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EFFECT OF ORAL ADMINISTRATION OF VITAMIN A ON BLOOD GLUCOSE LEVEL IN RABBITS AND ITS POSSIBLE INTERACTIONS WITH COMMONLY USED ORAL ANTIDIABETIC AGENTS

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Key words:

Vit A, Blood glucose, antioxidants, antidiabetic agents, glimepiride, gliclazide, metformin.

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ABSTRACT: In diabetes mellitus antioxidant vitamins are commonly employed to prevent or mitigate the long term complications of the disorder. Diabetic retinopathy, nephropathy, coronary and cerebral vascular insufficiency are examples of such complications. They are more common in Type 2 diabetes mellitus. The present study was conducted to observe the effect of Vit A on blood glucose level and its possible interactions with commonly prescribed oral antidiabetic agents i.e. glimepiride, gliclazide and metformin. The study was performed on healthy albino rabbits of either sex in which hyperglycemia was induced by giving oral glucose. We observed that Vit.A significantly lowered the blood glucose level but antagonized the effect of oral antidiabetic agents in co-administration therapy. It is therefore advisable that caution must be exercised when giving high doses of VitA to produce antioxidant effects in diabetic patients because it is not only unnecessary but may also have potentially deleterious effect on glycemic control.

INTRODUCTION: Diabetes mellitus is the commonest metabolic syndrome affecting > 382 million people in the world. [1] It has varied etiology and is characterized by prolonged hyperglycemia and derangement of carbohydrate, protein and lipid metabolism.[2, 3] Quantitative and/or qualitative deficiency of Insulin is the hallmark of diabetes. This may occur due to oxidative damage to the beta-cells as is seen in Type1 Diabetes mellitus (T1DM) [4] or due to development of Insulin resistance as occurs in Type 2 Diabetes mellitus. [5, 6]

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Lipid peroxidation, Advanced Glycated End products (AGEs), Sorbitol accumulation in the tissues , formation of Diacyl glycerol leading to activation of Protein kinase C and oxygen derived free radicals contribute to the pathogenesis of the disorder .[7, 8]

Various studies suggest that administration of Antioxidants like Vit A, Vit E, Vit C and selenium can prevent the long term complications of diabetes by free radical scavenging action. [9, 10, 11, 12]

Diabetic patients often require multiple drugs and therefore chances of drug interactions are quite high.[13]

Treatment of diabetes requires close supervision of blood glucose level because intensive blood glucose regulation has been reported to prevent or

significantly delay various vascular and non vascular complications of diabetes.[14]

At the same time avoidance of hypoglycemia is also of equal importance because episodes of hypoglycemia can lead to cerebral injury.[15, 16]

Various pharmacological agents are reported to have interactions with antidiabetic agents which can interfere with glycemic regulation.[17]

Vit A is commonly employed for its antioxidant effect in diabetic patients to retard the progression of diabetic retinopathy and other long term complications of diabetes.

It was therefore decided to undertake a study to explore the possibilities of drug interactions between Vit. A and common antidiabetic agents.

The aim of the this study was-

1. To assess if Vit A per se had any effect on blood sugar level.

2. To evaluate the possible effect of this antioxidant on the modification of blood sugar levels produced by commonly used antidiabetic agents.

Various drugs included in the study are the ones which are at present commonly employed (Vit A, gliclazide, glimepiride and metformin).

MATERIAL AND METHODS:

Present study was conducted on healthy albino rabbits of either sex weighing 1.5 - 2.0 kg. Study was approved by the meeting of IAEC held on 31st Aug, 2009 (circular No. 41/ AH/ RIMS&R/ 2009-10). Animals were made available to Department of Pharmacology by Central Animal House. They were maintained on standard pellet diet and water ad libitum.

Estimation of blood glucose level was done by using glucose oxidase - peroxidase method. Due to specificity of enzymes the enzymatic method is the most accurate. For this study rabbits were divided into 8 groups of 5 rabbits each.

Group I: Rabbits of this group were given 25 gm of glucose powder orally. This group shows normal pattern of blood glucose level after a glucose load and served as control.

Group II: Rabbits of this group were given vitamin A (10,000 I.U./Kg/d) orally for 7 days and 25 gm of glucose powder orally on 7th day. This group shows effect of Vitamin A on blood glucose level.

Group III: Rabbits of this group were given glimepiride (0.2 mg/kg) orally and 25 gm of glucose powder. This group shows normal pattern of antidiabetic action of glimepiride.

Group IV: Rabbits of this group were vitamin A (10,000 I.U./Kg/d) orally for 7 days and glimepiride (0.2 mg/kg) plus 25 gm of glucose powder were added on 7th day. This group shows effect of vitamin A on the pattern of blood glucose levels produced by glimepiride.

Group V: Rabbits of this group were given gliclazide (8 mg/kg) orally and 25 gm of glucose powder. This group shows normal pattern of antidiabetic action of gliclazide.

Group VI: Rabbits of this group were vitamin A (10,000 I.U./Kg/d) for 7 days and gliclazide (8 mg/kg) plus 25 gm of glucose powder were added on 7th day. This group shows effect of vitamin A on the pattern of blood glucose levels produced by gliclazide.

Group VII: Rabbits of this group were given metformin (100 mg/kg) orally and 25 gm of glucose powder. This group shows normal pattern of antidiabetic action of metformin.

Group VIII: Rabbits of this group were vitamin A (10,000 IU/Kg/d) for 7 days and metformin (100 mg/kg) plus 25 gm of glucose powder were added on 7th day. This group shows effect of vitamin A on the pattern of blood glucose levels produced by metformin.

- Rabbits were fasted overnight and during the study but were allowed water during this period.

- Samples were collected just before administration of drug and glucose (0 hr.) and after 2, 4 and 6 hrs. of administration.
- All drugs and glucose were given orally through nasogastric tubes, those not soluble in water were rendered soluble with the help of gum acacia.

Observations:

TABLE 1: BLOOD GLUCOSE LEVELS OF RABBITS RECEIVING 25 gm GLUCOSE POWDER AFTER OVERNIGHT FASTING

S.No.	Blood glucose level (mg%)& Time interval (hrs.)			
	0	**2**	**4**	**6**
1.	104.2	297.4	129.2	112.7
2.	111.0	288.8	133.1	108.5
3.	103.7	291.3	126.9	99.8
4.	98.9	302.0	119.3	118.0
5.	106.0	293.5	117.2	97.8
Mean	104.62	294.6	125.14	107.36
S.E. +	1.98	2.33	3.0	3.82

TABLE 2: BLOOD GLUCOSE LEVELS OF RABBITS RECEIVING VITAMIN A(10000 I.U./kg/d) FOR 7 DAYS AND 25 gm GLUCOSE POWDER AFTER OVERNIGHT FASTING

S. No.	Blood glucose level (mg%)& Time interval (hrs.)			
	0	**2**	**4**	**6**
1.	92.0	252.9	71.9	73.0
2.	86.0	317.6	89.0	87.4
3.	81.5	301.0	87.3	89.5
4.	115.7	293.8	93.4	82.0
5.	98.7	280.2	79.5	80.5
Mean	94.78	289.1	84.22	82.48
S.E. ±	5.99	10.90	3.82	2.90

TABLE 3: BLOOD GLUCOSE LEVELS OF RABBITS RECEIVING GLIMEPIRIDE (0.2 mg/kg) AND 25 gm GLUCOSE POWDER AFTER OVERNIGHT FASTING

S. No.	Blood glucose level (mg%)& Time interval (hrs.)			
	0	**2**	**4**	**6**
1.	104.2	112.0	101.8	98.3
2.	108.0	116.3	104.5	102.7
3.	112.9	127.1	98.3	104.9
4.	99.3	110.4	109.7	93.6
5.	102.0	109.8	112.0	90.5
Mean	105.28	114.96	105.26	98.00
S.E. ±	2.38	3.28	2.51	2.70

TABLE 4: BLOOD GLUCOSE LEVELS OF RABBITS RECEIVING VITAMIN A (10000 I.U./ kg/d) FOR 7 DAYS AND GLIMEPIRIDE (0.2 mg / kg) plus 25 gm GLUCOSE POWDER AFTER OVERNIGHT FASTING.

S. No.	Blood glucose level (mg%)& Time interval (hrs.)			
	0	**2**	**4**	**6**
1.	99.0	196.6	113.9	101.6
2.	107.8	183.0	161.4	107.0
3.	87.0	149.6	128.2	96.3
4.	93.6	160.0	143.0	91.9
5.	94.7	157.8	113.0	102.0

Mean	96.42	169.4	131.9	99.76
S.E. ±	3.44	8.79	9.21	2.60

TABLE 5: BLOOD GLUCOSE LEVELS OF RABBITS RECEIVING GLICLAZIDE (8 mg/kg) AND 25 gm GLUCOSE POWDER AFTER OVERNIGHT FASTING.

S.No.	Blood glucose level (mg%)& Time interval (hrs.)			
	0	**2**	**4**	**6**
1.	107.2	101.7	79.4	81.3
2.	100.0	91.4	76.0	90.3
3.	94.9	86.3	73.7	84.8
4.	98.8	88.0	81.2	91.7
5.	92.7	107.0	92.0	79.6
Mean	98.72	94.88	80.46	85.54
S.E. ±	2.50	4.05	3.17	2.39

TABLE 6: BLOOD GLUCOSE LEVELS OF RABBITS RECEIVING VITAMIN A (10000 I.U./ kg/d) fOR 7 DAYS AND GLICLAZIDE (8 mg / kg) plus 25 gm GLUCOSE POWDER AFTER OVERNIGHT FASTING.

S. No.	Blood glucose level (mg%)& Time interval (hrs.)			
	0	**2**	**4**	**6**
1.	87.0	138.3	104.0	96.3
2.	81.6	127.0	110.0	79.3
3.	103.9	141.8	121.6	91.0
4.	93.5	134.0	123.9	107.4
5.	96.8	119.0	97.3	93.6
Mean	92.56	132.02	111.24	93.52
S.E. ±	3.87	4.09	5.03	4.53

TABLE 7: BLOOD GLUCOSE LEVELS OF RABBITS RECEIVING METFORMIN (100 mg/kg) AND 25 gm GLUCOSE POWDER AFTER OVERNIGHT FASTING.

S. No.	Blood glucose level (mg%)& Time interval (hrs.)			
	0	**2**	**4**	**6**
1.	112.0	197.8	128.1	98.7
2.	108.3	186.4	118.7	101.3
3.	104.7	201.7	131.3	100.0
4.	113.9	211.9	124.8	103.8
5.	118.1	201.0	129.4	112.0
Mean	111.4	199.76	126.46	103.16
S.E. ±	2.30	4.10	2.21	2.37

TABLE 8: BLOOD GLUCOSE LEVELS OF RABBITS RECEIVING VITAMIN A (10000 I.U./ kg/d) FOR 7 DAYS AND METFORMIN (100 mg / kg) PLUS 25 gm GLUCOSE POWDER AFTER OVERNIGHT FASTING.

S. No.	Blood glucose level (mg%) Time interval (hrs.)			
	0	**2**	**4**	**6**
1.	103.5	210.7	100.0	93.8
2.	117.8	193.0	171.9	123.0
3.	98.3	139.2	128.5	103.8
4.	99.0	148.6	115.0	110.5
5.	87.8	159.0	127.3	108.0
Mean	101.28	170.1	128.54	107.82
S.E. ±	4.87	13.66	12.03	4.78

TABLE 9: STATISTICAL COMPARISON BETWEEN THE GROUP RECEIVING VIT. A PLUSGLUCOSE POWDER AND CONTROL GROUP (RECEIVING ONLY GLUCOSE POWDER).

Group receiving Vit A plus glucose powder (n = 5)	**Time interval (hrs.)**			
	0	**2**	**4**	**6**
Mean blood glucose (mg%)	94.78	289.1	84.22	82.48
SD +	13.39	24.37	8.54	6.48
Control group (receiving glucose powder only) (n = 5)	**Time interval (hrs.)**			
	0	**2**	**4**	**6**
Mean blood glucose (mg%)	104.62	294.6	125.14	107.36
SD +	4.43	5.21	6.71	8.54
't' value	1.56	1.01	8.43	5.19
'p' value	> 0.05	> 0.05	< 0.001	< 0.01

TABLE 10: STATISTICAL COMPARISON BETWEEN THE GROUP RECEIVING GLIMEPIRIDE PLUS VIT.A PLUS GLUCOSE POWDER AND THE GROUP RECEIVING GLIMEPIRIDE AND GLUCOSE POWDER.

Group receiving glimepiride, Vit. A and glucose powder (n = 5)	**Time interval (hrs.)**			
	0	**2**	**4**	**6**
Mean blood glucose (mg%)	96.42	169.4	131.9	99.76
SD +	7.70	19.68	20.63	5.82
Group receiving glimepiride and glucose powder (n = 5)	**Time interval (hrs.)**			
	0	**2**	**4**	**6**
Mean blood glucose (mg%)	105.28	114.96	105.26	98.0
SD +	5.32	7.33	5.61	6.04
't' value	2.11	5.79	5.52	0.61
'p' value	> 0.05	< 0.01	< 0.01	> 0.05

TABLE 11: STATISTICAL COMPARISON BETWEEN THE GROUP RECEIVING GLICLAZIDE PLUS VIT. A PLUS GLUCOSE POWDER AND THE GROUP RECEIVING GLICLAZIDE AND GLUCOSE POWDER

Group receiving gliclazide, Vit. A and glucose powder (n = 5)	**Time interval (hrs.)**			
	0	**2**	**4**	**6**
Mean blood glucose (mg%)	92.56	132.02	111.24	93.52
SD +	8.66	9.16	11.26	10.14
Group receiving gliclazide and glucose powder (n = 5)	**Time interval (hrs.)**			
	0	**2**	**4**	**6**
Mean blood glucose (mg%)	98.72	94.88	80.46	85.54
SD +	5.59	9.06	7.09	5.34
't' value	1.33	6.44	5.17	1.55
'p' value	> 0.05	< 0.01	< 0.01	> 0.05

TABLE 12: STATISTICAL COMPARISON BETWEEN THE GROUP RECEIVING METFORMIN PLUS VIT. A PLUS GLUCOSE POWDER AND THE GROUP RECEIVING METFORMIN AND GLUCOSE POWDER

Group receiving metformin, Vit. A and glucose powder (n = 5)	**Time interval (hrs.)**			
	0	**2**	**4**	**6**
Mean blood glucose (mg%)	101.28	170.1	128.54	107.82
SD +	10.90	30.59	26.94	10.70
Group receiving metformin and glucose powder (n = 5)	**Time interval (hrs.)**			
	0	**2**	**4**	**6**
Mean blood glucose (mg%)	111.4	199.76	126.46	103.16
SD +	5.14	9.17	4.94	5.30
't' value	1.88	2.07	0.16	0.87
'p' value	> 0.05	> 0.05	> 0.05	> 0.05

DISCUSSION: Aim of the present study was to see the effect of antioxidants on blood glucose level and their possible interactions with oral antidiabetic agents. Present study was conducted on healthy albino rabbits of either sex weighing 1.5 - 2 Kg. There were 8 groups in the present study each group comprising of 5 rabbits. The rabbits were fasted overnight. Blood samples (0.5 ml) were

withdrawn by disposable syringe each time from marginal pinna vein. Samples were taken in fluoride vials. Samples were centrifuged for 10 minutes at 3000 r.p.m. Supernatant was taken for estimation of blood glucose level. The estimation was done by glucose oxidase - peroxidase method. The observations obtained are shown in tables.

Table 1 shows blood glucose levels in fasted rabbits and at 2,4 and 6 hrs. Following administration of 25 gm glucose powder orally. The mean of blood glucose levels at 'O' hour (just before glucose) i.e. fasting value was found to be 104.62 mg%. The fasting values were found to be raised i.e. 294.6 mg% after 2 hrs., 125.14 mg% after 4 hrs. and 107.36 mg% after 6 hrs. following administration of glucose. These observations indicated that the blood glucose levels were significantly raised ($p< 0.001$) (about three times higher) than the fasting values following administration of larger dosage of glucose after 2 hrs. These values declined gradually reaching almost equal to fasting values after 6 hrs. This group served as control for the study.

Table 2 shows blood glucose levels of fasted rabbits following administration of vitamin A and glucose powder. Vitamin A was given in dose of 10,000 I.U./Kg/d for 7 days orally and 25 gm glucose powder was added on 7th day. The mean of blood glucose levels a '0' hr. (just before administration of drug and glucose) was 94.78 mg%, which became 289.1 mg% after 2 hrs., 84.22 mg% after 4 hrs. and 82.48 mg% after 6 hrs.These values were compared with control group in **Table 9**. A remarkable decrease in blood glucose level was noticed which was highly significant after 4 hrs. ($p<0.001$) and 6 hrs.($p<0.01$).

Table 3 shows blood glucose level of fasted rabbits following administration of 25 gm of glucose powder and glimepiride (0.2 mg/kg) orally. The mean of blood glucose levels at '0' hr. (fasting) was 105.28 mg%, which became 114.96 mg% after 2 hrs., 105.26 mg% after 4 hrs. and 98.0 mg% after 6 hrs. following administration of drug and glucose. On comparison to Table 1 it was found that glimepiride exhibit significant hypoglycemia at 2 and 4 hrs.

Table 4 shows blood glucose level in fasted rabbits following administration of Vitamin A, glucose and glimepiride. Vitamin A was given orally in dose of 10,000 I.U./Kg/d for 7 days regularly, 25 gm glucose and glimepiride (0.2 mg/kg) were added on 7th day and blood samples were taken. The mean of blood glucose levels at '0' hr. (fasting) was 96.42 mg% which became 169.4 mg% at '2' hrs, 131.9 mg% at 4 hrs.and 99.76 mg% at 6 hrs. following administration of drugs and glucose.

The values of Table 4 were compared with Table 3 in **Table 10**. The effect of glimepiride was observed to be modified when it was administered in combination with Vitamin A, Here we can see that vitamin A antagonized the hypoglycemic effect of glimepiride after 2 and 4 hrs. significantly ($p <0.01$).

Table 5 shows blood sugar levels of fasted rabbits following administration of glucose (25 gm) and gliclazide (8 mg/kg). The mean of blood glucose levels at '0' hr. (fasting) was 98.72 mg% which became 94.88 mg% at 2 hrs., 80.46 mg% at 4 hrs. and 85.54 mg% at 6 hrs. following administration of drug and glucose. Gliclazide produced significant hypoglycemia at 2, 4 and 6 hrs.

Table 6 shows blood glucose levels of fasted rabbits following administration of vitamin A, glucose and gliclazide. Vitamin A was given in dose of 10,000 I.U./Kg/d for 7 days regularly, glucose powder (25 gm) and gliclazide (8 mg / kg) were added on 7th day and blood samples were taken. The mean of blood glucose levels at '0' hr. (fasting) was 92.56 mg% which became 132.02 mg% at 2 hrs., 111.24 mg% at 4 hrs. and 93.52 mg% at 6 hrs. following administration of drugs and glucose.

These values are compared with values of Table 5 in **Table 11**. It can be seen that vitamin A when co-administered with gliclazide antagonized the effect of the latter. This effect was highly significant at 2 and 4 hrs. ($p<0.01$).

Table 7 shows blood glucose levels following administration of glucose powder (25 gm) and metformin (100mg/kg) in fasted rabbits. The mean of blood glucose levels at '0' hr. (just before

administration of drug and glucose) was 111.4 mg% which becomes 199.76 mg% after 2 hrs., 126.46 mg% after 4 hrs. and 103.16 mg% after 6 hrs. Metformin produced significant hypoglycemia at 2 hrs. as compared to control group.

Table 8 shows blood glucose levels following administration of Vitamin A, glucose and metformin in fasted rabbits. Vitamin A was given in dose of 10,000 I.U./kg/day for 7 days regularly, glucose powder (25 mg) and metformin (100 mg/kg) were added on 7th day and blood samples were taken. The mean of blood glucose levels at '0' hr. (just before administration of drugs and glucose) was 101.28 mg%, which became 170.1 mg% at 2 hrs., 128.54 mg% after 4 hrs. and 107.82 mg% at 6 hrs. These values were compared with those of Table 7in **Table 12**. It was observed that vitamin A had no significant role on metformin induced changes in blood glucose level.

CONCLUSION: Effect of vit. A and its possible interaction with oral antidiabetic agents (i.e. glimepiride, gliclazide and metformin) on blood glucose levels in rabbits have been reported in the present study. We observed that in studied conditions Vit A produced significant effect on blood glucose levels at 4 and 6 hr intervals in experimental rabbits. Administration of Vit A with glimepiride exhibited antagonistic effects on blood glucose levels.

However these effects in studied conditions were found to be significant at 2 and 4 hr intervals.

Vitamin A with gliclazide in these conditions had produced antagonistic effects at 2 and 4 hr intervals.

Vitamin A on administration with metformin did not produce any significant effect on metformin induced changes in blood glucose level.

Thus it is evident from the present study that Vit A inspite of its useful antioxidant properties have some inevitable action on blood glucose level and can adversely interfere with the action oral antidiabetic agents. Therefore in diabetic patients Vit A should be prescribed only if clearly indicated.

REFERENCES:

1. Guariguata L,Whiting DR, Hambleton I, Beagley J, Linnenkamp U, Shaw JE: Global estimates of diabetes prevalence for 2013 and projections for 2035. Diabetes research and clinical practice 2014: 103 (2): 137-149.
2. Fatani SH, Babakr AT, Nour Eldin EM, Almarzouki AA: Lipid peroxidation is Associated with Poor Control of Type-2 diabetes mellitus. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. Jan 2016 (accepted for upcoming issue).
3. Tangvarasittichai S: Oxidative stress, insulin resistance, dyslipidemia and type 2 diabetes mellitus. World Journal of diabetes 2015; 6(3):456.
4. Stambouli-Guerriche AB, Mokhtari-Soulimane N, Merzouk H, Merzouk SA, Bendedouche AS: Elevation of oxidative stress markers in Type 1 diabetic children. Journal of Diabetes and Endocrinology. Feb 2015; 6(2):5-11.
5. Wueest S, Lucchini FC, Challa TD, Müller W, Blüher M, Konrad D. Mesenteric fat lipolysis mediates obesity-associated hepatic steatosis and insulin resistance. Diabetes 2016; 65(1):140-8.
6. Perry RJ, Camporez JP, Kursawe R, Titchenell PM, Zhang D, Perry CJ, Jurczak MJ, Abudukadier A, Han MS, Zhang XM, Ruan HB: Hepatic acetyl CoA links adipose tissue inflammation to hepatic insulin resistance and type 2 diabetes. Cell.Feb 2015;160(4):745-58.
7. Li H, Horke S, Förstermann U: Oxidative stress in vascular disease and its pharmacological prevention. Trends in Pharmacological Sciences 2013; 34 (6): 313–319.
8. Singh VP, BaliA, Singh N, Jaggi AS:Advanced Glycation End Products and Diabetic Complications. Korean J PhysiolPharmacol2014; 18(1): 1–14.
9. Maret G, Traber AB, Jan F, Stevens AC: Vitamins C and E: Beneficial effects from a mechanistic perspective. Free RadicBiol Med 2011; 51:1000–13.
10. Costacou T, Zgibor JC, Evans RW, Tyurina YY, Kagan VE, Orchard TJ: Antioxidants and coronary artery disease among individuals with type 1 diabetes: findings from the Pittsburgh Epidemiology of Diabetes Complications Study. J Diabet Complications 2006; 20:387–94.
11. Milman U, Blum S, Shapira C, Aronson D, Miller-Lotan R, Anbinder Y et al: Vitamin E supplementation reduces cardiovascular events in a subgroup of middle-aged individuals with both type 2 diabetes mellitus and the haptoglobin 2-2 genotype. a prospective double-blinded clinical trial. ArteriosclerThrombVascBiol2008; 28:341–7.
12. Piero MN, Njagi JM, Kibiti CM, Ngeranwa JJN, Njagi ENM and Miriti PM: The Role of Vitamins and Mineral Elements in Management of Type 2 Diabetes Mellitus: A Review. South As J BiolSci 2012; 2(1):107 –115.
13. Freeman JS, Gross B: Potential drug interactions associated with treatments for type 2 diabetes and its comorbidities: a clinical pharmacology review. Expert Rev ClinPharmacol.2012; 5(1):31-42.
14. Ray KK, Seshasai SRK,Wijesuriya S etal: Effect of intensive control of glucose on cardiovascular outcomes and death in patients with diabetes mellitus: a meta-analysis of randomised controlled trials. The Lancet 2009: 373 (9677); 1765-1777.
15. Shafiee G, Mohajeri-Tehrani M, Pajouhi M, Larijani B: The importance of hypoglycemia in diabetic patients. J Diabetes MetabDisord2012;11:17.

16. Cardoso S, Santos RX, Correia SC et al: Insulin-induced recurrent hypoglycemia exacerbates diabetic brain mitochondrial dysfunction and oxidative imbalance. Neurobiology of Disease 2013; 49 (1): 1–12.

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