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Research Article

Weight Loss Associated with High Protein Diet Intake in Obesity: Interactions of Gut Microbiota in Protein Sources Influencing this Positive Effect

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Abstract

It has been known for some time that high protein diet prevents the development of diet induced obesity and may influence the association of metabolic disorders in mice. Dietary supplementation of various amino acids like leucine can partially mimic this effect. There has been a suggestion that high amino nitrogen intake may possibly lower storage and prevent insulin resistance. Other mechanisms include greater satiating effects of high protein diet as compared to high carbohydrate or high fat diet. This effect on satiety modulation involves multiple metabolic pathways. Protein intake induces signals leading to the release of peptide hormones like GLP-1 and PYY from the gastrointestinal tract. Also, Protein intake stimulates release of metabolic hormones which communicate energy status to the brain. Thus, long term intake of high protein diet seems to decrease food intake, weight and body adiposity in many well conducted studies. These effects are seen in 67% of population only with some gene effects as per the Dio Gene study. Still there had been a skepticism regarding a negative effect on kidney and bone health. In this review we have tried to highlight how it is not only protein per se but the additional components of nutrients which is contained in protein containing foods which influence the weight lowering ability of proteins, besides interfering with alterations in gut microbiota, which is already known as a well-known factor in influencing obesity development. Milk, dairy products have been found to be beneficial, contrary to lay press and social media belief that they need to be replaced by plant-based drinks.

Keywords: High Protein Diet; Leucine; Satiety; GLP1; PYY; Gut Microbiota; High Amino Nitrogen Intake

Introduction

In our series of work on obesity including role nutrients in metabolism, concentrating on fatty acid metabolism especially on ceramides [1], on role of PUFA's in health and obesity [2], nutrigenomics [3], here we have tried to summarize the role of high protein diets (HPD) in helping in achieving weight loss and its maintenance. Various proposed mechanisms have been highlighted besides the role of alteration of gut microbiota along with various kinds of protein sources in influencing the effect of protein on weight loss having different macronutrients contents which by themselves influence obesity like SFA, PUFA and besides interacting with gut microbiota and changing them. Also, the recent importance of POP gained from food specially sea food from environmental toxins influence impact on obesity. We have tried to tackle the controversies regarding the long-term consumption of high protein diet on bone mass and kidney dysfunction [4]. Also, other controversial topics like benefits/harm of use of milk and dairy products is considered [5]. Alongside that we have elaborated on the correlation of HPD and gut microbiota.

Materials and Methods

In this review we included data and relevant information through a PUBMED database search for articles published in English from 1985 to 2017, which included the terms weight loss, high protein diet, vegetarian, animal diet, different HPD foods, contraindications to HPD and tried to update our information regarding the role of HPD in aiding weight loss and modifications of this diet needed with different types of protein foods and changes in gut microbiota influencing the effects of these HPD in achieving the same.

Results

The electronic search yielded a total of 13,000 articles of which 7000 were relevant to HPD. After ruling out duplicate studies we selected 98 articles to update on knowledge regarding HPD in weight loss, different kinds of protein diets be it vegetarian, animal origin, those explaining normal recommendations of protein in diet and those dealing with controversies regarding use of HPD for weight loss and studies correlating changes in gut microbiota in relation to different kinds of protein diets and of persistent organic pollutants (POP) which get added with these diets. No meta-analysis was conducted.

Protein levels of a diet can be examined in relation to i) absolute amount consumed ii) proportion of total energy intake or the amount of protein/body weight. This increased protein diets are used for weight loss and maintenance, getting muscle hypertrophy and post exercise recovery.

On the basis of research in various decades FAO/WHO/UN University Expert consultation energy and Protein requirement gave a report in 1985 [6]. According to that the mean protein requirement should be set at 0.6g/kg/d with no differences in recommendation for men and women and > requirements for the elderly in view of lesser efficiency of protein utilization for them [6,7]. The Institute of Medicine has set the Recommended daily intake (RDI) of protein for 0.8g/kg body wt/d, which covers the 97. 5% of the population [8]. No Kidney problems have been shown in healthy individuals, but people having kidney disease should decrease their protein consumption. But because the acceptable macronutrient distribution range (AMDR) set by the Institute of Medicine is 10 - 35%, it should be considered high protein diet [8]. Important fact is that the quantity of protein needed to be consumed for getting optimal muscle and bone health seems to be different than that required to prevent deficiency [9]. They take a big part in achieving satiety, cellular signaling, thermogenic and glycemic regulation of the body and once protein intake is above the RDI, these metabolic processes are mostly seen [10]. No upper tolerable limit has been decided by the IMI in lieu of not much scientific evidence. But yet the risk of any side effects in healthy population at upper level seems to be very low [11]. In any case, the AMDR upper value of 35% does not match the RDI of 0. 8g/kg/day, given that if a 70 kg man consumed 2500 kcal/d and 35% came from protein, he would be consuming 219g protein/d or 3g/kg/d, which is almost 4 times the RDI for protein. Hence a modest consumption of 1.5g/kg/d can be included in the acceptable protein range for most individuals.

High protein intake might promote a negative fat balance and may be associated with decrease in fat stores. These have been shown in short term studies. The thermic effect of protein is much larger relative to carbohydrates or fat. Animal proteins have much more effect in contrast to vegetarian protein in lieu of differences in amino acid composition [12], but this needs further confirmation. Further protein causes a more satiety effect as compared to other macronutrients [13,14], irrespective of it being in drinks or in solid foods. Evidence is being provided that this effect of protein gets mediated in part by a synergistic effect of the gut satiety hormones like glucagon like peptide 1 (GLP1) and peptide YY (PYY), which get released through the small intestine [13-15]. Higher protein diets help in maintaining lean body tissue, which dictates the resting and 24h energy expenditure, which causes prevention of excessive decrease in energy expenditure [16]. This occurs more so when these high protein diets get combined with physical activity.

Astrup., *et al*. conducted a large scale multi centre trial in Europe namely The Diet, Obesity and Genes (DioGenes). This trial examined the importance of a slight increase in dietary protein content with decrease of carbohydrate and the importance of choosing low glycemic index (LGI) and high GI (HGI) for carbohydrates for weight control in 932 obese families. Adults alone were given a diet of 800 kcal/d for 8 weeks, following loss of 11 kg they were randomized to one of the following 5 energy ad libitum diets for 6 months. These diets were different in their protein content and GI. The HP diet group consumed 5.4% points more energy from protein than the normal protein (NP) groups and the LGI diet groups combination attained 5.1% lower GI than the HGI groups. The effect of HP and LGI was additive on weight loss and maintenance and this combination was further helpful in preventing weight regain and causing a reduction in dropout rates in the adults after the 11 kg weight loss. This diet simultaneously decreased body fatness and prevalence of overweight and obesity among their children and had definite beneficial effects on BP, blood lipids and inflammation in both parents and their children. Following 1 year, mainly the HP effects were maintained. Also, they identified putative genes which suggest that this diets efficacy is especially in 67% of population. Thus, they concluded that this Dio Genes diet was found to be effective for preventing weight regain and for weight reduction in overweight children under ad libitum conditions. The less restrictive dietary approach fits into a normal food culture and they transferred into popular diet and cook books in several languages [17].

Further Madsen., *et al.* 2017 studied the interaction between various diets, gut microbiota composition and obesity development. Evidence shows there is an association between intake of some dietary protein sources and obesity. They studied mainly in rodents and found that various protein sources differ, in their ability to either prevent or cause obesity. Protein sources like diets having casein, soy or beans, vegetables, dairy sea foods and meat vary in their amino acid composition. Also type of other factors like fatty acids and persistent organic pollutants differ between protein sources. All these factors can modulate the composition of the gut microbiota and hence affect these obesogenic properties [18].

There group showed that feeding obesity prone C57BL6 mice a high fat, high protein diet using casein, soy or filets of cod, beef, chicken (skinless) or pork as protein sources caused a marked difference in obesity development in thermoneutral conditions. Of these caseins was found to be maximum efficient for preventing weight gain and accumulation of adipose mass, as compared to mice in diet receiving high protein diet on basis of white meat (lean pork or chicken filets) had the highest increase in feed efficiency and adipose tissue mass [19] Also dairy and vegetarian protein sources is associated with protection against obesity, while intake of large portion of meat, especially red meats, suggests greater weight [20-22].

So far little is known on how different protein sources affect gut microbiota. Recently gut microbiota composition in caecum of rats fed protein from red meat (beef and pork), white meat (chicken and fish (along with casein and soy) were determined [23]. Animal feed consisted of 20% protein but had low 7% fat content. There was marked variation in both inter and intra group caecal composition of microbiota, with a more tight clustering of rats, fed the non-meat protein casein and soy, indicating that gut microbiota composition diverged between rats based on fed feed like meat and non-meat proteins [23]. Young rats fed a protein from chicken diet (17.7%) x 14 days had an increased relative abundance of genus Lactobacillus. But opposite pattern was observed in middle aged rats [23].

Holm., *et al.* showed that proteins from seafood caused lesser obesity as compared to terrestrial animals. Giving a mixture of Western diet which is a mixture of lean sea food namely ling, rosefish, cod wolf fish and muscle from Canadian scallop for 12 weeks in C57BL6 mice caused lower fat mass getting deposited than if mice were fed a western diet which was a mixture of skinless chicken breast, pork, tenderloin and beef sirloin [24]. When the gut microbiome was compared in the 2 groups of mice it was shown that there was relatively larger number of Bacteroides and Clostridiales, with genes which were involved in aromatic acid metabolism which was significantly higher in the microbiome of mice fed the seafood western diet [24]. Still its significance in normal physiology is not clear. Another study having similar dietary pattern, obesity development got attenuated in mice where lean pork meat was replaced by cod [19]. Also, uptake of lean seafood like white crab meat, scallop, and mixture of cod and scallop causes attenuation of diet induced obesity [25,26].

From these studies it is shown that in rodents it is the protein source which manipulates the obesity preventing effects of high protein diets, of which casein is very important for this function. These effects of proteins however do represent those of other milk derived proteins like whey, and this might be of importance in human beings. Studies have indicated that high intake of low fat dairy products causes obesity prevention [20,22]. More data show in humans that having a Dairy protein source containing 80% casein with 20% whey showed good weight lowering effects [27,28]. Unfortunately, a meta-analysis of randomized controlled trials (RCT) shows that dairy intake only promotes weight loss in combination with energy restriction [29]. Although data from group of madsen show casein causes anti-obesity effects in contrast to meat proteins from terrestrial animals and seafood [26,30], Other groups show that whey is somewhat more effective than casein [31-33] Along with decrease in weight gain whey protein intake caused lower stomach weight, along with intestinal length [33]. These animals received HFD with casein or a lactoferrin or lactoperoxide enriched whey protein isolate (WPI) at varying doses. WPI increased *lactobacillacea/Lactobacillus* and reduced *Clostridiaceae/clostridium* in HFD fed mice [33]. Shi., *et al*. gave 5%, 50% or 100% of dietary casein derived energy and exchanged it with WPI, which led to proportional decrease in body weight [34]. It was shown that as compared to casein, whey protein intake led to rise in lactobacilli and bifidobacterium rat model having colitis [35]. But drawing conclusions regarding differences in anti-obesity effects of casein, whey needs more study.

It is seen that few Bifidobacterium strains prevent obesity in rodents [36,37]. Although greater quantities of lactobacilli are seen in high fat diet fed mice [38], some particular strains of *Lactobacillus* like that of Lactobacillus planetarium [39] were found in human beings experiencing weight loss. Also adding *Lactobacillus curvatus* HY7601 and *L. Plantarium* KY1032 in diet induced obesity (DIO) mice was related to change in gut microbiome and decrease in obesity [40]. These 2 probiotic strains *L. planetarium* KY1032 and Lactobacillus curvatus HY7601 have also been shown to decease adipose mass in DIO mice [41].

Thus, studies prove that high protein diet from vegetarian sources and dairy is associated with obesity prevention [20,22], rats receiving protein from soy gain < body weight as compared to those getting beef, pork or turkey [42]. Results from both animal

and human studies have shown that soy food in general caused increased levels of Bifidobacterium and lactobacilli along with changing the ratio between Firmicutes and Bacteroides [43]. Though challenged a decreased Bacteroides-Firmicutes ratio has been associated with obesity in both human beings and animals [44,45]. Also, some strains of Bifidobacterium just like *Lactobacillus* help to prevent obesity in rodents [36,37,46]. More studies are still needed to give a causal relationship.

Role of Branched Chain amino acids (BCAA)

Besides causing protein synthesis amino acids take part in different steps involved in controlling metabolism. Intake of tryptophan or phenylalanine cause appetite regulation while that of arginine changes nitric oxide production and input of BCAA activates mammalian target of rapamycin complex 1 (mTOR1). Both casein and whey contain large amounts of BCAA like valine, leucine and isoleucine. Chronic increased levels of BCAA in mice where mitochondrial chain aminotransferase was blocked had increased energy expenditure [47]. In rats where HFD was given with addition of BCAA, obesity got attenuated [48]. Thus, because casein-whey have relatively greater amounts of BCAA it adds to their anti-obesity effects of dairy products. Adding leucine to a high fat diet having regular protein levels to that equivalent to that of diet containing high whey content, nipped obesity in bud as shown by Freudenberg [49,50]. Figure 1 highlights the various proposed mechanisms of how addition of amino acids helps in promoting weight loss, glucose homeostasis, lipid metabolism and metabolic syndrome though role of involvement of mTOR is controversial.

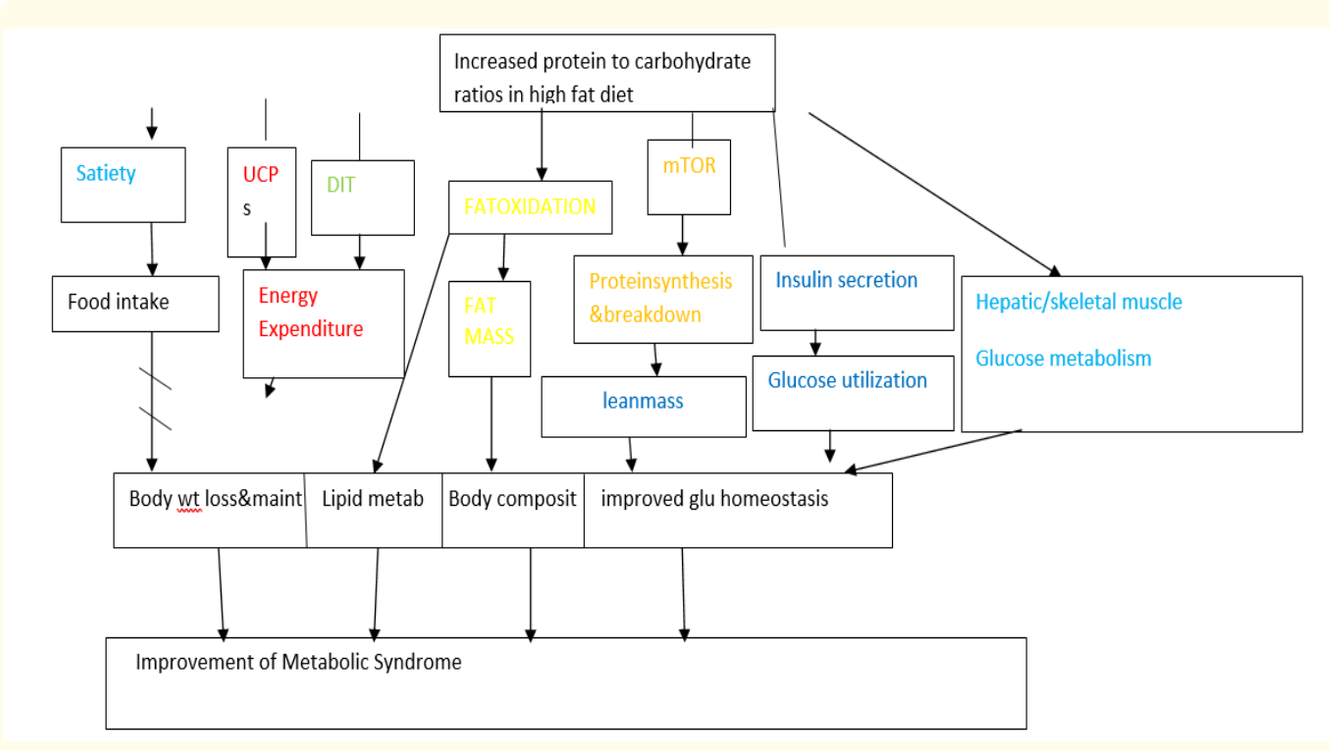

Figure 1: Simplified mechanisms of beneficial effects of dietary protein on the metabolic syndrome.
Abbreviations-UCP-Uncoupling Protein; DIT-Diet Induced Thermogenesis; Mtor-Mammalian Target of Rapamycin Complex1.

Adding BCAA in mice delayed age associated changes in the gastrointestinal tract (GIT) microbes [51]. Mice having BCAA supplementation had greater levels of *Akkermansia* and *Bifidobacterium* in the gut. Importance of this is shown by previous studies where *Akkermansia mucinphilia* is shown to protect against DIO [52,53]. Similar reports have been shown for some *Bifidobacteria* strains [34,36,46] Despite that the finding that equimolar supplementation with alanine decreased body fat mass gain in a short-term mice experiments just like that with leucine [50,54], points that some of the effects seen are not specifically caused by leucine but due to increased amino nitrogen consumption. This puts weight on fact that effect of BCAA on metabolism is complex and not well understood.

Role of Taurine

In contrast to terrestrial protein foods sea food protein contain a high level of taurine [55]. Adding taurine to the diet/drinking water prevents DIO and steatosis in rats [56-58]. In mice it seems that adding taurine decreased the abundance of Proteobacteria,

especially helicobacter and => increased short-chain fatty acids (SCFA) like acetate, propionate, butyrate, getting produced from non-digestible carbohydrates and might enter the systemic circulation and directly interfere with metabolism. Thus, SCFA generally counteract obesity in both rodents and humans [59]. But a recent examination showed that increased acetate production => hyperphagia and obesity in mice [60].

In mice fed obesogenic diets along with different taurine concentrations like chicken, cod, crab and scallop for 7 weeks, there was a correlation of intake of taurine and glycine negatively with body mass as well as total fat mass gain as shown by Tastesen 2014 [25].

Other factors determining efficacy of protein sources

Differences in fatty acids

Besides changes in amino acids various protein sources vary in different amounts of macronutrients, for development of obesity meat from terrestrial sources like red and processed meats are v high in saturated fatty acids (SFA), while meats from seafood like mackerel, halibut, salmon are rich in n3 polyunsaturated fatty acids (PUFAS). These fatty acids might affect development of obesity directly as well as indirectly by changing gut microbes. In animals it was seen that diets high in SFA's => increased adiposity and relatively low metabolic rate as compared to PUFA's [61,62]. In obese humans with abdominal obesity it was seen that SFA's promoted fat deposition in liver in contrast to PUFA'S [63]. Rosquist., *et al.* showed that in young healthy adults eating extra SFA's caused both increased fat deposits in liver and viscera in contrast to excessive n6 PUFA's consumption [64]. Once marine oils in salmon feed is exchanged with vegetable oil like soybean oil, it markedly increased the n6: n3 ratio, both in fish fillets and red blood cells (RBC's), which were drawn from mice consuming salmon [65,66]. This increased n6: n3ratio in RBC's of mice was associated with increased obesity [65-67] Even in humans n3 fatty acids promote loss of weight though more efficacy is seen in animals [68].

This high fat feeding is shown to change gut microbes as compared to obesity perse [69]. Even dietary fatty acid profile affects gut bacteriome, n3 PUFA'S as compared to n6 PUFA's feeding mice diets which were rich in SFA for 14 weeks duration reduced the Bacteroides-to Firmicutes ratio than did either PUFA diet' [70].

Akkermansia mucinphilia is also increased in DIO mice receiving fish oil, which also reduces fat mass increase and white adipose tissue (WAT) macrophage infiltration and betters gut barrier function and glucose metabolism [71]. Also, antibiotic treated mice getting gut bacteriome from a lard fed donor responded with increased adiposity and inflammation while if enriched with *Akkermansia mucinphilia* simultaneously there was part protection against obesity in those who were transplanted with microbes from fish oil fed mice [71].

Toll like receptors(TLR's) get activated by fatty acid saturated lipids from lard was proposed to induce inflammation via TLR signaling mediated by gut microbes [66]. Contrarily in middle age rat, fish oil feeding increased relative levels of Proteobacterium and genus *Desulfovibrio* along with induced inflammation as compared to rats receiving diets with soybean oil or lard [72].

Innate pathogen receptors, a part of 1st line defense against infectious agent, which include TLR, nucleotide oligomerization domain containing proteins and inflamassomes are considered a link between gut microbiota and host metabolism [73].

Also changes in gut permeability might be changed through the interaction between diet, host and gut microbes aiding access for proinflammatory molecules and activating inflammation which affects obesity development [74].

Adding lean fish in low energy diets was equally effective to addition of fatty fish or fish oil supplementation, increasing weight loss in humans [68]. Total level of n3 PUFA is much lower in lean as compared to sea food but most of fatty acids are present in phospholipid (PL) fraction [75]. Bioavailability of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) is believed to be > if they are PL bound. As the obesity affects, of PL bound n3 PUFA are better than n3 PUFA which are triacyl glyceride (TAG) bound in mice [76]. Greater biological activity of PL bound PUFA includes effects with gut mediated through endocannabinoid signaling system. The endocannabinoid signaling system links gut microbes to adipogenesis, Since cannabinoid 1 (CB1) receptors control gut permeability in an interaction with gut microbes [77]. Also changes in gut microbiome composition during obesity causes barrier dysfunction, which may cause leakage from gut of gram negative bacteria component and metabolic endotoxaemia which trigger onset of metabolic disorders related to obesity [78]. On the reverse adding intestinal bacteria *A. mucinphilia* to HFD fed mice => increase in intestinal level of 2 arachidonoyl glycerol, 2 oleoyl glycerol and 2 palmitoyl glycerol associated improved gut barrier and decreased metabolic endotoxaemia [52]. Still molecular mechanism which link gut microbes and endocannabinoid synthesis, or other bioactive lipids is not known and how they play important role in obesity development which needs to be deciphered.

Role of Persistent Organic Pollutants (POP's)

Food adds to > 90% of recent exposure to POP. This is mainly from food which is of animal origin like fish, dairy products or meat [79,80]. A lot of attention has been given to role of POP exposure and obesity in the obesity epidemic, which we are encountering. Importance has been given to how much polychlorinated bisphenyls (PCB's) and pesticides levels are present in circulation [81-83].

Definite relationship between exposure and obesity development has not been shown and inverse relationship between obesity and plasma levels of POP's, highly chlorinated PCB's has to be shown [84,85]. It is difficult to correlate directly POP exposure with obesity though PCB 153 [86] and PCB 7 7 [87] exacerbate obesity in mice. POP's from marine origin get deposited in adipose tissue along with obesity development in mice who get feeding from farmed Atlantic salmon [8I]. But mice who get increased POP's from whale meat feeding were thinner as compared to control casein fed mice, inspite of greater deposition of POP's in adipose tissue [88]. Midtbo decreased the levels of PCB's and DDT's by 50% in salmon fillets by particularly replacing fish oil with vegetable oil in this aquatic feed caused increase in insulin resistance and increased lipid diposition in liver, though PCB'S and DDT's levels got decreased [66].

There is a two directional relation between gut bacteria and environment pollutants [89]. POP exposure changes composition of gut microbes in mice. Gavage with increased mixture of PCB found in meat and fatty fish x 2 days decreased the overall levels of bacteria [90], development of which was prevented by exercise [90]. Also, it is shown that once exposed to 2, 3, 7, 8 tetra chloro-dibenzene (TCDF) shifts ratio of firmicutes: Bacteroides.

Secondly gut microbes can change the body burden by a lot of ways. Bacteria might change the enterohepatic circulation of environment chemicals as well as host detoxification capacity [91,92]. Also, Myrmel showed that dietary composition of macronutrients changes deposition of 4 important POP's in adipose tissue(AT) and liver in C57BL/6 mice [93].

Arciero., *et al*. examined the effects of protein pacing Caloric restriction in obese men and women. Short term protein pacing (P-;6meals/day, >30%protein/dayand calorie restriction (CR-25% energy deficit) improves tot al body fat, (TBF), Abdomical (ABF) andvisceral adipose tissue (VAT) fat loss, energy expenditure and biomarkers compared to heart healthy (HH) recommendations (3 meals/day, 15% protein/day) in obese adults. Yet much was not known regarding response of obese men and women to P-CR during weight loss (WL) and if mPCR is more effective than a HH diet during long-term (52 weeks) weight maintenance (WM.) So they tried to study the effect of i) PCR on TBF, ABF, RMR (resting metabolic rate) and biomarkers between obese men and women during WL (weeks 0-12) and ii) mPCR as compared to a HH diet during WM weeks (13 - 64) . During WL, men (n = 2) and women (n = 19) were assessed for TBF, ABF, VAT, RMR and biomarkers at weeks 0 (pre) and 12 (post). Both men and women had similar decreases ($p < 0.01$) in weight (10%), ABF (25%), VAT (33%), glucose (7 - 12%), insulin (40%), leptin (>50%) and increase in %lean body mass (9%). RMR (kcal/kg body weight) was unchanged and respiratory quotient decreased 9%. 24 subjects (mPCR, n = 10, HH, n = 14) completed WM, mPCR regained significantly less body weight (6%), TBF (12%) and ABF (17%) compared to HH ($p < 0.05$). Thus, they concluded their results showed that PCR increases weight loss and body composition and biomarkers, maintaining these changes for 52 weeks as compared to traditional HH diet [94].

Although high protein diet is effective in its satiating effects and achieving weight loss Cuenca Sanchez reviewed the controversies regarding negative effects of long-term consumption on bone mass loss and kidney dysfunction. However, they concluded it was only detrimental in patients having existing kidney dysfunction but not in healthy individuals [4].

Further their had been a controversy regarding use of milk and dairy products on health effects because of which there had been an increase in plant based drinks like soy, rice almond or oat. Thorning., *et al.* 2016 reviewed and found latest evidence tells that these milk and dairy products are associated with decreased risk of childhood obesity. Even in adults intake of milk and dairy products improved body composition and weight loss during energy restriction. Additionally, intake of these was associated with a neutral or reduced risk of T2DM and decreased risk of CVS disease especially stroke. Also, they had a beneficial effect on bone mineral density and no association of bone fracture fracture risk. Also, these products were inversely associated with colorectal cancer, bladder cancer and not associated with any risk of pancreatic cancer, ovarian cancer or lung cancer-although effects on prostate cancer were inconsistent. Thus, it was concluded that according to all scientific evidence milk and dairy products meet all nutrient recommendations and might protect against most chronic diseases currently seen [5].

Conclusion

Thus, this review highlights how HPD remains an efficacious method for achieving weight loss. Further modification like protein pacing calorie restriction is effective in improving total body fat, as well as abdominal body fat and VAT fat loss along with energy expenditure.

Different kinds of BCAA, like valine, leucine and isoleucine containing foods give additive effects and thus casein, whey which have high BCAA have high anti-obesity effects.

Besides that, various protein containing different levels of SFA's, PUFA's get their influence on the effects of protein either negatively or positively respectively with the detailed mechanism discussed.

Also, addition of POP which get added incidentally especially via seafood have influence on these HPD induced weight loss, which gets an important contributor with increasing environmental pollution. Also, how they influence gut microbiome is discussed.

How soy causes increased levels of *Bifidocacterium* and lactobacilli besides increasing bacteroides: firmicures ratio giving benefit of HPD as has been shown that the two probiotic strains *Lactobacillus curvatus* HY 7601 and *L. Plantarium* KY1032 cause decrease adipose mass in DIO mice. Whey protein have increased Lactobacillus and reduce clostridium in HFD fed mice.

No negative effects have been shown for long term HPD on bone mass or kidney function. Still it is considered that it may be detrimental in patients having existing kidney function, but not in healthy individuals.

Milk and dairy products have beneficial effect in childhood obesity and are useful in adults as well.

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