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Review Article

Trans Fats and their Effects on Various Diseases: A Review

Poonam Singhal*, Sidra Osmani and Ananda Sahithi Taduru

Department of Nutrition, St. Ann's College for Women, Hyderabad, Telangana, India

***Corresponding Author:** Poonam Singhal, Department of Nutrition, St. Ann's College for Women, Hyderabad, Telangana, India.

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Abstract

The fats consumed in the human diet can either be saturated or unsaturated. Trans fats are fats containing double bonds at the trans configuration determining the shape of the fatty acid. Trans bonds create a linear chain while cis forms a bent chain. Natural trans fats are obtained from a variety of sources of which ruminant animals are the major source. Artificial trans fats are produced by the partial hydrogenation of vegetable oils which results in the formation of trans double bonds. Literature has revealed that consumption of trans fats has a positive impact on lifestyle disorders like cardiovascular diseases, stroke, diabetes, cancer etc. This paper presents a systematic review of the intake of trans fats and its effect on various lifestyle disorders.

Keywords: Trans-Fats; Lifestyle Diseases; Double Bonds

Introduction

The fats consumed in the human diet can either be saturated or unsaturated. Saturated fats contain four bonds which have been satisfied by four atoms. In these, the double bonds are replaced by hydrogen atoms.

On the other hand, unsaturated fats, contain one or many double bonds at different positions along the carbon chain. Depending upon the location of the bonds saturated fats can either be 'cis' or 'trans'.

Trans fats are the fats containing trans double bonds, which determines the shape of the fatty acid. Trans bonds create a linear chain while cis forms bent chain [1].

Natural trans fats are obtained from a variety of sources of which ruminant animals are the major source. The hydrogenation of linoleic and linolenic acid by microbes in ruminant gut produces trans fatty acids. Certain representatives of trans fats are also derived from plants but these are seldom found in oils obtained from plants [2].

Artificial trans fats are produced by the partial hydrogenation of vegetable oils which results in the formation of trans double bonds within the fat instead of cis [3]. This process is extensively used by industries for the desirable fat qualities that it results in. Fats formed from partial hydrogenation have increased melting point, improved plasticity and are stable at room temperatures [1].

Initially the catalytic hydrogenation of vegetable oils was popular in food industry but it has lost charm because of the harmful health effects it leads to. Research has shown detrimental effects of trans fats on health as it has proved to have a direct connection with cardiovascular diseases by reducing HDL levels and increasing LDL levels [3,4]. It has also shown risk of breast cancer, shortening of pregnancy duration, problems in nervous system and vision of infants, diabetes, obesity and allergy [4].

Strategies to develop trans free hydrogenated oils have been developed which have desirable effects [5]. By careful oil and fat selection cooking products have been developed which contain less trans fats, less saturated fats and higher levels of desired PUFA [6].

India currently has no specific food law regarding regulation of amount of trans fats in processed foods. A strict stringent policy is required to regulate trans-fat content in foods to curb the rising levels of diabetes and cardiovascular diseases in India [4]. Additionally there is frequent re use of edible oils. A study by Swati Bhardwaj., *et al*. has shown that the trans fat content increases when oils are heated to temperatures of 180 degrees to 220 degree Celsius [7].

The Food and Drug Administration allows any product containing less than 0.5 gm of trans fat per serving to be labelled as trans fat free. This is adverse as a person may consume a product believing it to be trans fat free over the course of a day when in fact it may almost be equal to or exceed the 2gm limit which has been proposed by the American Heart Association [8].

Data from epidemiological studies has shown that death rate rises when trans fat percentage in the diet rises and the linoleic acid percentage goes down [8].

The main objective of this study is to determine the various effects of trans fats on cardiovascular health, and lifestyle disorders like diabetes, cancer, and Alzheimer's. From this study, the effect of trans fats on various diseases can be observed in positive and negative health aspects.

Trans fats and cardiovascular diseases

For many years lowering fat consumption in the diet has been recommended to lower the risk of heart disease. More than the amount of fat consumed, it is the type of fat consumed which determines the onset of coronary heart disease (CHD) [9]. Polyunsaturated fats like n- 3 and n- 6 fatty acids show a positive effect on cardiovascular disease [9,10]. Whereas it has been seen that a 2% increase in energy intake from trans-fat consumption increases the risk of heart disease by 23% [11].

Vascular inflammation and endothelial cell dysfunction play a key role in development of atherosclerosis. Observational as well as randomized studies have shown that intake of trans fats, increase the concentration of circulating inflammatory markers such as interleukin 6, tumor necrosis factor (TNF) or CRP [12].

In hydrogenated fat produced artificially, the saturated fatty acids contain a double bond in the trans configuration. This effects the serum lipoprotein cholesterol levels adversely when compared to unsaturated fats that contain double bond only in the cis configuration [13]. Numerous studies on randomized controlled trials have shown evidence of harmful effects of TFA on serum lipids, systemic inflammation and endothelial function due to saturated fat consumption [14].

A 20 year follow up study, conducted by Kyung won., *et al.* on nurses who initially did not suffer from any form of cardiovascular disease showed that a higher level of trans fat intake increased the risk of heart disease which was unaffected by other dietary factors and cardiovascular disease risk factors [10].

AAscherio., *et al*, researched a case control design to study the association of trans fatty acid intake with the risk of myocardial infraction in 239 patients from six hospitals in Boston. The trans-fat intake was calculated using a food frequency questionnaire. They concluded that the risk of acute myocardial infraction significantly increased with trans fatty acid intake. Margarine consumption-a rich source of trans fat also increased risk [15].

Alice., *et al*. conducted a study on 18 men and 18 women for 35 days from the hospitals in Boston area. Subjects were randomly assigned 6 diets, each of which was identical and 30% of calories were achieved from fats. In two of these diets, two third of the fat was provided from sources that gave less than 0.5 gm per 100 gm of trans fat. In three diets, two third of the fat was provided by sources that gave 7.4 gm, 9.9 gm and 20.1 gm per 100 gm of trans fat. This was compared to a high saturated fat diet rich in butter. It was observed that the LDL levels reduced on average by 12% and 11% in the diet that contained less than 0.5 gm of trans fat. Similar results were noted for both men and women [13].

Ingeborg, Anne., *et al.* concluded that the three classes of trans fatty acids namely ruminant trans fats, CLA and industrial transfatalso increase the LDL to HDL ratios. Ruminant trans fatty acids and CLA caused lesser change in the ratio than industrial trans fats, however the difference was not high. They summarized that both fats are co related to coronary artery disease [16].

Intake of both saturated and unsaturated fats is recommended to be restricted, as studies show that the ratio between total cholesterol and HDL level changes according to the type of fat consumed. Soyabean oil gave the lowest ratio, margarine, shortening, butter which are moderately hydrogenated gave intermediate ratios. Heavily hydrogenated margarine gave the highest ratio [13].

However, the amount of trans fats consumed from natural sources such as dairy is minor and it is not practically possible to extract transfat from meat and dairy [11]. While partially hydrogenated vegetable oils contain upto 50% of trans fat, dairy contains only 5% which is almost negligible, making it hard to calculate. Choosing low fat dairy products will help to lessen trans fat consumption and hence risk of coronary artery disease [17,18].

Triacyl rich lipoprotein concentration is raised postprandial due to consumption of a high fat diet. These have been related to the risk of CAD. The post prandial phase of high fat diets consequently elevates factor VII activity which leads to coronary thrombosis [18].

Katherine., *et al.* conducted a study on 501 healthy men to evaluate the combined effect of increased consumption of fruits and vegetables in the face of lowered saturated fat consumption. 76% risk of coronary heart disease was removed by consumption of greater than 5 servings/day of fruits and vegetables along with less than 12% energy derived from saturated fats. Their study has concluded not only lowering saturated fats but also increasing the servings of fruits and vegetables in a day will prevent mortality from CHD [19].

Numerous studies in addition to those mentioned above show that trans fats affect the heart adversely by lowering HDL levels and increasing the LDL level [20-22]. There are also others which show that there is no difference whether the fat consumed is saturated or unsaturated. The Strong Heart study was conducted on 4549 American Indians. The results from this indicated that, in the age group of 47 to 59 years, consumption of saturated fat, monounsaturated fatty acids and total fat all were risk factors for developing CHD in later life [23].

Trans fat and stroke

When blood flow to the brain is stopped it results in a stroke. While there is a directly proportional relationship between intake of trans fats and development of CHD, diabetes and Alzheimer, it is suggested that the relation with stroke in inversely proportional. 832 men from the Framingham Heart Study were examined to find the relation between incidence of stroke and fat and type of fat. After 20 years of follow up it was concluded that the incident of ischemic stroke is lesser with intake of saturated fat [24].

However it has also been hypothesized that trans fat or saturated fat in the diet may lead to stroke.

In one such study, the dietary intake of 69 patients with stroke in regard to the amount of saturated fat intake, monounsaturated fatty acid and hydrogenated fat intake was evaluated with the help of food frequency questionnaire. This was compared to a control of 60 subjects over a one-year period. It was observed that SFA and MUFA intake was more in the patients who suffered from stroke [25].

Another prospective study comprising of more than 17,000 individuals from the REGARD (Reasons for Geographic and Racial Differences in Stroke) cohort observed the relation between TFA intake and stroke. A median follow up was carried out for 7 years and results were compared with men versus women. It was concluded that results differ according to sex. In men the chance of stroke increased by 14% for every 2g/day increase in TFA intake. This was not seen in women [26].

3,183 stroke free subjects were assessed on their total dietary fat intake via FFQ over a mean period of 5.5 years. It was seen that the risk of ischemic stroke was higher in the upper quintile of total fat intake, specially more than 65 g when compared to the lowest quintile [27].

A prospective study on a large cohort of 87,025 healthy, postmenopausal women analyzed the relation of trans fats and ischemic stroke. As in the previous study it was observed that women in the highest quintile of trans fat intake were at a greater risk of stroke than the women in the lowest quintile. Here it was also concluded that use of aspirin inhibited the effect of trans fats [28].

While the above studies prove a relationship with trans fats there are others which do not show any relation between trans fat and stroke.

A study was conducted on the same cohort as above, the participants from the Women's Health Initiative Dietary Modification Trial. The intervention was to decrease the intake of fat to 20% of the calories and to increase the consumption of fruits and vegetables to 5 servings in a day, and grains to 6 servings per day. The mean fat intake reduced by 8.2% (saturated fat, MUFA and PUFA) at the end of 6 years when compared to the comparison group. 434 (0.28%) participants from the intervention group developed stroke and 642 (0.27%) participants in the comparison group. It was concluded that decrease in the fat intake and increase in fruit, vegetable and grain intake has no significant effect on stroke [29].

Though there is research on relation between trans fats and stroke the results have been extremely varied. Some concluded that there is no relation between the two, some resulted in showing a positive relation between them. Surprisingly others have shown that saturated fat intake helps to lower the risk of stroke [30].

Trans fats and diabetes

The aetiology of diabetes is complex and multifactorial. While a large number of genetic and environmental factors lead to diabetes the most significant is development of insulin resistance. High intake of saturated fats lead to insulin resistance and since TFA is a form of saturated fat it would mean that TFA could lead to insulin resistance as well [31,32]. The association between fat intake and diabetes mellitus is known since the late 1900's. Numerous studies have reported that the incidence of diabetes mellitus is low in eskimos who consume a diet rich in fish, which is dominantly composed of omega 3 and omega 6 fatty acids and low in saturated fat [33].

Dietary intervention trials to determine effect of TFA on development of diabetes are few. However improving the dietary quality

in terms of better carbohydrates (complex carbohydrates), fat (less of TFA and more or unsaturated fat), better protein could lead to an improve in blood glucose levels and serum insulin [34].

A study to determine the relation between circulating biomarkers of TFA and the incident of type 2 diabetes was conducted by pooling ten prospective cohorts of 22,711 individuals who were non prevalent to diabetes and belonged to five different countries. After an average maximum of 14 years of follow up it was concluded that biomarker levels of TFA were not significantly related to type 2 diabetes. However this could also be due the difference in the type of fat (ruminant or industrial) consumed by the population as well as the changes in dietary habits over a period of time [35].

A similar study was conducted on 4,219,457 individuals divided under three prospective cohort groups to assess the relation of TFA and diabetes. Years of follow up later it was concluded that intake of dairy fat is not associated to type 2 diabetes in comparison to calories from carbohydrates [36].

To determine if trans palmitoleate - a component of whole fat diary is linked with lower metabolic risk a prospective cohort study was conducted from 1992 to 2006. The levels of plasma phospholipid fatty acids, blood lipids, inflammatory markers, and glucose–insulin of 3736 individuals under the Cardiovascular Health Study, from four US communities was taken initially in 1992. Dietary habits were measured three years earlier. It was found that whole fat diary consumption is strongly associated with higher levels of trans palmitoleate and circulating trans palmitoleate was associated with lower insulin resistance and therefore incidence of diabetes [37].

Deposition of excess body fat specifically in the abdominal region leads to overweight which eventually may reduce insulin sensitivity. Insulin resistance if left unchecked for a period of time leads to the development of cardiovascular disease and diabetes. This resistance is effected by the quality of the fat consumed in the diet. Saturated fat worsens the condition whereas polyunsaturated, specifically omega 3 and omega 6, and mono unsaturated fats improve it [38-40].

Trans fats and cancer

The agents which cause cancer are referred to as the carcinogens. Multiple sources of food, natural as well as synthetic provide these substances in the diet. One of these sources are trans fats. The modification of dietary fat may help reduce the risk of cancer. The ruminant trans fatty acid, CLA has been studied experimentally to determine its relation with breast cancer.

Few studies have evaluated the relation of cancer risk and vaccenic acid, a type of ruminant trans-fat found mainly in beef, milk and butter. Out of 4 case control studies conducted 3 reported a direct association of vaccenic acid in the serum or erythrocyte to prostrate or breast cancer [42-44]. Ruminant trans fats, VA and CLA have shown a tumor reducing effect in some studies. However due to limited number of studies further clinical trials are needed to achieve conclusive results in relation to VA [41].

A meta analysis of a prospective cohort pooled the results of effect of TFA intake on risk of breast cancer. This study showed that no significant relation is present between total trans fatty acid and risk of breast cancer. However it concluded that risk of breast cancer and serum trans fatty acids intake showed a significant positive association in post-menopausal women [45].

A 6 year follow up was study conducted in Netherlands using a 150 food item food frequency questionnaire of specific fatty acids in European foods (obtained from the TRANSFAIR study) and found 941 incident cases of breast cancer. The mean intake of CLA was found to be 0.2g/d, out of this 29% was derived from butter, 21% from cheese, 24% from meat and 19% from milk and its products. But no association was observed for cheese, fresh meat, beef or processed meat to breast cancer incidence on the basis of a multi variate analysis. This study was unable to establish any protective effect of CLA on risk of breast cancer in post-menopausal women. On the contrary a positive association was found with trans unsaturated fatty acid, saturated fatty acids and trans vaccenic acid [46].

The relation between risk of ovarian cancer and intake of dietary fat has been studied but yielded inconsistent results. Few studies have shown that intake of a high fat diet does increase the risk of ovarian cancer [47].

A meta-analysis was conducted to determine effect of varying types of dietary fat, namely, animal fat, plant fat, monounsaturated fats, polyunsaturated fats and trans-fat on the risk of ovarian cancer. For trans fats two case control and two cohort studies summarized the RR as 1.25 (95% CI = 1.06-1.49, $P = 0.010$) for case control and 1.24 (95% CI = 0.85-1.81, $P = 0.285$) for cohort studies. It concluded that a significant positive association existed between trans fats and risk of ovarian cancer [48].

Trans fat and Alzheimer's

Cognitive degenerative diseases usually develop in later life. The most common manifestation is dementia, which is a form of Alzheimer's disease. Highly saturated fatty acids or trans fats increase the risk of dementia whereas high polyunsaturated and monounsaturated fatty acids decrease risk of dementia as suggested by evidence [49]. While sea food, rich in n - 3 fatty acids has a neuroprotective function the opposite that is cognitive decline occurs while consuming saturated and trans fats [50].

A ten year Japanese study on around 1600 community residents monitored the accumulation of trans fats using the trans fatty acid, elaidic acid as marker. The results showed that the subjects with greater amount of trans fat consumption had a greater chance of developing Alzheimer's in later life. Out the total participants, 377 did develop dementia [51].

Another study evaluated that high intake of trans fats in the face of high copper intake lead to faster cognitive decline. This comprised of about 3700 individuals above the age of 65 from Chicago whose cognitive function was evaluated every 3 three years for this 6 year study. Though copper is essential for brain function it was observed that when a diet rich in trans fat was consumed along with, it led to decline in cognitive function [52].

The Chicago Health and Aging Project (CHAP) comprised of a stratified sample of 815 individuals above the age of 65 and were observed for 3.9 years. It was observed that intake of trans fat was positively associated with the development of Alzheimer [53].

The Rotterdam study conducted in Netherlands on 5395 residents below the age of 55 showed development of dementia is positively associated with trans fat intake after a 2.1 year follow up. However after 6 years of observation of the same participants it was concluded that intake of trans fats have no effect on risk of development of dementia. It also showed that trans fat intake is negatively linked to development of Alzheimer [53,54].

It was concluded from another 21 year long study that moderate intake of saturated fats is related to increased risk of Alzhemier [55].

Therefore, trans fats do play a role in cognitive decline in later life. Dietary interventions are helpful in reducing these effects. Numerous studies have concluded that there is a positive association with intake of Mediterranean diet and cognitive function [56,57].

Figure 1: Trans fats and their effects on various disease.

Conclusion

Trans fats are the fats containing trans double bonds, which determines the shape of the fatty acid. The trans fatty acid consumption have shown effects on the cardiovascular diseases such as increase in the concentration of circulating inflammatory markers, post prandial phase of high fat diets consequently elevates factor VII activity which leads to coronary thrombosis. Also, trans fats affect the heart adversely by lowering HDL levels and increasing the LDL level. The effects of trans fat on stroke concluded that there is no relation between the two, but some resulted in showing a positive relation between them. High intake of saturated fats leads to insulin resistance and since TFA is a form of saturated fat it would mean that TFA could lead to insulin resistance as well. The ruminant trans fatty acid, CLA are studied which have relation with breast cancer. However few studies have concluded that the risk of breast cancer and serum trans fatty acids intake showed a significant positive association in post-menopausal women. Few studies have also shown that intake of a high fat diet does increase the risk of ovarian cancer. Decline in the cognition occurs while consuming saturated and trans fats, which over a period of time leads to Alzheimer's.

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