PJN
ISSN 1680-5194

PAKISTAN JOURNAL OF NUTRITION

ANSInet
308 Lasani Town, Sargodha Road, Faisalabad - Pakistan
Mob: +92 300 3008585, Fax: +92 41 8815544
E-mail: editorpjn@gmail.com

Pakistan Journal of Nutrition 8 (6): 900-904, 2009
ISSN 1680-5194

The Effect of Chromium Glycinate on the Blood Glucose Control and Blood Lipids of Normal and Diabetic Patients

R. Abdul-Wahab Hamad[1], M. Monzer Krishan[1], M. Jihad Quasem[1] and Ayman Suliman Mazahreh[2]
[1]Zarka University College, Al-Balqa Applied University, Jordan
[2]Department of Applied Sciences, Al-Balqa Applied University, Princes Alia University College, P.O. Box: 941941, Amman, 11194, Jordan

Abstract: The effect of chromium glycinate 200 µg was investigated for its effect on blood control and serum lipids in four groups were divided into normal subjects (n = 30), hyperglycemic (n = 28), no-insulin dependent diabetics (n = 20) and insulin-dependent diabetics (n = 20). The level of glucose and lipids profile in serum were analyzed before chromium glycinate supplements and periodically each two weeks throughout this study after chromium glycinate 200 µg supplements was taken for a period of four months. A significant improvements in the various parameters occurred in all groups of the study. The hyperglycemic group showed higher benefits in blood glucose control, lowered serum lipids and a decreased risk of coronary heart disease than other groups of no-insulin dependent diabetics and insulin-dependent diabetics.

Key words: Chromium glycinate, glucose tolerance factor, glycosylated haemoglobin HDL, LDL

INTRODUCTION

Chromium has been recognized as an essential trace element for nutrition. Recently, the National Academy of Sciences/National Research Council suggested that the daily intake of chromium for adults be between 50 and 200 µg (Anonymous, 1980). The chromium levels in the diet of the United States and Western Europe are lower than in the Near and Far East which is at least partly the result of processing (Althuis *et al*., 2002). A comprehensive review for determination of adult normal values of trace elements in Iraqi population (Abid *et al*., 2002) shows that 21.6 % of Iraqi volunteers under investigation had chromium deficiency compared with Iraqi adult normal value of Cr (55 ng/ml), they conclude that chromium deficiency were highly contributes in increase risk factors for diabetes in Iraq, therefore, organic chromium supplementation is highly recommended. Recently, two studies shows that the level of Se, Cr, Mg and Zn were significantly low in Iraqi patients (both sexes) with acute myocardial infarction unstable angina pectoris and hypertension (Abid *et al*., 2002; Al-Zamely *et al*., 2002).

Inorganic chromium compounds are poorly absorbed in man, amounting to 1-3% regardless of dose or dietary chromium status (Underwood, 1997). Organic chromium, such as found in brewer's yeast, is much better absorbed than inorganic chromium (Mertz, 1969). Over half of the chromium in brewer's yeast is in a volatile, organic form (Anderson, 2000; Anderson *et al*., 2001). This form of trivalent chromium, complexes with nicotinic acid and amino acids e.g. glycine, is known as Glucose Tolerance Factor (GTF). Among foods, brewer's yeast is the richest source of GTF. This biologically important form of chromium is hypothesized as a co-factor for the binding of insulin to membrane receptors in insulin-sensitive tissues (Mertz, 1969). GTF has been shown to be a requirement for normal carbohydrate metabolism (Doisy *et al*., 1976). When an animal or human is chromium deficient, the result is an impaired glucose tolerance. There is evidence to support the view that chromium deficiency occurs in normal human populations. It does appear that older individuals and those consuming large amounts of carbohydrates might be deficient. Tissue chromium levels have been found to dramatically decrease with age in the United States (Althuis *et al*., 2002). It has also been shown that chromium is mobilized from body stores as a response to administration of glucose by mouth (Doisy *et al*., 1976). High consumption of refined sugars and carbohydrates is thus likely to induce chromium deficiencies by excretion.

These refined carbohydrates are themselves low in chromium and contribute to the problem. Diabetics represent the most susceptible group of individuals toward chromium deficiency. Diminished chromium stores have been reported in the hair (Hambridge *et al*., 1968) and liver (Hambridge *et al*., 1968) of diabetic humans. Insulin-requiring diabetics have been shown to have an abnormal rate of chromium absorption. During the first 24 h after a single oral dose of chromium, these individuals absorb two to four times more chromium than normal subjects (Doisy *et al*., 1976). Recently, this effect was also seen in diabetic rats given radioactive-chromium. These rats, when given insulin after chromium, had their chromium levels restored to normal (Kraszeski *et al*., 1979).

Diabetics have been found to excrete in their urine twice the quantity as much chromium per day as do normal

individuals (Doisy *et al*., 1971).This is due to the fact that when insulin is taken, 20% of the chromium mobilized from the body stores is excreted in the urine. Thus, it appears that administration of insulin may result in an increased excretion of chromium and a tendency to chromium deficiency. This hypothesis is supported by the recent work of Thompson (Thompson, 1980) who found insulin treated diabetics to have significantly lower levels of plasma chromium than normal subjects.

In genetically diabetic mice with hyperglycemia and hyperinsulinemia, GTF administration, both acutely and chronically, reduced the elevated blood glucose levels to normal, inorganic chromium was completely without effect (Anderson, 2000). It was thus hypothesized that diabetic mice had an impaired ability to convert inorganic chromium into the biologically active GTF. If this impairment exists in humans it may explain the lack of success of chromium supplementation studies by Sherman (Sherman *et al*., 1968). This group and other groups used inorganic chromium for their studies. For instance, Levine found that the abnormal glucose tolerance of only 4/10 elderly subjects became normal after 1-4 months of inorganic chromium supplementation (Vladeva *et al*., 2005). This improvement of glucose tolerance was not due to retarded glucose absorption or to an increased rise in plasma insulin activity after the glucose load. In fact, in recent study, Doisy *et al*. (1976) found that the serum insulin concentration reached lower peak values after a glucose load, following an 8-month chromium supplementation, than before supplementation. This effect was seen in both normal subjects and siblings of diabetics. Thus, it appears that less insulin is required to keep glucose controlled when adequate chromium is present. A study with several offspring of an insulin-requiring diabetic Doisy *et al*. (1976) showed that inorganic chromium was ineffective in improving glucose tolerance while a six month supplement of brewer's yeast normalized the glucose tolerance as measured by the glucose tolerance test.

The present study is an attempt to verify the effect of a long-term supplementation of chromium glycinate on glucose control and lipids in patients.

MATERIALS AND METHODS

Ninety eight volunteered subjects (ages 25-63) were elected for the study. Thirty normal individuals (ages 38-63) served as controls. Twenty eight hyperglycemic individuals (ages 45-60) had abnormal blood glucose control as determined by % glycosylated haemoglobin (%GHb) and high normal fasting blood glucose. Twenty subjects (ages 41-59) were not insulin-dependent diabetics who were taking oral anti-diabetic medication. Twenty individuals (ages 16-55) were insulin-dependent diabetics, who had the disease at least four years. Their insulin requirement was stabilized.

The subjects in a seated position, after an overnight fast, venous blood was collected into a sample tube containing EDTA. The blood was frozen at -20°C until analysis. The %GHb in the blood was determined with an Isolab kit using the optimum room temperature and a control of known value. This column chromatographic method determines the fast haemoglobin HbA1 which equals HbA1a + HbA1b + HbA1c, with a reproducibility of approximately 5%.

Two other tubes of blood were taken. One was used for blood glucose measurements by a conventional automated enzyme method. The second tube contents were allowed to clot and the serum frozen until assay. The serum was analyzed for cholesterol and triglycerides by conventional automated methods. High-density Lipoprotein cholesterol (HDL) was determined after Mn^{+2} (ion) precipitation by a conventional automated enzymatic method. Low-density Lipoprotein cholesterol (LDL) was calculated from the formula, LDL Cholesterol = HDL – Triglycerides/5.

Chromium glycinate and Lipid profile: The chromium glycinate powder containing 16% chromium was locally synthesis and assayed by Atomic Absorption Spectroscopy (Model 760, Shimadzu AAS) on wave length 360 nm, flue air-actylene 3.0, slit 0.5 nm and a current 5 mA.

Lipids profile was analyzed by using kits such as LDL-Cholestrol kinetic determination (Syrbio diagnostic for Laboratories, France),

HDL-Cholestrol kinetic determination (Syrbio diagnostic for Laboratories, France).

Experimental design: All the parameters were determined in each subject before supplementation was initiated so that each subject served as his own control. Each subject then took orally each day a chromium glycinate tablet 200 µg. The %GHb and lipids were determined 2, 3 and 4 months after supplementation began. Statistical comparison with the pre-dose value was done.

RESULTS AND DISCUSSION

In this study, the % glycosylated haemoglobin (%GHb) was used to determine the subjects' glucose control. The %GHb is much easier to perform than the Glucose Tolerance Test (GTT) and has been found to correlate with the area under the GTT curve (Gabbay *et al*., 1977). The %GHb correlates with the degree of altered blood glucose control during the previous 1-3 month period (Gabbay *et al*., 1977; Koenig *et al*., 1976; Gonen *et al*., 1977) and decreases when control is improved. The results of the chromium supplementation on the %GHb of the groups is shown in Table 1.

There was slightly effect on %GHb for the normal subjects or the Non-Insulin-Dependent Diabetes as a

Table 1: Effect of chromium glycinate tablet 200 ug supplements on % GHB of human subjects

Groups	% GHB Before	% GHB 2 month after Cr Suppl.	% GHB 3 month after Cr Suppl.	% GHB 4 month after Cr Suppl.
Normal (n = 30)	7.40±1.61	6.35±1.15	6.15±1.02	6.14±0.85
Hyperglycemic (n = 28)	14.85±4.12	6.80±0.60	6.30±.95	6.25±0.71
Non –insulin dependent diabetes (n = 20)	8.81±1.45	7.56±1.20	6.84±1.23	6.94±1.42
Insulin dependent diabetes (n = 20)	12.12±2.85	6.60±0.80	7.51±0.25	8.30±2.12

Table 2: the effect of chromium glycinate 200 µg supplements on the serum level HDL in patients

Groups	HDL before mg/dl	HDL 2 month after Cr	HDL 3 month after Cr	HDL 4 month after Cr
Normal (n = 30)	46±12	64±11	58±14	61±13
Hyperglycemic (n = 28)	51±09	68±13	69±12	65±10
Non-insulin dependent diabetics (n=20)	47±12	51±13	49±11	53±14
Insulin dependent diabetics (n=20)	52±14	61 ±16	63±14	59±16

result of chromium supplementation. There was a transient improvement after two months for the Insulin-Dependent Diabetes but after four months the %GHb had slightly elevated compared with the two month periods. With a value which was significantly lower than the pre-dose level. A study by Rabinowitz *et al.* (1983) corroborates our results with diabetic groups. Rabinowitz *et al.* (1983); Rabinovitz *et al.* (2004) reported a double-blind crossover study of insulin-dependent and non-insulin-dependent diabetics supplemented with a brewer's yeast high in GTF (18 µg of Chromium/day) and a placebo for 4 months. No improvement in GTT was found in either group of diabetics. However, a recent study of reseachers (Offenbacher and Pi-Sunyer, 1980; Rabinovitz *et al.*, 2004) showed that elderly (average age, 78 years) non-insulin dependent diabetics had a 16% lower GTT after 2 months of a daily regimen of 11 µg of Chromium in the form of a chromium rich yeast. The present study showed a significant improvement in blood glucose control after 2 months. The highly significantly benefit group in the current study was the Hyperglycemic and control which had average 55% improvement in blood glucose control after 4 months of chromium glycinate. Every individual in this group had an improved %GHb by different values. A significant improvement of GTT was also found by Nordstrom (Nordstrom, 1982) after giving 4 µg of chromium in a brewer's yeast daily for 3 months to hyperglycaemic women aged 40-75 years. The improvement in GTT was more than 32%, less than the present study, but the dose and duration of the supplementation were less than the present study.

There were no significant changes in serum cholesterol of triglycerides in any of the groups after 4 months of chromium yeast. It was seen that the %GHb data, there were some improvements after 2 and 4 months in all groups. Offenbacher and Pi-Sunyer (1980) noted a significant decrease in serum cholesterol after 2 months of chromium yeast but some of this effect was found to be due to a non-chromium component of brewer's yeast. Several other studies (Riales, 1979; Racek *et al.*, 2006) also found decreases in serum cholesterol after several months of chromium yeast supplementation.

The date of High-density Lipoprotein cholesterol (HDL), which is that fraction of physiological cholesterol considered to be protective (Riales, 1979) against coronary heart disease. There was slightly change in insulin dependent diabetic groups after 4 months supplementation (Table 2).

Riales (1979) and Racek *et al.* (2006) observed significant increases in HDL. There were about 12-18% increase in normal after chromium yeast supplementation for 6 and 8 weeks, respectively. The present study also shows a slightly significant increase of HDL in the normal group, hyperglycemic and insulin-dependent diabetics after 4 months supplementation.

The results for the LDL determination are shown in Table 3. LDL is considered to be that protein of cholesterol, which carries cholesterol to the cell walls for the deposition that leads to atherosclerosis (Gordon *et al.*, 1977). The significant changes after 4 months were about 28% decline in the LDL of the Hyperglycemic and 18% in control groups. Railes (1979) showed that the short chromium yeast supplementation studies, found a significant decrease in LDL. Thus, the Hyperglycemic and control groups appears to have slightly significant of LDL lowering as a result of Cr supplementation, while no-insulin dependent and insulin-dependent diabetics showed non-significant changes.

The most significant risk factor with respect to coronary heart disease is the ratio of total cholesterol to HDL (Castell *et al.*, 1977; Racek *et al.*, 2006). The less the ratio, the less the risk of heart disease (Table 4).

All groups except the Non Insulin-Dependent Diabetics exhibited significant improvements, i.e. decreases in the Chol. /HDL ratio after 2 months of Cr. However, after 3 month, the control and Hyperglycemic and insulin dependent groups maintain a significant change with Chol. /HDL improvements ratio. The study of Riales (1979) also showed a slightly significant improvement

Table 3: Effect of chromium glycinate supplementation on the serum LDL of Human volunteers

Groups	LDL before Cr mg/dl	LDL 2 month after Cr	LDL 3 month after Cr	LDL 4 month after Cr
Normal (n = 30)	160±38	115±11	120±42	134±29
Hyperglycemic (n = 28)	151±19	124±30	109±41	114±39
Non –insulin dependent diabetics (n = 20)	147±51	151±43	143±45	142±38
Insulin dependent diabetics (n = 20)	163±41	156 ±38	160±41	153±54

Table 4: The effects of Cr supplementation on the Cholesterol to HDL Ratio (Chol/HDL)

Groups	Chol/HDL Before Cr	Chol/HDL 2 month after Cr	Chol/HDL 3 month after Cr	Chol/HDL 4 month after Cr
Normal (n = 30)	5.2±0.8	3.2±1.1	4.2±0.9	4.3±1.01
Hyperglycemic (n = 28)	4.5±0.8	3.7±0.9	3.1±0.7	3.3±0.8
Non –insulin dependent diabetics (n = 20)	6.1±1.1	5.4±1.4	5.6±1.3	5.1±1.6
Insulin dependent diabetics (n = 20)	5.2±41	3.6 ±1.1	3.8±1.4	3.5±1.3

in the Chol./HDL for normal individuals after 6 weeks of Cr supplementation. The Chol/HDL in the Hyperglycemic Group correlates with an average risk of coronary heart disease before supplementation and a less than ½ the average risk after chromium yeast supplementation.

REFERENCES

Abid, F.M., A.J. Shanshel, A.W.R. Hamad and M.H. Hamash, 2002. Determination of medically important trace elements in Iraqi peoples by using atomic absorption spectrophotometers., J. Babylon Univ. for Applied Science, 7: 1446.

Abid, F.M., K.M. Al-dori, H.I. Kalaf, R. Al_Kubisi, A.A. Salomi and A.W.R. Hamad, 2002. Measurments of essential trace elements in sera of cardiovascular patients compared normotensive control by AAS., J. Babylon Univ. for Applied Sci., 6: 283-302.

Al-Zamely, O.M., E.M. Al-Niami, F.M. Abid and R.Q. Atewei, 2002. study of essential trace elements and ultra trace elements level in sera of patients with angina pectoris and acute myocardial infarction., J. Babylon Univ. for Applied Sci., 7: 1498-1517.

Althuis, M.D., N.E. Jordan, E.A. Ludington and J.T. Wittes, 2002. Glucose and insulin responses to dietary chromium supplements: a meta-analysis. Am. J. Clin. Nutr., 76: 148-55.

Anderson, R.A., 2000. Chromium in the prevention and control of diabetes. Diabetes and Metabolism, 26: 22-27.

Anderson, R.A., A.M. Roussell, N. Zouari, S. Mahjoub, J.M. Matheau and A. Kerkeni, 2001. Potential antioxidant effects of zinc and chromium supplementation in people with type 2 diabetes mellitus. J. Am. Coll. Nutr., 20: 212-218.

Anonymous, 1980. Recommended Dietary Allowances, 9th Ed., Food and Nutrition Board, National Academy of Sciences, Washington, D.C., pp: 157.

Castell, W.P., J.T. Doyle and T. Gordon, 1977. HDL Cholesterol and other lipids in coronary heart disease. The co-operative lipoprotein in phenotyping study. Circulation, 55: 767.

Doisy, R.J., D.H.P. Streeten, J.M. Freeburg and A.J. Schneider, 1976. Chromium metabolism in man and trace elements in human health and disease. (E. Prasad, Editor), Nutrition Foundation Monograph, Academic Press, New York, p: 79.

Doisy, R.J., D.H.P. Streeten, M.L. Sourma, M.E. Kalafer, S.L. Rekant and T.G. Dalakos, 1971. Metabolism of chromium in human subjects in newer trace elements in nutrition (W. Mertz and W.E. Cornazen, Editors). Marcel Dekker, New York, p: 155.

Gabbay, K.H., K. Hasty, J.L. Breslow, R.C. Ellison, H.F. Bunn and P.P.M. Gallo, 1977. Glycosylated Haemoglobins and Long-term blood glucose control in Diabetes mellitus. J. Clin. Endocrinol. Metab., 44: 859.

Gonen, B., A.J. Rubenstein, H. Rochman, S.P. Tanega and D.D. Horowitz, 1977. Haemoglobin A1: An indicator of metabolic control of diabetic patients. Lancet, 2: 734.

Gordon, T., W.P. Castell and M.C. Hjortland, 1977. High density lipoprotein as a protective factor against coronary heart disease. Am. J. Med., 62: 707.

Hambridge, K.M., D.O. Rodgerson and D. O'Brien, 1968. Concentration of chromium in the hair of normal children and children with juvenile Diabetes mellitus. Diabetes, 17: 517.

Koenig, R.J., C.M. Peterson, R.L. Jones, C. Saudek, M. Lehrman and A.C. Cerami, 1976. Correlation of Glucose regulation and Haemoglobin Aic in Diabetes mellitus. New England J. Med., 295: 417.

Kraszeski, J.L., S. Wallach and R.L. Verch, 1979. Effect of insulin on Radio-Chromium distribution in rats. Endocrinol, 104: 881.

Mertz, W., 1969. chromium occurrence and function in Biological systems. Physiol. Rev., 49: 169.

Morgan, J.M., 1972. Hepatic Chromium content in Diabetic subjects. Metabolism, 21: 313.

Nordstrom, J.W., 1982. Trace mineral nutrition in the elderly. Am. J. Clin. Nutr., 36: 788.

Offenbacher, E.G. and Pi-Sunyer, 1980. Beneficial effect of chromium rich yeast on glucose tolerance and blood lipids in elderly subjects. Diabetes, 29: 919.

Rabinovitz, H., A. Friedensohn, A. Leibovitz, G. Gabay, C. Rocas and B. Habot, 2004. Effect of chromium supplementation on blood glucose and lipid levels in type 2 diabetes mellitus elderly patients. Int. J. Vitam. Nutr. Res., 74: 178-82.

Rabinowitz, M.B., H.C. Gonick, S.R. Levin and M.B. Davidson, 1983. Effects of Chromium and yeast supplements in carbohydrates and lipid metabolism in diabetic men. Diabetes Care, 6: 319.

Racek, J., L. Trefil, D. Rajdl, V. Mudrova, D. Hunter and V. Senft, 2006. Influence of chromium-enriched yeast on blood glucose and insulin variables, blood lipids, and markers of oxidative stress in subjects with type 2 diabetes mellitus. Biol. Trace Elem. Res., 109: 215-230.

Racek, J., L. Trefil, D. Rajdl, V. Mudrova, D. Hunter and V. Senft, 2006. Influence of chromium-enriched yeast on blood glucose and insulin variables, blood lipids and markers of oxidative stress in subjects with type 2 diabetes mellitus. Biol. Trace Elem. Res., 109: 215-30.

Riales, R., 1979. Influences of brewer's yeast on lipoprotein cholesterol concentrations in chromium in nutrition and metabolism. (D. Shapcott and J. Hubert, Editors), Elsevier, Amsterdam, p: 199.

Sherman, L., J.A. Glennon, W.J. Brech, G.H. Klomberg and E.S. Gordon, 1968. Failure of trivalent chromium to improve Hyperglycaemia in Diabetes Mellitus. Metabolism, 17: 439.

Thompson, D.A., 1980. Flameless Atomic Absorption Spectroscopy of plasma chromium. Am. Clin. Biochem., 17: 144.

Underwood, J.E., 1997. Trace elements in human and animal nutrition. Academic Press, New York, p:20.

Vladeva, S.V., D.D. Terzieva and D.T. Arabadjiiska, 2005. Effect of chromium on the insulin resistance in patients with type II diabetes mellitus. Folia Med., 47: 59-62.