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Associations between dairy foods, diabetes, and metabolic health: Potential mechanisms and future directions

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ABSTRACT

Epidemiological evidence supports an inverse relationship between adequate intake of dairy foods and susceptibility to type 2 diabetes (T2D). The biological mechanisms responsible for this association remain to be established. This review provides a current perspective on proposed mechanisms that may underlie these effects, and highlights how randomized clinical trials can be applied to investigate these relationships. Results from epidemiological studies generally support that consumption of milk and dairy products is associated with a lower incidence of T2D or improvements in glucose homeostasis indices, and studies of animal and cell models support a positive effect of dairy-rich diets or components on metabolic and inflammation factors relevant to T2D and insulin resistance. Emerging evidence indicates that dairy components that alter mitochondrial function (e.g., leucine actions on silent information regulator transcript 1 (SIRT1)-associated pathways), promote gut microbial population shifts, or influence inflammation and cardiovascular function (e.g., Ca-regulated peptides calcitonin gene-related peptide [CGRP] or calcitonin) should be considered as possible mechanistic factors linking dairy intake with lower risk for T2D. The possibility that dairy-derived trans-palmitoleic acid (tC16:1) has metabolic bioactivities has also been proposed. Pre-clinical and clinical studies focusing specifically on these parameters are needed to validate hypotheses regarding the potential roles of dairy products and their components on the determinants of glucose tolerance, particularly insulin sensitivity, pancreatic endocrine function, and inflammation in individuals at-risk for T2D development. Such experiments would complement epidemiological studies and add to the evidence base for recommendations regarding consumption of dairy products and their individual components.

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Abbreviations: T2D, type 2 diabetes; SIRT1, silent information regulator transcript 1; CGRP, calcitonin gene-related peptide; CDC, Centers for Disease Control and Prevention; DGA, Dietary Guidelines for Americans; RR, risk ratio; CI, confidence interval; NFDM, nonfat dry milk; DIO, diet induced obesity; PCG-1α, peroxisome-proliferator activated receptor gamma coactivator-1α; mTOR, mammalian target of rapamycin; YY1, yin yang 1; WAT, white adipose tissue.

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1. Introduction

Rapidly rising rates of type 2 diabetes (T2D) and other cardiometabolic disorders pose a significant threat to human health and raise healthcare costs worldwide. Data collected by the Centers for Disease Control and Prevention (CDC) show that 26 million Americans have diabetes, and approximately one third of U.S. adults are classified as having prediabetes and/or metabolic syndrome [1,2]. The health complications associated with diabetes are extremely taxing at both the individual and healthcare system levels. For instance, according to the CDC, diabetes is the leading cause of adult blindness in the U.S. and is also responsible for 44% of end-stage renal disease cases and 60% of lower limb amputations. The treatment and management of diabetes cost an estimated $176 billion annually in the U.S. alone, and the estimated indirect cost from disability, loss of work, and premature death related to diabetes is $69 billion [3]. Trends in the prevalence of obesity and T2D among pediatric and adolescent populations have also become a major public health concern. Obesity, a major risk factor for developing T2D and metabolic syndrome, has more than doubled in children and tripled in adolescents living in the U.S. over the past two decades [4,5]. During this time, the percentage of pediatric cases of diabetes classified as T2D has risen from less than 3% to 45% [6]. Diet and lifestyle interventions are the preferred treatment modality for these groups, and pharmacotherapy is only indicated if supervised lifestyle intervention fails [7,8]. In light of these sobering statistics, it is imperative that the clinical and scientific communities identify modifiable factors that can help prevent or mitigate T2D and other cardiometabolic diseases.

Recently, the relationship between dairy consumption, reduced T2D risk, and improved metabolic health has received increasing attention. The potential role for dairy consumption to reduce T2D risk was recognized in the 2010 Dietary Guidelines for Americans (DGA), which recommend 3 cups of fat-free or low-fat (1%) milk and milk products daily for individuals aged 9 years and above [9]. The DGA, established jointly by the U.S. Departments of Agriculture and Health and Human Services, are designed to provide science-based advice for Americans aged 2 years and above to help prevent chronic diseases and promote health. Recommendations for milk product intake have traditionally been based on their role as key contributors of essential nutrients, as well as on moderate evidence of a link to improved bone health. In 2010, the Dietary Guidelines Advisory Committee addressed a number of questions related to diet and disease risk using an evidence-based review process, and one of these questions was "What is the relationship between the intake of milk and milk products and incidence of T2D?" [10]. The Committee considered a systematic review with meta-analysis of four prospective studies, which reported that relative risk for T2D was 10% lower in people who had a high milk intake relative to those with low consumption [11]. Based on this, the Committee concluded that "Moderate evidence shows that milk and milk products are associated with a lower incidence of type 2 diabetes in adults," and in the Implications section, noted that "Research since 2004 shows that under-consumption of milk and milk products may lead to an increase in type 2 diabetes" [10].

This review aims to summarize recent meta-analyses that evaluated these potential links, to explore possible mechanisms, and to identify knowledge gaps to provide guidance and insight for future studies.

2. Summary of recent epidemiological evidence

Since the publication of the 2010 DGA report, studies have been published that support a possible protective effect of dairy product consumption on T2D incidence. In the following publications, the evidence reviewed is based on observational data obtained primarily through validated food-frequency questionnaires. While there is some variation among the dairy items included, the majority of studies defined total dairy intake as the combined intake of individual low-fat (skim milk, 1% milk, skim chocolate milk, sherbet, yogurt, cottage/ricotta cheeses) and high-fat (whole milk, cream, sour cream, ice-cream, butter, cream cheese and other cheeses) dairy products.

Tong et al. [12] completed a meta-analysis of studies on dairy consumption and risk of T2D, with seven cohort studies identified from a systematic literature review. When comparing the highest with the lowest dairy product intake, the combined diabetes risk ratio (RR) was 0.86 (95% CI, 0.79–0.92), with little evidence of heterogeneity. For subgroup analysis, the combined RRs were 0.82 (95% CI, 0.74–0.90), 1.00 (95% CI, 0.89–1.10), 0.95 (95% CI, 0.86–1.05) and 0.83 (95% CI, 0.74–0.93) for intake of low-fat dairy, high-fat dairy, whole milk and yogurt, respectively. Dose–response analysis showed that T2D risk could be reduced 5% for each one serving per day of total dairy products and 10% for each one serving per day of low-fat dairy products.

Kalergis et al., in a recent evidence-based review, reported that dairy intake is significantly associated with a reduced T2D risk and the relationship is dose-dependent [13]. There was consistent evidence to support an association between low-fat dairy consumption and T2D risk reduction, but a beneficial impact was also suggested for regular-fat dairy. The authors concluded that the roles of specific dairy products need to be clarified and that mechanistic studies should be conducted to expand on the current research. Another evidence-based review examining studies published just after the 2010 DGA report arrived at essentially the same conclusions [14].

Aune et al. [15] conducted a systematic review and dose–response meta-analysis of 17 cohort studies related to dairy intake and T2D risk. Summary RRs were estimated with a random-effects model. In the dose–response analysis, the summary RRs (95% CIs) were 0.93 (0.87–0.99) per 400 g total dairy products/day, 0.98 (0.94–1.03) per 200 g high-fat dairy products/day, 0.91 (0.86–0.96) per 200 g low-fat dairy products/day, 0.87 (0.72–1.04) per 200 g milk/day, 0.92 (0.86–0.99) per 50 g cheese/day, and 0.78 (0.6–1.02) per 200 g yogurt/day. Nonlinear inverse associations were observed for total dairy products, low-fat dairy products, cheese, and yogurt, with a flattening of the curves at higher intakes. The authors concluded that there