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ORIGINAL ARTICLE

A Comparative Study of Cholesterol Levels in Non-Pregnant Females Taking Ketogenic Versus Low Calorie Diet

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ABSTRACT

Introduction: Over the past few years, the population of Pakistan has become much aware of the need of weight loss and healthy lifestyle. We evaluated the cholesterol profiles to observe how keto diet and low-calorie diet influence the basic lipid profile of females.

Aims: The aim of this study was to compare the cholesterol and triglyceride levels in adult non pregnant females taking ketogenic versus low calorie diet for a one month

Methodology: The design of this study was a cross sectional study design. This study was conducted in lady reading hospital Peshawar and the duration of this study was from January 2022 to February 2022. 60 non pregnant females of age between 35-45 years with BMI ranging between 30-34.9 were included in the study. 30 were on low calorie diet, 30 were on keto diet. The serum cholesterol and triglyceride levels were calculated on day 1 and day 30 of the study.

Results: The serum chloesterol levels were significantly reduced in individuals taking low calorie diet as compared to keto diet over a period of thirty days. After few weeks, anthropometric and body composition measurements revealed a significant reduction significant decrease in glucose and insulin blood levels were observed, together with a significant improvement of body weight. There was a significant, slightly decrease of LBM. A significant decrease of triglycerides, total cholesterol and LDL were observed along with a rise in HDL levels. The LH/FSH ratio, LH total and free testosterone, and DHEAS blood levels were also significantly reduced. Estradiol, progesterone and SHBG increased. The Ferriman Gallwey Score was slightly, although not significantly, reduced.

Practical Implication: to determine the effects of a ketogenic diet (KD) in women age with a diagnosis of PCOS. We hypothesized that a modified KD (KEMEPHY diet) would lead to an improvement in body weight, plasma cholesterol, triglycerides, hyperinsulinemia, and hormonal outcomes

Conclusion: Low calorie diet was significantly better than ketogenic diet in reducing serum cholesterol and triglyceride levels in individuals on a 30-day diet plan of respective type. Our results suggest that a ketogenic diet may be considered as a valuable nonpharmacological treatment for Polycystic ovary syndrome. Longer treatment periods should be tested to verify the effect of a ketogenic diet on the dermatological aspects of Polycystic ovary syndrome.

Keywords: Cholesterol, Ketogenic Diet, Serum, Lifestyle, Low Calorie, Nutritionist

INTRODUCTION

Over the past few years, the population of Pakistan has become much aware of the need of weight loss and healthy lifestyle [1]. However, the commercialization of the need has led to formulation of a weight loss industry with various people practicing in the field, and various products available in the market. Moreover, with the advent of social media and blogging culture, numerous self-proclaimed dieticians and nutritionists have misguided the masses about the basics of weight loss. They opt for an easy and quick pathway for weight loss [(2)]. However, gross comparisons of these diet regimes in various populations are missing. In our study, we had enrolled a bunch of enthusiastic females visiting a nutrition and fitness clinic in a posh area of Lahore opting for either ketogenic diet or low calorie based on diet. After a span of one month, we evaluated their cholesterol profiles to observe how both these diet regimes influence their basic lipid profile.

Polycystic ovarian syndrome (PCOS) is considered the most common endocrine disorder in women in the reproductive age, with an estimated prevalence ranging from 6 to 15%, depending on the diagnostic criteria used. PCOS, in fact, is a heterogeneous condition with variable phenotypic expression leading to significant controversy on the diagnostic criteria [(1)]. Women with PCOS often seek care for menstrual disturbances (oligomenorrhea, amenorrhea, prolonged irregular menstrual bleeding), clinical manifestations of hyperandrogenism and infertility. Hirsutism is a common clinical presentation of hyperandrogenism occurring in up to 70% of women with PCOS and is evaluated using the Ferriman–Gallwey scoring system [2].

Common signs of PCOS not included in diagnostic criteria are represented by insulin resistance, reversal of the FSH/LH ratio and obesity, which is an important clinical feature of PCOS. Women with PCOS have increased visceral and subcutaneous body fat due to higher androgen levels. Obesity also plays a significant role in explaining the metabolic characteristics of PCOS: patients display an atherogenic lipid profile, associated with elevated levels of low-density lipoprotein, triglycerides and cholesterol, along with reduced levels of high-density lipoprotein [(3)]. However, it is important to remark that these metabolic abnormalities may also be present in nonobese patients [(4)]. The positive correlations between hyperinsulinemia and androgen levels suggested that insulin contributes to hyperandrogenism in women with PCOS. The ovaries of PCOS patients usually maintain a normal response to insulin. A partial elucidation of this mechanism is explained by the action of insulin on the ovary through the IGF-1 receptor. This binding occurs when insulin reaches high concentrations, as in compensatory hyperinsulinemia. Insulin actions on the ovary are also mediated by the glycan molecules that contain D-chiro-inositol (DCI) [(5)], a different second messenger from the classical one activated by phosphorylation of the receptor at tyrosine level in other tissues. Hyperinsulinemia stimulates thecal cell proliferation, amplifies LH mediated androgen secretion and increases expression of LH and IGF-1 receptor [(6)]. Furthermore, high insulin levels inhibit both the production of sex hormone binding globulin (SHBG) by the liver, causing increased levels of free testosterone [(7)], and the synthesis of IGF-BP1, increasing level of free IGF-1 [(8)].

Interestingly, excess carbohydrate intake and low-grade inflammation mutually interact with insulin resistance and hyperandrogenism to reinforce the metabolic phenotype of PCOS [(9)]. In fact, acute hyperglycemia is known to increase inflammation

and oxidative stress through generation of reactive oxygen species (ROS) [10]. PCOS women present a peculiar dietary pattern, characterised by reduced use of extra-virgin olive oil, legumes, seafood and nuts, a lower amount of complex carbohydrate, fiber, monounsaturated fatty acids, and higher simple carbohydrates, total fat and saturated fatty acid, compared to normal women. These nutritional habits are associated to an adverse body composition, characterised by reduced fat-free mass [11].

A univocal therapy for PCOS does not exist; the peculiar heterogeneity of this pathology requires that the treatment should be personalized, depending on the clinical presentation and needs of the patient.

The current guidelines as first-line treatment for menstrual irregularities, acne and hirsutism recommends hormonal contraceptives, at any age. Antiandrogens are suggested in the case that estroprogestinics are contraindicated or in the presence of severe hirsutism.

Metformin has long been used in therapeutic protocols, although alternatives are investigated, because of gastroenteric side effects; inositol represents an alternative approach. Anyway, metformin does not increase weight loss in patients treated with lifestyle modifications (diet and exercise programs). Therefore, diet and exercise, not metformin, should be the first line of therapy in obese women with PCOS. Metformin should be considered if the patient fails with diet and exercise [12]. Weight loss represents the most important factor to improve PCOS phenotype. A 5–10% weight loss improves ovulatory function and pregnancy rates, with reduction of insulin and free testosterone levels. However, even though lifestyle modification based on the principles of caloric restriction remains a primary therapy for PCOS and caloric restriction seems more important than macronutrient composition [13,14], little data are available about diet's macronutrient modification as therapeutic approach [15-17]. Indeed, it is controversial whether diet composition per se has an effect on reproductive and metabolic outcomes. Blood glucose levels are affected by carbohydrate intake and regulate insulin secretion from the pancreas, so very-low carbohydrates diets may be superior to standard hypocaloric diets in terms of improving fertility, endocrine/metabolic parameters, weight loss and satiety in women with PCOS [18]. Considering all aforementioned conditions, it would be reasonable that a ketogenic diet (KD) might has positive effects on PCOS. A KD is a nutritional protocol in which carbohydrates are lower than 30 g per day or 5% of total energy intake [19-21] relative increase in the proportions of protein and fat. The reduction of the amount of circulating glucose and insulin produces a reduction of the oxidation of glucose and an increase of the fat oxidation as showed by the reduction of the respiratory ratio [22] Another important effects of KD for PCOS is the activation of AMPK and SIRT-1, even in the absence of caloric deprivation [23]. Once activated, SIRT1 and AMPK produce beneficial effects on glucose homeostasis and improve insulin sensitivity [24].

The therapeutic role of KD has been investigated for a long time and several works have supported the thesis that physiological ketosis can be useful in many pathological conditions, such as epilepsy, neurological diseases, cancer (with a ketogenic isocaloric diet) and obesity, type 2 diabetes, acne, and the amelioration of respiratory and cardiovascular disease risk factors (with a generally low calorie ketogenic diet) [25]. This is an important aim, since the use of food as a drug has very relevant social and economic implications, both in economic and social terms. In PCOS, evidence for the effects of KD are scarce: only a small uncontrolled pilot study showed a significant reduction in body weight, free testosterone, LH to FSH ratio, and fasting insulin after a KD regimen, suggesting favorable effects in affected patients. Other data describe several mechanisms consistent with the favorable effects of such diet therapy [26]. A recent position statement of the Italian Society of Endocrinology suggested a weight-loss program with a very low-calorie ketogenic diet for overweight/obese patients with PCOS) not responsive to multicomponent standardized diet to improve insulin resistance, ovulatory dysfunctions and hyperandrogenemia, even if further controlled studies are deemed necessary to confirm the beneficial effects of KD in this clinical context [27]. Thus, aim of the present study was to determine the effects of a ketogenic diet (KD) in women age with a diagnosis of PCOS. We hypothesized that a modified KD (KEMEPHY diet) would lead to an improvement in body weight, plasma cholesterol, triglycerides, hyperinsulinemia, and hormonal outcomes.

METHODOLOGY

The design of this study was a cross sectional study design. This study was conducted in lady reading hospital Peshawar and the duration of this study was from January 2022 to February 2022. 60 non pregnant females are of age between 35-45 years with BMI ranging between 30-34.9 were included in the study. We used balloting method for sampling. The study was carried out with consent from all the participants.

Inclusion Criteria: Obese females (BMI 30-34.9) Ultrasound abdomen showing fatty liver Triglyceride and cholesterol levels on higher side

Exclusion Criteria: Use of anti-lipidemic drugs or supplements Pregnancy

The patients were divided in to two groups of 30 each patient. Low Calorie Diet group taking balanced diet with less than 1500 calories. They were given a monthly low calorie diet plan by the nutritionist. Their 1500 calories comprised of 40% fruits and vegetables, 25% fiber rich carbohydrates, 25% proteins and 10% fats[3].

Keto diet group which was given a monthly diet plan based on 70-80% fats, 20-25% proteins and 5-10% carbohydrates. Serum cholesterol levels of all females were calculated on Day 1 and Day 30 of the monthly diet plan. Serum triglyceride levels were calculated on Day 1 and Day 30 of monthly diet plan. Statistical analysis was done by graph pad prism version 6. One way and Two way Anova was used to assess difference between the groups. P value of less than 0.05 was considered significant. The study protocol complied with all tenets of the Helsinki declaration. All patients provided written informed consent before the beginning of the study. The study was approved by the ethical committee of the Department of Biomedical Sciences

RESULTS

Serum Cholesterol Levels: The serum chloesterol levels were significantly reduced in individuals taking low calorie diet over a period of thirty days. However serum cholesterol levels of individuals taking keto diet had no significant fall. There was also a significant reduction in cholesterol levels of low caolrie diet group as compared to keto diet group on day 30.

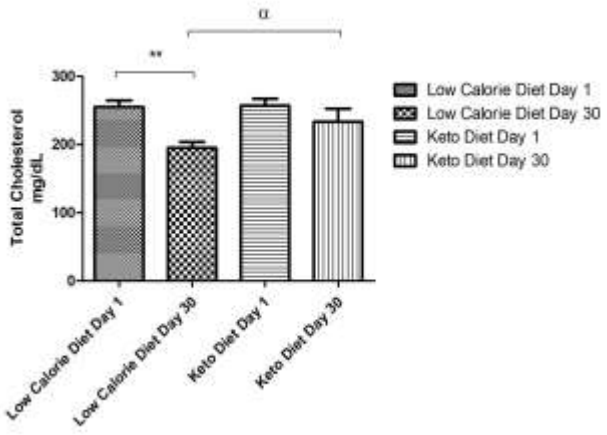

Figure 1:

Serum triglyceride levels

The serum triglyceride levels were significantly reduced in individuals taking low calorie diet over a period of thirty days. However serum triglyceride levels of individuals taking keto diet had no significant fall. There was no significant reduction in cholesterol levels of low caolrie diet group as compared to keto diet group on day 30.

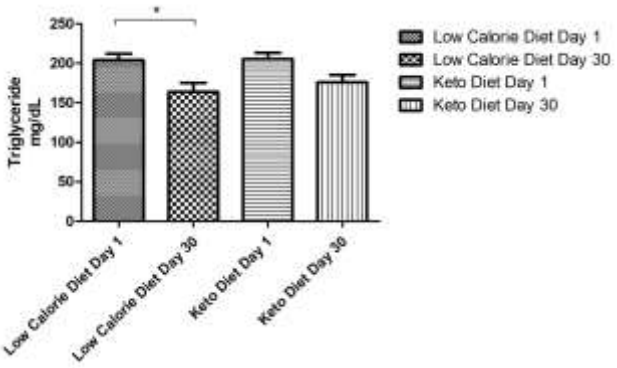

Figure 2:

DISCUSSION

The aim of our study was to assess two commonly used dietary regimes. Out of these two, low calorie diet is thought to have much safer profile as compared to keto diet [5]. There are many theories in support of this assumption. Keto diet is a quick way of losing weight. In process of rapid weight loss, patients, especially females are at higher risk of developing gall stones. Common short term side effects are characterized by fatigue headache, brain fog, constipation and upset stomach also known as keto flu.

Low level of carbohydrate intake is also associated with repeated hypoglycemic episodes. The short term use of ketogenic diet is associated with rise of serum cholesterol and triglyceride levels. Long term adverse effects include kidney stones, osteoporosis and liver disease as well [7]. However low-calorie diet is generally free of such adverse effects as it still provides all essential nutrients in correct portions but if low calorie diet goes beyond less than 1500 calories , it can lead to fatigue and development and gall stones [8]. In this study we evaluated the serum profile of both the dietary regimes and the superiority of low calorie diet was established here by significant reduction of cholesterol and triglyceride levels of females taking low calorie diet. Such reduction was not significant in the individuals taking keto diet. This may be due to the excessive fat intake as compared to normal diet when a person opts for keto diet.

Several dietary models have been proposed to correct the metabolic alterations of PCOS, but no one has reached, at the moment, a scientific validation as the best to recommend and it is still not clear even if normal weight, or overweight women may take benefit from a suitable dietary program to improve insulin resistance without caloric restriction. In this context KDs could be considered, as a nutraceutical therapy aimed to increase insulin sensitivity. The data available in the literature [26], although few, confirm the assumption that a KD, correcting hyperinsulinemia and improving body composition, can contribute to the normalization of the clinical picture in PCOS. During fasting or a carbohydrate restriction such as a KD, blood insulin concentration decreases, while glucagon increases to maintain the normal blood glucose level, first through glycogen stores, then through the β-oxidation of fatty acids stored in fat depots. Approximately 3–5 days after a very low carbohydrate diet, when the concentration of KBs begins to grow, hunger considerably decreases, but maintaining a state of well-being [28]. The advantage is further substantial if we compare common hypocaloric diets which are strongly restrictive towards the lipids, which keep the level of the orexigenic hormones up to 12 months from the suspension of the diet. In a physiological state of ketosis as during fasting, thanks to the considerable consumption of ketones by the CNS and the balance between insulin and glucagon, ketonemia reaches maximum levels of 7–8 mmol/L [6], with no change in the pH of the blood. During a LCKD the levels of KBs are usually between 0.5–0.6 and 4 and a nutritional ketosis could be defined as a blood ketones > 0.5 mmol/L [7–1] Indeed, our subjects showed an steep increase in blood BHB during the first 6 days reaching, at the end of the first week 0.55 ± 0.27 mmol/L BHB, whilst the mean value from day 7 to day 84 was 1.77 ± 0.55 BHB [29]. It is therefore essential to make a clear distinction between physiological ketosis (KD, fasting) and a pathological ketosis, such as that which can occur in diabetes when hyperglycemia and insulin deficiency cause uncontrolled rates of KBs and the ketonemia may exceed 20 mmol/L, exposing to the risk of severe acidosis. Fasting ketosis, however [30], leads to a loss of protein reserves, especially affecting muscle mass and generating a global state of decay. Conversely, the ketogenic diet, while maintaining a state of ketosis over time due to the limitation of carbohydrates, ensures an adequate supply of protein, preserving the tissues [20]. It is important to underline that a classic KD is not a high-protein diet, but usually has high-fat, adequate protein, low-carbohydrate content [31]. In fact, an excess of proteins increases gluconeogenesis in the long run, thus affecting the synthesis of KBs: in the first days of a KD the neoglucogenesis from amino acids represents the main source of glucose to keep the glycemia stable, then the demand for amino acids decreases and glucose is synthesized from the glycerol released from adipose tissue by triglyceride hydrolysis [32]. Our diet was a low-calorie ketogenic diet in which the amount of protein was high if we consider percentage (32%) but normal if we consider grams of protein per kilogram of body weight (1.23 g pro/ Kg bw). Such low-calorie approach is more feasible during a KD (LCKD) because it is well known that ketones reduce appetite probably through direct brain actions of KBs.

CONCLUSION

Low calorie diet was significantly better than ketogenic diet in reducing serum cholesterol and triglyceride levels in individuals on a 30-day diet plan of respective type. The results of our study are suggestive for a use of the KD as a possible therapeutic aid in PCOS, to be followed by a more balanced dietary regimen, but always with particular attention to the amount of carbohydrates. The duration of KD is still a question: there is no evidence of side effects in the short term, they are considered safe for short cycles. Less information is available on diets in the long term, but the experience gained in the field of epilepsy and GLUT-1 deficiency syndrome supports a possible use also for prolonged periods. It is plausible to hypothesize the setting of protocols to be repeated in cycles over time, interspersed with periods of balanced regime. Some limitations of the study need to be considered.

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