Correspondence

Renal function in male rats concurrently exposed to nicotine & ethanol

Sir,

Concurrent alcohol and nicotine consumption commonly occur together\(^1\). Long-term alcohol intake produces serious harmful effects on renal function\(^2\). Nicotine, being vasoconstrictive, increases blood pressure, potentially altering renal function\(^3\).

The incidence of smoking among individuals who abuse alcohol and opiates, is about 90 per cent, although alcoholic individuals smoke more cigarettes than those who abuse other substances\(^4\). The interactions between components of tobacco smoke and drugs have been of much concern and the subject of many investigations\(^5\). Although some workers investigated the influence of ethanol on renal function\(^6\) and nicotine on renal parameters\(^5\), very little information is available on the concurrent intake of nicotine and ethanol on renal function. Therefore, the current experimental study in rats was performed to determine whether nicotine interacts with ethanol to compromise renal function in chronic substance users.

Sprague-Dawley rats (300-345 g) (7 wk) (n = 8) were housed in metabolic cages and maintained on a 12 h light/12 h dark cycle, in Department of Physiology, University of Zimbabwe, Zimbabwe. Food and water were provided ad libitum. Licensing was obtained from the Director of Veterinary Services Zimbabwe (as stipulated in the Scientific Animal Experiments Act, 1963) for animal experiments performed within the precincts of the University of Zimbabwe. Chronically separate groups of 8 rats were administered 1.6 g/kg body weight (bwt) ethanol daily by gavage, nicotine at 0.1 mg/kg bwt, and concurrently for 4 wk. Control rats (n=8) were administered volumes of de-mineralized water equivalent to those for ethanol and/or nicotine. Urine volume and Na\(^+\)/K\(^+\) excretion were determined in 24 h urine samples.

At the end of the 4 wk, all chronically treated animals were anaesthetized with intra-peritoneal injection of sodium 5-ethyl-5’-(1-methyl-butyl)-2-thio-barbiturate at 0.11 g/kg, 1 bwt and challenged with intravenous hypotonic saline (0.077M NaCl) infusion via the right jugular vein. Following tracheotomy, cannulation, and urinary bladder incision, rats were placed on a warming tray at 37°C and equilibrated for 3 h. Thereafter, consecutive 20 min urine collections were made divided consecutively into 1 h control, 1 h 20 min treatment (nicotine and/or ethanol) and 1 h 40 min post-equilibration periods for determination of urine flow and Na\(^+\) and K\(^+\) excretion rates. Ethanol and/or nicotine were administered at 2.4 and 0.02 µg/min, respectively. Urine volume was determined gravimetrically. Na\(^+\) and K\(^+\) excretion rates were analysed using flame photometry. A control or vehicle infused group was set up to check the stability of renal function over the 4 h period.

Trunk blood was collected in pre-cooled vials directly after the 1 h 20 min treatment period and centrifuged at 2500 g/min. Arginine vasopressin (AVP) was extracted using previous methods\(^7\) using an AVP Radioimmunoassay kit supplied from Diagnostic Systems Laboratories, Texas, USA. AVP was extracted from plasma using Sep Pak C18 cartridges, the lower limit of detection being set at 0.5 fmol/l and intra- and inter-assay variations of 7.86 (n=15) and 12.32 per cent (n=15), respectively. Plasma aldosterone concentration was determined using Coat-A-Count by a Diagnostic Products kit, Los Angeles, USA. The test employed a solid-phase radioimmunoassay with an aldosterone-specific antibody immobilized to the wall of a polypropylene tube. The lower limit of detection was 44 fmol/l. Intra- and inter-assay coefficients of variation were 7.51 (n=15) and 7.93 per cent (n=15), respectively.

Data were statistically analysed using ANOVA-1 in MS-Excel (Analyse-IT Software, Ltd., Leeds). Scheffe’s
multiple comparison test was used to resolve any probable differences (CI = 95%).

Chronic nicotine administration did not significantly alter urine output, although there was a significant \((P<0.05)\) reduction of Na\(^+\) excretion by wk 4 compared with control animals \((5.64 \pm 1.02. vs. 7.10 \pm 1.11 \text{ ml/day}, \text{ respectively})\). Chronic ethanol administration initially reduced urine volume in wk 1 \((4.83 \pm 0.68 \text{ vs. } 6.03 \pm 0.86 \text{ ml/day}, \text{ respectively})\), but subsequently elevated in wk 4 \((9.81 \pm 1.02 \text{ vs. } 6.11 \pm 0.96 \text{ ml/day}, \text{ respectively})\) compared to control. The mean weekly urinary Na\(^+\) outputs were lower than control animals throughout the 4 wk treatment period. By wk 4, Na\(^+\) excretion was \(8.99 \pm 0.5 \text{ mmol/day} \) compared to \(11.98 \pm 0.9 \text{ mmol/day} \), in control rats. Concurrent ethanol and nicotine administration reduced weekly urine volume and Na\(^+\) output throughout the 4 wk period. At wk 4, urine volume and Na\(^+\) output in treated and control groups were \(4.63 \pm 1 \text{ vs. } 5.63 \pm 1 \text{ ml/day} \) and \(7.14 \pm 0.65 \text{ vs. } 9.01 \pm 1 \text{ ml/day} \), respectively. Urinary K\(^+\) outputs did not differ significantly from control rats throughout the 4 wk period. Plasma aldosterone levels at wk 4 were significantly \((P<0.05)\) elevated by chronic nicotine \((3.65 \pm 0.12 \text{ nmol/l})\), ethanol \((3.98 \pm 0.32 \text{ nmol/l})\), or in combination \((4.01 \pm 0.22 \text{ nmol/l}) \) vs. controls \((1.82 \pm 0.11 \text{ nmol/l})\). Plasma AVP concentrations by wk 4 were not significantly altered in nicotine exposed rats \((8.43 \pm 1.32 \text{ fmol/l})\), but significantly \((P<0.05)\) elevated by chronic nicotine \((9.81 \pm 1.02 \text{ fmol/l})\) and significantly \((P<0.05)\) reduced \((4.01 \pm 0.5 \text{ nmol/l}) \) vs. control. The mean weekly A VP concentrations 9. Discrepancies can be explained by differences in experimental design in the present study wherein chronically treated rats were acutely exposed to ethanol. The discrepancy between renal Na\(^+\) handling in chronic and acute exposures in the current study, suggests compromised tubular function that may be associated with a rise in blood pressure in chronic smokers. Chronic administration of nicotine and ethanol decreased urine flow and Na\(^+\) excretion rate in the present study. The effect is more marked when nicotine and ethanol were administered in combination, presumably lowering blood pressure through reduction in stroke volume via loss of Na\(^+\) and water. Nicotine acts in combination with ethanol to stimulate water and salt retention. This may have adverse consequences on renal function by elevating stroke volume and retaining metabolic waste. It would be interesting to investigate a timed chronic consumption of nicotine and/or ethanol and possible histological effects on renal structure.

Ross Gordon Cooper
Department of Physiology
College of Health Sciences
University of Zimbabwe
Mount Pleasant, Harare, Zimbabwe
Present address: Division of Physiology
Faculty of Health, UCE Birmingham
Baker Building, Room 701
Franchise Street, Perry Barr
Birmingham B42 2SU, UK
e-mail: rgcooperuk@yahoo.com

References


9. Musabayane CT, Cooper RG, Osim E, Balment RJ. Renal electrolyte and fluid handling in the rat following chloroquine and/or ethanol administration. Gen Pharmacol 2000; 34: 43-51.