

ORIGINAL

Gender differences in blood glucose and uric acid levels induced by varying doses of alcohol in man

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ABSTRACT. Objective. To study the gender differences in plasma glucose and uric acid levels caused by varying doses of alcohol.

Materials and methods. 64 (36 male and 28 female) healthy, light drinkers (< 20 g ethanol/day) between the ages of twenty-five and thirty-six years were selected as volunteers.

Results. The administration of 0.325, 0.650 and 1,300 g ethanol/kg body weight, reduced plasma glucose by 2, 11 and 16% respectively, in males and by 1, 4 and 7% in female subjects, respectively. These doses respectively increased plasma uric acid by 6, 20 and 32% in males and by 14, 40 and 56% in females ($p > 0.05$: except for the 56% difference).

Conclusions. Although, these changes were not demonstrated to be statistically significant, sex is implicated to influence the manner alcohol affects the metabolism of glucose and uric acid. Recently, hypoglycaemia and hyperuricaemia have been observed to be risk factors of brain damage and cardiovascular disorders, respectively. The involvement of chronic and excessive consumption of ethanol in brain damage and cardiovascular dysfunction via

disturbances in plasma glucose and uric acid levels, respectively, deserve further investigations.

KEY WORDS: glucose, uric acid, alcohol, hyperuricaemia, brain damage, hypoglycaemia.

Diferencias entre sexos en los niveles de glucosa y ácido úrico inducidos por diversas dosis de alcohol en seres humanos

RESUMEN. Objetivo. Analizar las diferencias entre sexos en los niveles en plasma de glucosa y ácido úrico producidos por diversas dosis de alcohol.

Material y métodos. Sesenta y cuatro personas (36 hombres y 28 mujeres) sanas, consumidoras «ligeras» de alcohol (< 20 g alcohol/día), de edades comprendidas entre los 25 y 36 años de edad fueron incluidas en el estudio, siendo su participación voluntaria.

Resultados. La administración de 0,325, 0,650 y 1.300 g etanol/kg de peso redujo la concentración de glucosa plasmática en varones un 2, 11 y 16%, respectivamente, y en mujeres en un 1, 4 y 7%, respectivamente. En estas dosis, se elevaron los niveles de ácido úrico en plasma en varones en un 6, 20 y 32%, y en las mujeres un 14, 40 y 56% ($p > 0,05$, excepto en la dosis más alta de alcohol).

Conclusiones. Aunque los cambios observados no son estadísticamente significativos, el género pudiera estar implicado en los efectos del alcohol sobre el metabolismo de la glucosa y ácido úrico. Recientemente se ha observado que la hipoglucemia e hipercalcemia son factores de riesgo del daño cerebral y

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Received: 31-07-2007

Accepted for publication: 23-07-2008

de los trastornos cardiovasculares, respectivamente. La implicación del consumo crónico y excesivo del alcohol en el daño cerebral y la disfunción cardiovascular, a través de alteraciones en los niveles plasmáticos de glucosa y ácido úrico, respectivamente, requieren posteriores investigaciones.

PALABRAS CLAVE: glucosa, ácido úrico, alcohol, hiperuricemia, daño cerebral, hipoglucemia.

Introduction

Alcohol is benign to metabolic processes when consumed in small dose¹ but when its intake is abused, it induces a wide range of pathobiochemical alterations². These alcohol 'effects' demonstrate its influence on central metabolic pathways. Reports on the effect of alcohol on glucose homeostasis are quite conflicting. Excessive consumption has been shown to precipitate hypoglycaemia in poorly nourished individuals³. Conversely, it could also produce the opposite (hyperglycaemia) effect in especially well nourished subjects⁴.

Plasma uric acid levels have been observed to increase during hangover period; hence, it is proving useful as a biological indicator of alcohol intoxication⁵. The association between alcohol consumption and gouty attack caused by the hyperuricaemic condition induced by alcohol has been supported by studies on moderate drinkers⁶. Alcohol is also known to decrease the urinary excretion of uric acid.

Great number of people consume alcohol being either ignorant or underscores the health implication. So, majority of drinkers suffer ill-health occasioned by the wrong use of alcohol.

This study attempts to highlight the changes induced by varying doses of alcohol consumption on plasma glucose and uric acid in both male and female individuals, all with the hope of discussing the medico-biochemical implications of such changes.

Materials and methods

Subjects and testing

Sixty-four consenting individuals (36 males and 28 females) in apparent good health, between the ages of 25 and 36 years were screened for drug use and selected for the study. Their mean \pm SD body weight is 63.6 ± 12.8 kg (range: 50-75 kg). The volunteers were light drinkers of alcohol (consume between 1-2 drinks/day) and they nei-

ther smoke cigarette nor snuff tobacco, or other addictive agents. They were not on any medication and they remained so throughout the period of investigation.

On arrival to the laboratory as scheduled, the participants willingly endorsed the agreement form provided by the Human Protection Agency as a means of obtaining their consent. They were then randomly separated into four experimental groups: A, B, C, and D. Group A (fruit juice; n = 16:9M, 7F), group B (0.325 g ethanol/kg; n = 16:9M,7F), group C (0.650 g ethanol/kg; n = 16:9M,7F), and group D (1.3 g ethanol/kg; n = 16:9M,7F).

During the first occasion, each member of a group was given the dose in parenthesis after 4 hours of taking a light meal eaten at about 4:00 pm. Details of what they ate were noted in order to allow duplication on later occasions. Timing of the meal was important because the condition of the stomach, whether full or empty⁷, and the time of the day, morning, afternoon or evening⁸ have been observed to influence alcohol metabolism and the associated biochemical changes. The ethanol was diluted to 28% with fruit juice before being orally ingested. The volume (ml) of alcoholic beverages ingested was calculated as follows⁹: volume (ml) of alcoholic beverages ingested = [dose of alcohol (g/kg) x body weight] / [specific gravity of drink x % alcohol in drink as decimal]. Each participant was thereafter rotated round the other remaining three test every forth-night. This rotation is important in order to eliminate intra-individual factors that may likely influence result outcome.

Collection of blood samples

Intravenous whole blood sample was collected after about 12 h post ingestion time, that is, at about 8.00 am before the individual takes breakfast meal and exercise. This timing was based on previous report¹⁰. Ethanol-induced changes in blood urate¹¹ and glucose¹² have been reported to be most observable between 10-15 hours post ingestion time. The collected whole blood was dispensed into a tube containing floride oxalate and mixed with the anticoagulant and glucose preserver by several times of gentle inversion. The specimen was then centrifuged at 1,200 xg for 5 min at room temperature to separate the plasma which was decanted into bijou bottle and analyzed within the hour of collection.

Analysis of serum samples

The methods previously described by Trinder¹³ and Caraway¹⁴ were used to determine the levels of gluco-

se and uric acid in the serum samples, respectively. The commercial kits containing the reagents used were supplied by Teco Diagnostics, USA.

The study was conducted in February and March, 2006 in the Alcohol Research Laboratory, Department of Medical Biochemistry, Delta State University, Abraka, Nigeria. The investigation was approved by our Faculty's Research and Bioethics Committee.

Statistical analysis

The data obtained were analyzed by repeat measure analysis of variance (ANOVA) followed by Dunnett's post hoc test for multiple comparisons using SPSS 10.0 computer software package (SPSS Inc. Chicago, U.S.A.). Statistical significant difference was established at $p < 0.05$.

Results

The results are shown in table 1. It can be observed that alcohol progressively reduced plasma glucose in a dose-dependent manner. The degree of such reduction was observed to be more among the male subjects. ANOVA shows no significant difference when compared with basal values.

Again, alcohol steadily increased plasma uric acid in relation to dose. The consumption of 1.3 g ethanol/kg produced significant increase ($p < 0.05$) in plasma uric acid among the female subjects.

Discussion

The dose of alcohol and the period of time over which such dose is consumed have been shown to influence the nature of alcohol-induced biochemical

changes¹⁵. The oral administration of 0.325, 0.650 and 1.300 g ethanol/kg body weight insignificantly reduced ($p > 0.05$) serum glucose of the male subjects by 2, 11 and 16% respectively, with very little decrease in those of the females: 1, 4 and 7%, respectively (table 1). This seems to agree with the observation of Winston and Reitz¹², who reported blood glucose levels to be decreased only in males after chronic alcohol ingestion. Thus, these findings probably suggest that sex could influence the way alcohol affects carbohydrate metabolism. Two important enzymes, phosphoglucomutase and UDP-glucose pyrophosphorylase, known to be involved in glycogen metabolism and glucose homeostasis have been demonstrated to be affected quite differently in male and female animals following chronic alcohol consumption. This could be the hallmark of the differences observed. Earlier study¹⁶, has shown that ethanol can decrease liver glycogen by more than half in animals fed nutritionally adequate diets, and that hypoglycaemia may follow complete depletion of glycogen⁸.

Apart from sex, which has been implicated in this study, nutritional status of the drinker has been reported to influence the pattern alcohol affects carbohydrate metabolism¹⁷ though in our study, nutrition was not a strong influencing factor because subjects' dietary intake was fairly adequate.

From this experimental demonstration, ethanol appears to gradually increase the concentration of serum uric acid, an observation that was significant in the female participants especially at the highest dose (table 1). Uric acid is the degradative end product of purine nucleotide catabolism. Hyperuricaemia¹¹, decreased urinary excretion of uric acid¹⁸ and gouty attack⁶ are indirect consequences of alcohol abuse. The results of this study (table 1), relate to earlier reports^{15,19,20} though, the females were more markedly affected. Ex-

Table 1. Changes in serum glucose and uric acid levels induced by different doses of alcohol in humans

	Male (n = 36)				Female (n = 28)			
	Doses of ethanol administered (g/kg)							
	0.000	0.325	0.650	1.300	0.000	0.325	0.650	0.300
Serum glucose (mmol/l)	4.81 ± 1.01	4.71 ± 1.21 (2.0)	4.28 ± 0.96 (11.0)	4.04 ± 1.26 (16.0)	4.33 ± 0.88	4.27 ± 0.94 (1.0)	4.16 ± 1.02 (4.0)	4.03 ± 1.08 (7.0)
Serum uric acid (mmol/l)	0.32 ± 0.06	0.34 ± 0.09 (6.0)	0.39 ± 0.07 (20.0)	0.42 ± 0.11 (32.0)	0.23 ± 0.08	0.26 ± 0.10 (14.0)	0.32 ± 0.09 (40.0)	0.36 ± 0.12* (56.0)

Values are expressed as mean ± SD for «n» subjects.

Values in parenthesis are percentage differences from basal (0.000 g ethanol/kg body weight) value.

*Significantly different from basal value ($p < 0.05$).

cessive generation of NADH due to hepatic metabolism of ethanol leads to an increase in blood lactate levels, and a secondary hyperuricaemia arises due to competition between lactate and uric acid for excretion in the renal tubules¹⁸.

This investigation implicates (although without statistically significant changes) sex to influence the pattern alcohol affects plasma glucose. It puts males at more risk of becoming hypoglycaemic. Gender difference also exists in the way ethanol affects uric acid metabolism. The turnover rate was more in females, exposing them to the risk of hyperuricaemia and other associated diseases, when compared with their male counterparts. Recent speculations implicate uric acid

as a risk factor of hypertension^{21,22} and hypoglycaemia has been reported to induce brain damage²³.

This study identifies gender differences, although these changes were not demonstrated to be statistically significant, but at higher amounts of alcohol both sexes have considerable measure of health risk. Males, the risk of hypoglycaemia and females, the risk of hyperuricaemia. Thus, the roles of hypoglycaemia and hyperuricaemia in respectively eliciting brain damage and cardiovascular dysfunction deserve further investigations.

Authors declared that there are not conflicts of interest.

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