

Effect of Zinc Sulfate Supplementation on Lipid and Glucose in Type 2 Diabetic Patients

Mohammad Afkhami - Ardekani, Mahdi Karimi, Seid Mohammad Mohammadi and Forough Nourani
Diabetes Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

Abstract: Type 2 diabetes mellitus is a chronic, progressive illness that causes considerable morbidity and premature mortality. More people are still having tendency to use herbal or alternative remedies. Zinc is a trace mineral which may be effective in diabetic patients. We evaluated the effect of zinc sulfate on biochemical markers of type 2 diabetic patients. In a randomized, controlled trial on diabetic subjects, forty patients received randomly either 660mg zinc sulfate or placebo for six weeks. Body Mass Index, Blood Pressure, Fasting Blood Sugar, 2-h postprandial glucose, Glycated hemoglobin, Triglyceride, cholesterol, low - density lipoproteins, high - density lipoproteins were checked before and six weeks after beginning of the study. HbA1C, BMI and Blood Pressure were measured after 12 weeks to evaluate the long term effect of drugs. The mean age of patients was 52.67 ± 8.60 . level of FBS, 2HPP, HbA1C decreased after six week treatment with zinc sulfate but it was not statistically significant. Due to zinc sulfate administration, significant decrease occurred in TG ($P=0.005$), chol ($p=0.02$), LDL (0.01) and systolic blood pressure ($p=0.02$). HDL was increased but it was not significant. No statistically significant differences were found prior to and after zinc treatment in BMI and diastolic blood pressure. After 12 weeks, there was a significant decrease in HbA1C ($P=0.04$) with zinc sulfate consumption. Zinc sulfate consumption in addition to other nutritional and pharmacological treatments in type 2 diabetic patients could be effective in lipid profile.

Key words: Zinc sulfate, Type 2 diabetes mellitus, lipid profile

Introduction: Type 2 diabetes mellitus is a polygenetic disorder resulting from interaction of both hereditary and environmental factors (Jinlin *et al.*, 2007). It is a chronic, progressive illness that causes considerable morbidity and premature mortality (Kleefstra *et al.*, 2007. Amos *et al.*, 1997). The worldwide prevalence of type 2 diabetes is high and is increasing steadily (King *et al.*, 1998). Approximately, 150 million people worldwide are affected by type 2 diabetes mellitus and this figure is expected to double in the next 20 years (Freeman and Cox, 2006). Prevalence of type 2 diabetes is 13.8% in Yazd province, Iran (Afkhami-Ardekani *et al.*, 2001). Type 2 diabetes is associated with the increased risk of microvascular and macro vascular complications (Nazimek-Siewniak *et al.*, 2002). Zinc is known to be an essential trace mineral which is necessary for health and growth and is also essential for the function and activity of over 200 metalloenzymes (Chen *et al.*, 1991). The ability of zinc to retard oxidative processes has been recognized for many years (Powell, 2000). Zinc is an essential mineral that is required for various cellular functions. Its abnormal metabolism is related to certain disorders such as diabetic complications (Song *et al.*, 2005).

Abnormal zinc and lipid plasma levels occur more frequently in metabolically uncontrolled diabetic patients. Yet, zinc sulfate supplementation may be a therapeutical resource to recover some functioning and improve life span (Partida-Hernandez *et al.*, 2006).

This article reports the effect of zinc sulfate on glucose and lipid profile of type 2 diabetes mellitus patients.

Materials and Methods

The study design was randomized, controlled trial. Subjects enrolled from Yazd Diabetes Research Center, Yazd, Iran. Inclusion criteria included type 2 diabetic patients with fixed drug dosage in past 6 months, fixed weight in past 3 months, without taking vitamins or mineral supplements in the previous 2 months and without clinical involvement of kidney, heart and lung. The subjects were fully informed of the purpose, procedures and hazards of trial and were free to leave the trial at any time. Written informed consent was obtained from all participants. The research protocol was approved by the ethics committee on human experimentation of Yazd University of Medical Sciences. Forty subjects divided randomly into two groups and supplemented daily with 660 mg zinc sulfate or placebo for six weeks. Zinc sulfate was manufactured by ALHAVI Company.

Subjects were instructed not to modify diet or activity level; each individual maintained dietary records at intervals throughout the experiment. Body Mass Index (BMI), Blood Pressure and biochemical markers included Fasting Blood Sugar (FBS), 2-h postprandial glucose (2hpp), Glycated hemoglobin (HbA1C), Triglyceride (TG), cholesterol (chol), low -density lipoproteins (LDL), high - density lipoproteins (HDL), Blood Urea Nitrogen (BUN), Creatinin (Cr), Alanine aminotransferases (ALT),Aspartate aminotransferases, (AST) were checked before the beginning of the study. BMI was calculated as the weight in kilograms per the

Afkhami-Ardekani et al.: Effect of Zinc on Glucose and Lipid in Type 2 Diabetes

square of height in meters and blood pressure measured with the person in the sitting position after a 5-min rest. All blood specimens were drawn at 8 a.m. after a period of 8 hours fasting. All patients were examined carefully and depending upon the treatment groups, each subject received drugs for a period of six weeks. Subjects eat zinc sulfate every eight hours by meal with a large glass of water (220 mg TDS).

BMI, blood pressure, AST, ALT and drug complications such as nausea, vomiting, abdominal pain, diarrhea, constipation, reduction of appetite were checked after 3 weeks.

At the end of 6 weeks all the indices checked as before the beginning and the drug complications were asked as well. HbA1C, BMI, blood pressure and complications were analyzed after 12 weeks to evaluate the long term effect of drugs.

Statistical analysis: All statistical analyses were performed by using SPSS, version 11.50. Data of continuous variables are expressed as means ± standard deviation. Differences between groups were assessed by the paired t test.

Results

All subjects completed the study. The mean age of patients was 52.67±8.60 with male constituting 40% of patients (16 male and 24 female). Mean duration of diabetes was 7.07±4.94 years. 17.5% and 22.5% of diabetic patients had hypertension and hyperlipidemia respectively. 65% and 62.5% ate metformin and glybenclamide respectively but only 5% had acarbose consumption. The characteristic and baseline biochemical markers of subjects are shown in Table 1. As it is seen in Table 2, level of FBS, 2HPP, HbA1C decreased after six week treatment with zinc sulfate but it was not statistically significant.

Due to zinc sulfate administration in diabetic patients, a significant decrease occurred in TG (P=0.005), chol (p=0.02), LDL (0.01) and systolic blood pressure (p=0.02).

Table 1: Characteristic and baseline biochemical markers of subjects

Variables	Mean±SD
BMI (kg/m ²)	27.60±5.92
FBS (mg/dl)	156.10±50.30
2hpp (mg/dl)	221.85±81.89
HbA1C (%)	7.83±1.53
TG (mg/dl)	216.92±113.92
Chol (mg/dl)	170.97±44.29
LDL (mg/dl)	92.45±34.63
HDL (mg/dl)	47.92±15.30S
BP (mmHg)	122.92±25.74
DBP (mmHg)	73.25±11.00

Body Mass Index (BMI), Fasting Blood Sugar (FBS), 2-h postprandial glucose (2hpp), Glycated hemoglobin (HbA1C), Triglyceride (TG), cholesterol (chol), low - density lipoproteins (LDL), high-density lipoproteins (HDL), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP).

HDL was increased but it was not significant (p=0.14). No statistically significant differences were found prior to and after zinc treatment in BMI and diastolic blood pressure.

Only two patients had mild abdominal pain. After 12 weeks, there was a significant decrease in HbA1C (P=0.04) in zinc sulfate group but a significant decrease didn't occur in BMI and blood pressure.

As it is seen in Table 2, no statistically significant differences were found prior to and after six weeks placebo treatment in different biochemical variables.

Discussion

Recently, diabetic patients have tendency to use complementary and alternative medicine beside routine therapies. Zinc is one of the minerals used by diabetic patients. Anderson *et al.* (2001) study on 110 type 2 diabetes mellitus with HbA1C > 7.5% revealed that more than 30% of the subjects may have been zinc deficient (Anderson *et al.*, 2001).

In present study, no statistically significant differences were found prior to and after 6 weeks zinc sulfate treatment in FBS, 2hpp, HbA1C, HDL, BMI and diastolic blood pressure.

Table 2: Biochemical parameters before to and after Zinc sulfate versus placebo consumption

Variables	Zinc sulfate			Placebo		
	Pre-trial	Post-trial	P-value	Pre-trial	Post-trial	P-value
BMI(kg/m ²)	28.33±6.6	26.75±5.08	0.16	26.86±5.15	26.75±5.08	0.16
FBS (mg/dl)	150.35±64.02	134.25±57.81	0.09	157.60±31.08	159.50±27.35	0.55
2hpp (mg/dl)	186.65±78.57	174.70±74.28	0.06	259.85±68.45	250.55±60.85	0.05
HbA1C (%)	8.13±2.03	7.35±1.62	0.05	7.53±0.71	7.46±0.73	0.62
TG (mg/dl)	227.85±130.61	138.30±75.43	0.005*	206±96.58	197.15±99.41	0.21
Chol (mg/dl)	161.05±47.82	126.40±33.27	0.02*	80.90±39.16	177.85±38.59	0.29
LDL (mg/dl)	85.85±38.39	56.55±21.08	0.01*	99.05±29.95	95.80±28.68	0.10
HDL (mg/dl)	49.50±10.17	56.80±21.85	0.14	46.35±19.28	46.55±19.26	0.51
SBP (mmHg)	134.25±18.48	129.50±18.48	0.02*	112.50±6.38	106.10±23.50	0.26
DBP (mmHg)	76.75±13.79	71.5±9.33	0.1	76.75±13.79	71.50±9.33	0.10

Body Mass Index (BMI), Fasting Blood Sugar (FBS), 2-h postprandial glucose (2hpp), Glycated hemoglobin (HbA1C), Triglyceride (TG), cholesterol (chol), low-density lipoproteins (LDL), high-density lipoproteins (HDL), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP). *Statistical significance when p<0.05.

Afkhami-Ardekani *et al.*: Effect of Zinc on Glucose and Lipid in Type 2 Diabetes

Due to zinc sulfate administration in diabetic patients, a significant decrease occurred in TG ($p=0.005$), chol ($p=0.02$), LDL ($p=0.01$) and systolic blood pressure ($p=0.02$). After 12 weeks, there was a significant decrease in HbA1C ($p=0.04$).

Some investigations indicated that a zinc-enriched diet has beneficial effects on basal and postprandial glycaemia, the content of cholesterol and triglycerides (Ghayour-Mobarhan *et al.*, 2005).

In Roussel *et al.* (2003) study on 56 diabetic patients (divided to zinc gluconate and placebo group) treated with 30 mg zinc gluconate, HbA1c decreased from 8.9 ± 0.4 to $7.7\pm 0.3\%$ following six months of zinc supplementation, but decreases were not significant and no changes was seen in FBS (Roussel *et al.*, 2003).our result about FBS and HBA1C was similar to it. Cunnane (1988) believed that zinc intimately affects many aspects of lipid metabolism through established enzymes but also has modulator effects whose mechanism is not obvious or established. In individuals with type 1 diabetes mellitus receiving 30 mg of zinc as zinc gluconate for three months, there were decreased lipid peroxidation and improvement in antioxidant status (Faure *et al.*, 1995; Faure *et al.*, 1993).

In Partida-Hernandez *et al.* (2006) survey on type 2 diabetic patients who received 100 mg zinc sulfate, there was no statistically change in FBS and HBA1C after 12 weeks (Partida-Hernandez *et al.*, 2006). In our survey HBA1C was statistically decreased after 12 weeks which may be related to the higher dosage of zinc sulfate in our study.

The diabetic patients had changes in their lipid profile after a 12-week zinc treatment as compared with placebo treatment in Partida-Hernandez *et al.* (2006) survey. The 100 mg zinc sulfate treatment was well tolerated, significantly reduced total cholesterol ($p=0.01$) and triglyceride concentrations (0.02) and increased those corresponding to zinc as well as HDL cholesterol in the bloodstream (0.002) but decrease in LDL was not significant (0.22) (Partida-Hernandez *et al.*, 2006). Differences with our study is related to drug dosage.

Results of randomized controlled trials of Hughes and Samman (2006) show that LDL, total cholesterol and triglycerides in plasma are unaffected by supplementation with up to 150 mg Zn/d. In contrast, HDL concentrations decline when zinc supplements provide a dose >50 mg/d (Hughes and Samman, 2006). Higher dose of zinc sulfate is needed to decrease the TG, total cholesterol and LDL similar to our study.

Hooper *et al.* (1980) study examined the effect of zinc administration on serum lipoprotein values in man. Twelve healthy adult men ingested 440 mg of zinc sulfate per day for five weeks. High-density lipoprotein-cholesterol concentration decreased 25% below baseline values (40.5 to 30.1 mg/dL). Total cholesterol,

triglyceride and low-density lipoprotein-cholesterol levels did not change throughout the study (Hooper *et al.*, 1980). In Roussel *et al.* (2003) study which indicated previously, no changes was seen in lipid profile. (Roussel *et al.*, 2003).

In Freeland-Graves *et al.* (1982) study, four levels of zinc supplements (0, 15, 50, or 100 mg/day) were given to 32 women for 8 weeks. No significant differences were seen in HDL-cholesterol over the 8 week except in the 100 mg group at week 4 (Freeland-Graves *et al.*, 1982). In conclusion, it seems that zinc is a proper mineral in diabetic patients due to their deficiency and consumption of zinc sulfate in addition to other nutritional and pharmacological treatments in type 2 diabetic patients could be effective in lipid profile.

References

- Afkhami-Ardekani, M., S. Vahidi, A. Vahidi and M.H. Ahmadi, 2001. Epidemiological survey of NIDDM in persons over 30 years old in Yazd province. J. Shahid Sadoughi Univ. Med. Sci. Health Services, 9: 22-27.
- Amos, A.F., D.J. McCarty and P. Zimmet, 1997. The rising global burden of diabetes and its complications: Estimates and projections to the year 2010. Diabet Med., 14 Suppl 5: S1-85.
- Anderson, R.A., A.M. Roussel, 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: 212-8.
- Chen, M.D., P.Y. Lin and W.H. Lin, 1991. Investigation of the relationships between zinc and obesity. Gaoxiong Yi Xue Ke Xue Za Zhi., 7: 628-34.
- Cunnane, S.C., 1988. Role of zinc in lipid and fatty acid metabolism and in membranes. Prog. Food Nutr. Sci., 12: 151-88.
- Faure, P., P.Y. Benhamou, A. Perard, S. Halimi and A.M. Roussel, 1995. Lipid peroxidation in insulin-dependent diabetic patients with early retina degenerative lesions: Effects of an oral zinc supplementation. Eur. J. Clin. Nutr., 49: 282-8.
- Faure, P., P. Corticelli, M.J. Richard, J. Arnaud, C. Coudray, S. Halimi, A. Favier and A.M. Roussel, 1993. Lipid peroxidation and trace element status in diabetic ketotic patients: Influence of insulin therapy. Clin. Chem., 39: 789-93.
- Freeland-Graves, J.H., B.J. Friedman, W.H. Han, R.L. Shorey and R. Young, 1982. Effect of zinc supplementation on plasma high-density lipoprotein cholesterol and zinc. Am. J. Clin. Nutr., 35: 988-992.
- Freeman, H. and R.D. Cox, 2006. Type-2 diabetes: A cocktail of genetic discovery. Hum. Mol. Genet., 15: R202-9.

Afkhami-Ardekani et al.: Effect of Zinc on Glucose and Lipid in Type 2 Diabetes

- Ghayour-Mobarhan, M., A. Taylor, S.A. New, D.J. Lamb and G.A. Ferns, 2005. Determinants of serum copper, zinc and selenium in healthy subjects. *Ann. Clin. Biochem.*, 42: 364-75.
- Hooper, P.L., L. Visconti, P.J. Garry and G.E. Johnson, 1980. Zinc lowers high-density lipoprotein-cholesterol levels. *JAMA.*, 244: 1960-1961.
- Hughes, S. and S. Samman, 2006. The Effect of Zinc Supplementation in Humans on Plasma Lipids, Antioxidant Status and Thrombogenesis. *J. Am. Coll. Nutr.*, 25: 285-291.
- Jinlin, F., W. Binyou and C. Terry, 2007. A new approach to the study of diet and risk of type 2 diabetes. *J. Post Grad. Med.*, 53: 139-43.
- King, H., R.E. Aubert and W.H. Herman, 1998. Global burden of diabetes, 1995-2025: Prevalence, numerical estimates and projections. *Diabetes Care*, 21: 1414-31.
- Kleefstra, N., S.T. Houweling, S.J. Bakker, S. Verhoeven, R.O. Gans, B. Meyboom-de Jong and H.J. Bilo, 2007. Chromium treatment has no effect in patients with type 2 diabetes in a Western population: A randomized, double-blind, placebo-controlled trial. *Diabetes Care*, 30: 1092-6.
- Nazimek-Siewniak, B, D. Moczulski and W. Grzeszczak, 2002. Risk of macrovascular and microvascular complications in Type 2 diabetes: Results of longitudinal study design. *J. Diabetes Complications*, 16: 271-6.
- Partida-Hernandez, G., F. Arreola, B. Fenton, M.Cabeza, R. Roman-Ramos and M.C. Revilla-Monsalve, 2006. Effect of zinc replacement on lipids and lipoproteins in type 2-diabetic patients. *Biomed Pharmacother*, 60: 161-8.
- Powell, S.R., 2000. The antioxidant properties of zinc. *J. Nutr.*, 130: 1447S-54S.
- Roussel, A.M., A. Kerkeni, N. Zouari, S. Mahjoub, J.M. Matheau and R.A. anderson, 2003. Antioxidant effectsof zinc supplementation in Tunisians with type 2 diabetes mellitus. *J. Am. Coll. Nutr.*, 22: 316-21.
- Song, Y., J. Wang, X.K. Li and L. Cai, 2005. Zinc and the diabetic heart. *Biometals*, 18: 325-32.