SINET: *Ethiop. J. Sci.*, 29(2):183–185, 2006

ISSN: 0379–2897

Short Communication

EFFECT OF ORAL FRUCTOSE ADMINISTRATION ON ALCOHOL-INDUCED INCREASE IN PLASMA URATE

Onyesom, I.

Department of Biochemistry, Delta State University, PO Box 144, Abraka
Delta State, Nigeria. E-mail: onyesominno@yahoo.co.uk

ABSTRACT: Oral fructose administration has been demonstrated to stimulate the oxidation of alcohol. However, its influence on alcohol-induced hyperuricemia is yet to be documented. This study therefore, reports the effect of fructose on alcohol- induced increase in plasma urate in adult albino rabbits. Twelve male adult albino rabbits, divided into A, B and C experimental groups were purchased from Yoha Farms, Warri, Delta State. Group A, the control animals (n=4) were given normal saline, while Group B animals (n=4) orally received 1.5 g (40%) ethanol/kg body weight as single daily dose for a routine period of fifteen weeks. Group C rabbits (n=4) were treated in a similar manner but 0.25 g fructose/kg body weight was usually given after about 10 min of administering the ethanol dose. The results obtained show that ethanol administration significantly increased ($P<0.05$) serum urate by 57.8% at the end of the 15-week treatment period but the serum urate levels for the ethanol + fructose-treated animals only increased by 10.6%, an increase that was not statistically significant at the 5% probability level. The stimulation of alcohol oxidative metabolism by fructose may not be accompanied by a threatening increase in serum urate, the aetiologic risk factor of gout, renal calculi and hypertension. Albeit, similar study designed for humans is needful in order to determine the suitability of animal model for predicting the possible human effect(s).

Key words/phrases: Alcohol, fructose, plasma, urate

INTRODUCTION

Urate is the catabolic end product of purines derived from both exogenous and endogenous sources (Fox, 1985). Recently, alcohol has been reported to increase serum uric acid in both regular and irregular alcohol consumers in Nigeria (Bartimaeus and Eno-Eno, 2002).

Alcohol consumption has traditionally been associated with hyperuricemia, and so could initiate gouty attacks in susceptible individuals (Vamvakas *et al.*, 1998). Determination of blood urate is becoming a useful diagnostic tool in clinical medicine, and recently it has been speculated to be amongst the aetiologic factors of hypertension (Itoh *et al.*, 1997).

The adverse consequences of alcoholism are seen in many different aspects of the individual's life, and its management has not been very successful possibly because of its socioclinical complexities. It is on this note, that the treatment value of some agents that could either reduce drinking behaviour or enhance blood alcohol clearance is currently being investigated for possible therapeutic benefit(s).

Fructose has been demonstrated to stimulate alcohol oxidative metabolism (Mascord, *et al.*, 1991), hence it is becoming a useful adjunct, but its effect on the reported increase in serum uric acid induced by alcohol consumption has not been reported. This study was, therefore, designed to investigate the effect of oral fructose therapy on alcohol- induced hyperuricemia.

MATERIALS AND METHODS

Twelve male adult albino rabbits (mean weight 1.43 kg) were purchased from Yoha Farms, Warri, Delta State, and growers mash was purchased from Bendel Feed and Flour Mill (BFFM), Ewu, Edo State. The animals were housed in metal hutches

and fed *ad libitum* on growers mash and water for 10 days to acclimatize them to the feed and laboratory environment. Thereafter, they were divided into three groups with four rabbits each and members of each group were housed singly in the metal hutches.

Rabbits in group A served as the control group and were given normal saline. Those in group B received 1.5 g (40%) ethanol/kg body weight as a single daily dose while those in group C were administered with ethanol as in group B but followed with 0.25 g fructose/kg body weight after 10 mins. Each animal was presented with about 50 g of the feed twice daily. Clean drinking water was provided *ad libitum* and the hutches were cleaned regularly.

The animals were treated and fed as described for a continuous period of 15 weeks. Whole blood samples were collected usually after the 5th, 10th and 15th weeks into clean, sterile bottles, allowed to clot, and then, centrifuged at 1,200 x g for 5 min at room temperature. The serum was collected into bijou bottles for urate assay.

Assay of urate

Urate concentration in the serum was assayed using the uricase method of Caraway (1963). Essentially, uric acid in sample (serum) is converted by uricase to allantoin and hydrogen peroxide. Under the catalytic influence of peroxidase, the latter oxidizes 3,5-dichloro-2-hydroxybenzene sulfuric acid and 4-amino-phanazone to form a red-violet quinoneimine compound whose intensity is determined spectrophotometrically at 520 nm. The colour intensity of the quinoneimine dye is proportional to the concentration of uric acid in the sample.

Commercial test kit containing the reagents used was supplied by Randox Laboratories Ltd., United Kingdom. The enzyme reagent was reconstituted with the Hepes buffer (pH 7.0) and then, allowed to stabilize at room temperature (about 29°C) for about 25 mins before use.

Three test tubes for blank, serum and standard were set and 0.2 ml of distilled water, serum and standard solution were respectively dispensed into the tubes followed by the addition of 1 ml of the reconstituted reagent to each of the tube. The contents of the tubes were thoroughly mixed and incubated for 5 min at 37°C in a Thermostatic Water Bath (BTI-BIO-TECH). Absorbance of serum and standard were measured against the blank at 520 nm using a spectrophotomer (SPECTRUM LAB 22). Then, the concentration of uric acid in serum was obtained by multiplying the sample: standard absorbance ratio by the concentration of the standard solution.

RESULTS

The results obtained from the study are shown in Table 1. The table reveals the changes in serum urate induced by the different treatment procedures and the statistical analysis demonstrates that the administration of 1.5 g (40%) ethanol/kg body weight, for a period of fifteen weeks, significantly ($P<0.05$) increased serum urate. Mean serum urate level for the B and C-group animals were found to be increased by 57.8%($P<0.05$) and 10.6% at the end of the 15-week exposure when compared with their respective basal (0 wk) values.

Table 1. Changes in serum urate induced in rabbits by alcohol and alcohol + fructose administrations.

Group		Serum urate concentration (μmol/L)			
A	Control (Normal saline)	144.0±6.7	150.0±7.4[a]	148.0±11.5[a]	142.0±5.2[a]
B	Ethanol (1.5g/kg body weight)	142.0±8.6	152.0±9.2[a]	164.0±8.3[b]	224.0±4.7[c]
C	Ethanol (1.5g/kg body weight) + Fructose (0.25g/kg body weight)	141.0±8.5	143.0±6.3[a]	148.0±10.6[a]	156.0±4.4[a]

n=4; values are expressed as mean± SEM.
Statistical significance was tested using Student's t-test.
For each group, value bearing different superscript differs significantly ($P<0.05$) from the control value.

DISCUSSION

The evidence available from this study suggests that ethanol administration increases serum urate (Table 1) and this further confirms a recent report (Bartimaeus and Eno-Eno, 2002). This hyperuricemic condition could increase the incidence of gouty attacks (Vamvakas *et al.*, 1998) and hypertension (Itoh *et al.*, 1997) among heavy consumers of alcoholic beverages.

The oxidation of ethanol and ethanal, its metabolite, respectively increases cytosolic and mitochondrial NADH/NAD^+ ratios, which in turn increase lactate/pyruvate and β-hydroxybutyrate/acetoacetate ratios. These altered ratios induce ketoacidosis that reduces the capacity of the kidney to excrete urate, leading to secondary hyperuricemia (Lieber *et al.*, 1962; Lefevre *et al.*, 1970).

However, in the presence of fructose, the increase in mean serum urate dropped from 57.8% to 10.6% (Table 1) indicating that fructose appears to interfere with the mechanism that build up urate in blood when ethanol is consumed. Although, the relationship is not well established, available reports (Tygstrup *et al.*, 1965; Scholz and Nohl, 1976) show that in the presence of ethanol, the metabolism of fructose is diverted from NAD^+ to NADH requiring pathways, which in turn generate NAD^+ needed for further alcohol oxidation. Also, this diversion consumes ATP that increases the mitochondrial oxidation of NADH to NAD^+. These effects may restore the intricate balance in NADH/NAD^+ ratio and reduce the associated secondary complications as observed in the changes in serum urate for the C-group animals.

Alcohol administration appears to either enhance purine breakdown or inhibit effective blood urate clearance via urine. But the co-administration of oral fructose seems to ameliorate the condition(s) that could produce the increase in serum urate. However, human investigation is required to establish whether animal-to-man extrapolation would be permissible, in case further studies on the anti- intoxicating property of fructose become imperative and desirable.

REFERENCES

1. Bartimaeus, E.S. and Eno-Eno, M. (2002). The effect of alcohol on uric level in consumers. *Journal of Applied Science and Environmental Management* **6**(1):5–7.
2. Caraway, W.T. (1963). Quantitative determination of uric acid. *Clinical Chemistry* **4**:239–243.
3. Fox, I.H. (1985) Adenosine triphosphate degradation in specific disease. *Journal of Laboratory and Clinical Medicine* **106**:101–110.
4. Itoh, T., Matsumoto, M., Nakamura, M., Okada, A., Shirashi, N., Hougaku, H., Hashimoto, H., Sakaguchi, M., Handa, N., Tekeshita, T., Morimoto, K. and Hori, M. (1997). Effects of daily alcohol intake on blood pressure differ depending on an individual's sensitivity to alcohol: Oriental flushing as a sign to stop drinking for health reasons. *Journal of Hypertension* **15**(11):1211–1217.
5. Lefevre, A., Adler, H. and Lieber, C.S. (1970). Effect of ethanol on ketone metabolism. *Journal of Clinical Investigation* **49**:1775–1782.
6. Liebeer, C.S., Jones, D.P., Losowsky, M.S. and Davidson, C.S. (1962). Interrelation of uric acid and ethanol metabolism in man. *Journal of Clinical Investigation* **41**:1863-1870.
7. Mascord, D., Smith, J., Starmer, G.A. and Whitfield. J.B. (1991) The effect of fructose on alcohol metabolism and the (lactate/pyrurate) ratio in man. *Alcohol and Alcoholism* **26**:53–59.
8. Scholz, R. and Nohl, H. (1976). Mechanism of the stimulatory effect of fructose on ethanol oxidation in perfused rat liver. *European Journal of Biochemistry* **63**:449–458.
9. Tygstrup, N., Winkler, K. and Lunquist, F. (1965). The mechanism of the fructose effect on ethanol metabolism in human liver. *Journal of Clinical Investigation* **44**:817–830.
10. Vamvakas, S., Teschner, M., Bahner, U. and Heidland, A. (1998) Alcohol abuse: potential role in electrolyte disturbances and kidney diseases. *Clinical Nephrology* **49**(4):205–213.