histotoxic symptoms may be due to these, but the exact mechanism of action of thiocyanates is not known.[4] Thiocyanate intoxication with blood concentrations above 200 mg/l may be rapidly corrected by haemodialysis, which reportedly removes several grams of the drug.[5] We tried peritoneal dialysis but in the absence of clearance studies, which we could not do, we cannot comment on the procedure for intoxication with this compound.

Distal part of oesophagus and stomach showing necrotic mucosa.

Requests for reprints should be sent to Professor Sharma.

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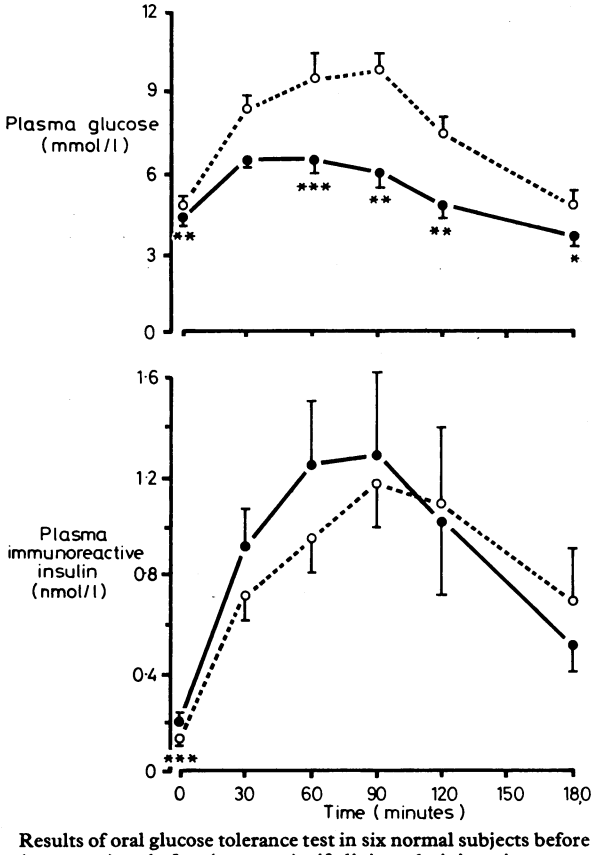
Hyperglycaemic effect of nifedipine

Nifedipine is widely used for the treatment of angina pectoris,[1] and no adverse metabolic side effects have been reported. We recently observed that a patient with maturity-onset diabetes had appreciably decreased mean glucose concentrations after nifedipine was stopped. This led us to investigate whether nifedipine possesses diabetogenic properties.

Patients, methods, and results

The effects of nifedipine on an oral glucose tolerance test (100 g of glucose) were studied in five women and one man. None had evidence of endocrinopathy or were receiving drugs. Mean age was 46 (range 26-55) years. Body weights were within 10% of the ideal weight. After an initial oral glucose tolerance test 20 mg of nifedipine was administered by mouth eight hourly for three days. A second test was performed two hours after the last dose of nifedipine. The subjects received a diet of 6·7 MJ (1600 kcal) (women) or 8·4 MJ (2000 kcal) (men) (45% carbohydrate), beginning three days before the first oral glucose tolerance test. Results are expressed as means $\pm$1 SEM. Differences in the responses before and after nifedipine were assessed by paired Student's *t* test.

Nifedipine induced distinct glucose intolerance (figure). Fasting plasma glucose concentrations showed a significant increase of 10%; basal insulin concentrations were significantly reduced (26%). During the oral glucose tolerance test plasma glucose concentrations were appreciably raised after administration of the drug, and at 60, 90, and 120 minutes values of 9·56, 9·89, and 7·67 mmol/l respectively were observed (172, 178, and 138 mg/100 ml). This contrasted with the normal glucose tolerance in all subjects before administration of nifedipine. In five subjects insulin concentrations were reduced at 30 and 60 minutes; in this subgroup the effect was significant. At 30 minutes the mean insulin concentrations were $0{\cdot}62 \pm 0{\cdot}12$ *v* $0{\cdot}85 \pm 0{\cdot}14$ nmol/l (90 ± 18 *v* 123 ± 20 μU/ml) ($p < 0{\cdot}01$); and at 60 minutes $0{\cdot}76 \pm 0{\cdot}17$ *v* $1{\cdot}13 \pm 0{\cdot}21$ nmol/l (110 ± 24 *v* 164 ± 30 μU/ml) ($p < 0{\cdot}05$). In the sixth subject plasma insulin concentration was increased twofold and fourfold at 30 and 60 minutes respectively. This subject was the only one whose plasma glucose concentrations remained normal during the second oral glucose tolerance test. Fasting plasma glucagon concentration was measured by radioimmunoassay (Unger's 30 K antiserum) in three subjects and five additional normal subjects. Glucagon concentrations were significantly increased by nifedipine ($0{\cdot}045 \pm 0{\cdot}008$ *v* $0{\cdot}034 \pm 0{\cdot}006$ nmol/l ($p < 0{\cdot}05$) (153 ± 27 *v* 115 ± 22 pg/ml).



Results of oral glucose tolerance test in six normal subjects before (●——●) and after (○ - - - ○) nifedipine administration.
*$p < 0{\cdot}05$; **$p < 0{\cdot}02$; ***$p < 0{\cdot}01$.
Conversion: SI to traditional units—Glucose: 1 mmol/l $\approx$ 18 mg/dl. Insulin: 1 nmol/l $\approx$ 145 μU/ml.

Comment

The present study shows that in subjects with normal glucose tolerance short-term administration of nifedipine increases fasting plasma glucose concentrations and induces appreciable glucose intolerance associated with a delay of the insulin response. Factors other than impaired insulin release may play a part in the nifedipine-induced glucose intolerance. Particularly relevant are the raised plasma glucagon concentrations that we observed, and the possibility of transient rises in plasma norepinephrine concentrations.[2]

While we were preparing this paper a study was reported in which the effects of nifedipine (30 mg/day by mouth for 10 days) on carbohydrate metabolism were measured.[3] In subjects with normal glucose tolerance raised fasting plasma glucose concentrations were observed; in contrast to our findings, however, an improvement in glucose tolerance, paradoxically associated with a reduced insulin response during the oral glucose tolerance test, was described. In patients with glucose intolerance nifedipine was reported to induce further

carbohydrate impairment. Glucagon concentrations were not investigated.

Because of the potential diabetogenic properties of nifedipine plasma glucose concentrations should thus be monitored in patients receiving this drug.

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Diagnosing tuberculous pleural effusion: comparative sensitivity of mycobacterial culture and histopathology

Establishing the specific causal diagnosis of tuberculous pleural effusion remains difficult because of the low yield of mycobacteria from sputum, gastric juice, and pleural fluid. Histopathological examination of pleura has been shown to give good results.[1] Mycobacterial culture of pleural tissue has been described[2 3] but has not become popular.[4 5] We have compared the sensitivity of pleural tissue mycobacterial culture and histopathology in establishing the diagnosis of tuberculous pleural effusion.

Patients, methods, and results

Twenty-four consecutive patients admitted to hospital with their first episode of exudative pleural effusion from March 1979 to August 1980 were studied. Patients with obvious underlying disease were not included. Closed pleural biopsy was performed with Abrams's needle, and two specimens of pleura were obtained from each patient. One piece was processed for mycobacterial culture and the other for histopathological examination. The specimen for culture was sent to the laboratory in sterile saline. It was ground in Teflon tissue grinder and inoculated in blood agar, in thioglycollate broth, and on two slopes of Lowenstein-Jensen culture medium. The slopes were incubated horizontally for one week and vertically for eight weeks. They were inspected for growth daily during the first week and weekly thereafter. All positive cultures were examined microscopically to confirm the presence of acid-fast bacilli. They were tested for niacin production and all were confirmed to be *Mycobacterium tuberculosis*. For histopathology, the pleural tissue was fixed in 10% formalin, processed through graded alcohol and chloroform solutions, and embedded in paraffin. Sections of 5 μm were cut, stained with hematoxylin-eosin, and examined for the presence of granulomas. In addition, 500-1000 ml of pleural fluid was collected in 2·5% sodium citrate solution (3 ml solution per 100 ml fluid). The entire specimen was centrifuged at 3000 rpm for 30 minutes and the sediment inoculated on to Lowenstein-Jensen culture medium.

Bacteriological or histopathological evidence of tuberculosis was obtained in 16 patients (see table); five patients had malignancy confirmed by pleural tissue histopathology; and in the remaining three no definite diagnosis could be reached. Among the 16 patients with tuberculosis, pleural tissue mycobacterial culture was positive in 14 (88%) but histopathology showed granulomas in only nine (56%). Pleural fluids from 11 patients were cultured and four (36%) were positive. Sputum and gastric juice smears were positive for acid-fast bacilli in only one patient in whom the pleural tissue and fluid grew mycobacteria. In five patients the diagnosis could be made only by pleural tissue culture, in one only by pleural tissue histopathology, and in another only by pleural fluid culture.

Comment

Mycobacterial culture of pleural tissue was found to be the most sensitive test for the diagnosis of tuberculous pleural effusion. Histopathological examination of pleura was less sensitive, but it was more sensitive than pleural fluid culture. Histopathology gives an answer more quickly and may occasionally be the only positive clue. Moreover, it helps in the early diagnosis of malignancy. Mycobacterial culture takes more time but gives a definitive diagnosis in most cases. Therefore, we recommend that mycobacterial culture and histopathological examination of pleural tissue should be done in all patients suspected to have tuberculous pleural effusion.

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Results of bacteriological and histopathological tests on 16 specimens of pleura

Specimen No	Pleural tissue		Pleural fluid		Sputum, gastric juice, or both
	Mycobacterial culture	Histopathology	Smear test for acid-fast bacilli	Mycobacterial culture	Smear test for acid-fast bacilli
1	+	−	ND	ND	−
2	+	+	−	−	−
3	+	−	−	ND	−
4	+	+	−	ND	ND
5	+	−	−	ND	−
6	+	−	−	ND	−
7	+	+	−	−	−
8	+	−	−	−	−
9	+	−	−	+	−
10	+	+	−	−	−
11	−	−	−	+	ND
12	+	+	−	+	−
13	+	+	−	−	ND
14	+	+	−	−	ND
15	−	+	−	−	ND
16	+	+	+	+	+
Total	16	16	15	11	11
No (%) positive	14 (88)	9 (56)	1 (7)	4 (36)	1 (9)

+ = Positive. − = Negative. ND = Not done.

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