discussed in other review articles (Hirai, et al., 2010; Jungbauer et al., 2012; Neuman et al., 2012).

In summary, the current evidence showed that either separation or combination of low GI, low saturated fat, and high fiber in a meal might be beneficial for alleviating chronic low-grade systemic inflammation during postprandial period.

Weight management

Whether the obesity magnifies the postprandial inflammatory responses is still controversial at the present time. Some studies found that postprandial inflammatory responses can be severer on obese individuals than the lean ones (Manning et al., 2008), however other studies showed no differences between the two groups of individuals (Alvarez, et al., 2009; MacEneaney, et al., 2009). It is believed that the excessive adipose tissue would be the main factor in the increase of the low-grade systemic inflammation. Therefore, we will further discuss the relationship between weight management and inflammatory responses.

Studies showed the body weight changes could be one of the major factors in alteration of postprandial inflammatory responses through the changes in adipocytes mass (Fain, 2006; Hirai, et al., 2010). It has been suggested that macrophage activation was influenced by adipose tissue since the hypertrophy of adipocytes may release monocyte chemoattractant protein-1 (MCP-1) (Bruun et al., 2005; Fain, 2006), which resulted in the infiltration and activation of macrophages in adipose tissue. Consequently, it might induce inflammatory responses (Bruun, et al., 2005; Hirai, et al., 2010). On the other hand, the elevations in blood glucose and FFA levels after a meal directly induced inflammatory responses by increased number of activated macrophages (Bruun, et al., 2005; Suganami et al., 2005). Two cross sectional studies have been carried out to investigate the postprandial inflammatory responses in children and adolescent boys with normal weight or overweight (Alvarez, et al., 2009; MacEneaney, et al., 2009). The results showed that after an oral fat tolerance test or a mixed-meal tolerance test, there were no differences between normal weight and overweight subjects on postprandial inflammatory responses. However, Manning, et al. (2008) examined the changes of postprandial cytokines responses on lean and obese women, and found the higher postprandial plasma IL-6 concentration in the obese women than in the lean ones (Manning, et al., 2008). Since IL-6 is proposed as a multi-functional cytokine playing both pro- and anti-inflammatory roles (Gleeson, 2007; Pedersen et al., 2001), the implication of elevated IL-6 concentration, such as pro- or anti-inflammation, is still uncertain. The current evidence was limited to weight gain augments in the postprandial inflammatory responses. However, it is convinced that weight gain increases low-grade systemic inflammation in fasting state (Holz et al., 2010). Further studies are warranted to investigate whether weight gain or weight regain after weight loss program may augment the postprandial inflammatory responses.

On the contrary, weight loss may be related to anti-inflammatory response. An article reviewed the associations between weight loss methods and immunological responses (Forsythe et al., 2008). The author suggested that weight loss itself might modify the adipose tissue mediated immune responses (Forsythe, et al., 2008). Moreover, it has been reported that weight loss could alleviate low-grade systemic inflammation, insulin resistance (Roth et al., 2010) and endothelial dysfunction (Mavri et al., 2010). When weight loss lasted more than 30 months, it might as well diminish arterial stiffness syndrome (Wolfson et al., 2010). One clinical investigation enrolled 20 obese patients, who experienced the laparoscopic adjustable gastric banding to induce weight loss. The results showed that the levels of IL-6, TNF-α and CRP were significantly reduced by the manipulation (Moschen et al., 2010). Furthermore, the study also compared mRNA expression in adipose tissue and liver, and suggested that the expressions of IL-6 and TNF-α mRNA were regulated by adipocytes. It could be suppressed by successful weight loss (Moschen, et al., 2010). This evidence indicated that the weight loss was associated with anti-inflammation and represented that weight loss might be a way to induce anti-inflammatory responses for ameliorates the negative effects during postprandial period.

It has been suggested that weight loss may lead to a significant reduction in postprandial inflammatory responses (Jellema et al., 2004; Plat et al., 2007). Studies investigated the effect of weight loss and consumption of fish oil on postprandial inflammatory markers (Jellema, et al., 2004; Plat, et al., 2007). The investigation was divided into two stages: nutritional intervention and weight loss. Eleven moderately obese men who were recruited firstly, were asked to daily consume either fish oil at a dose of 1.1g or placebo food for six weeks. Subsequently, eight subjects out of the eleven subjects were asked to consume a weight loss diet after two weeks of first stage. The results showed that the eight subjects successfully reduced their body weight by approximately 9.4 kg on average in the second stage with significant decrease in plasma markers of inflammation and endothelial dysfunction, whereas no effect was found in the fish oil trial during the first stage. The study demonstrated that successful weight loss could ameliorate postprandial inflammatory response.

Exercise

The anti-inflammation effect of exercise has been proposed in several studies (Gleeson et al., 2011; Moschen, et al., 2010). Chronic exercise training appeared to reduce adipose tissue and lead to an anti-inflammation condition, which might influence the adipocytes-modulated inflammation (Forsythe, et al., 2008; Gleeson, et al., 2011). On the other hand, as we discussed previously, the postprandial lipemia and high blood glucose concentration might develop inflammatory response after a meal. Studies showed that a single session of exercise reduced postprandial lipemia and blood glucose concentration (Maraki et al., 2010; Mitchell et al., 2008), which might correspondingly alter the inflammatory response. The underlying mechanism has been proposed that the single bout of prolonged exercise or long-term exercise training might diminish TLR expression (Gleeson, 2007; Gleeson et al., 2006; Oliveira et al., 2010), which would reduce inflammation response through blocking the NF-kB pathway. In addition, the contracting muscles released IL-6 (Petersen et al., 2005; Steensberg et al., 2003) also suggested to play an important role in anti-inflammatory reaction.

IL-6 is a multi-functional cytokine, which is responsible for both pro- and anti-inflammation. In resting conditions, IL-6 is produced by adipose tissue (Federico, et al., 2010; Mohamed-Ali et al., 1997), which may lead to an enhancement of the CRP synthesis (Federico, et al., 2010; Heinrich et al., 1990) in liver and CRP has been indicated to increase other risk factors in metabolic syndrome (Abbasi et al., 2010; Duvnjak et al., 2009). During exercise, IL-6 is produced by the contracting skeletal muscles (Pedersen et al., 2004), especially when muscle glycogen storage is low (Pedersen, et al., 2004). During exercise with depleted muscle glycogen, the IL-6 concentrations would be elevated as much as 100-fold compared to the initial bout of exercise (Mathur et al., 2008). The elevated level of IL-6 is considered to be associated with increased lipolysis, spared glucose utilization (Pedersen, 2007; van Hall et al., 2003) and improved insulin sensitivity via blocking TNF-α production (Gleeson, 2007). Furthermore, IL-6 has also been shown to promote the synthesis of IL-1ra and IL-10 (Steensberg, et al., 2003), which are important anti-inflammatory cytokines regarding the alleviation of the inflammation.

Despite of numerous explanations for exercise being an anti-inflammatory agent, yet no strong evidence demonstrates that exercise prior to a meal could alleviate the postprandial inflammatory responses, even the postprandial lipemia was obviously reduced after exercise. A recent research by Harrison et al. (2009) initiated 70% VO_2peak cycling for 100 minutes followed by an oral fat tolerance test in healthy young men. The results showed that exercise did not attenuate the postprandial elevations of IL-6 concentration and endothelial microparticles (Harrison, et al., 2009). Moreover, MacEneaney et al. (2009) demonstrated postprandial plasma concentration of inflammatory biomarkers in normal weight and overweight adolescent boys with 65% VO_2max treadmill exercise. The subjects exercised prior to a high fat meal. The results showed that exercise successfully attenuated the postprandial triglycerides concentrations, but did not lessen the postprandial increase in inflammatory biomarkers (MacEneaney, et al., 2009). Dekker et al. (2010) studied the impact of a 60 minutes treadmill walking (55% VO_2peak) prior to ingestion of a fat meal in hypertriacylglycerolemic men. The investigators found that exercise decreased IL-6 mRNA expression in adipose tissue, but did not influence the circulation of IL-6 level (Dekker et al., 2010).

Much evidence suggested that both aerobic and resistance exercise training ameliorated low-grade systemic inflammation and subsequently decreased risk factors in metabolic syndrome (Christiansen et al., 2010; Gleeson, 2007; Stensvold et al., 2010), however the differences in exercise type, intensity, duration, inflammatory biomarkers, and/or food elements might bring about dissimilar results. Therefore, further studies are warranted to investigate the possible mechanisms of how different exercises and foods affect low-grade systemic inflammation and postprandial inflammation.

SUMMARY

Postprandial response of inflammation may lead to chronic low-grade systemic inflammation. Previous evidence showed that after saturated fats-rich meal, the elevation of circulating free fatty acids and high levels of blood glucose might lead to increased postprandial response of inflammation via activated NF-κB pathway, whereas, dietary with low GI, low in saturated fats, and fiber-rich appeared to attenuate the postprandial inflammatory responses via down-regulating the NF-κB pathway. Furthermore, it has been suggested that weight loss may lead to a significant reduction in postprandial inflammatory responses. Many studies indicated that exercise is one of the anti-inflammatory factors, however, no sufficient and convincing evidence proves that exercise alleviated the subsequent postprandial inflammatory responses to date.

Therefore, more studies are encouraged to carry out to investigate the possible mechanisms of how exercises and foods affect low-grade systemic inflammation and postprandial inflammation in the future.

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