Dairy products and plasma cholesterol levels

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Abstract

Cholesterol synthesized in the body or ingested is an essential lipid component for human survival from our earliest life. Newborns ingest about 3-4 times the amount per body weight through mother's milk compared to the dietary intake of adults. A birth level of 1.7 mmol/L plasma total cholesterol will increase to 4-4.5 mmol/L during the nursing period and continue to increase from adulthood around 40% throughout life. Coronary artery disease and other metabolic disorders are strongly associated with low-density lipoprotein (LDL) and high-density lipoprotein (HDL) cholesterol as well as triacylglycerol concentration. Milk fat contains a broad range of fatty acids and some have a negative impact on the cholesterol rich lipoproteins. The saturated fatty acids (SFAs), such as palmitic acid (C16:0), myristic acid (C14:0), and lauric acid (C12:0), increase total plasma cholesterol, especially LDL, and constitute 11.3 g/L of bovine milk, which is 44.8% of total fatty acid in milk fat. Replacement of dairy SFA and trans-fatty acids with polyunsaturated fatty acids decreases plasma cholesterol, especially LDL cholesterol, and is associated with a reduced risk of cardiovascular disease. Available data shows different effects on lipoproteins for different dairy products and there is uncertainty as to the impact a reasonable intake amount of dairy items has on cardiovascular risk. The aim of this review is to elucidate the effect of milk components and dairy products on total cholesterol, LDL, HDL, and the LDL/HDL quotients. Based on eight recent randomized controlled trials of parallel or cross-over design and recent reviews it can be concluded that replacement of saturated fat mainly (but not exclusively) derived from high-fat dairy products with low-fat dairy products lowers LDL/HDL cholesterol and total/HDL cholesterol ratios. Whey, dairy fractions enriched in polar lipids, and techniques such as fermentation, or fortification of cows feeding can be used to produce dairy products with more beneficial effects on plasma lipid profile.

Keywords: bovine milk; low-density lipoprotein; high-density lipoprotein; saturated fatty acids; LDL/HDL quotients

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holesterol is an essential lipid component in cell membranes and a precursor of bioactive lipids such as bile acids and steroid hormones. Plasma cholesterol levels are also a well-known risk factor for cardiovascular disease (CVD). Mortality in the Western world is still caused to a high extent by CVD and a large amount of data related to CVD and other metabolic diseases concern our intake of fat. Two types of dietary fatty acids raise plasma cholesterol - saturated fatty acids (SFAs), mainly palmitic acid (C16:0), and trans-fatty acids (tFAs). Epidemiological as well as clinical data have shown that elevated low-density lipoprotein (LDL) cholesterol, especially small dense LDL particles, together with reduced high-density lipoprotein (HDL) cholesterol are associated with the risk of development of CVD. From 60 selected trials, Mensink et al. (1) summarized the effects of dietary fats on total cholesterol to HDL cholesterol ratios and concluded that replacing tFAs with unsaturated fatty acids gives the single most effective improvement in plasma lipids. Also, replacement of SFA with cis-unsaturated fatty acids reduces CVD risk (2, 3). One of the oldest and longest dietary intervention studies in the Nordic countries was the North Karelia Project, which started in the early 1970s. The main goal was to reduce the number of cardiovascular deaths by implementing a health promoting program on a large population. A major factor with high impact on this study was the change in intake of fat quality from butter to more unsaturated fat, which led to a 40% reduction in cholesterol concentrations (4, 5). There are prospective cohort studies and reviews (6-9) describing the effect of dairy fat on plasma cholesterol composition and the consensus is that there is no general relation between dairy intake and cardiovascular risk. Therefore, an

important question is whether a reasonable intake of dairy products in a balanced diet promotes health in other ways that outweigh the cholesterol raising effects. The aim of this review is to report an update on recent results from intervention studies with dairy products and their effects on cholesterol containing lipoproteins, and also to put current knowledge about milk components in relation to effects on plasma cholesterol.

Selection strategy

This review is primarily based on relevant original articles and recent reviews available in PubMed using the search words 'dairy intake,' 'milk fat,' 'cholesterol,' and 'human,' in combination with 'cardiovascular risk' or 'cardiovascular disease,' published from 2003, but with a focus on the recent 5 years. Additionally selected older publications are included to support the topic. The studies presented in Table 1 are randomized controlled trials performed from 2003 on the effects of different dairy products on plasma lipids with significant outcome.

Neonatal aspects

Milk is an optimal and natural food for a newborn baby. It is sometimes argued in adult nutrition that milk is a 'natural' food and could therefore not be harmful. Thus, there is reason to comment on the differences in cholesterol metabolism between adults and suckling babies. Cord blood has a different lipoprotein profile compared to adults. It contains one-third of the LDL concentration and one-half of the HDL concentration. At birth, LDL cholesterol and apolipoprotein B (apoB) concentrations are negatively associated with gestational age and total cholesterol concentration is around 1.67 mmol/L. During the first 5 days of nursing, the cholesterol concentration increases rapidly to the double (10). The following month the composition of LDL particles is modulated by the feeding mode. Both total- and LDLcholesterol concentrations are higher in breastfed babies than formula-fed babies and total cholesterol reaches almost 4 mmol/L for breastfed babies and around 3.5 mmol/L for formula-fed babies. The fat content in human milk and also its composition varies during the lactation period, whereas the cholesterol concentration decreases with the stages of lactation (11, 12). The daily cholesterol intake of 15-20 mg/kg is around 3-4 times the corresponding intake for adults. The intake of cholesterol in newborns and probably also the cholesterol synthesis subsequently match the need for cholesterol during rapid organ growth and the expansion of membrane cholesterol pools. Normal levels of plasma cholesterol for children and adolescents aged 2-19 years are 4-5 mmol/L and from 20 to 70 years of age, the plasma cholesterol increases by 30-45%. Subsequently, the need for dietary cholesterol is not the same when bovine milk and dairy products in general become an important part of basic food intake in adolescence and adulthood. It is also worth emphasizing that bovine milk differs from breast milk in that it contains rumen-derived short-chain fatty acids (C4:0–C8:0) - 3.5 times as much calcium and 2.5 times as much proteins - lower concentrations of unsaturated fatty acids and sphingomyelin, and more SFAs (12, 13).

Intervention studies

Numerous intervention studies have been published comparing the cholesterolemic effects of different dairy products on both healthy individuals and individuals with some metabolic disorder. Whereas the results for butter are consentient, trials with milk, fermented products, and cheese are less conclusive. In a study designed to compare the effects of the physical state of milk fat on plasma cholesterol diets providing 20E% (of which 16E% is SFA) as dairy fat either as whole milk, butter or hard cheese were compared (14) (Table 1). In this strictly controlled cross-over study on 14 healthy young men, they found no support for a hypocholesterolemic milk factor. The cheese diet resulted in 5 and 7% lower total cholesterol and LDL concentrations compared to butter, possibly as a consequence of the higher amount of calcium and fermentation of cheese. The overall decrease in triglycerides (TG) of 16-20% after all three diets could be explained by the lower content of carbohydrates compared to their normal diet. Others have obtained similar results (15) (Table 1). In a study by Biong et al. (16) (Table 1), the authors compared intake of cheese with butter enriched with casein or egg protein. The results from this study showed that at equal fat and protein content, cheese decreased total plasma cholesterol by 3%. but the LDL:HDL ratio was not different between the diets. Once again, the calcium content was higher in the cheese diet, which could promote the excretion of fat as calcium soaps. Also, one of the bacterial strains used in the fermentation of the cheese was found to have hypocholesterolemic effects on rats (17). Cheese is still a source of SFA and in a randomized controlled clinical trial with cross-over design, 31 subjects with mild hypercholesterolemia consumed 65 g of cheese per day made from either milk fat or rapeseed oil (18). After intervention, the total serum cholesterol and LDL cholesterol was reduced by 6.7 and 7% after 2 weeks and by 5 and 6.4% after 4 weeks with the rapeseed oilbased cheese. The HDL cholesterol concentrations were not significantly changed. A more recent intervention study undertaken simultaneously in Finland, Norway, and Sweden included 120 men and women with less than two symptoms of the metabolic syndrome (19) (Table 1). In this 6-month randomized parallel-group study the participants were allocated to a milk group or control group. The milk group was instructed to include 3-5 defined portions of dairy products in their daily diet while

Reference Tholstrup et al. [14]	Subjects (men+women) and intervention time		Dairy product (daily intake)	Significant effect on plasma cholesterol
	14 men	3 weeks	I.5 L milk, 64 g butter, 205 g cheese	Butter diet 7.9% increase LDL compared to cheese
Nestel et al. [15]	14+5	4 weeks	40 g butter or Cheddar cheese	Total and LDL cholesterol 9 and 15% higher after butter
Biong et al. [16]	9+13	3 weeks	150 g cheese, 52 g butter + protein	Total cholesterol 3% lower with cheese vs. butter meals
Wennersberg et al. [19]	4I +80	6 months	300 g more milk, 20 g more cheese, 5 g more butter than controls	Total cholesterol 4% higher in dairy group vs. control
Motard-Bélanger et al. [40]	48 men	4 weeks	Ruminant tFA high (10.2 g/2,500 kcal) or moderate (4.2 g/2,500 kcal), industrial tFA high or low (2.2 g/ 2,500 kcal) tFA	Total and LDL cholesterol increased 3 and 2% with high ruminant <i>t</i> FA and 6 and 5% with industrial <i>t</i> FA vs. control
Chardigny et al. [38]	19+21	3 weeks	Butter or cheese for ruminant <i>t</i> FA, cookies for industrial <i>t</i> FA. 4% of daily energy/67% of daily fat energy	In women: HDL cholesterol 6% lower with industrial <i>t</i> FA vs. ruminant <i>t</i> FA. LDL was 15% higher with ruminant <i>t</i> FA.Total cholesterol 11% increased with ruminant <i>t</i> FA
Andrade et al. [74]	34 women	4 weeks	125 g $ imes$ 3 fermented milk or plain yoghurt	Decrease of LDL (12,5 and 16%). Also decrease HDL 10–12%
Seidel et al. [77]	16+15	13 weeks	(a) 250 g regular milk, 150 g regular yoghurt and butter for cooking, (b) the same as a with modified milk, or (c) same as a with margarine	HDL increased 15%. LDL and LDL/HDL decreased 11% and 17.5% after modified milk

Table 1. The table presents intervention studies in which the aims were to investigate the effects of dairy products on plasma cholesterol concentrations and in which significant changes in cholesterol concentrations were seen

the control group continued with their habitual diet. The dairy group consumed 300 g more milk or yoghurt, 20 g more cheese and 5 g more butter than control group. The result was a moderate increase of 4% in serum total cholesterol in the milk group compared to control. A moderate increase in apoB in the milk group, especially in Sweden, was positively associated with the increase in C15:0, a biomarker of milk fat. The explanation might be the intake of more full-fat dairy products in the Swedish participants, whereas Norwegian and Finnish participants ate preferably low- to moderate-fat products (19).

Butter affects postprandial lipemia differently compared to vegetable oils. When 42–50 g of butter in a meal was compared with 35–40 g of olive oil, postprandial TG was lower with butter (20, 21) and in another study the size of the chylomicrons were smaller (22). This was seen both in healthy subjects and in overweight persons with non-insulin-dependent diabetes. By contrast, after-meals containing 100 g of butter compared with 80 g of olive oil, the postprandial TG concentrations are higher and the HDL cholesterol lower with butter both in healthy and type 2 diabetic individuals (23, 24). Whereas the presence of short-chain fatty acids in butter commonly explains the lower increase in postprandial plasma lipids in relation to other oils, the opposite relation occurring at a high lipid load has not been unraveled.

Factors in dairy products that affect plasma cholesterol

Milk contains a large number of bioactive compounds, but milk fat has the largest impact on plasma lipids. The lipid pattern in dairy fat is very complicated and more than 400 different fatty acids have been identified. About 70% of dairy fat contains SFAs of which the majority (45%) are of 12–16 carbon chain length and 2.7% are *t*FAs (13), and these have the ability to raise plasma cholesterol. Except for the concentration of different types of plasma lipoproteins that can be affected, their size and composition will change in response to different types of dietary fat. For example, it is suggested that larger sizes of lipoproteins are less atherogenic than smaller sizes (25) and some of the fatty acids typically found in milk fat have been associated with less dense LDL particles (26).

Other milk components like proteins, calcium, and lactose have been suggested to affect lipid metabolism directly or indirectly, but the strongest impact on plasma lipids emerges from the intake of milk fat.

Saturated fatty acids (SFA)

After absorption, the predominant dairy SFA palmitic acid (C16:0), but also myristic acid (C14:0) and lauric acid (C12:0) are preferentially directed to TG formation rather than to phospholipid acylation. These three longchain fatty acids raise total cholesterol, but their effects on LDL:HDL ratios are different. Palmitic acid is the major SFA in the diet and also in milk fat with a content of about 30%. Palmitic acid raises the LDL cholesterol more than it raises HDL cholesterol (27). Myristic acid represents 11% of the dairy fatty acids and increase total cholesterol as much as palmitic acid, but does not affect total cholesterol:HDL ratio (1, 28). Lauric acid is the most potent fatty acid in raising plasma total cholesterol, but dairy content is only 3.3%. The increase in HDL cholesterol induced by lauric acid is higher than the increase in LDL and thus the total cholesterol:HDL ratio was decreased when lauric acid was used to replace carbohydrates (1). Stearic acid represents 12% of the dairy fatty acids and improves the plasma cholesterol profile by decreasing total/HDL cholesterol ratio compared to other SFAs. But compared to polyunsaturated fatty acids (PUFA), stearic acid increases LDL and decreases HDL and increase total/ HDL ratio (29). Other SFAs are short- and medium-chain length and are mainly considered to be cholesterol neutral. At a certain amount of SFA intake, an increase in both LDL and HDL cholesterol can be seen, especially if the intake of unsaturated fatty acids is low (30, 31). In a recent metaanalysis of prospective epidemiological studies, intake of SFA and risk of CVD was studied (32). Six studies found a significant positive association between SFA intake and CVD, and 10 studies found no significant association. The author states, however, that there is a need for further studies to evaluate the CVD risks when replacing SFA with other specific nutrients.

The outcome of the meta-analysis (32) does not differ between men and women, but there are studies included suggesting that men and women have a different risk ratio from consumption of SFA with a slightly higher risk for men (33). In a recent meta-analysis of randomized controlled trials the pooled results from eight trials demonstrated a significant reduction in CVD events by replacing SFA with PUFA (34). In summary, if the target is to reduce plasma cholesterol, especially LDL, the intake of SFAs from dairy and other products should be replaced by low-fat dairy products or PUFA.

Unsaturated fatty acids

Although unsaturated fatty acids are a minor component of milk fat, monounsaturated fatty acids (MUFA), such as oleic acid (C18:1), is the second most abundant fatty acid representing 23% by weight in Swedish dairy milk (13). Dairy products together with meat and hydrogenated oils are actually a major source of MUFA in Scandinavia. Oleic acid is considered favorable since it has a cholesterol- and TG-lowering effect compared with SFA, and meals containing olive oil increase the size of postprandial TG-rich lipoproteins more than meals with butter (35), which is considered to be less atherogenic. By increasing MUFA at the expense of SFA, which can be done with modification of dairy products, larger postprandial chylomicrons can be formed (36). The overall effect of MUFA from dairy products is, however, not clear since the intake of oleic acid from other dietary products is high.

Trans-fatty acids (tFA)

Of the seasonal variation of fat in bovine milk, tFA have the largest variation and their concentrations are more than twice as high in summer milk as in winter milk (37), e.g. the variation in Swedish cows is from 0.6 to 3.9% with an approximate medium value of 2.7% (13). The dietary tFA of industrial origin that humans consume from eating cookies, pastries, and microwave popcorn are shown in many studies to be detrimental to our vascular health (38, 39). Milk fat is the major source of natural conjugated linoleic acid (CLA) and the predominant isoform is cis-9, trans-11 CLA, which accounts for 85-90%. The minor trans-10, cis-12 CLA isomer has been shown to have a more detrimental effect on plasma cholesterol than cis-9, trans-11 CLA since it increases total/HDL and LDL/HDL ratios. The effect of natural tFA, such as CLA and trans 18:1, found in dairy products and meat and of industrial tFA on human plasma lipids has been investigated. The study by Motard-Belanger et al. (40) suggests that ruminant tFAhave little impact on cholesterol homeostasis (Table 1). In this 4-week randomized, cross-over-controlled study on 38 healthy men, they found that a moderate intake of ruminant tFA had neutral effects on plasma lipids, whereas high amounts of both ruminant and industrial tFA increased both the total plasma cholesterol by 3 and 2%, respectively, and LDL cholesterol by 6 and 4.6%. In a quantitative review of 39 carefully selected original articles, only including randomized controlled trials in a parallel or cross-over design, the authors conclude that all tFA increases the LDL/HDL ratio in a linear fashion (41). The effect of ruminant tFA and CLA on the LDL/ HDL ratio was less than that of industrial tFA. In the TRANSFACT study, a randomized controlled trial, 46 healthy subjects consumed 11-12 g/day of either industrial or ruminant tFA (38) (Table 1). The major finding was that the natural sources of tFA significantly increases HDL- and LDL-cholesterol concentrations in women but not in men, and the HDL-lowering effect is mainly associated with industrial tFA. The differences in cholesterol concentrations observed in women were also associated with the size of lipoproteins and tFA from natural sources increases the proportion of larger

particles. Thus, reducing the intake of ruminant fat will decrease the plasma cholesterol concentration and an improvement of the LDL/HDL ratio is likely. The mechanisms underlying the gender effects and type of isoforms need further investigation.

Medium-chain fatty acids (MCFA)

Medium-chain fatty acids (MCFA) are caproic acid (hexanoic acid, C6:0), caprylic acid (octanoic acid, C8:0), and capric acid (decanoic acid, C10:0). MCFA are present at about 6.8, 6.9, 6.6, and 7.3% (of total fatty acid) in butter, milk, yogurt, and cheese, respectively (42). MCFA are rapidly hydrolyzed in the gastrointestinal tract (GI-tract) and are directly transported to the liver and into the mitochondria of the hepatocytes for oxidation (43) but some, especially decanoic acid (C10:0) will be incorporated to chylomicron TG. Several studies report effects such as increased lipid oxidation, decreased body weight, increased thermogenesis and energy expenditure from consumption of MCFA and a few studies report a lowering of total cholesterol, LDL, and an increase of LDL particle size (44, 45). Whether the long-term effects on plasma cholesterol levels and an improvement of LDL:HDL ratios are caused by weight reduction or are an actual effect of the MCFA itself is not fully clarified. In a randomized controlled intervention study on 17 healthy individuals, a high intake of 70 g of MCFA per day for 3 weeks was, however, detrimental to plasma lipids with a 12% increase both in LDL cholesterol and LDL/HDL ratio (46). In another study, intake of moderate amounts (10 E%) of MCFA for 6 weeks had no effect on plasma cholesterol concentrations (47). The intake of MCFA from dairy products will be of little significance with regard to concentration, whereas the interaction with other dairy lipid components might have an effect on plasma lipids, but no such data are available.

Polar lipids

The milk fat globule membrane contains 2–3% of polar lipids, mostly phosphatidylcholine (PC) (30–35%), but also sphingomyelin (25%). Some studies showed that human milk has higher levels of sphingomyelin (SM) than of PC (11). In a Western diet, the intake of SM from bovine milk is approximately 4–12 mg/dl (48). Studies on rats and mice have shown that dietary SM from milk inhibits cholesterol absorption (49–51). We recently performed a 4-week intervention study on 48 healthy subjects where participants consumed a sphingomyelin-enriched milk drink every day with their habitual diet. Our main hypothesis of a cholesterol-lowering effect was unconfirmed but there was a trend that the SMenriched drink counteracted the effects emerging from an increased energy intake. The increased plasma concentrations of cholesterol and TG caused by the elevated energy intake, mainly caused by the test drinks, were counteracted by the SM-enriched drink (52). There are several potential mechanisms by which dairy products enriched in polar lipids can promote vascular health and reduce risk, such as affecting the cholesterol absorption and being a source of unsaturated fatty acids. Presently, there are only few studies within this area and human intervention trials are warranted.

Proteins

There are studies supporting the hypothesis that dairy products have anti-obesity effects and the bioactive compounds such as calcium and proteins augmenting this effect have been discussed (53, 54). In the 1990s, it was suggested that whey proteins had more hypocholesterolemic effect than casein and soy proteins in rats (55, 56). A decade later, four peptides formed from tryptic cleavage of bovine β-lactoglobulin: IIAEK, GLDIOK, ALPMH, and VYVEELKPTPEGDLEILLQK were found to inhibit cholesterol absorption by increasing fecal output of steroid. Of the four peptides, IIAEK had a higher effect than β -sitosterol (57). In a recent *in vitro* study on a human intestinal cell line (NCI-H716), the effects both of the specific amino acids leucine, isoleucine and valine, and of whey, skim milk and casein on expression of lipidregulating genes was examined (58). It was found that isoleucine, leucine, valine, and whey down-regulated Niemann-Pick C1-like 1 (NPC1L1), a protein carrier with a critical role for intestinal cholesterol absorption. They conclude that dairy products such as whey, with a high content of branched-chain amino acids can have an effect on cholesterol absorption and possibly also on the plasma cholesterol concentration. The hypocholesterolemic effect of whey has now been confirmed also in humans (59). A comparison of whey proteins and casein with glucose as control was recently conducted on overweight/ obese subjects. After 12 weeks of daily intake, results showed that whey significantly decreased total and LDL cholesterol compared to both casein and control. Furthermore, Nyberg et al. (60) found evidence of an acid sphingomyelinase present in human milk, which may generate ceramide from hydrolysis of milk SM in the stomach, and recent investigations in human intestinal Caco-2 cells showed that the presence of ceramide inhibited the cellular uptake of cholesterol more effectively than that of SM (61). Taken together, whey proteins but not casein seems to have hypocholesterolemic effects by inhibiting intestinal absorption of cholesterol. Whether acid sphingomyelinase is present in bovine milk and, if so, has any effect on digestion of dairy SM in the stomach is not known.

Calcium

Calcium as a food supplement has been shown to increase HDL cholesterol and decrease total- and LDL-cholesterol concentrations, thereby improve the HDL:LDL ratio (62– 64). Dairy products are the richest source of calcium and the concentration is highest in hard cheese. It was shown in an intervention study on 18 healthy men that milk and yoghurt containing different concentrations of calcium decreased postprandial lipid response in a dose-dependent manner (65). The results by Lorenzen et al. (65) and from other trials (66) indicate that an increase in dairy calcium promotes fecal fat excretion, but support as to whether this affects plasma cholesterol concentrations is lacking.

Lactose

It is hypothesized that lactose can affect lipemia by promoting calcium absorption. In humans, it has been hypothesized whether lactose is a risk factor for ischemic heart disease (IHD) in a study based on data from 43 countries (67). The study compares populations with different grades of lactose malabsorption and milk intake. They propose that there is a correlation between populations with high occurrence of lactose malabsorption and lower incidence of mortality from IHD. This is, however, contradicted in several studies where the risk ratios for myocardial infarctions are <1 with a high milk consumption (68, 69). In older human studies, ingesting 80 g of lactose per day as whey resulted in a decreased serum cholesterol (70). Furthermore, 50 g/day of added lactose to patients with CVD significantly reduced serum cholesterol over a 3-week period (71). In a study comparing high-fatfed mice with mice fed both high-fat and lactose, plasma lipids were significantly lower in the group fed high fat with lactose. The body weight gain was also slightly lower for mice-fed lactose, but cholesterol levels were not investigated (72). There seems to be no newer human data on plasma cholesterol after intake of lactose-free dairy products compared to the lactose-containing counterparts.

Fermented dairy products

The effects of fermented dairy products have been studied since the 1970s. The first studies showed that unpasteurized yoghurt decreased serum cholesterol by 5–9%. Later, results from some studies showed no effects of fermented products, but this was explained by the fact that the subjects in the study had a baseline cholesterol concentration of <5.0 mmol/L. Since then, many studies have displayed hypocholesterolemic effects on hypercholesterolemic subjects (73). In a recent study on 34 women, an intake of 125 g of fermented milk three times a day for 4 weeks decreased plasma LDL cholesterol by 12.5–16%. There was also a significant decrease of HDL cholesterol of 10-12% (74) (Table 1). It is concluded that many strains of fermentation bacteria, but not all are viable enough to reach the lower part of the gut and exert effects on the microbiota, thereby increasing the amount of propionate that has a cholesterol-lowering effect. The second effect by which bacteria may influence cholesterol level is by hydrolyzing glycine and taurin-conjugated bile acids (15, 75). By deconjugating bile acids, the excretion of bile acids in feces is increased, which promote the use of cholesterol for synthesis of new bile acids. The use of fermented milk instead of normal milk may therefore be a method to reduce or maintain the plasma cholesterol levels, but the effects on LDL/HDL ratio should be further investigated.

Modified dairy products

Of the main milk components, fat is the most sensitive to dietary changes (76). Except for seasonal variations in bovine milk fat composition, fortified feeding of cows may affect the milk fat composition. By feeding cows 400 g of rapeseed oil, Seidel et al. (77) were able to reduce SFA (C12:0, C14:0, and C16:0) by 20% and increase the milk content of unsaturated fatty acids by about 33%. In the following intervention study divided into three periods of 18 days each, both normo- and hyperlipidemic subjects increased their HDL cholesterol and reduced the LDL cholesterol after the period with modified milk. This was not seen after periods with regular fat or margarine (77) (Table 1). In this study, normolipidemic subjects responded more sensitively to changes in HDL and LDL cholesterol than those with hyperlipemia. By modification of cow-feeding regimes, the fatty acid composition of milk might be adjusted to contain less SFA and consequently more healthy dairy products can be produced.

Conclusion

The impact on our plasma lipid levels from dairy intake is depending on amounts, fat concentrations, and also on gender, age, and metabolic capacity of the consumer. Certain dairy products are also often part of a healthconscious lifestyle, which promotes maintaining or loss of weight with a subsequent improvement of plasma cholesterol profile. Also, when it comes to choices of food within the same group, women tend to choose low-fat dairy products more often than men do.

Despite the complexity of this nutrient, we find some conclusions that can be made regarding milk fat and cholesterol.

Dairy fat contains a high concentration of SFA and since dairy products are a considerable part of habitual diets, they have also generally been a target for restriction advice in order to reduce intake of saturated fat. Intake of saturated fat with chain length C12–C16 and *t*FA increases plasma LDL which is an independent risk factor for CVD. The presence of *t*FA in dairy fat increases the LDL/HDL linearly with dose and, theoretically, by lowering the *t*FA intake by 0.5% of energy, this might reduce

the cardiovascular risk by 1.5-6%. Palmitic acid is the predominant fatty acid in milk fat and increases the LDL:HDL ratio more than lauric and myristic acids do. It can be calculated how much a change in SFA intake will affect the LDL cholesterol and the risk of developing CVD. By substituting 30 g of butter per day containing about 11 g of SFA with a margarine rich in unsaturated fatty acids containing 2.4 g of SFA, would reduce LDL cholesterol by 0.2 mmol/L and subsequently reduce the risk of CVD in the order of 6–10%. In light of this, the increase of 4.9 g/day SFA intake in the milk group in the study by Wennersberg resulted in a slight increase in LDL cholesterol of 0.1 mmol/L. In some cohorts with a rather high baseline intake of dairy fat, correlations between dairy intake and plasma cholesterol would therefore be scarce. However, dairy SFA is not only C12-C16, but around 25% is represented by short- and medium-chain fatty acids, which have the ability to affect the digestion of milk fat already in the stomach through digestion by gastric lipase and isomerization of fatty acids in the partially hydrolyzed TG. It is necessary to distinguish between the effects of butter and other dairy products, since butter increases plasma cholesterol, especially LDL cholesterol, more than other dairy products. Dairy fat raises both LDL and HDL cholesterol, but the evidence for a detrimental effect of high plasma LDL levels is stronger than the positive effects from an increased HDL concentration. Intervention studies that focus on reducing dairy fat intake and other studies as well, must be aware of the effect on HDL cholesterol, both regarding size and concentration, since a reduction in HDL size and concentration may not improve health or reduce CVD risks.

On the basis of controlled and randomized dietary intervention studies with different dairy products and recent meta-analyses of both epidemiological and controlled studies, the present approach to limit the intake of high-fat dairy products on behalf of low-fat products is unchallenged. A reasonable intake of cheese, low-fat and fermented milk reduced plasma cholesterol levels, mainly LDL cholesterol, in the order of 3-15% compared to butter or other high-fat dairy products, but not compared to nutrients containing more PUFA. The levels of milk components, e.g. MUFA, MCFA, and other polar lipids, have little individual impact on plasma cholesterol concentrations, but there are only few studies for consensus and no studies on concerted action of selected components. There is still no satisfactory explanation for the term 'milk factor,' although some unknown mechanism might yet be found in the interaction between calcium, proteins, lactose, and fatty acids.

Conflicts of interest

The author declares no conflict of interest regarding this review.

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