THE EFFECTS OF ASCORBIC ACID ON MEMBRANE TRANSPORT OF GLUCOSE

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The level of glycemia and ascorbic acid was tested of oral glucose-tolerance test (OGTT). This test was done on thirty healthy normoglycemic adult women, between 18 and 30 years of age, who showed no clinical signs of endocrine disturbances.

At the beginning of the experiment the level of ascorbic acid and the level of glycemia were determined twelve hours after the last meal. In the following seven days eash of the examined women was given, beside the usual nourishment, 1.000 mg ascorbic acid (two times a day of 500 mg with breakfast and lunch). The level of ascorbic acid the last taken dosage of ascorbic acid. The achieved results of OGTT at the beginning and in the end of the test showed the ascorbic acid in the dosage of 1.000 mg/per day for seven days intensified the level glycemia during OGTT.

This hyperglycemy is probably the consequence of the receptor obstruction in cellular membrane by ascorbic acid. *Acta Medica Medianae 2004; 43 (1):39–41.*

Key words: *level of glycemia, ascorbic acid, oral glucose - tolerance test*

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Introduction

In most species, the hepatic metabolism of glucose includes the synthesis of ascorbic acid (1). In man, monkey and guinea pigs, however, the absence of one enzyme in that pathwey (2) necessitates the dietary intake of a micronutrient. Term „antiscorbutic chemical“ in citrus fruits was well appreciated long before Szent-Georgi's (3) isolation of ascorbic acid itself in 1928.

In particular, the cellular uptake of ascorbic acid is regulated by both glucose and insulin and the renal reabsorption of ascorbic acid is impeared by hyperglycemia (4). This evidence also suggests that vitamin C supplementation may be beneficial in countering the pathophysiologies resulting from the chronic hyperglycemia of insulin-dipendent diabetes mellitus (IDDM).

Levels of ascorbic acid are decreased in various tissues of animals with experimental diabetes (5). Mann suggested (6) in 1974 that glucose and vitamin C might occupy the same membrane transport system. He subsequently reported with Newton (7) that elevated glucose levels interfered with cellular ascorbic acid transport in erythrocytes. Others have observed inhibition by glucose of ascorbic acid in vitro by human lymphocytes (8) and bovine endothelial cells (9). Bigley et al. (10) described competitive inhibition between the in vitro uptake of dehydroascorbic acid and glucose analogues by human polymorphonuclear leucocytes (PMN) and fibroblasts, and concluded on the basis of kinetic data that the competing ligands utilized the same membrane carrier.

In this study we compared the effects of ascorbic acid on the glucose levels in the plasma.

Materials and methods

During 2002. the level of glycemia and ascorbic acid was tested at Gynecology clinic in Nis. This test was done on thirty healthy normoglycemic adult women, aged between 18 and 30, who had no clinical signs of endocrine disturbances.

At the beginning of the experiment the level of ascorbic acid and the level of glycemia were determined twelve hours after the last meal. In the following seven days each of the examined women was given, beside the usual nourishment, 1.000 mg ascorbic acid (two times a day of 500 mg with breakfast and lunch). The level of ascorbic acid and glycemia was determined on the eight day of the experiment, tventy-four hours after the last taken dosage of ascorbic acid. The achieved results of oral glucose-tolerance test (OGTT) at the beginning and in the end of the test were shown in a table and on diagram.

The results

In the case of thirty normoglycemic adult women, aged between 18 and 30, the oral glucose tolerance test was done with 75 g of glucose. The achieved values of glycemia were shown in table 1.

Table 1. The values of glycemia during OGTT (mmol/L) at the beginning of the experiment

Time (min)	0	30	60	90	120
glucochemy	3,77	6,82	7,93	7,04	4,1

After OGTT was done, and after taking 1.000 mg of ascorbic acid every day, the oral glucose-tolerance test was determined. The achieved values were given in table 2.

Table 2. The values of glycemia during OGTT (mmol/L) in the end of the experiment

Time (min)	0	30	60	90	120
glucochemy	4,16	9,1	10,71	9,04	6,82

The above given results show the existence of the level of glycemia in the case of all examined normoglycemic adult women, after taking 1 g of ascorbic acid during the period of seven days. This difference is more obvious on the following diagram (diagram 1).

Namely, the level of glycemia, after applying ascorbic acid is higher in all the intervals of determining of oral glucose tolerance test (OGTT). These differences are more important statistically ($p < 0{,}001$).

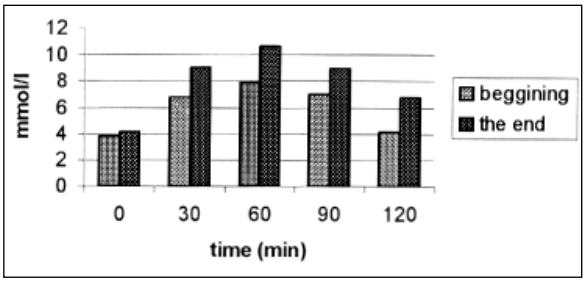

Diagram 1. The values of glycemia during OGTT (mmol/L) at he beginning and at the end of the experiment

Discussion

In most species, the hepatic metabolism of glucose includes the synthesis of ascorbic acid. Glucose has a similar structure, and is the precursor for the vitamin in species that synthesize it (11). Although the biosynthetic relationship between glucose and vitamin C is absent in man, on the basis of in vitro examination of tissue homogenate extracts Burns (2) concluded that, man, monkey and guinea pig were unable to convert L-gulonolactone to l-ascorbic acid, and that this was the „missing step" in the biosynthesis in the livers of these species which made them dependent on exogenous ascorbic acid for their vitamin C requirements. Chatterjee et al. (12) concluded that there existed an additional „missing step", namely that performed in other species by the enzyme L-glucuronolacton oxdidase in converting D-glucuronolactone to L-gulonolactone. More specifically Burns (2), Stone (13) and Chatterjee et al. (12) considered that the „missing step" was due to gene deletion.

In his seminar paper „Evolution and the Need for Ascorbic Acid" Linus Pauling (14) concluded that the loss of the ability to synthesize ascorbic acid probably occurred in the common ancestor of the primates. A rought estimate of the time when this mutational change occurred is twenty-five million years ago.

Weighty experimental and theoretical considerations will advise in favour of the thesis that vitamin C deficiency in a number of species including humans is not due to rotal inability to biosynthesis ascorbate, but rather to a very limited biosynthetic ability which normally cannot be stopped to meet the minimum metabolic/physiological requirements (15,16,17,18).

The cellular uptale of ascorbic acid from plasma can occur by two mechanisms. An active transport of ascorbic acid is documented (4,19). With regard to this active transport, insulin has been proved to accelerate ascorbic acid clearanse from plasma, and presumably into cells since there is no increase in urinary excretion (20, 21).

Hyperglycemia has been shown to inhibit ascorbic acid transport. This inhibition seems to paradoxically give the evidence suggesting that insulin promotes both ascorbic acid and dehydroascorbic acid (DHA) uptake by cells. The inhibition of ascorbic acid uptake by hyperglycemia was demonstrated in vitro in the absence of insulin and may not, therefore, be important in normal physiology. Hyperglycemia is also known to enhance renal ascorbic acid lowes (4, 20,23).

The glucose transport system also transports the minor oxidized and uncharged species, DHA with a presumed subsequent intracellular reduction to ascorbic acid. Cunningham (24) showed that DHA competed for glucose transport system transported on an equimolar basis with the transport surrogates 2-deohy-glucose and 3-O-methyl glucose. Earlier studies (10) clearly show an enhancement of leucocyte DHA uptake by insulin, consistent with the requirement of glucose transport system transporters from the cytosol to membrane surfaces. Much emphasis has been placed on this potential uptake mechanism (24).

Conclusion

The results of this experiments autorized us to conclude:

Taking of the ascorbic acid in the dosage of 1.000 mg/per day for seven days, intensifies the level of glycemia druging OGGT.

This hyperglycemy is probably the consequence of the receptor obstruction in cellular membrane by ascorbic acid.

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UTICAJ PERORALNOG UNOSA ASKORBINSKE KISELINE NA NIVO GLIKEMIJE KOD ZDRAVIH OSOBA

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U medicinskoj literaturi postoje mnogobrojni podaci o efektima askorbinske kiseline na pojedine aktivnosti organizma. Međutim, relativno mali broj radova obrađuje problem efekata askorbinske kiseline na nivo glikemije i sistem glikoregulacije.

Izučavan je uticaj askorbinske kiseline na nivo glikemije kod 30 zdravih, normoglikemičnih žena, starosti između 18 i 30 godina, koje nisu imale kliničke simptome nekog endokrinog poremećaja. Kod svih ispitanica urađen je oralni glikozo-tolerans test (OGTT) sa 75 g glikoze, na početku ogleda. Narednih sedam dana, svaka ispitanica, per os, unosila je po 1.000 mg askorbinske kiseline na dan. Osmog dana (24 h posle poslednje doze unete askorbinske kiseline), kod svake ispitanice, urađen je OGTT. Dobijeni rezultati pokazuju da postoji značajna razlika u nivou glikemije, pre i posle uzimanja askorbinske kiseline. Posle sedmodnevnog uzimanja askorbinske kiseline nivo glikemije je značajno viši, duže traje i sporije se vraća na početnu vrednost. Ova razlika u nivou glikemije, mogla bi biti posledica kopetitivnog delovanja askorbinske kiseline i glikoze na zajedničke receptore transportnog mehanizma u celularnim membranama. *Acta Medica Medianae 2004; 43 (1):39 – 41.*

Ključne reči: *askorbinska kiselina, glikemija, oralni glikozo-tolerans test*