

The effect of oral alcohol on gastroenteropancreatic hormones in volunteers

W W Dinsmore, M E Callender, Dorothy McMaster, A H G Love, K D Buchanan

Accepted 10th June 1985.

SUMMARY

This study has examined changes in gastrointestinal hormones induced by alcohol. Ten normal volunteers consumed an orange and carbohydrate-containing drink on two separate occasions, with and without 50g alcohol. There was a significant hyperglycaemia associated with alcohol ingestion but no difference was noted in insulin or gastric inhibitory polypeptide in the two groups. Gastrin release was stimulated by alcohol but pancreatic polypeptide release and N-terminal glucagon release were both suppressed by alcohol. There was no difference in release of secretin or C-terminal glucagon in either group.

INTRODUCTION

Gastroenteropancreatic hormonal changes induced by alcohol may be responsible for many of the effects of alcohol, including gastritis, diarrhoea and abnormal carbohydrate metabolism.¹ The responses of gastroenteropancreatic hormones in normal subjects to oral alcohol are either unknown or in dispute.¹⁻⁹

The aim of the study was to assess gastroenteropancreatic hormone changes induced by alcohol. Therefore we have studied normal volunteers who had oral alcohol in an orange and glucose drink. Assessment was made of serial alcohol, glucose and gastrointestinal hormones (insulin, gastrin, gastric inhibitory polypeptide (GIP), pancreatic polypeptide (PP), secretin and glucagon).

PATIENTS AND METHODS

Normal fasting volunteers (six male and four female, mean age 22 years, range 18-34 years), with no history of diabetes mellitus or excess alcohol intake were included in the study. The project had the approval of the Royal Victoria Hospital Ethical Committee. Written informed consent was obtained from each volunteer.

Royal Victoria Hospital, Grosvenor Road, Belfast.

W W Dinsmore, MD, MRCP, Registrar.

M E Callender, MRCP, Consultant Physician.

The Department of Medicine, Queen's University, Belfast.

Dorothy McMaster, PhD, Senior Research Officer.

A H G Love, BSc, MD, FRCP, FRCPI, Professor of Medicine.

K D Buchanan, PhD, MD, FRCP, Professor of Metabolic Medicine.

Correspondence to: Dr W W Dinsmore, Royal Victoria Hospital, Belfast BT12 6BA.

The experiment started at 9.00 a.m. when 10 volunteers (who were fasted from 10 p.m.) each had 50g 95% alcohol, diluted with 450 ml pure unsweetened orange juice containing 34g fructose, to which was added 34g glucose. Each volunteer was assessed on two mornings at least two weeks apart, having at random the drink with alcohol on one morning and without alcohol on the other morning. An indwelling cannula was inserted at time -15 minutes when an arterial blood sample was taken for analysis. Blood samples were immediately transferred to chilled heparinised tubes and stored on ice prior to centrifugation. A second sample was taken at time zero and the volunteers were then given the orange drink which was consumed orally with blood samples at time 15, 30, 45, 60, 90, 120, 180 and 240 minutes. The cannula was flushed out after each sample with 0.5 ml physiological saline (0.9% NaCl) and the first 3 ml of the venous sample were discarded to prevent contamination.

All samples were analysed for glucose and alcohol by colorimetry. Insulin, GIP, gastrin, N and C glucagon, secretin and PP were measured by radioimmunoassay.

Statistical analysis was performed using Wilcoxon matched-pairs signed-ranks test. Results are given \pm standard error.

RESULTS

Serum alcohol was increased to 2.4 mmol/l (± 0.4) after 15 minutes and reached a peak of 12.4 mmol/l (± 1.1) at 90 minutes. There was an overall elevation of serum glucose with alcohol with significantly higher glucose at 45 mins, 60 mins ($p < 0.01$) and 90 mins ($p < 0.05$) (Figs 1 and 2).

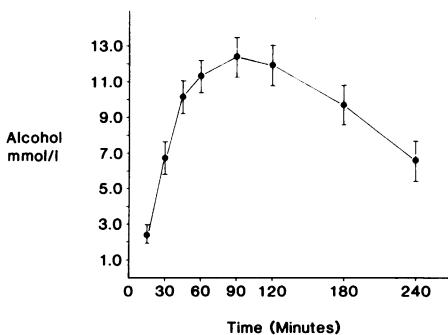


Fig 1. The change in serum alcohol (mmol/l) (\pm SEM) measured for 240 mins in 10 normal volunteers who each had 50g alcohol in an orange drink containing 34g fructose and 34g glucose

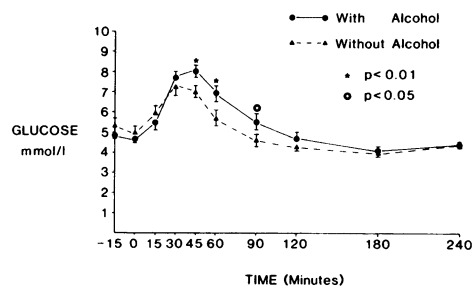


Fig 2. The change in serum glucose concentrations (mmol/l) (\pm SEM) in 10 normal volunteers measured over 240 mins following an orange drink containing 34g glucose and 34g fructose, both with and without alcohol. (The p values refer to the corresponding times comparing with and without alcohol).

Plasma insulin reached a peak of 74.7 mU/l (± 5.3) without alcohol and was suppressed with alcohol, reaching a peak of 59.0 mU/l (± 7.8) ($p < 0.05$) at 45 minutes. There was, however, no significant difference in the area under the curves, with or without alcohol. Plasma GIP was stimulated both with and without alcohol. There was no significant difference at any time and there was no overall difference in GIP release in the two groups assessed by the area under the curves (Figs 3 and 4).

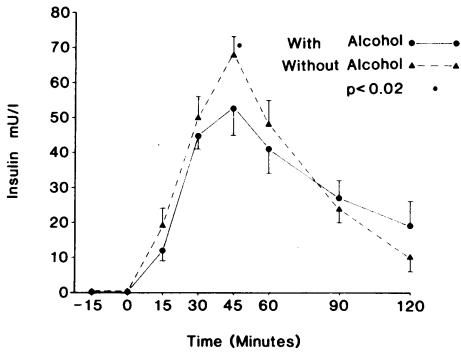


Fig 3. The change in plasma insulin concentrations (mU/l) (\pm SEM) in 10 normal volunteers measured over 120 mins following an orange drink containing 34g glucose and 34g fructose, both with and without alcohol. (The p value refers to 45 mins, comparing with and without alcohol).

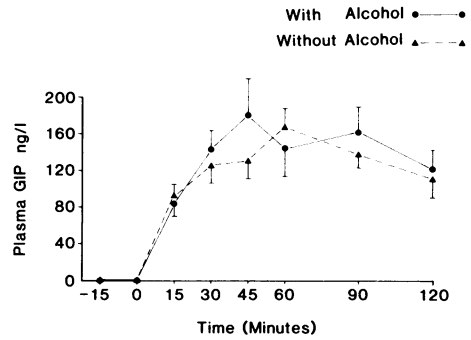


Fig 4. The change in plasma gastric inhibitory polypeptide (GIP) concentration (\pm SEM) in 10 normal volunteers measured over 120 mins following an orange drink containing 34g glucose and 34g fructose, both with and without alcohol.

Gastrin was stimulated with and without alcohol ($p < 0.001$), comparing peak values with baseline values. Alcohol produced further stimulation of gastrin release with significantly greater elevation of plasma gastrin at 45 and 90 minutes ($p < 0.05$), when compared with the controls without alcohol. The area under the gastrin curve with alcohol was 4129 ng/1/2h (\pm 821) and this was greater than the area under the curve without alcohol, 2019 ng/1/2h (\pm 367) ($p < 0.05$). There was no significant effect on secretin release with or without alcohol. N-terminal glucagon was stimulated by the orange drink without alcohol and was higher than with alcohol at times 45 minutes ($p < 0.005$), 90 minutes and 120 minutes ($p < 0.05$). The area under the curve without alcohol was 2089 ng/1/2h (\pm 813) and with alcohol was -69 ng/1/2h ($p < 0.05$) (Figs 5 and 6).

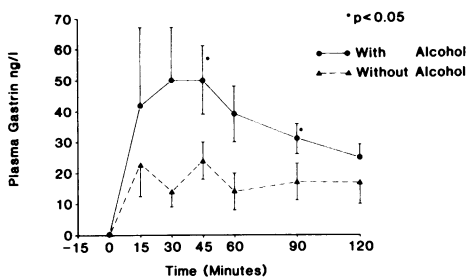


Fig 5. The increase in plasma gastrin concentrations (ng/l) (\pm SEM) in 10 normal volunteers measured over 120 mins following an orange drink containing 34g glucose and 34g fructose, both with and without alcohol. (The p values refer to the corresponding times comparing with and without alcohol).

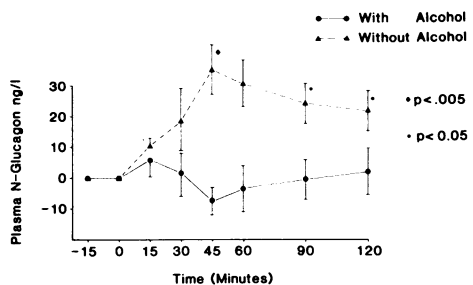


Fig 6. The increase in plasma N-terminal glucagon concentration (ng/l) (\pm SEM) in 10 normal volunteers measured over 120 mins following an orange drink containing 34g glucose and 34g fructose, both with and without alcohol. (The p values refer to the corresponding times comparing with and without alcohol).

There was a tendency towards higher values of C-terminal glucagon without alcohol at all recorded times, but this was not statistically significant. Lower mean levels of pancreatic polypeptide were recorded at all times in the volunteers who had alcohol, but this was only significant at time 90 minutes ($p < 0.05$). The area under the curve with alcohol in two hours was 1560 ng/1/2h, but without alcohol it was 3334 ng/1/2h (Figs 7 and 8).

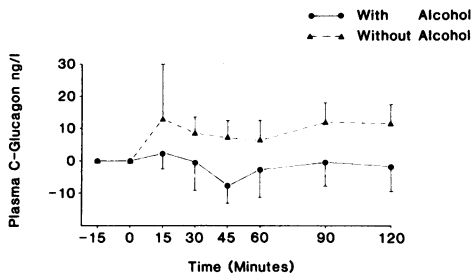


Fig 7. The change in plasma C-terminal glucagon concentration (ng/l) (\pm SEM) in 10 normal volunteers measured over 120 mins following an orange drink containing 34g glucose and 34g fructose, both with and without alcohol.

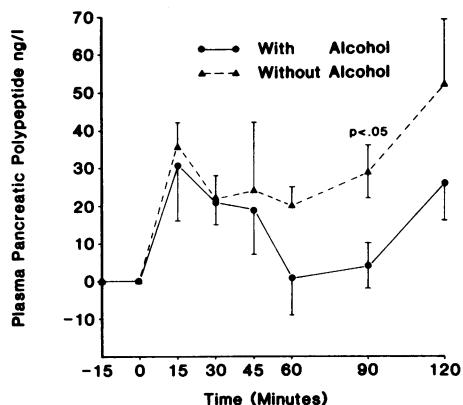


Fig 8. The change in plasma pancreatic polypeptide (PP) concentration (ng/l) (\pm SEM) in 10 normal volunteers measured over 120 mins following an orange drink containing 34g glucose and 34g fructose, both with and without alcohol. (The p value refers to 90 mins, comparing with and without alcohol).

DISCUSSION

The experiment was constructed to mimic a common situation, i.e. alcohol taken with a carbohydrate-containing mixer. The total alcohol consumed was approximately equivalent to five U.K. measures (50g) and after dilution with orange juice would be in a concentration of approximately 10% V/V, which is readily absorbable.¹⁰ The peak alcohol concentration (12.4 mmol/l) was at 90 minutes and was still under the limit for legally driving a motor car in Northern Ireland.

Serum glucose was significantly higher in the group with alcohol, as other workers have noted.^{11, 12} Alcohol is known to produce vasodilation and this may have promoted the uptake and transport of the glucose. Previous studies with a carbohydrate load given with alcohol have produced hypoglycaemia three to four hours after administration of the test dose.⁴ In contrast, our lowest serum glucose recorded was 2.9 mmol/l in one subject at 180 minutes. There was no significant difference in the mean glucose concentrations at 180 and 240 minutes either with or without alcohol and no volunteer complained of hypoglycaemic symptoms. In O'Keefe's study⁴ the blood alcohol concentrations were 50% higher than in the present study, and this higher alcohol concentration may have been related to the observed hypoglycaemia in his subjects.

Despite a higher insulin peak with alcohol, there was a similar total release of insulin in both groups and the volunteers with higher serum glucose concentrations did not respond with hyperinsulinaemia. This contrasts with O'Keefe⁴ who noted hyperinsulinaemia associated with alcohol administration.

Release of GIP is also glucose-dependent and, while there was a marked response to the orange drink in both groups, there was no overall difference between the volunteers with and without alcohol and this is in keeping with the insulin results. Several authors^{2,9} have noted an increase in serum gastrin after oral alcohol and our results confirm this finding. Stimulation of gastric secretion by oral alcohol is well documented.^{13, 14} This may be due to two factors: a direct effect of alcohol on the parietal cells^{13, 14} and release of gastrin from the antrum after local action of alcohol.¹⁴ In addition, gastrin release is now known to be stimulated by intravenous alcohol and this seems to be a specific effect of alcohol on the gastrin cells.¹⁵

As secretin administration has produced all stages of acute pancreatitis in animals¹⁶ and pancreatitis is common in alcoholism, there has been much interest in secretin levels and their relationship to alcohol ingestion. We have found no significant alteration in secretin levels after alcohol; this corresponds with the findings of Henry³ but is in contrast with the results of Straus⁸ and Llanos,⁹ both of whom noted secretin stimulation after 60 ml neat vodka taken orally. The previously noted increase in gastrin would be likely to stimulate gastric acid secretion and hence stimulate release of secretin, so it is surprising not to find an overall effect of alcohol on secretin levels. This may be because changes in acid production were not great enough to stimulate any significant release of secretin or because delayed gastric emptying induced by alcohol¹⁷ has reduced the rate of release of acid from the stomach into the duodenum.

The suppression of glucagon by alcohol has not previously been reported. The N-terminal glucagon is more suppressed than the C-terminal glucagon. The C-terminal glucagon antibody reacts predominantly with pancreatic glucagon and the N-terminal glucagon reacts with both pancreatic glucagon and 'enteroglucagon'. Therefore this suggests that alcohol has produced a greater reduction in the 'enteroglucagon' component of glucagon than in the pancreatic component of glucagon. While the physiological functions of 'enteroglucagon' are still unclear, it is thought to be trophic, producing hyperplasia of the small intestinal cells.¹⁸ Since alcohol is known to induce mucosal damage in alcoholics,¹⁹ it is possible that low 'enteroglucagon' levels induced by the alcohol will reduce the gut mucosal response to the alcohol insult. The glucagon findings in the present study are in keeping with those in previous studies of volunteers³ in which alcohol in the form of 60 ml neat vodka was taken orally and produced no significant change in glucagon when compared with the fasting levels.

The suppression of pancreatic polypeptide (PP) with alcohol is in keeping with previous studies,⁶ in which depression of PP levels was noted after a meal with white wine compared with a meal with distilled water. An increase in plasma PP is thought to produce a decrease in exocrine pancreatic secretion²⁰ and, since alcohol also produces inhibition of exocrine pancreatic secretion in both man²¹ and dogs,²² it has been suggested that PP is the hormonal mediator involved. This hypothesis is refuted by our experiment and by the work of Singer,⁶ in which a depression of PP was associated with alcohol ingestion.

In this study, we have found that hyperglycaemia was induced by alcohol but this was not associated with significant overall change in either insulin or GIP levels. While there was stimulation of gastrin release associated with alcohol ingestion, there was no change in secretin release. Pancreatic polypeptide was suppressed in the alcohol group. Suppression of N-terminal glucagon associated with alcohol in this study has not previously been documented.

REFERENCES

1. Bloom SR, Polak JM. Gut hormones. *Adv Clin Chem* 1980; **21**: 177-244.
2. Becker HD, Reeder DD, Thompson JC. Gastrin release of ethanol in man and in dogs. *Ann Surg* 1974; **179**: 906-909.
3. Henry RW, Lavery T, Buchanan KD. The effect of alcohol on gastroenteropancreatic hormones. *Ulster Med J* 1981; **50**: 120-22.
4. O'Keefe SJD, Marks V. Lunchtime gin and tonic—a cause of reactive hypoglycaemia. *Lancet* 1977; **1**: 1286-88.
5. Staub JL, Sarles H, Chayvialle JA, Descos F, Lassman V, Vague P. Relationship between intravenous ethanol, alcohol-induced inhibition of pancreatic secretion and plasma concentration of immunoreactive pancreatic polypeptide, vasoactive intestinal peptide and somatostatin in man. *Regul Pept* 1981; **2**: 61-68.
6. Singer MV, Eysselein V, Goebell M. Pancreatic polypeptide response to ethanol in humans and dogs. *Regul Pept* 1983; **6**: 13-23.
7. Fink RS, Adrian TE, Margot DH, Bloom SR. Increased plasma pancreatic polypeptide in chronic alcohol abuse. *Clin Endocrinol* 1983; **18**: 417-21.
8. Straus E, Urbach HJ, Yalow RS. Alcohol-stimulated secretion of immunoreactive secretin. *N Engl J Med* 1975; **293**: 1031-32.
9. Llanos OL, Swierczek JS, Teichmann RK, Rayford PL, Thompson JC. Effect of alcohol on the release of secretin and pancreatic secretion. *Surgery* 1977; **81**: 661-67.
10. Royal College of Psychiatrists. Alcohol and alcoholism. London: Tavistock, 1979.
11. Dornhorst A, Ouyang A. Effect of alcohol on glucose tolerance. *Lancet* 1971; **2**: 957-59.
12. Phillips GB, Safrit HF. Alcoholic diabetes: induction of glucose intolerance with alcohol. *JAMA* 1971; **217**: 1513-19.
13. Woodward ER, Robertson C, Ruttenberg MD, Schapiro H. Alcohol as a gastric secretory stimulant. *Gastroenterology* 1957; **32**: 727-37.
14. Irvine WT, Watkin DB, Williams EJ. The mechanism by which alcohol stimulates acid secretion. *Gastroenterology* 1960; **39**: 41-47.
15. Eysselein VE, Singer MV, Wentz H, Goebell H. Action of ethanol on gastrin release in the dog. *Dig Dis Sci* 1984; **291**: 12-18.
16. Herman RE, Davis JH. The role of incomplete pancreatic duct obstruction in the etiology of pancreatitis. *Surgery* 1960; **48**: 318-329.
17. Fairclough PD, Clark ML. Alcohol related disease of the gastrointestinal tract. In: Clark PMS, Kricka LJ, eds. Medical consequences of alcohol abuse. Chichester: Ellis Horwood, 1980: 87-101.
18. Gleeson MH, Bloom SR, Polak JM, Henry K, Dowling RH. Endocrine tumour in kidney affecting small bowel structure, motility and absorptive function. *Gut* 1971; **12**: 773-782.
19. Wilson FA, Moyumpa AM. Ethanol and small intestinal transport. *Gastroenterology* 1979; **76**: 388-403.
20. Greenberg GR, McCloy RF, Adrian TE, Chadwick VS, Baron JH, Bloom SR. Inhibition of pancreas and gall-bladder by pancreatic polypeptide. *Lancet* 1978; **2**: 1280-82.
21. Mott C, Sarles H, Tiscornia O, Gullo L. Inhibitory action of alcohol on human exocrine pancreatic secretion. *Am J Dig Dis* 1972; **17**: 902-10.
22. Bayer M, Rudick J, Lieber CS, Janowitz HD. Inhibitory effects of ethanol on canine exocrine pancreatic secretion. *Gastroenterology* 1972; **63**: 619-626.