resolution of urinary symptoms. He presented on this occasion with a two-week history of abdominal distension with vomiting for three days. He had the signs of intestinal obstruction but was not acutely ill. Rectal examination showed an empty rectum and a normal prostate. Sigmoidoscopy to 25 cm was normal but clear bubbly mucus was seen coming from above. Plain *x*-ray examination of the abdomen showed a few fluid levels and barium enema examination suggested carcinoma of the sigmoid colon.

After a defunctioning colostomy a formal laparotomy was performed. Rock-hard faeces were impacted in the sigmoid colon and extended back to the caecum. Manual removal by a colotomy was carried out, after which there was no evidence of carcinoma or any other mural lesion in the colon.

Discussion

This man had a clinical and radiological syndrome which exactly resembled carcinoma of the colon. The very severe constipation was probably precipitated by orphenadrine. This drug was probably additionally implicated in the patient's previous urinary retention. Most anti-Parkinsonian agents have atropinic properties, and the smooth muscle relaxation so produced leads to bowel stasis.

Warnes *et al*[2] have described six patients in a psychiatric institution who developed intestinal obstruction caused by impacted faeces. All had been taking atropinic anti-Parkinsonian agents as well as their phenothiazine treatment.

Orphenadrine is structurally dissimilar to other anti-Parkinsonian agents and is related to diphenhydramine hydrochloride.[3] It does, however, have atropinic properties, though fewer than those of benzhexol.[4] It thus seems likely that any of the anti-Parkinsonian agents, with the possible exception of amantadine hydrochloride and levodopa, may cause smooth muscle stasis that may be severe. Parkinsonian patients on these drugs should be asked regularly about their bowel habit. An episode of atropinic side effects such as urinary retention should cause consideration of a change of treatment.

We thank Professor S J G Semple and Mr D Ralphs for allowing us to report details of a patient under their care.

[1] Simpson, J, in *Textbook of Medical Treatment*, ed Alstead and Girdwood. London, Churchill, 1974.
[2] Warnes, H, Lehmann, H E, Ban, T A, *Canadian Medical Association Journal*, 1967, 96-112.
[3] Esphri, D W, in *The Pharmacological Basis of Therapeutics*, ed Goodman and Gilman. London, Macmillan, 1970.
[4] Friend, D, *Clinical Pharmacology and Therapeutics*, 1963, 4, 815-22.

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Metabolic effects of oral salbutamol

The selective β2-adrenergic agonist salbutamol is widely used to relieve airways obstruction. Non-selective β-adrenergic agonists like isoprenaline stimulate insulin and non-esterified fatty acid (NEFA) release,[1] but it is uncertain whether these actions are mediated by β1- or β2-adrenoceptors. Salbutamol causes insulin release in dogs.[2] We report here the results of a double-blind, placebo-controlled study of some metabolic effects of oral salbutamol in man.

Methods and results

Ten healthy non-obese men aged between 18 and 25 years volunteered for study. They reported on each of two mornings 72 hours apart, having fasted for 12 to 16 hours, and lay semi-recumbent during the study. After 30 minutes' rest two basal venous blood samples were withdrawn and a 4-mg tablet of salbutamol or of placebo was given orally, in random order. Further venous samples were withdrawn after 30, 60, and 120 minutes, and each sample was assayed for plasma levels of insulin (immunoassay), glucose (glucose oxidase method), NEFA (measured as palmitic acid with the Duncombe colorimetric technique), free glycerol and triglyceride (enzymatic method), and potassium (flame photometry).

There was a small but significant sustained increase in plasma insulin after salbutamol, with a more gradual increase in glucose (see table). No such changes occurred after placebo. Plasma NEFA and free glycerol levels increased slowly after both salbutamol and placebo, but the NEFA increase occurred earlier (at 60 minutes) after salbutamol. After salbutamol plasma potassium concentrations decreased progressively from the basal level of 4·1 ± 0·1 mmol/l (4·1 ± 0·1 mEq/l), but the fall was statistically significant only at the 120-minute level (3·9 ± 0·1 mmol/l, $P<0.05$). Plasma triglyceride levels were unchanged.

Changes in plasma constituents after salbutamol or placebo (mean ± SEM)

Plasma constituent		Mean basal	30 min	60 min	120 min
Salbutamol	Insulin (mU/l)	25 ± 1·6	36 ± 3·7*	37 ± 3·0*	36 ± 4·5†
	Glucose (mmol/l)	5·3 ± 0·15	5·6 ± 0·17	5·9 ± 0·16*	6·0 ± 0·22‡
	NEFA (μmol/l)	472 ± 26	497 ± 41	633 ± 51*	574 ± 51
	Glycerol (μmol/l)	102 ± 7·6	100 ± 10·9	114 ± 11·9	133 ± 10·9†
Placebo	Insulin (mU/l)	23 ± 2·7	23 ± 2·5	23 ± 2·5	22 ± 2·1
	Glucose (mmol/l)	5·2 ± 0·20	5·2 ± 0·17	5·2 ± 0·17	5·3 ± 0·20
	NEFA (μmol/l)	439 ± 45	470 ± 42	507 ± 62	598 ± 64†
	Glycerol (μmol/l)	98 ± 6·5	91 ± 6·5	109 ± 9·8	114 ± 8·7†

Significant difference from mean basal level *$P<0.01$. †$P<0.05$. ‡$P<0.001$.

Conversion: SI to traditional units—Glucose: 1 mmol/l ≈ 18 mg/100 ml. NEFA: 1 μmol/l ≈ 0·26 mg/l. Glycerol: 1 μmol/l ≈ 0·0092. mg/100 ml.

Discussion

Insulin secretion in man is influenced by adrenergic mechanisms, being increased by β-adrenoceptor stimulation or α-adrenoceptor blockade, and decreased by α-adrenoceptor stimulation or β-adrenoceptor blockade.[3] Whether the pancreatic β-receptor which mediates insulin release is of β1 or β2 subtype is not known, nor indeed is it certain that the subtype hypothesis is fully applicable to man.

Our findings agree with those of two studies[4 5] of intravenous infusion of salbutamol, which showed appreciable increases in plasma insulin. Nevertheless, the magnitude of the other metabolic changes after intravenous salbutamol seem to differ from those of oral salbutamol. Goldberg *et al*[4] found that after intravenous salbutamol the most striking change was an increase in NEFA. The increase in plasma concentration of insulin after salbutamol might be due to direct stimulation of pancreatic β-receptors, to increased plasma NEFA levels, or to hyperglycaemia. Our finding of a prompt and substantial increase in plasma insulin at a time when changes in NEFA and free glycerol were absent or insignificant suggests that the insulin increase is probably not secondary to a rise in NEFA level. In addition, the more rapid rise in insulin than in glucose seen in this study, together with the fact that intravenous salbutamol in low dosage causes no change in blood sugar but an increase in plasma insulin which is abolished by pretreatment with propranolol,[5] indicate that salbutamol probably causes insulin release by stimulation of pancreatic β2-adrenoceptors.

[1] Porte, D, *Diabetes*, 1967, **16**, 150.
[2] Loubatieres, A, *et al*, *Diabetologia*, 1971, **7**, 127.
[3] Porte, D, *Journal of Clinical Investigation*, 1967, **46**, 86.
[4] Goldberg, R, *et al*, *Postgraduate Medical Journal*, 1975, **54**, 53.
[5] Massara, F, *et al*, *Hormone and Metabolic Research*, 1975, **7**, 94.

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