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Trans Fatty Acid: TFA Implication: Does it helpful or harmful?

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Abstract

The sources oftrans fatty acif (TFA) mostly are from processing of natural cis unsaturated fatty acids. In Indonesia, the main sources of TFA are deep fryingfoods, products of dehydrogenated fat such as margarine shortened hydrogenated vegetable oil (HVO), breads, packaged snacks, chips, cereals, biscuits. There is not so many data available yet for TFA intake in Indonesia and also there is no awareness to write down TFA on label of food in Indonesia. In order to find out the TFA in food, so we should do laboratory analysis. Result of the laboratory analysis of hawker foods which are often consumed by Semarang citizens were examined at the Institut Pertanian Bogor (IPB) Integrated Laboratory 2011, TFA contain shows ranged from 0,01% (-2,4%) of total fat. Beef tripe fried rice is a kind of culinary product which containing highest TFA, this food consists of rice, margarine, eggs, gut and beef tripe fried-cook altogether using vegetables oil and margarine. A high intake of TFA has a bad effect on the lipid profile which is a predictor of atherosclerosis, and is a major underlying cause of cardiovascular disease (CVD). TFA also increases the ratio of LDL to HDL cholesterol. Giving high TFA without an increase in calories, causing an increase in intra-abdominal fat deposit, insulin sensitivity failed, his efficiency decreased signal transduction of insulin. Research used Sprague-dawley (SD) rats proved that there is a strong positive correlation degree between the meaningful high feed intake of TFA with a weight of rats.

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Observational studies and randomized controlled trials showed that a high intake of trans fatty acids generally increase the occurrence of systemic inflammation through changes in the levels of inflammatory mediators.Research in mice suggests that granting SD TFA increase the levels of NO and necrosis of pancreatic beta cells in a meaningful.High intake of TFA can lead to the occurrence of peroksidasi lipid cell membrane, it would cause the onset of oxidative stress.

Keywords: Trans Fatty Acid; Diabetes Mellitus; Beta Cells Pancreas.

1. Introduction

Recently, there is increasing number of people using trans fatty acid resulted from changes of life style, such as shifting of traditional diet to western diet or fast food which is consist of high calories, fat, including trans fatty acids (TFA) [1,2]. The sources of TFA mostly are from processing of natural is unsaturated fatty acids. In Indonesia, the main sources of TFA are from products of dehydrogenated fat such as margarine *shortened hydrogenated vegetable oil* (HVO), breads, packaged snacks, chips, cereals, and biscuits [3]. All of these products have the benefits that they are tasty, crispy, not easily to get rancidity and easily to bring because of their form [4]. Another foods which are prepared by *deep frying such as chips also contribute the highest TFA intake* [5]. Naturally, TFA also could be obtained from ruminance products such as milk, cheese, butter, and meat [3].

US Dietary Guidelines Advisory Committee recommend that consumption of TFA is should be 1% maximum of total energy intake, even in the reality it is increase range 2-3% of total energy intake. There is not so many data available yet for TFA intake in Indonesia and also there is no awareness to write down TFA on label of food in Indonesia. In order to find out the TFA in food, so we should do laboratory analysis. Researcer [5] demonstrated that in average, consumption of TFA is 0.71% of total energy intake [5]. Result of the laboratory analysis of hawker foods which are often consumed by Semarang citizens were examined at the Institute Pertanian Bogor (IPB) Integrated Laboratory 2011, TFA contain shows ranged from 0,01% (-2,4%) of total fat. Beef tripe fried rice is a kind of culinary product which containing highest TFA, this food consists of rice, margarine, eggs, gut and beef tripe fried-cook altogether using vegetables oil and margarine [6]. TFA consumption is currently very interesting to be researched because the dilemma relating to the benefits and adverse effects on health than saturated fatty acids that were previously regarded as a type of fat that adversely affect health [7].

A high intake of TFA have a bad effect on the lipid profile which is a predictor of atherosclerosis, and is a major underlying cause of cardiovascular disease (CVD) [8]. Observational studies and randomized controlled trials showed that a high intake of trans fatty acids generally increase the occurrence of systemic inflammation through changes in the levels of inflammatory mediators such as interleukin 6 (IL-6), C-reactive protein (CRP) is an independent risk factor for the occurrence of degenerative diseases such as diabetes mellitus [9]. The purpose of this paper is to review the current evidence from animal and human studies on the topic of TFA in relation to its impact to health of TFA in addition to depict the role of TFA in the pathogenesis of diabetes mellitus.

2. Trans Fatty Acids Sources

Trans Fatty Acids (TFA) actually is an unsaturated fatty acid containing one or more double bond and then changed the configuration for processing. The presence of double bonds in unsaturated fatty acids, allowing the geometric isomers that depends on the orientation of the atoms or groups around the double bond axis. Form or cis configuration has two parts carbon chains tend to confront each other while the trans form has two parts of the carbon chain is almost linear. Unsaturated fatty acids are long chains found in nature almost all have the cis configuration, in which the molecules form an angle of 120 degrees at the double bond. At low temperatures, the carbon chain of unsaturated fatty acids form a zigzag pattern when it is extended. At higher temperatures, most of the bond held resulting in a shortening of the chain rotation. Derived by those characteristics that are why TFA has configurations and characters almost like saturated fatty acids [10, 11].

Products like biscuits, donuts and other products that use softener fat (shortening) are some mentioned sources of TFA in the daily food. Fried fast food, bakery products, packaged snacks, margarines and crackers are also major sources of TFA by Bhagavan. Butter contains 2-5% TFA, while hydrogenated margarine amounts 15-40% TFA. Other studies mentioned that in margarine containing> 60% TFA. TFA found in lard in small quantities, and not found in canola oil, soybean oil, olive oil, and corn oil [5]. TFA in margarine is obtained by the process of partial hydrogenation of vegetable oils. Hydrogenation is the process of adding hydrogen to the substrate, with the aim of reducing the double bond so that the fat does not quickly broken [12]. Hydrogenation is the process of heating of unsaturated fatty acids at high temperatures between 140-2250C with the addition of elementary hydrogen assisted by a metal catalyst (usually using a nickel). Industrial hydrogenation is the largest source of TFA (90%). The existence of margarine is considered beneficial because it has a high melting point that is equal to the melting point of saturated fatty acids. In Indonesia, margarine is also potentially as a source of TFA. The Data content of TFA on margarine in Indonesia that is between 0-8.44% of the total fatty acids, found in the highest levels of TFA import margarine. TFA content of fatty acids total within margarine in Australia's is 3,44 - 4.75%, in New Zealand s 7.6-9.6% while Sweden of 2-50%.

The lowest levels of TFA are present in margarine are created through the process of using a phase of stearine. This process makes use of stearic acid to produce the desired functional properties. Industry in Indonesia is already using the process, so that the margarine circulating in the market there are also not contain TFA or low TFA content. The low soft margarine in the TFA also remains still contain unsaturated fatty acids and it's still better than butter is composed of saturated fatty acids. The product brand "Blue Band margarine" and "Simas" added niacin that aims to lower serum cholesterol levels. While mentioning that margarine is made from Indonesia's palm oil without going through the process of partial hydrogenation, but through a process of blending of the emulsion (a mixture of) oil, thus gained consistency as desired and does not form the TFA. Up to this point the lower TFA margarine low in saturated fatty acids have not found at the same time yet [5].

Vegetable oils (soybean, corn, sunflower seeds and canola) are heated repeatedly or used for deep frying will produce the TFA content due to the unsaturated fatty acid of about 87-93% and is in the form of a cis configuration is very sensitive to warming [13, 14]. Research shows that by doing a warm up on some sample cooking oil from various kinds of oils like corn oil, canola, and the rice bran with temperature more than 200^{o}C

were repeated four times showed that TFA formation simply applied is different for each type of oil. Canola oil warming resulted provide the highest levels of TFA.

3. Health Implications of TFA

Negative effects of TFA started from the United States in the laboratory publication mentioning that swine with rations of vegetable fat hydrogenated for 8 months experience more severe atherosclerosis than controls [15]. According to the Institute of Shortening and Edible Oils (ISEO) mentioned that the consumption of excessive amounts of TFA is not to cause a negative effect on health, other researchers said TFA consumption of 1-3% have been able to bring up a heart attack for adulthood. TFA interfere with conversion of essential fatty acids linoleic into arachidonat, this will disrupt the system in the metabolism of fatty enzymatic reactions that can affect the development of the nervous system, because nerve cells are in dire need of essential fatty acids.

The results of research in the last decade show that the high presence of TFA beneath food pose a negative impact on health that is triggering the onset of coronary heart disease that cannot be ignored. In addition, research has shown that influence of TFA are worse than the negative effects of saturated fatty acids and cholesterol [16]. Various studies show that TFA intakes can cause increased levels of total cholesterol in the blood, similar to the influence the consumption of saturated fatty acids. Epidemiological studies suggest that a reduction in the consumption of TFA in the diet can significantly lower the risk of occurrence of PKV [12]. TFA also have the effect of inhibiting the activity of the enzyme fatty acid elongase and desaturase at high levels, TFA may inhibit the enzyme works lecithin cholesterol acyltransferase (LCAT). LCAT roles in lipid metabolism, take for example the function of cholesterol from tissues and removing lipoprotein. This mechanism leads to formation of HDL2 is hampered and the excess cholesterol cannot be transported back to the heart. Associated HDL2 concentration in reverse with the incidence of atherosclerosis coroner's [17]. In addition to lowering the levels of HDL, the TFA also lead to HDL may not function properly. TFA hypercholesterolemic effects may also be due to a failure in the formation of bile acids from cholesterol due to a decline in the amount of lipoprotein HDL cholesterol carry on duty from extra hepatic tissues to the liver. Cholesterol levels continuously depending on the conversion into bile acids, chaos in that process takes effects of cholesterol levels against arthritis [18].

TFA also increases the levels of triglyceride blood fats than the other [19], and to improve lipoprotein A (Lpa). High amounts of TFA can increase the activity of cholesterylester protein transfer this enzyme plays a role in transferring cholesterol from HDL to LDL and very low-density lipoprotein (VLDL). This increase in activity may decrease the amount of HDL and LDL and VLDL levels increase, lowering cholesterol LDL particle size, and further increase the risk of cardiovascular disease. TFA clearly have the effect of serum triglyceride levels adverse to [20, 19], while saturated fatty acids had no effect on HDL levels decrease [21]. TFA also increases the ratio of LDL to HDL cholesterol, which is a strong predictor of the risk of cardiovascular disease.

On a relative basis stated that influence consumption of TFA are more harmful to health than saturated fatty acids consumption. This is because the TFA consumption mainly cause increased LDL cholesterol and reduced HDL cholesterol, thus in total the influence of TFA is consumption on LDL cholesterol: HDL ratio is very real,

almost doubled when compared with the effects of the consumption of saturated fatty acids. The levels of oxidized LDL represented the ratio of LDL cholesterol: HDL, therefore the effects of TFA toward health way much worse than saturated fatty acids [13].

4. The influence of Trans Fatty Acids and Increased Weight Gain

Results of research with animals are trying to show that TFA is an independent factor in increasing weight. Giving high TFA without an increase in calories, causing an increase in weight gain, an increase in intra-abdominal fat deposit, insulin sensitivity failed, his efficiency decreased signal transduction of insulin. This causes the onset of obesity accompanied by increased intra-abdominal fat buildup. Not known clearly regarding the effect on the process of lypogenic, but causes the elongation and desaturation TFA, an increase in the size of cells adiposity, Phospholipids composition changes in the scelet muscle cell membrane resulting occurrence of resistance insulin and obesity. There are associations between central obesity and insulin resistance and abnormal insulin receptor binding post signal transduction. Protein kinase B (PKB) is a center within the insulin receptors of the signal connecting phosphorylace intracel glucose for transport through the cell membrane. decline in PKB activity, may cause a decrease in transport glucose to the muscles, resulting in an increase in glucose in circulation, for glucose intake from scelet muscles is important in determining body glucose disposal and insulin sensitivity [22]. Other studies toward rats, which were granting of a diet high in TFA led to an increase in body weight, insulin resistance, fat mass accumulation of triglycerides in the liver organs primarily as a result of the decline of lipid oxidation and increased fatty acid synthesis, which in turn can trigger the onset of obesity, metabolic syndrome and lypotoxysity [23].

Research used SD rats [6] proved that there is a strong positive correlation degree between the meaningful high feed intake of TFA with a weight of rats. There is a positive correlation also seems very strong degree of meaning between high feed intake of TFA with delta weight gain. Research in humans and animals indicate there is a causal relationship between obesity and insulin resistance, an increase or decrease in weight is closely correlated with insulin sensitivity [24]. Other research shows that TFA is also an independent factor in increasing weight, giving greater height, TFA in increasing weight, and intra-abdominal fat deposit heightens, insulin sensitivity, decreased efficiency failed signal transduction of insulin, although without any additional calories in the diet. This causes the onset of obesity accompanied by increased intra-abdominal fat buildup [25].

An increase in body weight that a lot more rats who got high TFA may be due the failure of the process of beta oxidation of fatty acids occurs, so that the buildup of long chain fatty acid complexes-koA (LC-COA), and resulted in disruption to the activity of uncoupling protein 2 (UCP-2), which will eventually hinder the formation of energy, one of its manifestations is improving intra-abdominal fat deposit [26, 27]. Other studies have concluded that the State can improve hyperglycemia concentration malonil koA in the cytosol. The number of malonil increased causing the disruption of the COA process of beta oxidation due to barriers of carnitine palmitoil transferase enzyme activity-1 found on the side of the membrane in mitochondria Externa. These barriers lead to failure of acyl CoA transport into the mitochondria, and result in the formation of oxidation process of disruption of energy via the Krebs cycle [28].

5. The Role of Trans Fatty Acids on Oxidative Stress, Inflammation and Blood Glucose Levels

Oxidative Stress is the state in which the level of reactive oxygen exceeds the endogenous antioxidant defense. This situation causes the body of excess free radicals, which can react with lipids, proteins, nucleic acids, which can lead to cellular damage to certain organs and local dysfunction. Lipids are molecules that are vulnerable to the attack of free radicals, thus going on peroxides' lipids [29]. Oxidative Stress significantly contributed to the many diseases associated with impaired blood flow whiles the creation of energy disruptions [30-32].

ROS plays an important role in the physiological condition as well as vascular, ROS pathologis intracellular is produced in a number of slightly, thus ROS worked as second messengers, biochemical pathway modulators to mediate the various responses as the growth of smooth muscle cells of blood vessels. But when ROS are produced in large quantities, then the ROS can damage DNA, is toxic, and can cause apoptosis. Oxidative stress causes increasing stimulus reactive oxygen species (ROS), one of which is the generation of molecular NO. NO normal amounts of a molecule that is protective for the life of the cell, but the increasing number of NO and NO continuous exposure causing energy depletion that resulted in the occurrence of necrosis of cells. Oxidative stress significantly contributed to the many diseases associated with impaired blood flow and formation of a temporary energy, such as atherosclerosis, diabetes, and hypertension [30-32].

ROS plays an important role in the physiological condition as well as vascular, ROS pathologist intracellular is produced in a little amount, then the ROS work as second messengers, biochemical pathway modulators to mediate the various response as the growth of smooth muscle cells of blood vessels. Nitric Oxide (NO) as one of the compounds, ROS, under normal circumstances is produced in small quantities, NO nontoxic relative against its own cells and prevent the occurrence of cell death, but if there is, then NO hypoxia causes ATP depletion through necrosis, caused due to inhibition of respiration, poly ADP-ribose dehydrogenas (PARD), the blocked and glutation depletion due to Glycolysis. The lack of antioxidants, giving support to NO as a result of the production of ROS and RNS that causes necrosis of the cells. Obstacles in the process of Glycolysis resulted in the production of ATP to be reduced, thus causing a slowdown in metabolic energy, when this happens continuously then it can cause necrosis [33, 34]. Research in mice suggests that granting SD TFA increase the levels of NO and necrosis of pancreatic beta cells in a meaningful [6].

Inflammation is the response of an organism against pathogens and cause change through a series of reactions that occur on the network. Systemic inflammation is an independent risk factor for the occurrence of a wide range of degenerative diseases such as insulin resistance, DM, other, and heart failure, in which multiple inflammatory mediators like IL6, CRP plays a role in the process of the various diseases [9]. Systemic inflammatory activation measured CRP, IL-6, which is associated with abnormal lipids, cardiovascular disease, metabolic syndrome and insulin resistance, so that the CRP and IL-6 is also a predictor of disease of DM [10].

TFA modulate the activity of monocytes and macrophages with manifestations of inflammatory mediator production improvements, such as tumor necrosis factor-alpha (TNF-α), interleukin 1 (IL-1), interleukin-6 (IL-6) and C reactive protein (CRP) (Madge and Pober, 2001), and TNF receptor Monocyte Chemoattractant Protein (MCP-1) [10]. Other studies have proved that the granting of TFA of 10% after 4 weeks of CRP levels increase

significantly and the increase in the higher by administering up to 8 weeks [6]. This may be mediated by the effect of membrane receptors are influenced by specific membrane phospholipids, such as endothelial nitric oxidation (NO) synthase by directly binding the trans fatty acids which results in modulation of gene transcription regulation pengkode TNF-α, reactive oxygen species (ROS), nuclearfactor-kB (NF-kB), and the massanger RNA (mRNA), and arthritis in the endoplasmic reticulum (ER). Proinflamatori effects of TFA intake may improve insulin resistance, endothelial cell function failure, lipid oxidation, increase and decrease Tissue plasminogen activity post prandial [35].

Research on animals, try to mention that awarding a diet with 10% TFA content affect nutrient metabolism in treatment of liver, adipose tissue, muscle skelet and induces insulin resistance [23]. Awarding of the 6.7% TFA may increase TNF-α which is important in the formation of atherosclerosis by increasing the permiabilitas endothelial cells, promoting change, induces monocyte adesi macrophage foam cell formation, promote, and stimulate the growth of smooth muscle cells [36].

TFA may increase the production of IL-1 are produced by monocytes and macrophages and monocytes and recruitment function for infiltration into the endothelial cells. The inclusion of the fatty acid into the endothelial cells will increase the activity of the cells that leads to changes in cell function, it is supported by the easy nature of TFA joined endothelial cell membrane phospholipids, so change the cellular and molecular components of the membranes of the blood vessels, which can lead to changes in the nature of antihemostatik, changes in vascular tone, hiperadesi against leucosis, migration increases the production of cytokines and growth factors. High intake of TFA is also damaging the endothelial functions indirectly through decreased HDL cholesterol levels, LDL oxidation which triggers. Adipose tissue is an important endocrine organ, in which a diposit can produce bioactive proteins, including IL-6 and TNF-α. This phenomenon can change the structure of cell membranes, including the series of lipids are essential to cellular signal, because it provides a place to membrane receptors, co-receptor, and mediators including adhesion molecule-40. Improvement of adhesion molecules expression is often associated with inflammatory endothelial cell phenotypes. Long-term exposure to the TFA on Endothelial Activation can be chronic and cumulative can promote the development of atherosclerosis.

Inflammation of the arteries will stimulate increased levels of TNF-α and synthesis, IL-1 and CRP, which will stimulate endothelial to ICAM-1 and is tied with leucocyte function-associated antigen (LFA), so will be bound on the surface of monocyte endothelial and into subendotel for diapedesis. This process leads to monocyte macrophage turns into the so-called macrophage scavenger type A and B that serves to phagocytosis continuously against LDL and VLDL and produce foam cell. Foam cell would express the growth factor and other cytokines to form plaque. TFA also has an effect on the occurrence of inflammatory, via the specific [37]. TFA modulate inflammatory processes through the Phospholypid macrophages membrane and signaling. Pro-inflammatory effects of TFA may also be able to explain the effect of TFA on other experimental observations, for example, TFA increase insulin resistance, endothelial cell function, frustrate increases lipid oxidation [35]. Inflammatory processes enable the cells into producing cytokines-cytokines, which are enhancing the activity of TNF-α and Il-6 production increases, increased production of IL-6, spur production of CRP, increase lipolysis of fat cells, and disruption of the GLUT 4 causing the onset of insulin resistance.

Research toward animals tried to mention that supplying diet with 10% TFA content affect nutrient metabolism in treatment of liver, adipose tissue, muscle scelet and induces insulin resistance, through a path that is not yet clear [23]. High intake of TFA can lead to the occurrence of peroksidasi lipid cell membrane, it would cause the onset of oxidative stress [38].

6. Conclusion and Future Prospects

TFA is one type of fatty acids which is generally obtained from the results of processing, impact to health aspect badly, one of a kind is against lipid profile, causing systemic inflammatory through increasing cytokines, levels of CRP, obesity with increased intra-abdominal fat, triglyceride accumulation in liver cells, oxidative stress and pancreatic beta cell necrosis.

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