Iranian Journal of Pharmaceutical Sciences
2014: 10 (3): 63- 68
www.ijps.ir

Original Article

Effect of Nano-magnesium Oxide on Glucose Concentration and Lipid Profile in Diabetic Laboratory Mice

Noushin Naghsh, Shaghayegh Kazemi*

Islamic Azad University of Istahban, Istahban, Farss, Iran.

Abstract

Nano-sized drugs have better distribution than their identical forms. Magnesium is the cofactor of various enzymes in lipid and glucose metabolism. In this study, the effect of nano-magnesium oxide (nano-MgO) on glucose concentration and lipid profile in diabetes induced mice was evaluated in 21 laboratory mice. Mice were randomly divided into three equal groups (control, treatment, and placebo). Diabetes was induced in treatment and placebo group by injection of 60 mg/kg streptozotocin while control group was injected by saline. Treatment group was injected by 2 mg/kg of nano-MgO every 48 hours until the day 45. Serum glucose was measured at 3, 46, and 48 days. Concentration of triglyceride (TG), cholesterol, high density lipoprotein (HDL) and low density lipoprotein (LDL) was measured at day 48. Treatment and placebo group had higher glucose level at day 3 but treatment group at days 46 and 48 had lower glucose levels than placebo group. Diabetic mice had higher levels of TG, cholesterol, LDL and lower levels of HDL than control group in their serum samples. Treatment with MgO ameliorated change in glucose, TG, HDL and LDL level in treated mice. Our study has showed that administration of nano-MgO decreased glucose concentration and ameliorated TG, HDL and LDL levels in diabetes induced mice.

Key words: Diabetes, glucose, lipid profile, nano drug, nano-magnesium oxide.

Corresponding Author: Shaghayegh Kazemi, Islamic Azad university. Istahban. Fras,Iran
Tel: +989133294209
E-Mail: shaghayegh_113@yahoo.com
Cite this article as: Naghsh N, Kazemi Sh, Effect of Nano-magnesium Oxide on Glucose Concentration and Lipid Profile in Diabetic Laboratory Mice.Iranian Journal of Pharmaceutical Sciences, 2014, 10(3): 63-68.

1. Introduction

Using nano sized drugs have been noticed in recent years and growing number of studies have used these drugs in treatment of various diseases [1]. Magnesium is the fourth most abundant cation in living organisms which plays role in more than 300 enzymes [2] including those responsible for glucose and lipid metabolism [3-5].These enzymes have role in glucose oxidation, glucose transport, and insulin release. Magnesium may also act as a cofactor in

ATPase and adenylat cyclase enzymes [6]. Since it has modulatory effect on glucose transporters [3], magnesium deficiency may contribute to insulin resistance [7]. Previously magnesium was used as complementary therapy in diabetic patients [8]. Treatment with magnesium has also ameliorated lipid profile in fructose fed rats. Nano-Magnesium oxide (nano-MgO) has been formerly used in various areas [1]. It has been best known for its bactericidal effect [9]. Nano-MgO has been previously known for its bactericidal effect. The effect of nano-magnesium compounds in diabetic patients was not studied yet. The aim of this study is to evaluate the possible effect of nano-mgO on serum glucose levels and lipid profile in diabetic laboratory mice.

2. Materials and Methods

2.1. Materials

Nano magnesium oxide was obtained from Neutrino CO. It was 10 nm in diameter. Streptozotocin obtained from Merck Co.

2.2. Animals and Treatments

In this study 21 male laboratory mice (Mus musculus) weighing initially between 25-30 grams were divided randomly into three equal groups and allowed five days of adaptation prior to study. They were given free access to rodent diet and water in 20-25°C temperature and 60-70% humidity. Diabetes was induced in treatment and placebo groups by intraperitoneal administration of 60mg/kg streptozotocin while control group was injected by the same volume of normal saline. Treatment group was injected intraperitoneally by 4 mg/kg of nano-MgO every alternative day until the day 45. Placebo group was injected by same value of normal saline in same period. Blood samples were centrifuged to separate serum. This experiment was performed under the approval of the state committee on animal ethics, Islamic Azad university, Istahban, Iran. Also, the recommendations of European Council Directive (86/609/EC) of November 24, 1986, regarding the protection of animals used for experimental purposes, were considered.

2.3. Blood Glucose Measurement

Blood samples were taken from tail at days 3 (1 hour before the first treatment) 46 and 48 after induction of diabetes (24 and 72 hours after the last treatment respectively). Glucose concentration was assayed by Accu-Chek active blood glucose meter

2.4. Evaluation of Serum Lipid Profile

At the end of study (day 48) blood samples were taken from heart and were centrifuged to separate serum. Serum samples were used for measuring lipid markers. Triglyceride was measured using an enzymatic method by Bucolo and David (1973) [10] modified by Fossati and Prencipe (1982) [11]. Cholesterol level was determined using an enzymatic method by Allain et al 1974 [12]. HDL was assayed by direct method using commercial kit by Man

Company [13-15]. Serum LDL was measured by direct method [16].

2.5. Statistics

Results were expressed as Mean ± SEM. Data were analyzed by one way ANOVA followed by Bonferroni's post hoc test using software IBM SPSS (Statistical Package for the Social Sciences) version 22. P-value less than 0.05 were considered statistically significant.

3. Results and Discussion

3.1. Blood Glucose Measurement

Change in glucose concentration is shown in Fig. 1 and table 1. Three days after administration of streptozotocin glucose concentration of serum was higher in treatment (P<0.001) and placebo groups (P<0.001) compared with control group. At day 46, one day after the last injection, glucose concentration in treated mice was lower than that of placebo group (P<0.001); however it was higher than control group (P<0.001). At day 48, three days after the last injection, glucose level in treated mice was still lower than placebo group (P=0.037) but simple T test has shown that glucose level in treatment group was higher than glucose level at day 46 in the same group (P=0.026).

3.2. Evaluation of Serum Lipid Profile

Evaluation of serum biochemical data is given in table 1. Our laboratory data has revealed that triglyceride level was higher in placebo group compared with control group (P<0.001). Concentration of triglyceride in treated group showed no difference with control group (P=0.055). Serum cholesterol concentration in treatment and placebo groups were higher than control group (P<0.001). Cholesterol levels in mice received the treatment was lower than that of placebo group but not

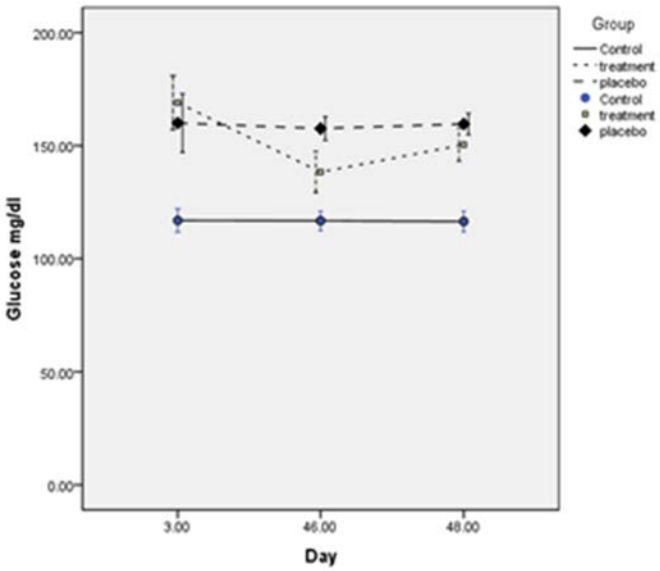

Figure 1. Change in serum glucose levels in three groups of mice at days 3, 46 and 48.

Table 1. Biochemical profile in serum samples. Data are expressed as mean±S.E.M. N=7 for each group.

	Glu3* (mg/dl)	Glu46* (mg/dl)	Glu48* (mg/dl)	TG† (mg/dl)	Cho† (mg/dl)	HDL† (mg/dl)	LDL† (mg/dl)
Control	116.9±2.11	116.7±1.74	116.3±1.74	141.3±4.13	81.9±2.56	72.1±1.71	10.0±0.81
Treatment	169.0±4.88	138.3±3.71	150.4±3.00	124.4±1.29	100.7±1.55	71.7±0.97	15.6±0.48
Placebo	160.0±5.31	157.6±2.15	159.6±1.95	251±6.69	107.6±1.29	60.6±3.60	19.28±0.64

*****Glu 3, glu 46 and glu 48 represents glucose concentration at days 3, 46 and 48 respectively.
† TG, Cho, HDL and LDL represents triglyceride, cholesterol, high density lipoprotein and density lipoprotein levels in serum in day

significantly (P=0.057). HDL levels in placebo group was lower than control group (P=0.008). Mice treated with nano-MgO showed higher levels of HDL than placebo groups (P=0.011) and it showed no difference with control group (P=1). Serum samples of diabetic mice in placebo group had higher levels of LDL than control group (P<0.001). Treated mice showed lower levels of LDL compared with placebo group (P=0.003) but it was higher than control group (P=0.001).

3.3. Discussion

Our study has revealed that nano-sized magnesium oxide decreased glucose concentration in diabetic mice. It was evidenced by lower concentration of glucose in treated group compared with placebo group one day after the last injection. Previously the effect of magnesium supplements was studied in diabetic patients [8]. These studies have shown that magnesium chloride and magnesium pidolate are able to decrease fasting glucose in type II diabetic patients [17-19]. However others have reported that magnesium pidolate [20], magnesium citrate [21], magnesium aspartate [22] and magnesium citrate [23] had no effect on glucose concentration. Lima et al 1998 have reported that magnesium oxide has no effect on hyperglycemia [2]. In our knowledge this is the first administration of a nano-sized mineral compound in diabetic patients. The difference between our results and Lima et al 1998 may be due to the fact that nano size particles have large specific area and high biological activity [24]. Our results have shown that the effect of nano-MgO lasts three days after the last injection. It has been suggested that nanoparticles because of their long retention in host tissue has the ability to repeat their catalytic activity [25].

Our study has shown that nano-sized magnesium oxide has also ameliorated change in lipid profile. It prevented changes in triglyceride and HDL and decreased change in LDL concentration. Magnesium has an important role in enzymes responsible for lipid metabolism. Increased magnesium uptake improves insulin sensitivity and lipid profile [5]. Previously it has been reported that magnesium is able to decrease

the activity of lipogenic enzymes in liver and increase lipoprotein lipase activity [26.[

Since nano particles have high biologic activity [24] their application in treatment of different diseases were investigated [27, 28]. Nano particles may transfer easily through cell membrane [29, 30]. As seen in our laboratory data nano-mMgO is not able to reduce glucose concentration to normal level and it can't be used as the only therapy but it may be used as a supplementary therapy. However the possible side effect of such therapy is not known well and must be studied later.

4. Conclusion

From this study it was concluded that nano-MgO is able to decreased glucose concentration in diabetic mice. It has also ameliorated glucose and lipid profile in diabetic mice.

Acknowledgement

The authors thank to Mr. Koohi for his help on animal care and Dr. Hashempour for his help on preparation of the paper.

References

[1] Singh, R, Lillard, JW, Jr. Nanoparticle-based targeted drug delivery. Exp Mol Pathol (2009)86(3): 215-223.

[2] de Lordes Lima, M, Cruz, T, Pousada, JC, Rodrigues, LE, Barbosa, K, Cangucu, V. The effect of magnesium supplementation in increasing doses on the control of type 2 diabetes. Diabetes Care (1998)21(5): 682-686.

[3] Mooradian, AD, Failla, M, Hoogwerf, B, Maryniuk, M, Wylie-Rosett, J. Selected vitamins and minerals in diabetes. Diabetes Care (1994)17(5): 464-479.

[4] Tosiello, L. Hypomagnesemia and diabetes mellitus. A review of clinical implications. Arch Intern Med (1996)156(11): 1143-1148.

[5] Olatunji, LA, Soladoye, AO. Increased magnesium intake prevents hyperlipidemia and insulin resistance and reduces lipid peroxidation in fructose-fed rats. Pathophysiology (2007)14(1): 11-15.

[6] Dasgupta, A, Sarma, D, Saikia, UK. Hypomagnesemia in type 2 diabetes mellitus. Indian J Endocrinol Metab (2012)16(6): 1000-1003.

[7] Alzaid, AA, Dinneen, SF, Moyer, TP, Rizza, RA. Effects of insulin on plasma magnesium in noninsulin-dependent diabetes mellitus: evidence for insulin resistance. J Clin Endocrinol Metab (1995)80(4): 1376-1381.

[8] Guerrero-Romero, F, Rodriguez-Moran, M. Complementary therapies for diabetes: the case for chromium, magnesium, and antioxidants. Arch Med Res (2005)36(3): 250-257.

[9] Huang, L, Li, DQ, Lin, YJ, Wei, M, Evans, DG, Duan, X. Controllable preparation of Nano-MgO and investigation of its bactericidal properties. J Inorg Biochem (2005)99(5): 986-993.

[10] Bucolo, G, David, H. Quantitative determination of serum triglycerides by the use of enzymes. Clin Chem (1973)19(5): 476-482.

[11] Fossati, P, Prencipe, L. Serum triglycerides determined colorimetrically with an enzyme that produces hydrogen peroxide. Clin Chem (1982)28(10): 2077-2080.

[12] Allain, CC, Poon, LS, Chan, CS, Richmond, W, Fu, PC. Enzymatic determination of total serum cholesterol. Clin Chem (1974)20(4): 470-475.

[13] Pelliniemi, TT, Viikari, J, Nieminen, L. Effect of hyperlipidaemic diet and clofibrate treatment on rat

erythrocyte lipids. Scand J Haematol (1976)17(2): 117-122.

[14] Demacker, PN, Hijmans, AG, Vos-Janssen, HE, van't Laar, A, Jansen, AP. A study of the use of polyethylene glycol in estimating cholesterol in high-density lipoprotein. Clin Chem (1980)26(13): 1775-1779.

[15] Widhalm, K, Pakosta, R. Precipitation with polyethylene glycol and density-gradient ultracentrifugation compared for determining high-density lipoprotein subclasses HDL2 and HDL3. Clin Chem (1991)37(2): 238-240.

[16] Rifai, N, Iannotti, E, DeAngelis, K, Law, T. Analytical and clinical performance of a homogeneous enzymatic LDL-cholesterol assay compared with the ultracentrifugation-dextran sulfate-Mg2+ method. Clin Chem (1998)44(6 Pt 1): 1242-1250.

[17] Rodriguez-Moran, M, Guerrero-Romero, F. Oral magnesium supplementation improves insulin sensitivity and metabolic control in type 2 diabetic subjects: a randomized double-blind controlled trial. Diabetes Care (2003)26(4): 1147-1152.

[18] Paolisso, G, Sgambato, S, Gambardella, A, Pizza, G, Tesauro, P, Varricchio, M, D'Onofrio, F. Daily magnesium supplements improve glucose handling in elderly subjects. Am J Clin Nutr (1992)55(6): 1161-1167.

[19]Yokota, K, et al. Clinical efficacy of magnesium supplementation in patients with type 2 diabetes. J Am Coll Nutr (2004)23(5): 506S-509S.

[20] Paolisso, G, Scheen, A, Cozzolino, D, Di Maro, G, Varricchio, M, D'Onofrio, F, Lefebvre, PJ. Changes in glucose turnover parameters and improvement of glucose oxidation after 4-week magnesium administration in elderly noninsulin-dependent (type II) diabetic patients. J Clin Endocrinol Metab (1994)78(6): 1510-1514.

[21] Eibl, NL, Kopp, HP, Nowak, HR, Schnack, CJ, Hopmeier, PG, Schernthaner, G. Hypomagnesemia in type II diabetes: effect of a 3-month replacement therapy. Diabetes Care (1995)18(2): 188-192.

[22] de Valk, HW, Verkaaik, R, van Rijn, HJ, Geerdink, RA, Struyvenberg, A. Oral magnesium supplementation in insulin-requiring Type 2 diabetic patients. Diabet Med (1998)15(6): 503-507.

[23] Gullestad, L, Jacobsen, T, Dolva, LO. Effect of magnesium treatment on glycemic control and metabolic parameters in NIDDM patients. Diabetes Care (1994)17(5): 460-461.

[24] Zhu, MT, et al. Comparative study of pulmonary responses to nano- and submicron-sized ferric oxide in rats. Toxicology (2008)247(2-3): 102-111.

[25] Limbach, LK, Wick, P, Manser, P, Grass, RN, Bruinink, A, Stark, WJ. Exposure of engineered nanoparticles to human lung epithelial cells: influence of chemical composition and catalytic activity on oxidative stress. Environ Sci Technol (2007)41(11): 4158-4163.

[26] Odonkor, JM, Rogers, MP. Effects of ethyl-CPIB (clofibrate) on tissue lipoprotein lipase and plasma post-heparin lipolytic activity in rats. Biochem Pharmacol (1984)33(8): 1337-1341.

[27] Langer, R, Cleland, JL, Hanes, J. New advances in microsphere-based single-dose vaccines. Adv Drug Deliv Rev (1997)28(1): 97-119.

[28] Torres-Martinez, CL, Kho, R, Mian, OI, Mehra, RK. Efficient Photocatalytic Degradation of Environmental Pollutants with Mass-Produced ZnS Nanocrystals. J Colloid Interface Sci (2001)240(2): 525-532.

[29] Renwick, LC, Donaldson, K, Clouter, A. Impairment of alveolar macrophage phagocytosis by ultrafine particles. Toxicol Appl Pharmacol (2001)172(2): 119-127.

[30] Hoet, PH, Bruske-Hohlfeld, I, Salata, OV. Nanoparticles - known and unknown health risks. J Nanobiotechnology (2004)2(1): 12.