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The Impact of High-Protein Diet Models on Weight Loss in Obese People and the Mechanisms at Work

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Abstract. Current studies have inadequately investigated the regulatory mechanisms that high-protein diets (HPD) use to modulate basal metabolism during weight loss in obese people. To fill this gap, this research looks into the regulatory mechanisms and effects of HPDs on the basal metabolism of obese people losing weight. We analyze these mechanisms and impacts from multiple perspectives: the weight loss efficacy of HPDs, their mechanistic pathways in promoting weight loss in obese individuals, practical implementation protocols, associated adverse reactions and mitigation strategies, and short- and long-term effects. The research findings show that HPDs markedly improve body weight and metabolic indicators by adjusting satiety-related factors, increasing the thermic effect of food, and influencing blood lipids and lipid metabolism. More favorable results are obtained when HPDs are combined with fitting physical movement and other dietary weight-loss tactics. This research gives a theoretical basis for integrating HPD patterns with artificial intelligence and big-data technologies in the future. But, current studies of the short- and long-term effects of HPD interventions on the renal function of overweight/obese individuals are limited. Future research should work on refining these mechanistic frameworks to consolidate the theoretical foundation for HPDs.

Keywords: High-protein diets, weight loss, overweight and obese.

1. Introduction

Obesity, being a chronic metabolic disorder, is defined by an over-growth of adipose tissue. It's generally diagnosed when the body mass index (BMI) goes beyond 28. 0 kg/m². 0 kg/m², yet regional adjustments are commonly made to account for population-specific physiological traits). The pathogenesis of it is multifactorial. The main modifiable risk factors are long-term excessive eating of high-energy, high-fat diets and lack of physical activity. Usually, clinical weight management strategies give importance to nutritional modulation. It consists of balancing the sufficient supply of essential energy for basal metabolic needs and reducing excessive caloric intake, a central principle of evidence-based weight loss strategies. But a major limitation of traditional hypocaloric diets is the possibility of lacking micronutrients, arising from reduced dietary variety and limited food access among obese people.

Against this backdrop, high-protein diets (HPDs) have shown up as a promising nutritional approach to harmonize weight loss goals and the upkeep of essential nutrient status. A HPD is a

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dietary pattern where protein makes 20–30% of total daily energy intake (TEI), going beyond the Recommended Dietary Allowance (RDA) of 0. The amount for healthy adults is 8 g/kg body weight (BW), and it usually ranges from 1. 2 to 2.2 g/kg BW in order to manage weight. Mechanistically, high-protein intake supports muscle protein synthesis (MPS) by providing sufficient essential amino acids (EAAs), particularly leucine, which acts as a key signaling molecule to activate the mammalian target of rapamycin (mTOR) pathway—critical for preserving lean body mass (LBM) during energy restriction. Besides, dietary protein enhances the production of anorexigenic gastrointestinal hormones, such as GLP-1 and CCK. These hormones delay the emptying of the stomach and transmit satiety signals to the hypothalamus, so as to reduce ad libitum caloric intake. It also promotes the peristalsis of the intestines and preserves the gut barrier function, decreasing the probability of constipation, a common negative consequence of low-calorie diets.

Empirical research shows HPDs are associated with positive outcomes in obese people. These include better body composition (less fat mass compared to LBM), regulated glucose balance (higher insulin sensitivity), and normal lipid profiles (lower triglycerides and LDL-C). But, there are still gaps in comprehending the underlying metabolic regulatory mechanisms, especially how high-protein intake regulates basal metabolism, the browning process of adipose tissue, and gut microbiota composition when losing weight.

This study intends to methodically explore the impacts and mechanistic bases of HPD patterns on weight loss and metabolic regulation in obese people. Specifically, it will address four core objectives: (1) quantify the dose-dependent effects of high-protein intake on weight loss efficacy and body composition changes; (2) elucidate the molecular mechanisms linking HPDs to appetite regulation, energy expenditure, and adipose tissue metabolism; (3) evaluate the safety profile of HPDs, including potential adverse effects (e.g.such as the burden on the kidneys and bone mineral loss) and the targeted strategies for mitigation. (4) Compare short-term (≤12 weeks) and long-term (≥12 months) outcomes to give sustainable dietary recommendations. Through the incorporation of clinical data, molecular biology assays, and microbiome analyses, this research aims to develop bespoke HPD protocols for different obese phenotypes (e.g., metabolically healthy vs. Metabolically unhealthy obesity), make weight-loss more efficient, and expand the clinical and nutritional usages of HPD strategies.

2. The means of HPD in achieving weight loss

In recent years, accumulating clinical and experimental studies on the effects of dietary patterns on body weight and metabolic parameters in overweight/obese individuals have consistently demonstrated that an HPD can significantly reduce body weight, BMI, body fat percentage, and visceral fat area [1,2]. HPD shows favorable regulatory effects on metabolic indicators, like blood glucose, blood lipids, and urinary metabolic profiles.

2.1. The regulation of hunger-associated peptide hormones

Hunger and satiety are tightly managed by a complex peptide-hormone network. GLP-1, CCK, and ghrelin are important mediators in this regulation. GLP-1 is an incretin hormone mostly secreted by intestinal L cells, whereas CCK is a polypeptide hormone produced and released by enteroendocrine cells of the small intestine. Both hormones are sensitive to nutrients. After ingesting proteins, carbohydrates, or fats, they get secreted to bring about physiological effects such as improving satiety perception, slowing gastric emptying, and modulating central appetite through the gut-brain axis. In contrast, ghrelin—a 28-amino acid polypeptide hormone primarily secreted by P/D1 cells in

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the gastric fundus—acts as an orexigenic signal: it binds to its receptor in the hypothalamus to stimulate food intake, promote adipose tissue synthesis, and reduce energy expenditure, thereby contributing to weight gain and obesity.

Studies have found that HPD can robustly increase the secretion of GLP-1 and CCK. They transmit satiety signals to the CNS and peripheral nervous system through neural and endocrine paths, ultimately suppressing hunger drive [1]. In particular, a time-course study of the dynamics of ghrelin secretion showed that HPD also holds back ghrelin release, causing a decline in serum acylated ghrelin (AG) levels. The down-regulation of AG then causes a drop in appetite for obese individuals, a decrease in daily caloric intake, and a halt to adipose mass increase [3].

2.2. Improved thermogenic effect of food

TEF is the energy the human body expends while going through the digestion, absorption, and metabolism of nutrients. Among macronutrients, protein shows the most remarkable thermogenic effect, taking 30%–40% of its caloric value. Carbohydrates come after at 5%–6%, and fats are around 0%–3%. An HPD regimen strengthens the proportion of protein intake, and as a consequence, it raises the energy expenditure for the metabolic conversion of nutrients into heat in obese individuals. Actually, the synthesis of body proteins from dietary amino acids uses more energy than the direct change of fats or carbohydrates into thermal energy [4]. The combined action of these mechanisms results in a rise in daily energy expenditure in obese patients using an HPD, making weight loss interventions more efficient.

2.3. Effects on blood lipid profiles as well as lipid metabolism

In a clinical trial involving overweight or obese participants, an HPD was found to exert significant ameliorative effects on dyslipidemia, characterized by reductions in serum triglycerides (TG), total cholesterol (TC), LDL-C, and high-density lipoprotein cholesterol (HDL-C). Remarkably, in relation to a standard-protein diet pattern, the high-protein intervention was more successful in reducing TG and HDL-C levels in this population. Another complementary experimental study's results showed that HPDs are able to bring down very low-density lipoprotein (VLDL) concentrations while maintaining lean muscle mass [5-7]. These results show that HPDs effectively relieve dyslipidemic states.

Given that lipid metabolism disorders are established risk factors for chronic conditions such as coronary heart disease—a conclusion supported by clinical investigations into chronic disease pathogenesis—the favorable regulatory effects of HPDs on lipid metabolism hold implications for both the prevention of chronic metabolic disorders and the improvement of disease prognosis. Then, HPDs give a practical framework for long-term dietary management [2].

Simultaneously, increasing evidence from studies examining the effect of HPDs on liver function suggests that weight loss achieved by means of HPD interventions is beneficial to liver health [2,8,9].

3. Real implementation of the HPD model

HPD models often need to be integrated with other weight management strategies to get the most out of interventions.

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3.1. One HPD combined in combination with lifestyle intervention

A clinical study involved obese patients who met the WHO diagnostic criteria for obesity. Researchers looked into the effects of an HPD combined with lifestyle intervention over 1-and 6-month follow-up times. It was shown by the results that serum TC, TG, HDL-C, etc. In the intervention group, levels were significantly decreased at both time points (all $P < 0.05$). Notably, the amount of these diminutions was more pronounced after 6 months of unbroken lifestyle/behavioral intervention ($P < 0.05$). The data shows that an HPD, along with lifestyle changes such as regular physical activity, can effectively reduce central obesity and improve glucose and lipid metabolism in obese people [10].

3.2. The joint consequence of HPDs and weight loss methods

An energy-balanced diet with a precisely controlled calorie deficit, in combination with balanced nutrient intake, is a means of achieving sustainable weight loss. Compared to isocaloric energy-balanced diets, HPDs show better weight loss results, such as greater body weight reductions and the preservation of fat-free mass (FFM) [11].

While low-carbohydrate diets cause obvious short-term weight loss, their long-term effectiveness and safety are still to be fully determined. When combined with HPDs, the satiety-promoting and metabolic advantages of high-protein intake can be put to use to further improve weight loss [11].

Intemittent fasting may bring more substantial metabolic improvements than conventional energy-balanced diets. But no significant difference in the magnitude of weight loss has been detected between them. When integrated with a HPD, intermittent fasting is able to support the maintenance of weight-loss effects and the improvement of metabolic health by enhancing satiety and upping the metabolic rate [11].

3.3. Specific suggestions for HPD

Regarding diet, the Chinese Residents Dietary Guidelines propose increasing the consumption of high-quality proteins, including lean meat, fish, eggs, legumes, and dairy items. When put against standard protein diets, this dietary approach is more apt to preserve FFM and maintain the baseline muscle mass. Research on the muscle-protective effects of protein intake showed that a daily protein intake of up to 1. A quantity of 3 g/kg body weight (BW) is good for keeping muscle. Directly taking branched-chain amino acids (BCAAs) can also contribute to muscle mass upkeep [12]. In a randomized, double-blind, placebo-controlled trial, 84 elderly individuals with inadequate protein intake were part of it, and it was shown that 3 weeks of having a complete nutritional drink with 2. 2 g of eicosapentaenoic acid (EPA) together with 5 g of BCAAs significantly increased the muscle mass and strength of the right arm [13]. In fact, the timing and type of protein supplementation are vital for results. Supplementation following strength training yields better effects, and milk/whey protein is more effective than soy protein.

3.4. Harmful outcomes and countermeasures of HPD

A study was carried out to look into the influence of HPD intervention on body weight and metabolic parameters in overweight/obese patients who attend the Nutrition Weight Loss Clinic of the First Hospital of Shanxi Medical University. The intervention joined dietary and exercise schemes, with strict supervision and follow-up to check the results. Among 88 overweight/obese participants, over 10 individuals reported adverse reactions: 15 experienced hunger, 14 constipation,

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11 dizziness, 10 diarrhea, 2 fatigue, and 1 reduced attention. These results show that obese patients could experience discomfort when undergoing HPD intervention, including dizziness, diarrhea, constipation, hunger, fatigue, and less attention. A possible mechanism is the inadequate intake of carbohydrates during the intervention, which causes short-term intolerance [2].

It is recommended to adjust the diet plan in a timely manner to deal with adverse reactions. For example, adding probiotics can relieve constipation, while suitable glucose intake can reduce hunger.

4. Census of the effects on kidneys and individualized use of HPDs

Current research into the adverse renal effects of short-term HPDs faces three main limitations.

At first, a large number of studies are aimed at specific populations (e.g. (college students, overweight/obese individuals), so there is limited generalizability, especially for groups with pre-existing renal dysfunction or chronic diseases. Additionally, intergroup variations (e.g. Gender, age, and ethnicity in renal reactions to high-protein intake are commonly under-explored, weakening the external validity of findings [14].

In the second place, cross-sectional designs and short follow-up times (e.g. A 3-year study that observed but was not able to track the long-term pattern of renal adverse effects restricts the assessment of sustained impacts [15].

Third, the origin and quality aspects of protein (animal vs. Plant-based elements have separate effects on the renal system. But, many studies don't perform detailed stratification according to protein type, which makes result interpretation difficult [5,14].

There is an ongoing controversy about long-term HPD interventions and renal function. Newly-found evidence points out that these diets may harm the kidneys, especially in undiagnosed mild CKD cases. Suggested mechanisms involve glomerular hyperfiltration, which causes chronic renal damage, fibrosis, and mesangial cell proliferation, yet the exact biological pathways are unclear [16]. In-depth study of mechanisms is essential to explain these pathways and support targeted interventions. In CKD patients, suitable protein intake is a key element in disease management. So, long-term HPD studies can give scientific proof for dietary care, helping to manage the disease and slow its progress. More longitudinal studies are urgently demanded to clarify the long-run renal outcomes of HPDs.

HPDs display a relatively high degree of adherence. But individualized adjustments are crucial to balance long-term weight loss effectiveness and metabolic safety. The research on individualized optimization has transitioned from a "one-size-fits-all" mode to precision stratification, combining genetic, microbiome, metabolic, and behavioral factors to boost both efficacy and safety. But, challenges stay, including high prices of genetic/microbiome testing and poor evidence for vulnerable populations (e.g. , children). Future research can make use of single-cell sequencing and artificial intelligence to develop the personalized use of HPD patterns.

5. Conclusion

Finally, an HPD is an effective means for weight loss and metabolic betterment, particularly for those who are overweight or obese. By controlling factors associated with satiety, increasing the thermic effect of food, and regulating blood lipid profiles and lipid metabolism, this dietary pattern markedly improves body weight and metabolic indicators. Remarkably, when an HPD is combined with right physical exercise and complementary dietary weight-loss tactics, synergistic effects are found, resulting in better outcomes. However, in the course of carrying out the implementation,

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individual variations and possible adverse effects have to be closely monitored, and timely changes should be made as required.

There are ongoing limitations in current research. The specific mechanisms of certain regulatory pathways are not fully grasped, and studies looking at the short-and long-term effects of HPD interventions on renal function in overweight/obese people are constrained. Future research ought to focus on a more in-depth exploration of these theoretical mechanisms to improve the framework for the short and long-term physiological effects of HPDs. In fact, the integration of AI and related technologies will make it easier to apply HPDs in an individualized and precise way.

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