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Commentary
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Recent Perspectives for Clinical Effects of Whey Protein on Post-Prandial Hyperglycemia (PPH)

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Abstract

As the development of continuous glucose monitoring (CGM) progresses, the clinical effects of whey protein on postprandial hyperglycemia (PPH) have been identified. Whey protein includes milk protein, yogurt, casein, almond milk, and so on. Milk protein supplementation has been shown to reduce fasting blood glucose (FBG) by -1.83 mg/dL, fasting insulin by -1.06 μU/mL, and HOMA-IR by -0.27. Whey protein was administered in doses of 0–30 g before breakfast, and the incremental area under the curve (AUC) was reduced when taking 15–30 g. Premeal whey showed a lower glucose peak by -1.0 mmol/L (-18 mg/dL) in patients with gestational diabetes mellitus (GDM). Further research development is expected for PPH.

Keywords

Whey Protein, Post-Prandial Hyperglycemia, Incremental Area Under the Curves, Dairy Matrix, Biomarkers of Food Intake

Abbreviations

PPH: Post-Prandial Hyperglycemia; AUCs: Incremental Area Under the Curves; BFIs: Biomarkers of Food Intake

Commentary

Adequate diabetic control has been proposed using the *Standards of Care in Diabetes* by the American Diabetes Association (ADA) for a long time [1]. Recently, glucose variability has been precisely detected by continuous glucose monitoring (CGM), which has contributed greatly to better diabetic control [2]. The authors have continued beneficial analyses of CGM by applying smartphone technology [3]. From our study, pre-prandial milk intake showed a beneficial effect on post-prandial hyperglycemia (PPH) [4]. As α-glucosidase inhibitors (α-GI), such as miglitol, can reduce PPH, milk is known to show similar clinical efficacy. In this article, several valuable reports about the relationship between PPH and whey protein will be described.

The degree of PPH depends on several factors, such as the type and concentration of carbohydrates, and the physicochemical properties of the food matrix [5]. It determines the uptake rate of monosaccharides into the bloodstream, gastric emptying, and other related processes. In the case of milk, the influence on PPH would be multi-faceted, such as gastric emptying, the uptake rate of glucose/galactose into the bloodstream, insulin secretion, and so on. A clinical study on PPH was conducted for three groups taking dairy as 0, 1, or 2 items [6]. As a result, total glucose area under the curves (AUCs) showed lower values in 1-D and 2-D than in none-D ($p<0.05$). Therefore, replacing a carbohydrate-rich breakfast with one to two dairy servings can be beneficial for reducing PPH and improving glycemic control. From these data, isoenergetic replacement of a carbohydrate-rich breakfast with one serving of dairy can improve post-prandial glycemic control, amino acid availability, and bone metabolism.

Supplementation with milk-derived proteins (milk protein/whey/casein) has been known to improve fasting blood glucose and homeostasis model assessment of insulin resistance (HOMA-IR). It suggests that short-term intervention would provide beneficial clinical effects for PPH. A total of 36 RCTs (1851 cases) were included in the pooled analysis [7]. Consequently, milk protein (MP) supplementation effectively reduced fasting blood glucose (FBG) by -1.83 mg/dL, fasting insulin by -1.06 μU/mL, and HOMA-IR by -0.27. With short-term administration of a lower daily dose of whey protein (<30 g), FBG showed a considerable decrease. In addition, fasting IRI also showed a remarkable decrease with long-term supplementation using moderate-to-higher daily doses of whey protein.

In nutritional research, the validation and identification of biomarkers of food intake (BFIs) have been important but rather difficult projects. A current study included both milk and yogurt for 14 healthy young and 14 older participants [8]. After a 3-week dairy exclusion period from the diet, they drank 600 mL of milk or yogurt and were followed for 6 hours concerning the BFIs. In comparison with milk, several delayed serum kinetics were found for 22–45 minutes in lysine, tyrosine, phenylalanine, threonine, lactose, galactonate, and galactitol. Consequently, we can identify candidate BFIs of milk or yogurt based on several modified post-prandial responses. Furthermore, future studies should include population-specific factors to obtain more specific and accurate BFIs.

The clinical efficacy of almond milk for PPH was studied in comparison with cow milk [9]. Patients with type 2 diabetes (T2D) (n=22) participated in the study, and almond milk versus carbohydrate- or caloric-matched 2% milk was served with oatmeal. The glucose incremental AUC (iAUC-240) was compared, and post-prandial markers were measured, such as insulin, glucagon, TG, free fatty acids (FFAs), and gastrointestinal (G-I) hormones. As a result, no significant differences were detected among the three groups. However, the values of iAUC-240 for insulin/glucagon were higher in carbohydrate-matched 2% milk versus almond milk. Consequently, almond milk did not show any particular additional glycemic benefit over 2% milk or post-prandial effects on TG, FFAs, or leptin. Nevertheless, carbohydrate-matched milk revealed a higher insulin/glucagon response than almond milk.

To investigate whether whey protein lowers PPH, patients with gestational diabetes mellitus (GDM) and patients with normal glucose tolerance (NGT) were provided with whey or placebo (each n=12) [10]. Whey protein was given at doses of 0, 10, 15, 20, and 30 g before breakfast. As a result, the incremental area under the curve (AUC) was reduced by taking 15–30 g of whey protein. Furthermore, premeal whey showed a lower glucose peak by -1.0 mmol/L with GDM and -0.7 mmol/L without GDM compared with placebo. Consequently, premeal whey (20 g) showed a dose-dependent reduction in incremental glucose peaks by -2.0 mmol/L in GDM compared with placebo.

The regular consumption of high-protein dairy-based products seems to improve the nutritional status of the elderly. In a nutritional study, 25 elderly participants with a mean age of 71.4 years consumed either high-protein or energy-enriched berry purées [11]. Compared with the protein-free group, the dairy product group showed a remarkably higher insulin response, lower blood glucose, and reduced post-prandial NEFA rebound. These findings may be beneficial for improving muscle protein and energy metabolism in the elderly. Consequently, these effects will benefit elderly individuals with impaired glycemic control and muscle metabolism.

The dairy matrix influences the digestion and absorption of lipids, which is associated with the risk of cardiovascular diseases (CVDs). The study investigated post-prandial glucose, lipid, and appetite responses for 8 hours after consuming different matrices of isoenergetic dairy meals [12]. During four days, one of four different dairy products was served, which were made of cheese, micellar casein isolate (MCI), cream, or gel from MCI drink. As a result, time × meal interactions were found in glucose, insulin, and FFAs ($p<0.001$). The post-prandial TG response was higher after MCI gel, suggesting that casein network types influence lipid responses.

From the findings mentioned above, recent reports on PPH and whey protein are summarized in (**Table-1**). Several types of study designs are included. In conclusion, the current article will hopefully serve as a useful reference for future research and practice on diabetes, PPH, whey protein, and milk.

Conflict of Interest

The authors have read and approved the final version of the manuscript. The authors have no conflicts of interest to declare.

Table-1: Recent English Papers on Milk and Postprandial Blood Glucose

No	Author	Journal	Design	Subjects	Main finding	Year	PMID
1	Smedegaard	Diabetes Care	Randomized crossover trial	Gestational diabetes	Premeal whey protein reduced postprandial glucose excursions	2025	39775593
2	Dhaver S	Nutrients	Randomized clinical trial	Type 2 diabetes	No significant iAUC difference, milk increased insulin response	2025	40647197
3	Hilkens L	J Nutrition	Randomized crossover trial	Adults, breakfast interv	Dairy replacement lowered postprandial plasma glucose tAUC	2024	38092152
4	Mohammadi S	Nutrition J	Systemat Rev/meta-analys	Adults, various trials	Milk protein improved fasting glucose and insulin resistance markers	2023	37798798
5	Shkembi B	Foods	Review	Human narrative review	Milk matrix slows gastric emptying, lowers glycemic response	2023	36765982
6	Törrönen R	Clin Nutr ESPEN	Rand. single-blind crossov	Older adults	Dairy protein snacks increased insulin response, lowered glucose	2022	36184209
7	Kim J	Front in Nutrition	Randomized crossover trial	Young to older adults	Milk and yogurt shape different postprandial metabolic responses	2022	35600812
8	Kjølbæk L	Am J Clin Nutr	Randomized crossover trial	Healthy adults	Different dairy matrices produced varied glycemic and lipid responses	2021	34477812

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