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Role of Chromium in Polycystic Ovarian Syndrome

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Abstract

Polycystic ovarian syndrome is the disorder of female reproductive system. Obesity, hyperandrogenism and inflammation are known to play a role in its pathophysiology. It can cause menstural irregularities, insulin resistance, infertility, dyslipidemia, acne, hairsuitism and glucose intolerance. Unhealthy lifestyles like high intake of fatty and sugary foods, decrease in physical activity also play a role in causing obesity and metabolic dysfunction. Chromium is an important element in carbohydrate and lipid metabolism. In this review we will find out how chromium improves metabolic dysfunction, lipid and carbohydrate metabolism, menstural irregularities and ovarian problems. We will also find out how chromium can be used as a treatment strategy for polycystic ovaries.

Keywords: PCOS • Glucose metabolism • Insulin resistance • Chromium • Menstural irregularities

Introduction

PCOS is an endocrine disorder that affects female of reproductive age. Cysts formation in the ovaries causes irregularity in menstural cycle. It is mainly related to unhealthy lifestyle pattern [1]. The cause of PCOS is unclear. It is a multifactorial disease with overlapping symptoms and complex pathophysiology. It is a major cause of infertility in females [2]. High level of androgens is present in PCOS females. Its clinical signs and symptoms include menstural irregularities, acne, and hairsutism [3]. The clinical manifestation of PCOS includes menstural irregularities, acne, hairsuitism and obesity. Disturbance in androgens synthesis and action is typically common. It also involves impaired glucose intolerance, insulin resistance, dyslipidemia and disturb ovulatory function [4]. Some female also experience depression and anxiety. They also have low energy levels and fatigue due to sleep disturbances. Hormonal changes can cause abnormal hair growth in them. Dark skin patches are also associated with PCOS. They gain weight easily and face difficulties in losing weight. Menstural disturbances include oligomenorrhea, Amenorrhea and prolonged bleeding. Pelvic pain and headache is also common with heavy periods [5].

A study conducted in ISRA University Hyderabad, Sindh concluded that the prevalence of PCOS is high in Pakistan. The main risk factor of this disease is genetic predisposition and the frequently observed clinical feature is menstural irregularities [6]. Women with PCOS have high risk of hypertension, high serum triglycerides concentration and low serum HDL concentration [7]. The cause of PCOS is genetic and environmental. Unhealthy eating pattern can cause obesity which increases the level of inflammation in our body. Insulin resistance can also be the cause of PCOS. Insulin is secreted by beta cells of pancreas and it facilitate the uptake of glucose by cells. High level of adipose tissue in our body can cause insulin resistance [8].

Long term consequences of PCOS includes glucose intolerance, gestational diabetes, type 2 diabetes mellitus, hypertension, cardiovascular disease, atherogenic dyslipidemia, non-alcoholic fatty liver disease, coronary heart disease and coagulation disorders [9]. Micronutrient deficiencies are also common in obese people [10].

The management of PCOS includes adopting a healthy lifestyle pattern, decreasing the intake of calories and increasing the physical activity. Drug therapy for losing weight includes orlistat. Bariatric surgery also shows some improvement in weight loss Weight loss in PCOS females improves hormonal, reproductive, metabolic and cardiovascular health [11]. PCOS females also deals with environmental and mental stress that keep their confidence level low and as its consequence they face a lot of difficulties in changing their lifestyle pattern and losing weight [12].

Chromium is an essential element. It has an important role in metabolism of glucose, insulin and lipids. Different studies show that chromium improves hyperglycemia, insulin resistance and fasting glucose levels [13]. Restriction of chromium in early life effect insulin signaling pathway and may cause irreversible insulin resistance [14]. A randomized, double blind, placebo control study was conducted on 40 PCOS female. They were divided into two half groups. One group was given 200 microgram of chromium per day and the other group was given placebo for 8 weeks. Result showed that chromium supplementation improves fasting glucose, insulin resistance, and serum triglycerides level and increase antioxidant capacity [15].

Literaturu Review

PCOS pathophysiology

Hyperandrogenism, chronic low grade inflammation and insulin resistance are associated with polycystic ovarian syndrome [16]. Elevated plasma levels of trimethylamine N oxide which is an organic compound is associated with PCOS pathogenesis without hyperandrogenism. It is also associated with high levels of systemic inflammation (Figure 1) [17].

Hyperandrogenism due to insulin can impair beta cell function of pancreas, increase subcutaneous fat and lipid storing capacity which leads to hypertrophy of intra-abdominal adipocyte and lip toxicity which will increase insulin resistance [18]. Large number of PCOS patients with normal circulating androgen levels have high levels of follicular fluid androgens and insulin resistance [19]. Circadian misalignments in PCOS female which is

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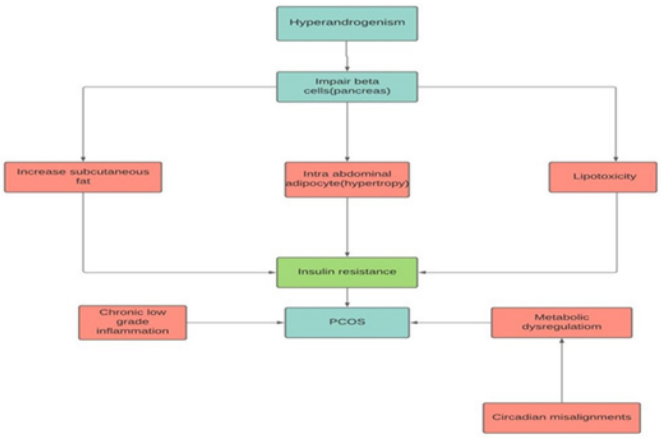

Figure 1. Pathophysiology of PCOS.

characterized by delay in melatonin off set relative to normal sleep timing can cause metabolic dysregulation. Later melatonin offset can increase serum free testosterone levels and decrease insulin sensitivity [20].

Dietary treatment and supplementation

Selenium is an important element required for normal reproductive function. It involves in the process of fertilization, gametogenesis and gonadal formation [21], levels of serum selenium is low in polycystic ovarian syndrome female compared with healthy female [22].

A study was conducted on 24 female rats to find the effect of selenium in polycystic ovarian syndrome. Rats were treated with 0.1 mg of selenium per kg of body weight. Selenium improves endocrine and metabolic phenotypes that are associated with PCOS comparable to metformin and it could be used in treating PCOS [23].

Zinc is a trace element and it plays an important role in the metabolism of carbohydrate, proteins and fats. It also takes part in the formation and releasing of insulin. It also reduces the level of oxidative stress by synthesizing enzymes that are important in reducing free radicals [24].

A study concluded that deficiency of zinc is also plays a role in polycystic ovarian syndrome pathogenesis [25]. A study conducted on mouse and human skeletal muscle shows that zinc has insulin like effect on cell signaling that are involve in homeostasis of glucose. Zinc also increases glucose consumption by cells. Phosphorylation events that are associated with insulin signaling are also mirrored with zinc treatment [26].

Vitamin E is a fat soluble vitamin and it consists of mixture of tocotrienols and tocopherols. Reactive oxygenated species is one of the main cause of female reproductive disorders. They damage the cell of reproductive system. Vitamin E acts as an antioxidants and it regulate the over production of reactive oxygenated species [27]. A study concluded that dietary intake of antioxidant nutrients had a protective effect on metabolic syndrome [28].

Vitamin D is a fat soluble vitamin, normally present in our body in inactive form. It require sunlight to get activated [29]. Serum vitamin D level is significantly lower in PCOS female compared with healthy female. Lower vitamin status is also associated with unfavorable lipid profile and insulin resistance [30].

Vitamin D deficiency is also associated with low chances of ovulation in women with PCOS [31]. Vascular endothelial growth factor has been known for playing a role in polycystic ovarian syndrome pathogenesis. Vitamin D supplementation decreases the level of serum vascular endothelial growth factor and triglycerides level in PCOS females [32].

Chromium and metabolic dysfunction

Chromium is essential mineral for lipid and carbohydrate metabolism [33] Chromium enhance insulin signaling pathways inside the cells by decreasing cholesterol content in membranes which enhance the transportation of glucose [34-36]. Restriction of chromium in early life effect insulin signaling pathway and may cause irreversible insulin resistance [14].

A study conducted by Elizabeth joseph chromium supplementation lower triglycerides levels in diabetic patients [35]. Chromium malate improves lipid metabolism by reducing the level of total cholesterol, triglycerides levels and LDL levels and increase serum HDL levels (Figure 2) [36].

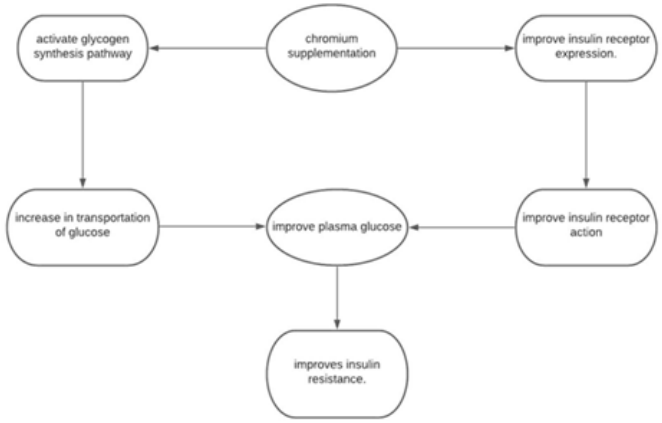

Figure 2. Chromium improves metabolic dysfunction.

A study concludes that chromium increase insulin receptor kinase activity [37]. A study conducted on mice chromium enriched bacillus subtilis enhanced the expression of insulin receptors and improved chromium concentration in body tissues. It also decreases the level of plasma glucose and LDL cholesterol and increase the level of HDL cholesterol [38].

In a study complex of chromium with sulfated rhamnose polysaccharides is synthesized to find its effect on type 2 diabetes mice. Mice were fed with high sucrose and high fat diet. SPRC treatment were given to them for 11 weeks daily. SPRC treatment activate the signaling pathway of glycogen synthesis and also enhance the transportation of glucose. It increase glycogen content of tissues, reduce body mass and improve oral tolerance of glucose [39]. In a study conducted on 24 female mice to find the effect of chromium supplementation. The end result showed that chromium supplementation improves the level of fasting glucose and fasting insulin [40].

Chromium and BMI

High BMI levels means high percentage of fat in body which worsens the condition of polycystic ovarian syndrome. Abnormal subcutaneous fat concentration increase the production of adipokine [41]. Another study concluded that central obesity increase apolipoprotein B/apolipoprotein A1 ratio. Apoliprotien includes the potentially anthrogenic compounds. Apolipoprotien A1 is the main component of HDL [42]. In a study chromium and carnitine co supplementation decreases body weight, BMI, fasting glucose and improves lipid profile all of which has a beneficial effect in polycystic ovaries [43]. Supplementation of chromium picolinate modify the mRNA levels related to metabolism of glucose and lipogenesis to impart the positive effect on glucose homeostasis which leads to the beneficial effect in whole body composition. And improvements in BMI also [44].

Chromium and lipid metabolism

Dyslipidemia is common in women with polycystic ovaries which involves disturbance in lipid metabolism and lipid profile. Mostly abnormal level of cholesterol is present [45]. A study concluded that a high fat diet before the age of puberty plays an important role in the development of polycystic ovaries. It causes ovarian changes and disturbance in metabolism [46].

An experiment was conducted on broilers to find the effect of chromium on lipid metabolism. Chromium decreases the fat percentage in abdomen. It also decreases the activity of fatty acid synthase, hormone sensitive lipase, acetyl CoA carboxylase and lipoprotein lipase. There is also increase in fatty acid synthase and lipoprotein lipase genetic expression [47].

Hepatic steatosis is a condition in which there is accumulation of abnormal fat percentage in liver. Metabolism of lipids is disturbed in this disease [48]. Chromium reduced the accumulated of fatty acids and lipids in hepatic steatosis which shows that chromium has a beneficial effect in metabolism of lipids [49] (Figure 3).

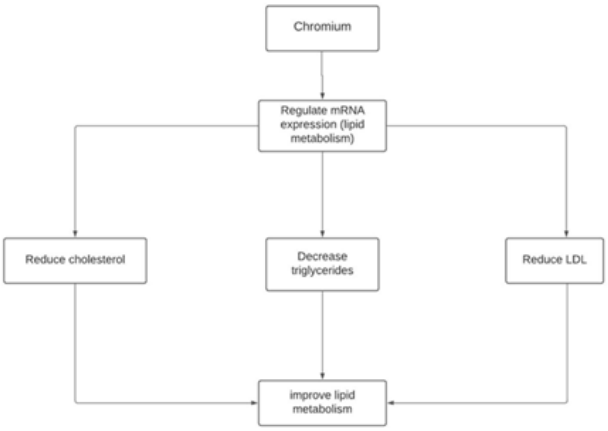

Figure 3. Chromium improves lipid profile.

miRNA expression related to lipid metabolism is regulated by chromium. There is improvement in the level of triglycerides, LDL and cholesterol which all are the negative biochemical indicators related to lipid metabolism. It also regulates accumulation of lipid and it can be used in treating hyperlipidemia [50].

Chromium and blood glucose

A study was conducted on type 2 diabetes patients to find out the effect of low and high plasma chromium levels. Hyperglycemia, hyperinsulinemia, insulin resistance was associated with low plasma chromium levels. Favorable fat distribution is associated with high plasma chromium levels [51]. A study conducted on non-diabetic individuals finds out that high urinary chromium excretion is associated with high levels of insulin resistance [52].

A study was conducted on streptozotocin induced diabetic rats. They were administered chromium picolinate (1 mg per kg of body weight daily) in the duration of four weeks. The end result showed improvement in plasma glucose levels and it is also beneficial in weight loss, polyphagia, polydipsia. It also normalize the glycogen content in liver. It increases the activity of glycolytic enzymes and decreases the activity of gluconeogenic enzyme [53]. A study was conducted on type 2 diabetic rats. They were treated chromium malate for 8 weeks. High dosage of chromium malate increases the antihyperglycemic activity. It increases the levels of hepatic glycogen, glucokinase and glucose 6 phosphatase dehydrogenase [36] (Figure 4).

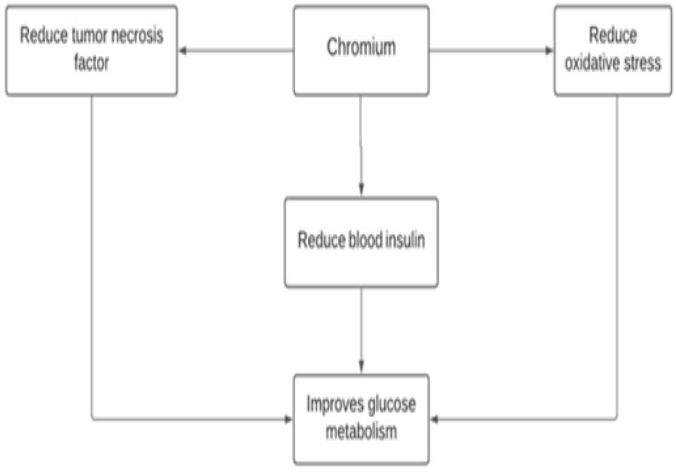

Figure 4. Chromium improve glucose metabolism.

A study was conducted on obese people with type 2 diabetes mellitus. The duration of study was 90 days and a supplementation of chromium picolinate with biotin were given to them which improves fasting glucose levels in all participants [33]. In another study conducted on type 2 diabetes. Patient's supplementation of chromium and cysteine improves insulin resistance. It also reduces blood levels of insulin, tumor necrosis factor and oxidative stress [54].

Chromium and hormonal imbalance in menstural cycle

Menstural cycle consists of the following phases. Menstural phase, Follicular phase, Pre-ovulatory phase, Luteal phase and Pre-menstural phase. In first half of menstural cycle estrogen levels are low and follicle stimulating hormone and leutinizing hormone are at peak. In second half of menstural cycle estrogen level rises [55].

A study was conducted on 40 female PCOS patients to find the disturbance in their hormonal profile. The samples of blood were taken during the 2 to 4 days of menstural cycle. The result of these PCOS patients was compared with healthy female control group. The hormones that were evaluated in this study included follicle stimulating hormone, oxytocin, prolactin, testosterone, luteninzing hormone. The end result showed that there is elevated level of all these hormones in PCOS females [56].

A study was conducted on 54 participants to find the effect of chromium and carnitine co- administration on hormonal parameters. The age of these participants is 18 to 40 years old. The end result showed that there is decrease in the level of testosterone hormone [57]. A study was conducted on 35 adolescent girls with PCOS. For 6 months chromium supplementation the amount of 1000 micro gram were given to them. The result showed improvement in the level of free testosterone and decrease menstural irregularities [58].

Chromium and ovarian problem management

In a randomized control trial chromium picolinate reduced the level of BMI, fasting insulin levels, increases the chance of ovulation and regular menstural cycle [59]. A study was conducted on PCOS females to find the effect of selenium, chromium, myoinositol and L-tyrosine. The result showed restoration in ovulation, regular menstural cycle and increase level of progesterone in luteal phase [60].

A study was conducted on 60 female PCOS females to find the effect of metformin versus chromium picolinate. It shows that chromium is better tolerated. While both improve the improve the level of leutinizing hormone, follicle stimulating hormone, hairsutism score and ovarian volume [61]. Increase number of small follicles is present in ovaries of women with PCOS and it shows hyperstimulation in ovaries [62]. Chromium by reducing total follicular count in ovaries proves beneficial in treating ovarian problems in women with PCOS. Reduce follicular count also decrease the volume of ovaries [58].

Chromium and PCOS management

Insulin resistance is the main feature of polycystic ovaries which involves high level of serum insulin also called hyperinsulinemia but cells are resistance to insulin may be due to the presence of high amount of lipid dysfunction in them [63]. Chromium is reported to improve insulin resistance and fasting glucose to insulin ratio which shows that it is useful in treating polycystic ovary syndrome [59]. Elevated testosterone levels, obesity and inflammatory markers can increase insulin levels, fasting glucose levels and cause insulin resistance [64]. A study conducted on PCOS females concluded that central obesity despite of normal weight had increased risk of causing insulin resistance and dyslipidemia compared with PCOS female of normal weight without central obesity [65]. Women with polycystic ovaries show abnormal lipid profile such as high levels of low density lipoprotein, triglycerides and low levels of high density lipoprotein which effect their overall body composition and play a role in pathophysiology of PCOS [66].

A randomized control trial was conducted on 64 PCOS women. They were divided into two equal groups. One group was given 200 microgram of chromium picolinate and the other group was treated with placebo for 8 weeks. The result showed that there is improvement in most of the clinical features of PCOS such as the level of serum insulin, serum triglycerides and cholesterol. Improvement in all these parameters also improves insulin resistance, BMI levels, metabolism of lipids and glucose.

Discussion

Polycystic ovarian syndrome is an endocrinal disorder which disturbs the reproductive function of females. Hairsuitism, acne and menstural irregularities are the common feature of polycystic ovaries. It is the most common cause of infertility in females. Lipid and carbohydrate metabolism is disturbed in this disorder. Excessive fat in body tissues is present which prevent insulin to perform its action, as a result high level of insulin is secreted by pancreas and it cause insulin resistance. Polycystic ovaries cause metabolic dysfunction in body which is improved by the action of chromium on metabolic pathways. Chromium has a positive effect on lipid metabolism. It decreases the level of triglycerides, free cholesterol and LDL levels. By decreasing body fat levels it also decreases the body mass index levels. Chromium also has a positive effect on carbohydrate metabolism. It improves the level of insulin, improve insulin action and normalize plasma glucose levels in the body. It also decreases the level of insulin resistance. To improve glucose metabolism it decreases gluconeogenic enzymes and increase glycogenic enzymes. It also improves glycogen content in body tissues. Chromium improves hormonal profile. It regulates the level of testosterone, follicle stimulating hormone and leutinizing hormone. Improvements in all these hormonal levels regulate menstural cycle and increases the chances of ovulation. It also decreases the volume of ovaries. Above all mentioned effects of chromium suggest that it can be used in the treatment of polycystic ovaries.

Conclusion

PCOS effects females of reproductive age. It cause disturbances in their menstural cycle and cause infertility. Acne, fatigue and hairsuitism are its common symptoms. Chromium is an important element that is beneficial in treating polycystic ovaries. It regulates the metabolism of carbohydrates and fats, improve body composition and decrease the level of BMI. It also regulates the disturbances of hormonal profile due to polycystic ovaries. Regulation of menstural cycle and increase in the chance of ovulation are also its benefits.

Acknowledgement

None

Conflict of Interest

Authors declare no conflict of interest.

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