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Intestinal effects of captopril

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Captopril, an angiotensin converting enzyme inhibitor, should reduce all the effects caused by angiotensin II and III. Angiotensin affects the gut,¹ and we report on six patients with adverse gastrointestinal effects that were associated with captopril and consistent with inhibition of some aspect of the agonist effect of angiotensin on intestinal function. We also review other similar cases reported to the World Health Organisation.

Patients, methods, and results

Captopril has been monitored by the New Zealand Medicines Adverse Reactions Committee through its intensive medicines monitoring programme since 1981. The clinical events reported are analysed by at least two clinicians, and reports of new or serious events are followed up for an assessment of causality. The completeness of the cohorts from the monitoring of prescription data by pharmacists is about 85%.

Out of a total cohort of 4124 patients, 169 were reported as having 220 events (mostly medicine related). Of these events, four (1.8%) were of gastrointestinal disturbance, at that time.

The table shows the clinical details of six patients reporting constipation and diarrhoea associated with taking captopril. The severity of the event was sufficient to prompt withdrawal of treatment in five of them, and causality with captopril was highly likely in all of them. In cases 1 and 2 the causal relation was strong because captopril was the only drug changed in the treatment and there was no confounding underlying illness. The temporal relations were feasible both for onset and for disappearance of symptoms. The striking feature was the severity of the condition. No treatment was given in either case, but the symptoms resolved soon after captopril was withdrawn. Diltiazem may have interacted with captopril in case 1.

Three further cases of uncomplicated constipation were reported to the intensive medicines monitoring programme (three women aged 65-80 taking 25-75 mg captopril daily). In two no other medicines were used, and in none were symptoms severe enough to withdraw the drug. Forty three cases were recorded in the WHO's international database to the end of June 1991.

The four cases of diarrhoea in the table were probably due to captopril. Again, withdrawal of captopril resulted in rapid resolution of symptoms. In two patients captopril was the only drug taken. Another seven patients (three men, four women, age 46-87) taking 18.75-150 mg captopril daily had less severe diarrhoea (without vomiting in three patients). This did not result in withdrawal of captopril and causality was speculative. The WHO's database had 186 reported cases of diarrhoea to the end of June 1991.

Discussion

Angiotensin stimulates intestinal motility¹ and its blockade may be expected to result in atony and constipation. Though the mechanism of this response is unclear, in rats prostaglandin inhibition failed to prevent the stimulating effects of angiotensin II.² In dogs Walus *et al* showed an angiotensin induced increase in intestinal activity in vivo with reduced blood flow, though oxygen consumption was unaltered.³ Inhibition of angiotensin converting enzyme should therefore reduce motility with an increase in blood flow and may be beneficial in intestinal (ileal) ischaemia as well as causing constipation.

Angiotensin II blocks the secretion of water and electrolytes in the ileum and colon in rats⁴; thus its inhibition would increase water and electrolyte concentrations in the intestine. Levens discussed a biphasic action of angiotensin II, low doses increasing sodium and water absorption from the intestine, high doses having the reverse effect.⁵ The low dose effect is secondary to local release of noradrenaline, but inhibition of absorption at high doses is thought to be due to prostaglandins. This biphasic dose-response makes prediction of the effects of angiotensin converting enzyme inhibitors difficult. Aldosterone, too, enhances colonic absorption.

Clinical details of six patients taking captopril who reported constipation and diarrhoea

Case No	Sex	Age (years)	Daily dose (mg)	Duration of treatment before onset (days)	Other drugs	Indication	Comment	Time till resolution after stopping captopril
<i>Constipation</i>								
1	F	61	25	21	Diltiazem	Congestive heart failure	Atonic bowel; megacolon	3 days
2	M	44	75	7	None	Hypertension	Complete bowel atony	24 hours
<i>Diarrhoea</i>								
3	M	62	75	17	None	Hypertension	With vomiting	24 hours
4	F	43	12.5	28	None	Hypertension	With vomiting	Treatment not stopped
5	F	74	25		Frusemide, sulindac, ethinyloestradiol, alginic acid (Gaviscon)			
6	M	61	25	First dose	Cimetidine, prazosin	Congestive heart failure Hypertension	With vomiting Abdominal distension	2 days 24 hours

The symptoms were severe enough in five out of six of our cases for captopril to be withdrawn, and causality of captopril seems likely. The background physiology is complex but suggests that captopril and other angiotensin converting enzyme inhibitors may cause various gastrointestinal side effects. These, however, are rarely reported.

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Glass injuries to children

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Age and distribution of glass injuries in children

Age (years)	No	
	Boys	Girls
<1	4	1
1	14	15
2	31	16
3	21	27
4	27	14
5	39	23
6	14	17
7	14	11
8	39	10
9	24	14
10	30	9
11	24	15
12	22	12
13	18	12
14	31	9
15	10	6

We investigated injuries caused by glass in children attending the accident and emergency service at the Royal Liverpool Children's Hospital in an attempt to identify preventive measures.

Patients, methods, and results

In the five months from 1 March to 31 July 1990 there were 24 082 new attendances at the department, of which 587 (2.4%) were for injuries caused by glass. One hundred and seventy of these were in children aged under 5 years, and injuries were twice as common in boys as in girls (table). Injuries occurred evenly throughout the study period.

In 219 cases the injury occurred in the street; 196 happened at home. Only 47 occurred in play areas. The type of glass was not known in 267 cases. The most frequently identified objects were bottles (158). Architectural glass caused 70 injuries. Forty six injuries, all of which were more than 12 hours old at presentation, were infected.

Radiographs were taken in 546 cases, revealing retained glass in 57. Most cases were managed in the department. Four hundred and one children required suturing or the application of Steri-Strips. Six children, four of whom had injured themselves on architectural glass, required immediate admission: two needed primary repair of nerves or tendons, two underwent wound exploration, one was a drunk adolescent, and one toddler had an associated skull fracture. A further 20 children were referred to other specialties. Four children developed wound infections that required inpatient care.

Hands and fingers were the most common sites of injury and were affected in 224 cases. Eighty five per

cent of all injuries (498) affected the limbs, 217 the legs and 275 the arms. The face and head were injured in 61 children. Only 25 had multiple lacerations.

Comment

In our hospital accidents account for half the new attendances in the accident and emergency department and 5% of all injuries are caused by glass. Glass injuries accounted for 1.1% of paediatric accidents in Sheffield¹ and for 9.3% in Philadelphia.²

Most injuries in our series occurred in the street or home; if our streets were clear of glass 37% of these injuries could be prevented. The quantity of glass on the streets would be less if cartons replaced bottles, if people disposed of litter responsibly, and if the streets were frequently swept.

Architectural glass, however, caused the more severe injuries. British Standards specifications have been set for the type and strength of glass to be used in tabletops and trolleys (BS7376:1990), but specifications are needed for all glass in doors and low windows.³

Parents often appeared unaware or careless of potential glass hazards at home. Some lacked understanding of their child's developmental stage: glass was left within reach of toddlers, or children were allowed to play "catch" near glass doors.

Glass injuries cost this hospital at least £62 060 annually. This figure was arrived at by adding together the costs incurred in the five months of this study—initial visits (£10 566), radiography (£3949), admissions and operative procedures (£2200), and review visits (£9144)—but it takes no account of the cost to specialist clinics and district nurses—or of the emotional cost to the children themselves.

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ONE HUNDRED YEARS AGO

HORSE MEAT

It will probably be a long time before the people take to eating horse meat—not because it is not excellent, nourishing, wholesome, and well flavoured—but because they do not know how to cook it, or indeed any other kind of meat, except by boiling, broiling, or roasting. Of bouillon, for which horse meat is excellent, of the *pot-au-feu*, of braising meat, of the succulent and savory cive of *filets au chasseur*, of *patés* they have not an elementary idea. No doubt—since a great deal of excellent horse meat is, we believe, sold in London—we get some in our sausages, in our meat extracts, and in the dishes of the foreign restaurateur of the second and third class, who have lately flourished and multiplied in London. But consciously we do not eat it; the rich have no reason to seek it out, and the poor condemn and despise it; so much the

worse for us, and for the horses, who would have a happier and less toilsome old age if they were fattened for the butcher instead of being worn out and tortured in their last days, till they are dragged to the knacker's yard, or the Zoological Gardens. Here are the details of the bill for horse meat in Paris, and no one will deny to the Parisians that they know how to eat and what to eat. The people of Paris have consumed within the year 21,291 horses, 229 donkeys, and 40 mules, the meat weighing, according to the returns, 4,615 tons. At the 180 shops and stalls where this kind of food is sold the price has varied from 2d. a pound to 10d., the latter being the price of superior horse steaks. But only about one-third of the meat is sold fresh and undisguised; the rest is used in making sausages, and it should be added that 402 horses were seized and condemned as unfit for food.

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