date. Renal biopsy was not performed for any of these patients because of the risk of damaging the remaining kidney. Renal arteriograms were not considered necessary as the blood pressure could be controlled successfully by low doses of anti-hypertensive agents. Apparently, these three cases belonged to the benign arterial hypertension category of Luxton.¹

Shapiro *et al*³ reported a case of Hodgkin's disease in which irradiation caused arterial hypertension to develop 10 years later. In their patient one kidney was shrunken owing to direct radiation damage and was the cause of the raised blood pressure. In all three patients reported in the present study, however, the remaining kidney was larger than average, thus showing that even a compensatorily hypertrophied kidney can be the cause of hypertension.

Because of the combination of various types of treatment, the number of children with malignant tumours who can be treated successfully is increasing. Every physician should therefore be aware of the side effects of such treatment and of the complications which can develop at a much later date. These case reports indicate that arterial hypertension is a delayed complication of radiotherapy which, however, is easily detected and controlled. If undetected it causes irreversible vascular damage. Thus, the

traditional five-year follow-up after successful treatment of malignant disease is not long enough, as problems may arise much later at any age.

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High dose of antacid (Mylanta II) reduces bioavailability of ranitidine

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Abstract

To investigate the effect of antacid on the bioavailability and disposition of ranitidine six healthy volunteers were studied on two occasions one week apart. In the first study they received ranitidine 150 mg with 60 ml water, and in the second study they received ranitidine 150 mg plus 30 ml of an aluminium/magnesium hydroxide mixture (Mylanta II) and 30 ml water. Giving antacid reduced both the maximum plasma ranitidine concentration and the area under the curve by one-third; elimination of the drug was not changed.

Thus giving a high dose of antacid significantly diminished the bioavailability of ranitidine.

Introduction

The efficacy of the histamine H₂-receptor antagonist ranitidine in the treatment of peptic ulceration is related to the plasma drug concentration achieved.¹ Antacids are commonly prescribed with H₂-receptor antagonists; in the case of cimetidine co-administration of antacid reduces bioavailability by one-third.^{2,3} The aim of the present study was to investigate the effect of antacid on the bioavailability and disposition of ranitidine.

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Subjects, methods, and results

Six healthy volunteers (three men, three women) aged 21-29 years and weighing 56-83 kg were each studied on two occasions a week apart. In the first study, after an overnight fast each subject received ranitidine as a 150 mg tablet (Zantac) with 60 ml water (control study). In the second study the ranitidine tablet was taken with 30 ml of an aluminium/magnesium hydroxide mixture (Mylanta II; neutralising capacity 150 mmol (5.5 g) hydrochloric acid/30 ml) plus 30 ml water (antacid study). On each occasion blood was sampled at intervals to 12 hours and urine to 24 hours and assayed as previously described.⁴

The maximum plasma concentration and the time taken to reach it were obtained directly from each subject's plasma concentration-time profile. The area under the plasma concentration-time curve from

Mean ± SEM plasma ranitidine concentrations (n=6) after control (●—●) and antacid (○---○) studies, showing significant reduction in bioavailability with antacid.

time 0 to infinity, the terminal-phase elimination half life, and the renal clearance of ranitidine were calculated by standard-model-independent pharmacokinetic formulae.³ Differences between studies were tested using the paired *t* test, *p* < 0.05 being taken as statistically significant. Data are presented as means $\pm$ SD.

The figure shows the mean plasma ranitidine concentration-time data in the two studies. Co-administration of antacid with ranitidine significantly reduced the maximum plasma concentration (from 613 ± 188 to 432 ± 249 $\mu\text{g/l}$) and the area under the curve (from 3613 ± 1090 to 2394 ± 496 $\mu\text{g h/l}$). Elimination of ranitidine, however, was unchanged, as shown by the similar values for the terminal-phase elimination half life (control study 2.30 ± 0.55 h; antacid study 2.58 ± 0.46 h) and renal clearance (control study 17.5 ± 6.0 l/h; antacid study 18.4 ± 5.7 l/h). These results indicate that absorption of ranitidine was reduced by one-third in the presence of the antacid. The similar times to reach peak plasma concentrations, however, show that the rate of absorption was not significantly altered. The percentage of the dose excreted in the urine as unchanged ranitidine was significantly reduced in the antacid study ($28.7 \pm 7.7\%$ v $38.2 \pm 7.9\%$). Recovery of the desmethyl metabolite also tended to be lower in the antacid study ($2.1 \pm 0.9\%$ v $2.5 \pm 0.8\%$).

Discussion

Co-administration of cimetidine with high doses of antacid (neutralising capacity 35-42 mmol (1.3-1.5 g) hydrochloric acid/10 ml; dose given 30 ml) results in a 22-35% reduction in bioavailability of the drug,^{2,3} although lower doses (neutralising capacity 10-15 mmol (0.36-0.55 g) hydrochloric acid/10 ml; dose given 20 ml) show no effect.⁵ Until now the influence of antacids on the bioavailability of ranitidine has not been reported.

In the present study co-administration of antacid at a high dose significantly diminished the bioavailability of ranitidine. This was shown by the reduced area under the curve and by

the comparable reduction in the urinary recovery of unchanged drug. The unchanged values for renal clearance and terminal-phase elimination half life indicate that the efficiency of renal elimination was not significantly affected. These results strongly suggest that the interaction between ranitidine and antacid occurs in the gastrointestinal lumen.

As with cimetidine,⁵ ingestion of less potent antacid preparations with ranitidine may minimise or avoid the interaction shown in this study. Moreover, because ranitidine is a more potent H_2 -antagonist¹ a one-third reduction in bioavailability may not be of such clinical importance. Since the effect of ranitidine on secretion of gastric acid is closely related to the plasma drug concentration,¹ however, we recommend that simultaneous ingestion of ranitidine and antacids be avoided.

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Acceleration of ventricular rate by amiodarone in atrial fibrillation associated with the Wolff-Parkinson-White syndrome

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Abstract

Amiodarone has proved to be a valuable drug in atrial fibrillation associated with the Wolff-Parkinson-White syndrome. When it was administered to a patient with this syndrome in atrial fibrillation, who had previously suffered an inferior myocardial infarction, the ventricular rate accelerated from 170 to 230 beats/minute.

This unusual case emphasises the need for full electro-physiological assessment of patients with the Wolff-Parkinson-White syndrome for whom amiodarone treatment is being considered.

Introduction

Previous reports have shown the efficacy of amiodarone in treating arrhythmias associated with accessory atrioventricular

pathways.¹⁻³ We describe a case in which intravenous amiodarone accelerated the ventricular rate in atrial fibrillation associated with the Wolff-Parkinson-White syndrome, thus potentially increasing the risk of dangerous ventricular arrhythmias.

Case report

A 69-year-old man was admitted to hospital in March 1982 with a 10-day history of shortness of breath, ankle swelling, orthopnoea, and bouts of fast palpitation. He had suffered myocardial infarctions in 1973 and 1974 and had a four-year history of unexplained bouts of dizziness and sudden losses of consciousness. He had also been admitted elsewhere with documented supraventricular tachycardia associated with ischaemic chest pain, although cardiac enzyme activities were not raised.

On admission there was clinical and radiological evidence of left ventricular failure and various irregular narrow- and broad-complex tachycardias with rates of between 130 and 170 beats/min that failed to respond to intravenous verapamil, disopyramide, or lignocaine. Plasma electrolyte concentrations and cardiac enzyme activities were normal. Because of difficulty in controlling the arrhythmias 800 mg amiodarone was administered by mouth and he was transferred to this hospital for further management. Previous cardioversions had failed to sustain sinus rhythm.

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