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Editorial

Dietary proteins, metabolic syndrome, and sarcopenia: Focus on Asian Indians

The traditional diets consumed by our pre-agricultural hunter-gatherer ancestors consisted of animal protein and wild plants, and low intake of carbohydrates [1]. In recent times, protein content and types depend on nutrition transition, capacity to buy foods, and vegetarian status of individuals. While importance of proteins for health is well understood in general, its relevance in context of obesity and co-morbid metabolic diseases continues to be debated. It is particularly important to underline emerging gluco-regulatory role of various proteins, particularly dairy based proteins [2]. Role of proteins in glucose-insulin metabolism should be properly contextualized in background of rapidly increasing diabetes in south Asians [3] and in populations of other developing countries [4].

Many research studies suggest that high-protein diets may confer some advantages, particularly for overweight individuals with features of the metabolic syndrome [5–7]. For example, a meta-analysis of 6 randomized control trials in Caucasians reported a 7% reduction in body weight in the subjects on high protein diet ($p < 0.01$) vs. 3% body weight reduction in the subjects on energy controlled diet [8]. Importantly, even a small amount of weight loss is important for the prevention of diabetes and other obesity-related non-communicable diseases. For example, it has been shown in the Diabetes Prevention Program that a 1 kg weight loss is associated with about 16% reduction in the risk of developing diabetes [9]. Further, as compared to high carbohydrate diets, diets high in proteins lead to preservation of lean body mass and reduce fat mass, even when weight loss is not significant [10]. Overall, these changes in body composition support improvement of insulin sensitivity.

In this issue of journal, Badely et al. [11], reviewed data from 27 published randomized controlled trials (n , 2377), and show that intake of whey protein causes improvement of all components of the metabolic syndrome. Similar effects of high protein intake in Asian Indians who are vegetarian or have metabolic syndrome has been shown by us [7]. However, research findings may vary on this issue due to multiple factors such as total energy intake, source of protein and carbohydrates, physical activity, sample size, study design etc.

In this context some ethnic groups need special mention. Asian Indians, largely vegetarian, have relatively lower intake of proteins as compared to predominantly non-vegetarian populations in developed countries [12]. In addition, they have lower skeletal muscle mass (“sarcopenia”) than whites [12,13]. Importantly, sarcopenia alone could determine occurrence of type 2 diabetes in this ethnic group as compared to whites and blacks [14]. It is possible

that increase in protein intake along with resistance exercises in Asian Indians, or other predominantly vegetarian individuals could improve metabolic status and also impede tendency for diabetes. This interesting issue remains to be tested.

Sources of proteins warrant a special mention here. Animal proteins contain a good balance of all the amino acids and have a higher protein digestibility corrected amino acid score (PDCASS) but are also high in saturated fat and cholesterol content. On the other hand, plant proteins are lower in fat content and have no cholesterol but the PDCASS is lower in comparison to animal proteins. As compared to plant-derived proteins such as soya, animal proteins may also lead to increased protein oxidation and energy expenditure. Dairy proteins are a combination of slow acting casein and fast acting whey protein and has PDCASS of 1. Both these variety of protein have unique role in weight loss and increasing the muscle mass when combined with physical activity. Studies show that some compounds present in whey proteins act as natural angiotensin-converting-enzyme inhibitors, which may play a role in lowering the blood pressure [15]. It has also been observed in OmniHeart trial that increasing protein at the expense of carbohydrates in the diet can lower blood pressure in pre-hypertensive and hypertensive subjects and reduce cardiovascular risk [16].

Multiple mechanisms of protein-induced weight loss have been discussed. The beneficial effects of high protein diets such as increased satiety may be due to inhibition of appetite, and reduction of food intake. The postprandial amino acid concentration influences satiety, through the stimulation of gastrointestinal hormones glucagon-like peptide-1 (GLP-1), peptide YY (PYY), and cholecystokinin [17–19]. The hypothalamic control of energy balance, mostly in the arcuate nucleus is influenced by high-protein diets. It has also been observed that reward-driven eating behavior or motivation to eat in the mesolimbic system is reduced by diets rich in protein. It is probably because of these mechanisms of action of high-protein diet on satiety and food intake, that most of the studies report increased satiety with high-protein diets [20]. Of all the essential amino acids, leucine is of particular interest, and has been shown to be crucial for muscle protein synthesis [21]. Leucine aids muscle protein synthesis through the activation of mTOR-signaling pathway and AMPK in hypothalamus [22]. Further, high-protein diets lead to weight loss by playing an important role in energy balance through diet-induced thermogenesis and ketosis pathways. It is important to note that diet-induced thermogenesis is highest after protein ingestion (~30%), as compared to that after carbohydrate ingestion (10%) and fat ingestion (5%) [23]. One possible reason could be that amino acids, in comparison with fatty

acids and glucose, are catabolized less efficiently, yielding lower net amounts of ATP [24].

Although high-protein diets are associated with various beneficial effects as discussed above, their adverse effects are a point of debate, specifically with respect to their effect on renal functions. Detrimental long-term elevation in glomerular filtration rate (GFR) has been reported after consumption of high-protein diets [25]. Although high-protein diets are considered to be relatively safe in healthy individuals, but they are not recommended in individuals with those with compromised renal functions [25].

Finally, in view of generally beneficial effects of dietary proteins on metabolism and appetite in obesity and metabolic syndrome, larger trials of such diets for prevention of diabetes are warranted, especially in south Asians/Asian Indians.

References

- [1] Konner M, Eaton SB. Paleolithic nutrition: twenty-five years later. *Nutr Clin Pract* 2010 Dec;25(6):594–602.
- [2] Comerford KB, Pasin G. Emerging evidence for the importance of dietary protein source on glucoregulatory markers and type 2 diabetes: different effects of dairy, meat, fish, egg, and plant protein foods. *Nutrients* 2016 Jul 23;8(8).
- [3] Hills AP, Arena R, Khunti K, Yajnik CS, Jayawardena R, Henry CJ, et al. Epidemiology and determinants of type 2 diabetes in south Asia. *Lancet Diabetes Endocrinol* 2018 Dec;6(12):966–78.
- [4] Misra A, Gopalan H, Jayawardena R, Hills AP, Soares M, Reza-Albarran AA, et al. Diabetes in developing countries. *J Diabetes* 2019 Jul;11(7):522–39.
- [5] Krieger JW, Sitren HS, Daniels MJ, Langkamp-Henken B. Effects of variation in protein and carbohydrate intake on body mass and composition during energy restriction: a meta-regression 1. *Am J Clin Nutr* 2006 Feb;83(2):260–74.
- [6] Gulati S, Misra A, Tiwari R, Sharma M, Pandey RM, Yadav CP. Effect of high-protein meal replacement on weight and cardiometabolic profile in overweight/obese Asian Indians in North India. *Br J Nutr* 2017 Jun;117(11):1531–40.
- [7] Bhardwaj S, Misra A, Gulati S, Anoop S, Kamal VK, Pandey RM. A randomized controlled trial to evaluate the effects of high Protein Complete (IActo) VEgetarian (PACER) diet in non-diabetic obese Asian Indians in North India. *Heliyon* 2017 Dec;3(12):e00472.
- [8] Heymsfield SB, van Mierlo CA, van der Knaap HC, Heo M, Frier HI. Weight management using a meal replacement strategy: meta and pooling analysis from six studies. *Int J Obes Relat Metab Disord* 2003 May;27(5):537–49.
- [9] Hamman RF, Wing RR, Edelstein SL, Lachin JM, Bray GA, Delahanty L, et al. Effect of weight loss with lifestyle intervention on risk of diabetes. *Diabetes Care* 2006 Sep;29(9):2102–7.
- [10] Piatti PM, Monti F, Fermo I, Baruffaldi L, Nasser R, Santambrogio G, et al. Hypocaloric high-protein diet improves glucose oxidation and spares lean body mass: comparison to hypocaloric high-carbohydrate diet. *Metabolism* 1994 Dec;43(12):1481–7.
- [11] Badely M, Parastouei K, Sepandi M, Samadi M, Ttaghdi M. The effect of whey protein on the components of metabolic syndrome in overweight and obese individuals; a systematic review and meta-analysis. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*; 2019 (current issue).
- [12] Gulati S, Misra A. Abdominal obesity and type 2 diabetes in Asian Indians: dietary strategies including edible oils, cooking practices and sugar intake. *Eur J Clin Nutr* 2017 Jul;71(7):850–7.
- [13] Misra A, Khurana L. Obesity-related non-communicable diseases: south Asians vs white Caucasians. *Int J Obes* 2011 Feb;35(2):167–87.
- [14] Ntuk UE, Celis-Morales CA, Mackay DF, Sattar N, Pell JP, Gill JMR. Association between grip strength and diabetes prevalence in black, South-Asian, and white European ethnic groups: a cross-sectional analysis of 418 656 participants in the UK Biobank study. *Diabet Med* 2017 Aug;34(8):1120–8.
- [15] De Leo F, Panarese S, Gallerani R, Ceci LR. Angiotensin converting enzyme (ACE) inhibitory peptides: production and implementation of functional food. *Curr Pharmaceut Des* 2009;15(31):3622–43.
- [16] Appel LJ, Sacks FM, Carey VJ, Obarzanek E, Swain JF, Miller 3rd ER, et al. Effects of protein, monounsaturated fat, and carbohydrate intake on blood pressure and serum lipids: results of the OmniHeart randomized trial. *J Am Med Assoc* 2005 Nov 16;294(19):2455–64.
- [17] Paddon-Jones D, Westman E, Mattes RD, Wolfe RR, Astrup A, Westerterp-Plantenga M. Protein, weight management, and satiety. *Am J Clin Nutr* 2008 May;87(5):1558S–61S.
- [18] Wren AM, Seal LJ, Cohen MA, Brynes AE, Frost GS, Murphy KG, et al. Ghrelin enhances appetite and increases food intake in humans. *J Clin Endocrinol Metab* 2001 Dec;86(12):5992.
- [19] Kissileff HR, Carretta JC, Geliebter A, Pi-Sunyer FX. Cholecystokinin and stomach distension combine to reduce food intake in humans. *Am J Physiol Regul Integr Comp Physiol* 2003 Nov;285(5):R992–8.
- [20] Wycherley TP, Moran LJ, Clifton PM, Noakes M, Brinkworth GD. Effects of energy-restricted high-protein, low-fat compared with standard-protein, low-fat diets: a meta-analysis of randomized controlled trials. *Am J Clin Nutr* 2012 Dec;96(6):1281–98.
- [21] Kurpad AV, Raj T, El-Khoury A, Kuriyan R, Maruthy K, Borgonha S, et al. Daily requirement for and splanchnic uptake of leucine in healthy adult Indians. *Am J Clin Nutr* 2001 Dec;74(6):747–55.
- [22] Cota D, Proulx K, Smith KA, Kozma SC, Thomas G, Woods SC, et al. Hypothalamic mTOR signaling regulates food intake. *Science* 2006 May 12;312(5775):927–30.
- [23] Cuenca-Sanchez M, Navas-Carrillo D, Orenes-Pinero E. Controversies surrounding high-protein diet intake: satiating effect and kidney and bone health. *Adv Nutr* 2015 May;6(3):260–6.
- [24] Westerterp-Plantenga MS, Nieuwenhuizen A, Tome D, Soenen S, Westerterp KR. Dietary protein, weight loss, and weight maintenance. *Annu Rev Nutr* 2009;29:21–41.
- [25] Friedman AN. High-protein diets: potential effects on the kidney in renal health and disease. *Am J Kidney Dis* 2004 Dec;44(6):950–62.

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