www.ayurpharm.com
ISSN: 2278-4772

Ayurpharm Int J Ayur Alli Sci., Vol. 11, No. 1 (2022) Pages 1 – 12

REVIEW ON KETOGENIC DIET WITH SPECIAL REFERENCE TO AVAPEEDAKA SNEHAPANA

Maya Mohan A[1*], Smitha AV[2]

1. *Associate Professor, Dept. of Panchakarma, PNNM Ayurveda Medical College, Shoranur, Kerala, India.*
2. *Associate Professor, Dept. of Swasthavritta, PNNM Ayurveda Medical College, Shoranur, Kerala, India.*

Received: 09-01-2022; Revised: 22-01-2022; Accepted: 26-01-2022

Abstract

Ketogenic diet is a high fat adequate protein, low carbohydrate diet used primarily to treat metabolic syndrome, epilepsy, disorders of urinary system and neurodegenerative disorders. *Avapeedaka snehapana* is a type of *Samana Snehapana* (oral administration of medicated lipids for alleviation of disease) in which ghee is administered in two divided dose - *Pragbhaktha Snehapana* (oral administration of lipids before food) and *Jeernanthika Snehapana* (administration of lipids after digestion of food and ghee). This *Snehapana* is similar to ketodiet where fat given in large amount induces ketogenesis. This review helps to know about ketogenesis induced by *Avapeedaka Snehapana*, the mechanism involved in treating neurodegenerative disorders, metabolic syndrome etc. This paper also focuses on adverse effect of long-term use of ketogenic diet.

Keywords: Ketogenic diet, *Avapeedaka Snehapana, Pragbhaktha Snehapana, Jeernanthika Snehapana*

***Address for correspondence:**
Dr. Maya Mohan A,
Associate Professor,
PNNM Ayurveda Medical College,
Shoranur, Kerala, India – 679 123
E-mail: dr.mayaattoor@gmail.com

Cite This Article

Maya Mohan A, Smitha AV. review on ketogenic diet with special reference to Avapeedaka snehapana. Ayurpharm Int J Ayur Alli Sci. 2022;11(1):1-12.

www.ayurpharm.com
ISSN: 2278-4772
Ayurpharm Int J Ayur Alli Sci., Vol. 11, No. 1 (2022) Pages 1 – 12

INTRODUCTION

The ketogenic diet is a high-fat, adequate protein, low carbohydrate diet that in medicine is used primarily to treat diseases like metabolic syndrome, epilepsy, neuro degenerative diseases.[1] This diet forces body to burn fats rather than carbohydrates and thus inducing ketogenesis in the body.

According to Susrutha Samhita, our body is considered as the essence of *Sneha* (lipids). Lipids form the structural and functional unit of human body and all the vital functions depend on it, hence lipids are considered as the ultimatum in the maintenance of health. [2] Therapeutically, lipids are used in various forms and modes. The lipids when used in the form of oral ingestion is termed as *Snehapana* and it is the most effective of all other modes of application of *Sneha* (lipids). Therapeutic applications of lipids are gaining much importance due to its wide indications, faster action, and easy drug delivery.

Avapeedaka snehapana (a type of lipid intake), is detailed here with its probable mode of action of ketogenesis. This is a type of *Samana snehapana* (administration of medicated lipids for alleviation of diseases), in which ghee in *Uttamamatra* (dose of ghee which digests in 24 hours) is administered in two doses - *Pragbhakta* (before food) and *Jeernanthika* (after digestion of ghee and food).[3] Thus this type of administration is similar to ketodiet, where fats are given in large amount. Here ghee induces ketogenesis in the body by breaking down of the fatty acid. Thus, produces ketosis in gradual. Ketosis is a process that happens when the body doesn't have enough carbohydrates to burn for energy. Instead, it burns fat and release ketones, which is used as source of energy. Starvation, high-fat or low-carbohydrate diet, and muscular exercises are the few natural conditions leading to ketosis.

This research paper aims to know about

- Ketogenic diet and *Avapeedaka snehapana*
- role of *Ghrita* (ghee) in inducing the ketogenesis
- the effect of a ketogenic diet on our body
- How ketogenesis is induced by *Avapeedaka Snehapana*
- to know about the mechanism of the ketogenic diet in treating neurodegenerative disorders and in reducing the bodyweight
- Comparison of indications of *Avapeedaka snehapana* with that of therapeutic indications found effective by using ketogenic diet.

Here papers have been taken related to ketogenic diet and is compared with that of *Avapeedaka Snehapana*. This will bring *Avapeedaka Snehapana* into the mainstream of practice.

KETOGENIC DIET

There are 4 different ketogenic diet available-traditional 'classic' ketogenic diet (KD), the medium-chain triglyceride (MCT) ketogenic diet, the modified Atkins diet (MAD) and the low glycemic index treatment (lGIT). The composition of the diets is discussed in Table 1. [4]

Action of *Avapeedaka snehapana* is similar to classical ketogenic diet or medium chain triglyceride ketogenic diet. Ghee is nutritionally superior to other fats because of its MCFAs (medium chain fatty acids) content, which are absorbed directly by the liver and burned to provide energy. This energy can be used to burn other fats in the system and to lose weight. Thus it helps to get into ketosis faster by increasing the ketone bodies. So it is found best for keto recipes.

www.ayurpharm.com
ISSN: 2278-4772
Ayurpharm Int J Ayur Alli Sci., Vol. 11, No. 1 (2022) Pages 1 – 12

Table 1: Composition of Ketogenic diets

Diet	Composition
Classical KD	Can be any ratio but typically 3-4:1 Based on 4:1 ratio: 90% calories come from fat, 4% carbohydrate, 6% protein
Medium Chain Triglyceride	Can be any ratio Based on 4:1 ratio: 10% LCT fat, 60% MCT fat, 20% carbohydrate, 10% protein
Modified Atkins	Approx 1.1:1 ratio 65% fat, 10% carbohydrate, 25% protein
Low glycemic index diet	Approx 0.6:1 ratio 60% fat, 10% carbohydrate, 30% protein This does not produce prominent ketosis

Ghee exclusively contains butyric acid which contribute to its distinct flavor and easy digestion. MCT (medium chain triglycerides) from ghee is used by the body to have instant energy so one does not feel fatigued even with less diet. It is observed that MCT is adsorbed quicker than LCTs (long chain triglycerides). Ghee contains no transfat, no carbohydrate, no fibre and no proteins. It has some micronutrients including vitamin A, D, E and K and essential fatty acids such as linolenic acid and arachidonic acid along with omega 3 and 6 fatty acids and choline. One table spoon of ghee contains approximately 112 calories and total fat content of 12.7 grams (7.9 g saturated and 4.2g unsaturated) as well as 32.6 milligrams of cholesterol. [5] Study shows that intake of MCT ketogenic diet resulted in increased BOHB (beta hydroxyl buteric acid) at all time, improve time to ketosis, might reduce adverse effects of keto-induction and thus increasing tolerability of very low carbohydrate diets.[6]

AVAPEEDAKA SNEHAPANAM

Avapeedaka Snehapana is a special method of internal administration of *Sneha dravya* (unctuous medicine) mentioned in the classical ayurveda texts. It is mainly indicated in *Mutravegarodhajanyavikara* (diseases due to the suppression of urge of micturition). Because of the lack of adequate review and analysis, this method of administration of *Snehapana* is losing its significance from the practices and the concept remains unexplored. *Avapeedaka snehapana* is a special pattern of *Snehapana* in which *Sneha* is administered in 2 *Kala* (period) at a stretch, that is, *Pragbhakta* (before food) and in *Jeernanthaavastha* (after the digestion of food) in *Uttamamatra* (maximal dose that digest in a period of 24 hours) respectively.[7] The word *Avapeedaka* implies the meaning of either *Peedana* (pushing down) of *Dosha* (bodily humor) or the *Peedana* of *Ahara* (food).[8] It is a type of *Samana sneha* and it can be practiced in different ways- 1/4th of ghee is taken before food,3/4th taken after digestion or 1/3rd of ghee is taken before food, 2/3rd taken after digestion as said by *Vakyapradeepika* commentary.[9] Some practitioners are also administering in the format of 1/2 part of ghee is taken before food, next half is taken after digestion. Some are practicing in a way that *Prakbhakta* dose is given as before evening meals and *Jeernanthika* dose is given in next day morning as one gets hunger. According to texts, ghee is preferred for this type administration. Oil is not preferred as it cause *Badhavitkata* [hardening of stools] and *Alpamootrata* [decreased urine production].[10] Any way many clinicians are using oils also for *Avapeedaka snehapana* and getting good results.

This *Snehapana* incorporates the concept of *Oushadhakaala* (time of administration of medicine), which helps to counter mainly *Apana* and *Vyanavayu*. *Avapeedaka snehapana* is

www.ayurpharm.com
ISSN: 2278-4772
Ayurpharm Int J Ayur Alli Sci., Vol. 11, No. 1 (2022) Pages 1 – 12

indicated in *Mootravegarodhajanyavikaras, Mootrajataram, Adhonabhija vathavyadhi*(diseases due to vitiation of vata below the umbilicus) *chikitsa*, *Raktaarsas* (bleeding piles) conditions.[7,11,12] According to Kashyapa samhita it cures diseases of *Pitta* and *Vayu*, strengthens the portions like *Uru* (thighs), *Katee* (hips). It has got *Urjaskara* (produce vigour), *Vajikarana* (aphrodisiac) and *Sramaghna* (relieves tiredness) action.[13]

As *Avapeedaka Snehapana* is indicated for *Samana* (alleviation of disease). [14] It can be used continuously up to *Samana* of disease. Administering ghee in this high dose, with little carbohydrate and proteins for some days results in ketogenesis. This clearly verify that the result of *Avapeedaka Snehapana* can be due to added on effect of ketogenesis and drug effect.

PATHOPHYSIOLOGY

Carbohydrates are the primary source of energy in our body. Glucose enters the glycolytic pathway for glucose breakdown and is then used in the form of energy. Most of the fats we eat are digested in the small intestine with the help of bile salts, pancreatic lipolytic enzymes, and intestinal lipase. After digestion, it is absorbed by intestines and are transported to the liver. In the liver, they are converted into triglycerides which is then hydrolyzed and converted into glycerol and fatty acids. Then it moves to the target tissues.

On low-carbohydrate diet, Glycogen stores deplete and certain metabolic changes happens in our body. Then the energy requirement is supplied from the oxidation of fat. For this, fats are mobilized from the depots and brought to the liver. The liver utilizes 2 metabolic processes to feed the bodies, namely gluconeogenesis as well as ketogenesis. Then, fat oxidation takes place at a fastened rate.

Gluconeogenesis is a metabolic pathway that results in generation of glucose from certain noncarbohydrate substrates like aminoacids. When glucose availability is reduced further, the endogenous production of glucose is not able to keep up with the needs of the body and the ketogenesis begins. If one consumes lots of protein in a ketodiet, gluconeogenesis may prevent ketogenesis. In general, it should take 2-4 days to enter ketosis. After 2 days of ketogenic diet, energy is generated by the oxidation of fatty acids in mitochondria, resulting in the production of large amounts of acetyl-CoA, which enters the Krebs cycle to form CO2, H2O and ATP (adenosine triphosphate). In the liver two acetyl CoA condenses to form aceto-acetyl CoA, which again produces aceto-acetate. The Aceto-acetate is either reduced to form β- hydroxybutyric acid or to acetones after decarboxylation. Aceto-acetic acid, β-hydroxybutyric acid and acetone are together called ketone bodies. The process of formation of ketone bodies is called ketogenesis. The ketones are formed at a faster rate than can be used in ketosis. They come out of the cell and enter the bloodstream. When blood level of ketone bodies rises above the renal threshold, they are eliminated through urine. [15] Excretion of acetone through the lungs, causes the fruity-sweet odour of ketosis. Normally, ketone bodies are used in the body by many tissues with the production of carbon dioxide and water without being accumulated. The end-products of the ketogenesis are ATP molecules and H+ ions.

The metabolism remains in the ketotic state, as long as the body is deprived of carbohydrates. This is referred to as "nutritional ketosis". This is considered quite safe, as ketone bodies are produced in small concentrations without any alterations in blood ph. It differs from ketoacidosis, which is a life-threatening condition.

www.ayurpharm.com
ISSN: 2278-4772
Ayurpharm Int J Ayur Alli Sci., Vol. 11, No. 1 (2022) Pages 1 – 12

In this condition, ketone bodies are produced in extremely larger concentrations, altering blood ph to an acidotic state. Once ketone bodies achieve a blood concentration similar to that of glucose, they can be transported preferentially.[16]

Ketone bodies produced in the body can be easily utilized for energy production by the heart, muscle tissue, and kidneys. Ketone bodies can cross the blood-brain barrier, thus providing an alternative source of energy to the brain. RBCs and the liver cannot utilize ketones because of lack of mitochondria and enzyme diaphorase respectively.

CLINICAL CONDITIONS WHERE KETODIET IS USED

When an adult enters the phase of ketosis, they may continue to enjoy the health advantages that come with it. Ketodiet reduces appetite, helps with faster weight loss, improves blood sugar control for patients with type2 diabetics and is effective against metabolic syndrome. It improves physical stamina so used by sportsmen for endurance events. It improves sleep, immunity, anxiety, mood changes and overall feeling of wellbeing.

Due to its neuroprotective benefits now, it is also used to treat different disorders such as refractory epilepsy, Parkinson's diseases, Alzheimer's disease, traumatic brain injury, and amyotrophic lateral sclerosis. The intake of low carbohydrate-containing food changes the body's metabolism by initiating fatty acid oxidation and thus increases the life span of the person. In this diet calories are restricted, so it also gives benefit by reducing the risk of different diseases.

AVAPEEDAKA SNEHAPANA WRT THERAPEUTIC KETOGENIC DIET

The ghee is administered as *Avapeedaka Snehapana* and *Raktashali* (brown rice) is used as diet in the form of *Yavagu* (rice gruel). Ghee contains almost 99.5 g of fat with minimal protein and zero carbohydrate per 100 g while the gruel of brown rice contains 0.9 g of fat, 2.6 g of protein, and 23 g of carbohydrate. Thus, *Avapeedaka Snehapana* shows similar combination as a ketogenic diet. [15]

Most people eat a high-carb diet, and the body uses carbohydrate for energy supply. The body can store around two-thousand calories of excess carbohydrate at any period. As the intake of carbohydrates is reduced, it produces the biochemical effect of fasting. Then the body is forced to fatty acid oxidation. Ketogenesis occurs in the body and sufficient calories are made available for normal daily activity. The transition from the use of circulating glucose to the breakdown of accumulated fat as an energy source (for starting ketogenesis) typically occurs over 3 to 4 days of consuming less than 40 or 50 grams of carbohydrates each day.

Ketosis is readily understood as the ketones can be detected in the urine and can be recognized by a characteristic smell of the individual's breath. Whenever the participant urinates, the presence of ketones and specific gravity are checked. The specific gravity tells how concentrated the urine is, and is a good indicator of dehydration.[17]

The prophylactic properties of the ketogenic diet build up with time. During the hospitalization, the participant has their blood sugar checked every six hours to watch for hypoglycemia, and treated if needed.

www.ayurpharm.com
ISSN: 2278-4772
Ayurpharm Int J Ayur Alli Sci., Vol. 11, No. 1 (2022) Pages 1 – 12

It is anticipated that as the body's carbohydrate stores are used up, their blood sugar will drop up to around 40. At this point, the body's fat stores begin to be metabolized, and the blood sugar levels go back to the normal range.

DISCUSSION

AVAPEEDAKA SNEHAPANA AS COMPARED TO KETODIET IN VARIOUS DISEASED CONDITION WITH PROBABLE MODE OF ACTION

Metabolic Syndrome

Ketogenic diet prevents weight gain and decrease appetite and cravings. Weight reduction is mediated by a reduction in hunger and an increase in energy expenditure (resting and postprandial). Lipogenesis is reduced. Lipolysis is increased. Gluconeogenesis has an increased metabolic cost. This leads to ketogenesis utilizing body fat stores.[18] KD-induced weight loss is accompanied by a mitigation in increase of circulating ghrelin. This helps avoid hunger and cravings and contribute to maintenance of weight loss. [19]

When the body burns ketone bodies, the sequencing of single-cell RNA occurs in adipose tissue, so tissue protective gamma delta and T cells become active, thus preventing inflammation in adipose tissue. This reduces diabetic risk and improves the body metabolism.

In the early morning, lower insulin levels that result from deprivation of glucose during ketogenic diets generally stop the body from producing more cholesterol.[20] This may contribute to weight reduction.

Ketogenic diet acts by inducing a state of physiological ketosis. As in this diet carbohydrate substrate is minimized, the insulin requirement comes down. This leads to resolution of insulin resistance and reduction in insulin secretion from pancreas, with a concomitant fall in glucagon production. This not only reduces rate of glucose utilization by the tissue but also decreases the fat storage, which favours fat metabolism.[21][22][23] Several hormonal changes also take place to promote rapid fatty acid mobilization in the adipose tissue. Also, epinephrine, norepinephrine, glucocorticoids, growth hormones and thyroid hormones have an influence on the fat metabolism. Keto diet can alter GnRH levels, thus can cause reduction in oestrogen. Thus, keto genic diet can be used in the treatment of PCOD as it normalizes blood sugar and oestrogen level. [24] In menopausal age, keto diet improves insulin sensitivity and improve hormonal imbalances. Insulin resistance may be linked to higher level of hot flushes. Thus overall, it is found effective in metabolic syndrome by reducing insulin resistance.

Prameha is caused due to vitiation of *Mootravaha srotas*. In *Mootravahasroto vikaras*, *Avapeedaka snehapana* is indicated. It may be understood that *Avapeedaka Snehapana* can also mobilize the fat in the body. Almost 50% fat depositions in the body are found in the perirenal tissues, mesenteries, and omentum. These areas are present in the *Adho nabhipradesha* (below the umbilicus), which is one among the indications of *Avapeedaka Snehapana*.

Neuroprotective action of Ketodiet

Ketogenic diet shows neuroprotective effects and studies show its efficacy for a number of neurological disorders including epilepsy, Alzheimer's disease, Parkinson's disease, sleep disorders, headache, traumatic brain injury, amyotrophic lateral sclerosis, autism. Ketone bodies are used as an alternative source of energy in the brain instead of glucose. During prolonged starvation, the human brain can use an

www.ayurpharm.com
ISSN: 2278-4772
Ayurpharm Int J Ayur Alli Sci., Vol. 11, No. 1 (2022) Pages 1 – 12

appreciable amount of ketones bodies. In brain, ketone bodies are transformed into acetyle CoA and this enter tricarboxylic acid cycle in the mitochondria of brain, which ultimately leads to production of ATP. Thus, it is understood that *Avapeedaka Snehapana* is an advisable method of treatment for neurological disorders.1n 2008, Neal.et.al conducted first randomized controlled trail to assess the efficacy of KD in epilepsy in children. KD group experienced 75% reduction in seizure frequency after 3 months compared to controls. When epilepsy is drug resistant, other options like KD can be used for epilepsy control. [25] Childrens of ASD (Autism Spectrum Disorder) display an array of mitochondrial dysfunction. Studies in murine models shows that ketogenic diet improves mitochondrial function by enhancing mitochondrial biogenesis.[26]

Oxidative stress and mitochondrial dysfunction are the central features of brain neurodegenerative diseases like including Alzheimer's Disease and Parkinson's Disease. The goal of neuroprotection is either a slowing down or a complete stop of the processes, which leads to neuronal death in the CNS.[27]

Increased production of ketone bodies by the liver and reduction in blood glucose concentration are key factors for the therapeutic effects of Ketogenic Diet.

Mitochondrial dysfunction and enhanced apoptosis, accompanied by a poor antioxidant status are the mechanisms of Alzheimer's Disease pathogenesis. The gradual and selective loss of dopaminergic neurons in the substantia nigra pars compacta and imbalance in dopamine metabolism due to oxidative stress forms the pathology of Parkinsons Disease.[28]

Ketogenic diet increases mitochondrial respiration via an increase in ATP (adenosine triphosphate) production. This may be responsible for neuroprotective action. It should be mentioned that β-hydroxybutyrate provides more energy for the brain per unit of oxygen than glucose. Ketogenic diet also reduces the production of free radicals by improving the efficiency of the mitochondrial respiratory chain complex increasing NADH (nicotinamide adenine dinucleotide) oxidation and inhibiting mitochondrial permeability transition. [29] Antioxidant action of KD results also from the increase in glutathione and glutathione peroxidase activity. In research on rats, it is observed that the increase in antioxidant activity in the hippocampus was accompanied by an increase of glutathione peroxidase. It is suggested that the higher activity of this enzyme, induced by the ketogenic diet in the hippocampus, might contribute to the protection of this structure from neurodegenerative changes. [30] Next discussed mechanism of KD action is the ability to abate apoptosis. In addition to this, KD control the stabilization of nerve-cell synapse functions. Moreover, the selected polyunsaturated fatty acids (e.g., arachidonic acid, docosahexaenoic acid, and eicosatetraenoic acid) may promote excitability of neuron-cell membranes, by reducing inflammatory conditions and suppressing the production of free radicals. [31]

Additionally, the restriction of calories exert a neuroprotective effect by (a) improving mitochondrial functions, leading to the reduction of reactive oxygen species (ROS) production and increased energy output (b) by decreasing inflammatory and pro-apoptotic activities (c) increasing levels of neuroprotective factors, such as neurotrophins (brain-derived neurotrophic factor (BDNF), neurotrophin-3–NT-3, glial cell line-derived neurotrophic factor (GDNF)) and molecular chaperones (proteins that prevent aggregation of polypeptides into potentially toxic components). Caloric restriction also has anti-inflammatory effects. It reduces levels of NFκB, the central component of the inflammatory

www.ayurpharm.com
ISSN: 2278-4772
Ayurpharm Int J Ayur Alli Sci., Vol. 11, No. 1 (2022) Pages 1 – 12

process and block the synthesis of interleukins (IL1β, IL2, IL4, IL6), tumor necrosis factors (TNFα) and suppresses the activity of cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS). [32]

Some theories have been advanced about how it modifies the neuronal metabolism and excitability in epilepsy in order to reduce the seizure frequency. Possibly, the real mechanism of reduction of cortical hyper excitability involves multiple factors. Metabolic changes in the blood and cerebrospinal fluid (CSF), including a decrease in glucose levels and an increase in ketone bodies may be the cause for seizure reduction. The mitochondria function and energy reserve may also play a role in the KD mechanisms, resulting in synapse stabilization and excitatory decrease. [33]

Abnormal glucose metabolism uptake, diminished mitochondrial-associated brain energy metabolism, changes in neurotransmitter release, and increased inflammatory response are the key pathophysiological metabolic alterations observed in Alzheimer's Disease. KD may modulate metabolic and signaling changes underlying the pathophysiology of neurodegenerative disorders. It is associated with improved cognitive performance in elderly adults with Alzheimer's Disease. The improvement of the cognitive outcomes depends on the level and duration of ketosis. The best results of KD treatment are expected in early pre symptomatic stages of Alzheimer's Disease.

Avapeedaka snehapana can be compared to *Samudga prayoga* which is said in *Oushadhakala* [time of administration of medicine]. *Samudga prayoga* is the administration of medicine given before and after light food. This type of administration is indicated in *Kampa* [tremors], *Akshepaka* [convulsions], *Hidma* [hiccups] etc. conditions which can be correlated to Parkinsons like neuro degenerative conditions. [34]

Disorders of urinary system

In ketosis, the ketone is formed at a faster rate than can be used. When blood level of ketone bodies rises above the renal threshold, they are excreted in the urine. This is known as ketonuria. During ketosis, there is a high number of acids in the urine and is associated with acidosis in the body. During the maintenance of the acid-base balance, Na ions are lost from the plasma. Thus, there is loss of body fluids resulting in the dehydration. Thus, ketogenic food can increase the urine output. Thus, we can explain the effect on *Mutravegarodhajanya vikara* and *Mutravahasrotodushti*.

Mutravegarodhajanyavikara (diseases due to suppression of urge of urine) includes *Angabhanga* (body pain), *Asmari* (urinary calculi), *Vastivedana* (pain in urinary bladder), *Medravedana* (pain in penis), *Vankshanavedana* (pain in the inguinal region).[7] In all these conditions, frequent micturition is important to pacify the condition, so diuresis is adopted as main line of treatment.

Studies found that ketogenic diet is effective in the treatment of infections of urinary tract. In the study they gave lipids: others in ratio 3.5:1. It was found that rapid initial fall in urinary pH by 5 days and which is then maintain low till 3rd week. Acetone bodies were produced in urine and is appeared in greatest amount during first 5 days and by the end of 3 weeks it had become very much diminished. This makes bacterial colony die. The successful use of the ketogenic diet in the treatment of urinary infections is dependent on the bactericidal action of beta-oxybutyric acid at a certain degree of acidity.[35]

In another study, the effect of Ketogenic Diet in testosterone propionate induced BPH is

www.ayurpharm.com
ISSN: 2278-4772
Ayurpharm Int J Ayur Alli Sci., Vol. 11, No. 1 (2022) Pages 1 – 12

investigated. Prostatic tissue weight gain is a marker of BPH progression. The weight reduction might be related to the ability of Ketogenic Diet to modulate the synthesis of hormone testosterone. KD ingestion leads to decrease in circulating testosterone as well as gonadotrophins - LH and FSH. LH is responsible for testosterone synthesis. Its decrease would have repressed the testosterone synthesis. Thus, inhibiting BPH progression. HMG CoA (3-hydroxy-3-methyl-glutaryl coenzyme A) reductase enzyme in cholesterol synthesis is decreased in KD consumption. This leads to inhibition of cholesterol synthesis (a precursor of testosterone synthesis) which will subsequently reduce incidence and progress of BPH.[36]

Fasting plasma insulin has been linked to BPH and incident aggressive and lethal prostate cancer. Nearly all of normal cells have flexibility to adapt to using ketone bodies for fuel in place of glucose. But prostate cancer cells do not have this metabolic flexibility. Hence, they effectively starve to death, while all normal cells operate more efficiently than before. Thus, by keto diet, the cancer cells starve. So, it can be given in other cancers also.[37]

Apanavata is responsible for the proper functioning of micturition, defecation, semen ejaculation, menstrual blood, and childbirth.[38] *Apanavayu* is hampered in the clinical conditions like *Ashmari* (urinary calculi), *Udavarta* (upward movement of *vata*) and *Mutrakrichra* (dysuria). So *Avapeedaka snehapana* can be clinically administered. Ketogenic food can increase the urine output and thereby may have an influence on *Mutravegarodhajanya vikara* and *Mutravahasrotodushti vikaras*.

In ketogenic diet, calories are restricted and benefits by reducing the risk of different diseases. Thus increases the life span of the person.

Keto diet produces health benefits in short term. Researches has shown that ketogenic-diets generally work only in the short term and could be unhealthful.

Adverse effects of the Ketogenic diet

Studies on the adverse effects of KD administration is limited in the adult population. Some effects such as hypoglycemia and dehydration are seen. KBs were considered toxic resulting from the association of therapeutic ketosis with diabetic ketoacidosis, which results in ketone concentrations higher than 20 mm, which can be reversed with insulin administration.[39] Hyperketonemia due to insulin deficiency may lead to severe acidosis and even death of the individuals.[46][40] The adverse effects frequently reported by patients are gastrointestinal effects, weight loss, and transient hyperlipidemia.[44] Gastrointestinal side effects include constipation, nausea, vomiting, and lower appetite.[44][41] Weight loss by ketogenic diet should be monitored and regulated. It is seen that the change in lipid profile, such as fasting total serum cholesterol, triglycerides, and low-density lipoprotein (LDL) cholesterol is increased at the beginning of the KD treatment then it normalizes after 1 year.[42] Moreover, dehydration, hepatitis, pancreatitis, hypoglycemia, hyperuricemia, hypertransaminasemia, hypomagnesemia, and hyponatremia are also seen as adverse effects of the KD.[45][41] Also prolonged use of ketogenic-diet produces progressive loss of bone mineral content associated with poor bone health status.[46]

On the other hand, prolonged KD may cause enhanced atherosclerosis, cardiomyopathy, nephrolithiasis, impaired hepatic functions, neuropathy of the optic nerve, anemia, and deficiencies of vitamins and mineral components.[45] Chronic KD treatment may cause disturbances in catabolism and reduced

www.ayurpharm.com
ISSN: 2278-4772
Ayurpharm Int J Ayur Alli Sci., Vol. 11, No. 1 (2022) Pages 1 – 12

synthesis of functional proteins. Considering the loss of appetite and lower organoleptic attractiveness, it would be difficult to achieve an appropriate supply of protein and nutrients. The nutritional deficiency or insufficient protein intake may produce severe consequences for health.[45][47] But any significant adverse effects were not observed in 83 obese patients when the KD was administered for 24 weeks.[43] Additionally, in patients with Alzheimer's Disease, KD may significantly affect food consumption via disturbances in the senses of smell and taste, neurological symptoms, such as apraxia, dysphagia, and behavioral disturbances during eating.[45]

CONCLUSION

Avapeedaka snehapana can be given as medication for many diseases. As this type of *Snehapana* produces ketosis in the body, it can be told to be like ketogenic diet. This can be correlated to classical KD or MCT KD. Here ghee is preferred as it gets into ketosis easily. But not recommended for long term use as it could be unhealthy as it can cause deficiency of many nutrients which are essential. Also, *Avapeedaka Snehapana* is told as *Samana Sneha*, which is medicine used for alleviation of disease, and it is to be used up to the *Samana* of disease. In *Avapeedaka Snehapana*, special care should be taken while doing on diabetic patients who is taking oral medicines / insulin as there is chance of serious hypoglycemia and also ketoacidosis. So short term use of *Avapeedaka Snehapana* is advisable for many clinical conditions and is found effective with least side effects.

REFERENCES

1. Ketogenic diet. Retrieved from: https://en.wikipedia.org/wiki/Keto_genic_diet [Accessed on: 02/01/2022]
2. Susrutha. Susrutha Samhitha, Vol. 2. Srikanthamurthy KR, editor. 2nd ed. Varanasi: Choukambha Orientalia; 2004. Chikitisasthana, 31/ 4. p.507.
3. Vagbhata. Astanga Hridaya. Bhisagacharya Harishastri Paradkar, editor. 1st ed. Varanasi: Chaukambha Krishnadas Academy; 2019. Sootrasthana, 4/6-7. p.48.
4. Dhamija R, Eckert S, Wirrell E. Ketogenic diet. *Can. J. Neurol. Sci.* 2013;l40:159-160.
5. Kumar A, Tripathi S, Hans N, Falguni Pattnaik, Naik SN. Ghee: Its Properties, Importance and Health Benefits. LIPID UNIVERSE, 2018;64.
6. Cliff J. d C. Harvey, Grant M Schofield, Micalla Williden, Joseph A. McQuillan. The Effect of Medium Chain Triglycerides on Time to Nutritional Ketosis and Symptoms of Keto-Induction in Healthy Adults: A Randomised Controlled Clinical Trial. Hindawi Journal of Nutrition and Metabolism, 2018. Retrieved from: https://doi.org/10.1155/2018/2630565 [Accessed on: 02/01/2022]
7. Vagbhata. Astanga Hridaya. Bhisagacharya Harishastri Paradkar, editor. 1st ed, Varanasi: Chaukambha Krishnadas Academy; 2019. Sootrasthana, 4/6-7. p.48.
8. Vagbhata. Ashtanga Hridayam (Commentaries of Sarvangasundari of Arunadatta and Ayurveda Rasayanam of Hemadri). Murthy KRS, editor. 5th ed. Varanasi: Chowkhambha Krishnadas Academy; 2001. Sutrasthanam, 4/6. p.50.
9. Vagbhata. Ashtanga Hridayam (Vakyapradeepika commentary by Parameswara), Part 1. 1st ed. Kottayam: Vaidyasarathy Press; 1950. Sootrasthana, 4/6-7. p.53.
10. Vagbhata. Astanga Hridaya. Bhisagacharya Harishastri Paradkar, editor. 1st ed. Varanasi: Chaukambha Krishnadas Academy; 2019. Sootrasthana, 4/6-7. p.54.
11. Vagbhata. Astanga Hridaya. Bhisagacharya Harishastri Paradkar, editor. 1st ed. Varanasi: Chaukambha Krishnadas Academy; 2019. Chikitsa sthanam, 21/15. p.723.
12. Vagbhata. Astanga Hridaya. Bhisagacharya Harishastri Paradkar, editor. 1st ed. Varanasi: Chaukambha Krishnadas Academy; 2019. Chikitsa sthanam, 8/24. p.510.
13. Vriddha Jeevaka. Kasyapa Samhita. Tewari PV, editor. 1st ed. Varanasi: Chaukhambha Visvabharathi; 2013. Sootrasthanam, 22/47. p.34.
14. Vagbhata. Astanga Hridayam (Hridayabhodhika commentary by Sridharapandita), Part 1. 1st ed. Thiruvananthapuram: Ayurveda department, Travancore State Government; 1940. Sootrasthanam, 16/18. p.120.

15. Kadambari PB, Dharmarajan P, Prathibha CK, Anandaraman PV. Critical Review on the Concept of Avapeedaka Snehapana - A Special Mode of Lipid Administration. J Evidence-Based Integrative Medicine, 2018;23:1-5.
16. Wajeed Masood, Pavan Annamaraju, Kalyan R. Uppaluri. Ketogenic Diet. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022.
17. Alharbi A, Al-Sowayan NS. The Effect of Ketogenic-Diet on Health. Food and Nutrition Sciences, 2020;11:301-313.
18. Hall KD, Chen KY, Guo J, et al. Energy expenditure and body composition changes after an isocaloric ketogenic diet in overweight and obese men. Am J Clin Nutr. 2016;104(2):324-333.
19. Sumithran P, Prendergast LA, Delbridge E, et al. Ketosis and appetite-mediating nutrients and hormones after weight loss. Eur J Clin Nutr. 2013;67:759-764.
20. Dowis K, Banga S. The Potential Health Benefits of the Ketogenic Diet: A Narrative Review. *Nutrients*, 2021;13(5):1654.
21. Raghad A Alarim, Faris A Alasmre, Hammam A Alotaibi, Mohammed A Alshehri, Sara A Hussain. Effects of the Ketogenic Diet on Glycemic Control in Diabetic Patients: Meta-Analysis of Clinical Trials. *Cureus*, 2020;12(10):e10796.
22. Jornayvaz FR, Jurczak MJ, Lee HY, et al. A high-fat, ketogenic diet causes hepatic insulin resistance in mice, despite increasing energy expenditure and preventing weight gain. Am J Physiol Endocrinol Metab. 2010;299:E808-815.
23. Paoli A, Rubini A, Volek JS, Grimaldi KA. Beyond weight loss: A review of the therapeutic uses of very-low-carbohydrate (ketogenic) diets. Eur J Clin Nutr. 2013;67(8):789-796.
24. Antonio Paoli, Laura Mancin, Maria Cristina Giacona, Antonino Bianco, Massimiliano Caprio. Effects of a ketogenic diet in overweight women with polycystic ovary syndrome. J Transl Med. 2020;18(104):1-11.
25. Neal EG,Chaffe H, Schwartz RH, Lawson MS, Edwards N, Fitzsimmons G, Whitney A, Cross JH. The ketogenic diet for the treatment of childhood epilepsy: A randomized controlled trail. Lancet Neurol. 2008;7(60):500-506.
26. Selfridge JE, Wilkins HM, E L, Carl SM, Koppel S, Funk E, Fields T, Lu J, Tang EP, Slawson C, Wang W, Zhu H, Swerdlow RH. Effect of one month duration ketogenic and non-ketogenic high fat diets on mouse brain bioenergetic infrastructure. *J Bioenerg Biomembr*. 2015; 47:1–11.
27. Rusek M, Pluta R, Ułamek-Kozioł M, Czuczwar SJ. Ketogenic Diet in Alzheimer's Disease. Int J Mol Sci. 2019;20(16):3892.
28. Włodarek D. Role of Ketogenic Diets in Neurodegenerative Diseases (Alzheimer's Disease and Parkinson's Disease). Nutrients. 2019;11(1):169.
29. Susan A. Masino, Jong M Rho. Mechanisms of ketogenic diet action. Jeffrey L Noebels, Massimo Avoli, Michael A Rogawski, Richard W Olsen, Antonio V Delgado-Escueta, editors. In: Jasper's Basic Mechanisms of the Epilepsies [Internet]. 4th ed. Bethesda (MD): National Center for Biotechnology Information (US); 2012.
30. Ziegler D.R., Ribeiro L.C., Hagenn M., Siqueira I.R., Araújo E., Torres I.L., Gottfried C., Netto C.A., Gonçalves C.A. Ketogenic diet increases glutathione peroxidase activity in rat hippocampus. *Neurochem. Res.* 2003;28:1793–1797.
31. Stafstrom CE, Rho JM. The ketogenic diet as a treatment paradigm for diverse neurological disorders. *Front. Pharmacol.* 2012;3:59.
32. Maalouf M, Rho JM, Mattson MP. The neuroprotective properties of calorie restriction, the ketogenic diet, and ketone bodies. *Brain Res. Rev.* 2009;59:293–315.
33. D' Andrea Meira I, Romão TT, Pires do Prado HJ, Krüger LT, Pires MEP, da Conceição PO. Ketogenic Diet and Epilepsy: What We Know So Far. Front Neurosci. 2019;13:5.
34. Vagbhata. Ashtanga Samgraham (Sasilekha commentary). Shivprasad Sharma, editor. 1st ed. 19th Series. Varanasi: Choukhambha Sanskrit Series Office; 2006. Sootrasthanam, 23/20.p.180.
35. Robb DC. The ketogenic diet in the treatment of infections of the urinary tract. Br Med J. 1933;2:1158-1162.
36. Omowumi Titilola Kayode, Adetomiwa Victor Owolabi, Azeez Abideen Abolanle Kayode. Biochemical and histomorphological changes in testosterone propionate-induced benign prostatic hyperplasia in male Wistar rats treated with ketogenic diet. Biomed Pharmacother. 2020;132:110863.
37. Daniela D Weber, Sepideh Aminazdeh-Gohari, Barbara Kofler. Ketogenic diet in cancer therapy. *Aging*, 2018;10(2):164-165.
38. Marta Rusek, Ryszard Pluta, Marzena Ułamek-Kozioł, Stanisław J Czuczwar. Ketogenic Diet in

Alzheimer's Disease. Int J Mol Sci. 2019;9;20(16):3892.
39. Sami A Hashim, Theodore B VanItallie. Ketone body therapy: from the ketogenic diet to the oral administration of ketone ester. J. Lipid Res. 2014;55(9):1818-1826.
40. Ryszard Pluta, Mirosław Jabłoński. The ketogenic diet for epilepsy therapy in children: quo vadis? Nutrition 2011;27(5):615–616.
41. Marzena Ułamek-Kozioł, Ryszard Pluta, Anna Bogucka-Kocka, Stanisław J Czuczwar . To treat or not to treat drug-refractory epilepsy by the ketogenic diet? That is the question. Ann. Agric. Environ Med. 2016;23(4):533-536.
42. Pavel Klein, Jaromir Janousek, Arkady Barber, Randi Weissberger. Ketogenic diet treatment in adults with refractory epilepsy. Epilepsy Behav. 2010;19(4):575-579.
43. Hussein M Dashti, Thazhumpal C Mathew, Talib Hussein, Sami K Asfar, Abdulla Behbahani, Mousa A Khoursheed, Hilal M Al-Sayer, Yousef Y Bo-Abbas, Naji S Al-Zaid. Long-term effects of a ketogenic diet in obese patients. Exp. Clin. Cardiol. 2004;9(3):200-205.
44. Tanya J. W. McDonald and Mackenzie C. Cervenka. Ketogenic Diets for Adult Neurological Disorders. Neurotherapeutics. 2018;15(4):1018-1031.
45. Włodarek D. Role of ketogenic diets in neurodegenerative diseases (Alzheimer's disease and Parkinson's disease) *Nutrients.* 2019;11:169.
46. Antonio Paoli, Antonino Bianco, Ernesto Damiani, Gerardo Bosco. Ketogenic diet in neuromuscular and neurodegenerative diseases. *Biomed. Res. Int.* 2014; 2014:474296.
47. Matthew K Taylor, Debra K Sullivan, Jonathan D Mahnken, Jeffrey M Burns, Russell H Swerdlow. Feasibility and efficacy data from a ketogenic diet intervention in Alzheimer's disease. Alzheimer's Dement. (NY) 2018;4:28-36.

Source of Support: Nil Conflict of Interest: None Declared