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AN ASSESSMENT OF GASTRIC EMPTYING BY BREATHALYSER

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1 A breathalyser has been used to measure blood alcohol levels at short intervals to produce an absorption curve which we have shown is reproducible.

2 Changes in the rate of absorption which reflect changes in gastric emptying times produced by metoclopromide and propantheline have been demonstrated.

3 The breathalyser technique described appears to offer a simple method of studying the effects of drugs on the rate of gastric emptying.

Introduction

Drug interactions can occur at many sites in the body and the administration of a second drug may seriously modify the efficacy of a patient's original medication. Drugs which modify intestinal function have been shown to affect absorption and to reduce or increase the blood levels of other drugs taken by the patient. This effect has been demonstrated by giving propantheline and metoclopramide with paracetamol (Nimmo, Heading, Tothill & Prescott, 1973) and digoxin (Manninen, Apajalahti, Melin & Karesoja, 1973). These drugs alter intestinal motility and this probably accounts for their effect on the blood levels of the digoxin and paracetamol. Other drugs may have similar effects. It is, however, relatively difficult to demonstrate that gastrointestinal motility has been altered. It is possible to intubate the upper gastrointestinal tract and to measure pressure changes or flow rates (Connell & Texter, 1968). One can follow markers in transit either radiologically or by scanning (Griffiths, Owen, Campbell & Shields, 1968), or alternatively by noting their appearance in the stool. Changes in motility can also be inferred from changes in the absorption curves of drugs or other substances but this has the disadvantage of requiring either multiple venepunctures or repeated cannulation of a vein followed by analysis of large numbers of blood samples by techniques of variable complexity.

Alcohol is absorbed slowly from the stomach and rapidly from the small intestine, therefore the rate of absorption is determined largely by the rate of gastric emptying (Rinkel & Myerson, 1941; Kalant, 1971). Furthermore, alcohol is excreted in the expired air and the amount exhaled is directly proportional to the arterial blood level since the alveolar air is in equilibrium with pulmonary capillary blood at all times. Thus a breathalyser can be used to estimate blood alcohol levels because alcohol will diffuse into the alveolar air according to Henry's Law so that the ratio of the concentration in the air to that of blood is constant at a given temperature. This relationship has been demonstrated by both *in vivo* and *in vitro* techniques (Liljestrand & Linde, 1930). At 37°C the blood : air ratio has been repeatedly shown to be 2100 : 1 (Liljestrand & Linde, 1930; Harger, Laney, Bridwell & Kitchel, 1950; Harger, Forney & Barnes, 1950).

In this study we have used a breathalyser technique to obtain frequent blood levels after the ingestion of alcohol to produce an accurate absorption curve. We then studied the reproducibility of the blood level curve and the effects of metoclopramide and propantheline to determine whether this technique offers a simple way of assessing the effects of drugs and other factors on intestinal motility.

Methods

Subjects

Five informed fasting volunteers aged 20-30, two of whom were female, participated in this study. All of them drank alcohol on social occasions but had no alcohol on the evening before the test.

Procedure

Each volunteer was given 40 ml absolute alcohol diluted to 200 ml with water and flavoured with

low calorie lime juice. This was swallowed as quickly as possible and was immediately followed by 100 ml water. The mouth was then washed out with water. Blood alcohol levels were determined by the breathalyser described below at 5 min intervals for up to 4 hours. Throughout the test the subject remained seated.

The effect of altering gastrointestinal motility was studied by giving metoclopramide (10 mg) and propantheline (30 mg) intravenously on subsequent occasions 10 min before ingesting the alcohol. The study was then repeated exactly as described above. The treatments were given in a randomized order.

Breath analysis

The breath analysis was performed by a Gas Chromatograph Intoximeter (Lion Laboratories, Cardiff) which uses a flame ionization detecting system. It traps 0.25 cm^3 of alveolar air from a single breath by a precision sampling valve after 1 litre of tidal air has been collected in a waste bag. When a button is pressed, the machine analyses the alveolar air, calculates the area under the curve, multiplies the answer by the blood/air ratio and gives an estimation of the blood alcohol level in about 3 minutes. The intoximeter is calibrated by injecting known concentrations of alcohol and the error for analysing repeat samples is less than 1%.

Results

The reproducibility of the method was studied by performing repeat tests on the same subject under standardized conditions. The heights and times taken to reach the peak in these repeat studies are set out in Table 1 and a two-way analysis of variance is presented in Table 2.

The effects of increasing and decreasing gastrointestinal motility by metoclopramide and propantheline respectively in two individuals are shown in Figure 1. These show clearly the more rapid rise in blood levels and the higher peak caused by metoclopramide and the flattening of the absorption curve which follows the administration of propantheline. A summary of the results obtained on all five subjects studied, is given in Table 1.

Discussion

There is a current interest in factors which influence the absorption of drugs (Welling, 1972;

Table 1 The effect of metoclopramide (10 mg) and propantheline (30 mg) on the time taken to reach the peak and the peak concentration of alcohol in five subjects. The reproducibility is indicated by the results of the repeat studies.

			Peak times (min)			*Peak concentration (mg/100 ml)*		
Subject	*Weight (kg)*	*Sex*	*Metoclopramide*	*Control*	*Propantheline*	*Metoclopramide*	*Control*	*Propantheline*
1	124	M	15	20	30	84	54	36
				30			48	
				20			58	
2	61	F	35	45	70	86	98	73
			30	70		113	93	
				55			87	
3	54	F	35	55	85	134	122	73
				55			115	
4	65	M	30	75	80	97	52	50
				70			60	
5	68	M	45	60	75	102	69	54
				65			68	
Ratio			1	1.82 (0.405)	2.18 (0.365)	1.844 (0.234)	1.326 (0.189)	1

s.d. in parenthesis.

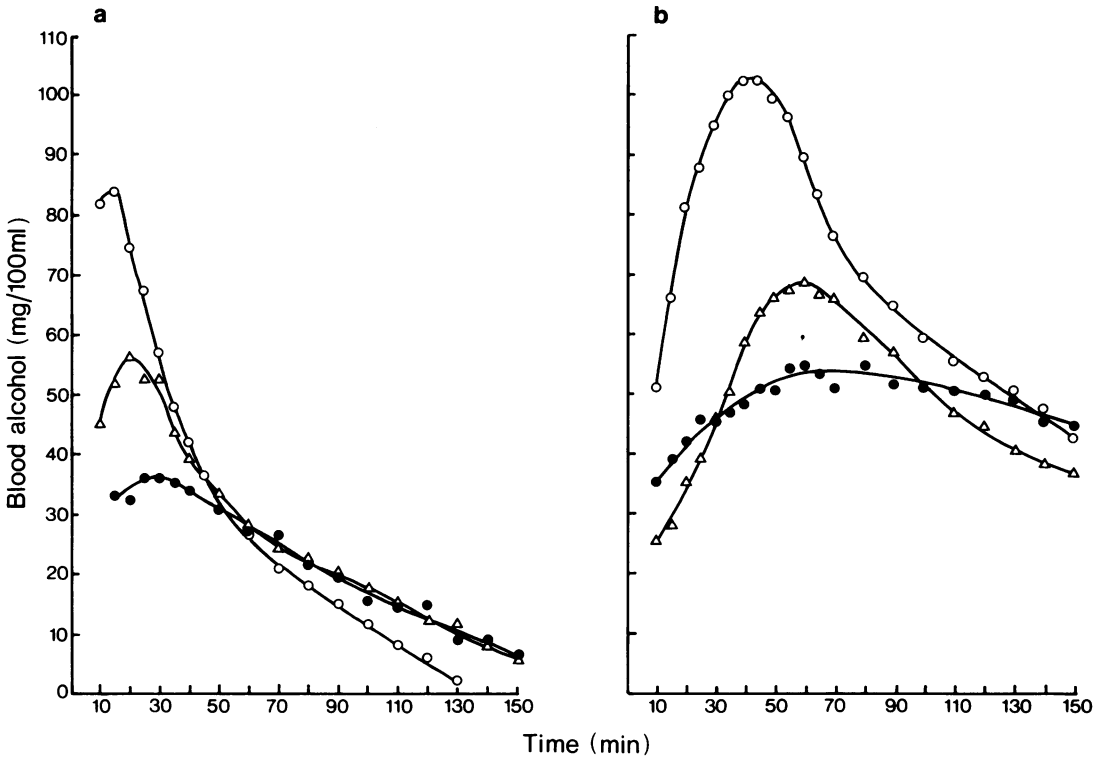

Fig. 1 Blood alcohol levels after ingestion of 40 ml absolute alcohol diluted to 200 ml with water in two different individuals (a and b), showing the control values obtained (△) and the effect of metoclopramide (○; 10 mg, i.v.) and propantheline (●; 30 mg, i.v.) administered 10 min before the alcohol.

Kendall & Chan, 1974) and it has been shown that the rate of gastric emptying and intestinal motility is important in this context. The technique described provides a way of assessing the action of drugs on gastrointestinal motility.

The blood alcohol/time profiles as influenced by metoclopramide or propantheline show a consistently similar pattern. Analysis of the peak height (Table 1) shows that intersubject peak alcohol concentrations vary by no more than ±10% and that the ratio of peak concentration of blood alcohol alone to metoclopramide and to propantheline is reasonably constant. There is more variation in the time of peak alcohol concentrations (±20%) and the deviation from the mean ratio value is greater. The analysis of

Table 2 Two-way analysis of variance of peak alcohol times and concentrations

			Peak alcohol times			*Peak alcohol concentration*		
Source		*Degrees of freedom*	*Sum of squares*	*Mean of squares*	F	*Sum of squares*	*Mean of squares*	F
Main effects	Subject	4	3,146	786.5	10.12*	4,662	1165.5	12.36*
	Drug	2	3,392	1696	21.8**	5,336	2668.0	28.3**
Interaction (residual)	Subject x Drug	8	621.6	77.7		754.5	94.3	

** Significant at 0.1% level.
* Significant at 1.0% level.

variance confirms that there is a statistically significant intersubject variation in both peak alcohol concentration and times. In view of this, the procedure is now being modified in order to reduce the variation in peak concentrations by giving a weight related amount (0.5 ml/kg) of alcohol. In spite of the variation, the effect of metoclopramide on both the peak alcohol time and concentration was significant ($P < 0.01$). The effect of propantheline on peak time was less marked ($P < 0.05$) but was significant on peak concentration ($P < 0.025$).

Analysis of the areas under the curves has provided no useful information. It is assumed that at 'infinite time' the areas under the blood/alcohol/time curve for alcohol taken alone, after metoclopramide or after propantheline would be similar. This is at present being investigated. Comparison of the areas for different intervals of time (10-50, 60, 70, 80 and 90 min) failed to reveal a consistent pattern. It should be noted that values obtained in the first 10 min are not significant as these may be contaminated by traces of alcohol and alcohol vapour in the pharynx and buccal cavity.

Nimmo *et al.* (1973) showed that metoclopramide significantly increased and propantheline decreased the rate of absorption of paracetamol. The results of the present study demonstrates that metoclopramide also increases the rate of alcohol absorption and that propantheline decreases the rate. The results obtained by Manninen *et al.* (1973) who demonstrated higher plasma digoxin levels after propantheline and lower after metoclopramide are more difficult to interpret and emphasize the need for further investigation.

The method which we have described for the assessment of upper gastrointestinal motility is as accurate as most others currently available, it is simple to perform and causes no serious discomfort for the subject studied. Measurement of the peak blood alcohol concentration would seem to offer a valuable way of dividing drugs into those which increase, decrease or have no significant effect on gastric emptying and upper intestinal motility.

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