recommendations for hydrallazine therapy and previous evidence.^{1,3} One report is consistent with our experience.⁵ Autoimmune phenomena were also more frequent in asymptomatic slow acetylators receiving 200 mg hydrallazine a day or less. This has previously been reported only in patients taking over 200 mg hydrallazine daily.²

Our study indicates that conventionally "safe" doses of hydrallazine may cause both asymptomatic autoimmune phenomena and a lupus syndrome which is not always mild or transient and may require steroids. Potentially serious hydrallazine toxicity is a possibility in all patients taking this drug even after many months of uncomplicated treatment, but especially in slow acetylators in whom constant vigilance for early symptoms is necessary.

Correspondence should be addressed to Dr R F Bing, Department of Medicine, Clinical Sciences Building, Leicester Royal Infirmary, Leicester LE2 7LX.

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(Accepted 28 April 1980)

Department of Medicine, University of Leicester, Leicester

R F BING, MB, MRCP, lecturer in medicine
G I RUSSELL, MB, MRCP, clinical research associate
H THURSTON, MB, MRCP, reader in medicine
J D SWALES, MD, FRCP, professor of medicine

Neonatal systemic candidiasis treated with miconazole

Fortunately systemic candidiasis is uncommon in the newborn baby. Amphotericin B may be used only with caution because of the risks of severe side effects, particularly on the kidney. In this case study we describe our experiences with another antifungal agent, miconazole, an imidazole derivative widely used in adults but to our knowledge rarely used in the neonate.

Case report

A baby girl, birthweight 890 g, was born after 26 weeks' gestation. Between day 3 and day 11 she developed recurrent neonatal apnoea which was managed in turn by intermittent mask ventilation, continuous positive airways pressure, and intravenous aminophylline. On day 6 total parenteral nutrition was started by a central Silastic catheter introduced through a scalp vein. On day 9 the baby became unwell, and *Staphylococcus epidermidis* was isolated from blood culture. The Silastic catheter was removed and nasogastric feeding and flucloxacillin begun. On day 21 apnoeic episodes recurred, and she was again given parenteral nutrition. Intravenous chloramphenicol was started.

On day 16 *Candida albicans* was isolated from the mouth and groin and the baby was treated with oral and topical nystatin. *C. albicans* was then isolated from blood culture taken on day 21. The minimal inhibitory concentration of miconazole for the *C. albicans* isolates was determined by dilution tests in broth and recorded as the lowest antifungal concentrations that gave total inhibition of growth after 48 hours at 37°C. The minimum inhibitory concentration for miconazole was 25 mg/l but partial inhibitory effects were noted in vitro at much lower concentrations.

The central Silastic catheter was withdrawn, but *Candida* was not grown from the catheter tip. Nasojejunal feeding was begun. On day 28 an indurated area on the left thigh was seen to be discharging a large quantity of pus from which *C. albicans* was later isolated. Chloramphenicol was discontinued, and a course of intravenous miconazole was started at a daily dose of 10 mg/kg given in two divided doses, each lasting two hours. The baby's general condition improved, and the candida abscess showed signs of resolution. A serum miconazole concentration measured within one hour of administration of 1.6 mg/l was determined by bioassay. On the fifth day of treatment,

however, frequent episodes of ventricular tachycardia were noted and miconazole was discontinued.

On day 40 the baby once again became ill. There was persistent purulent discharge from the abscess on the left thigh and a similar abscess had now developed on the right thigh from which *C. albicans* was isolated. Blood culture was sterile. Intravenous miconazole was restarted but, because the drug had an irritant effect on the veins which caused frequent venous thrombosis, oral miconazole was added, and the thigh abscesses were irrigated with the intravenous preparation of the drug. During this second course the serum concentration of miconazole was 2.8 mg/l. Intravenous miconazole was continued for six days, and the thigh abscesses were irrigated for 12 days. Over this time the abscesses healed.

Comment

We encountered two major problems with miconazole. The first was an intermittent ventricular tachycardia. This has been reported in adults after rapid injections of a bolus (manufacturers' data), but in our baby it occurred between infusions: it is interesting that the problem did not recur during the second course of treatment. Clearly it is unwise to administer miconazole intravenously without facilities for heart-rate monitoring. The second problem was frequent superficial thrombophlebitis at the site of intravenous administration which resulted in considerable practical difficulties in giving the recommended dose of miconazole.

At the end of an intravenous infusion of a therapeutic dose of miconazole blood concentrations in most patients are between 1 and 10 mg/l.¹ The concentrations of serum miconazole in our baby were in this range, and we gained a strong impression that clinical improvement was due to miconazole. With a minimum inhibitory concentration of 25 mg/l it might be argued that the improvement was coincidental. Nevertheless, it has been suggested that azole antifungal minimum inhibitory concentrations in vivo do not necessarily correlate with effective doses,² and our experiences tend to support this notion.

Correspondence should be addressed to Dr D P Davies.

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(Accepted 29 April 1980)

Neonatal Unit, Leicester Royal Infirmary Maternity Hospital, Leicester

M CLARKE, MB, MRCP, senior house officer
D P DAVIES, MD, MRCP, senior lecturer

Department of Microbiology, University of Leicester

F ODDS, BSC, PHD, lecturer

Public Health Laboratory, Leicester

C MITCHELL, MB, MRCPATH, consultant microbiologist

Impotence in diabetic and non-diabetic hospital outpatients

Although the reported incidence varies greatly, impotence is widely accepted as being more common in diabetics than the general population. Since the Kinsey Report¹ is the only source giving the incidence in the general population by age, we undertook a small survey of impotence in men attending a diabetic clinic compared with non-diabetic hospital outpatients.

Patients, methods, and results

We studied 83 consecutive male patients aged 15-60 years attending this clinic and 50 non-diabetic patients within the same age range attending hospital outpatient follow-up clinics in the same area. All answered a short questionnaire about their libido and potency or, if they did not have a sexual partner, whether they experienced morning erections; the non-diabetics were also asked whether, if their sexual performance was unsatisfactory, they had any condition that might cause this. We did not validate the questionnaire, and relied on the patients' own assessments of their sexual performance.

The table shows that the overall incidence of impotence was 23% (19/83) among the diabetics and 20% (10/50) among the non-diabetics. No difference in libido emerged between the groups. Of the impotent men, 10 diabetics and four non-diabetics rarely or never experienced sexual desire whereas nine diabetics and six non-diabetics often did. All impotent subjects aged under 50 had "normal" libido, except for one diabetic aged 45.

Incidence of impotence in diabetic and non-diabetic hospital outpatients

Age (years)	Diabetics		Non-diabetics	
	No of subjects	No impotent	No of subjects	No impotent
15-20	9	0	1	0
21-30	4	1	11	1
31-40	9	1	8	0
41-50	24	3	12	4
51-60	37	14	18	5
Total	83	19 (23%)	50	10 (20%)

Although 19 diabetics admitted to impotence, only three had sought help for this. One, aged 28, had had diabetes mellitus for 12 years with impotence of recent origin associated with severe marital problems. He and his wife subsequently separated and he later attempted suicide. The second, aged 47, had had marital problems during three marriages over 15 years and had received oral testosterone before becoming diabetic. The third, aged 56, had had diabetes for four years. He had been treated elsewhere with testosterone propionate injections for two years. All 19 impotent diabetics were examined for clinical evidence of autonomic neuropathy. Only one, aged 31, had postural hypotension and a significant reduction in sinus arrhythmia on deep respiration.

Comment

Assessment of impotence is difficult to standardise, so that large discrepancies occur in the reported incidence in diabetics. Joslin regarded impotence as uncommon in diabetics, whereas Rubin and Babbott found that 55% of 198 diabetic men suffered from it.² Despite the subjective nature of the disorder and its diagnosis there has been no controlled investigation of the comparative incidence of impotence in diabetics and non-diabetics.

The present study is too small to yield definitive results, but it indicates that the incidence of impotence in diabetic men attending a hospital clinic may be little different from that in other men of the same age living in the same geographical area and attending other hospital outpatient clinics. Thus impotence in diabetics may not necessarily be a specific complication of the disease but may perhaps be related to the general condition of not feeling completely well or at least attending hospital. This would account for the difficulty in showing any relation between the incidence of impotence and the severity of diabetes,² diabetic angiopathy,³ or autonomic neuropathy.⁴ A study of 30 diabetics complaining of impotence showed that two-thirds had normal nocturnal erections.⁵ The authors concluded that the impotence was psychological rather than organic and wondered why it appeared to be so common in diabetics. Our findings indicate that impotence is equally common in other hospital outpatients. By the loose criteria applied in most studies "impotence" might even be more common in the general (non-hospital) population of this country than in the population studied by Kinsey *et al* with stricter criteria in the USA in 1948, although a detailed investigation would be needed to confirm or refute this.

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(Accepted 28 April 1980)

Diabetic Clinic, North Middlesex Hospital, London N18

EVA LESTER, MB, MRCPATH, consultant chemical pathologist

A J GRANT, MB, CHB, clinical assistant

F J WOODROFFE, MSC, FRCP, physician in charge

Generalised allergy to porcine and bovine monocomponent insulins

Before the introduction of highly purified insulins allergy to insulin was relatively common; local reactions occurred in up to 56% of patients and systemic reactions were found in 0.1-0.2%.¹ Only one report has been published on a generalised allergic reaction to monocomponent insulin.²

Case report

A 48-year-old woman with diabetes was treated for 10 years with diet and oral hypoglycaemic agents—apart from two periods, totalling two months, when she was given Lente insulin because of concurrent illnesses. When admitted for surgery to a breast abscess, control of her diabetes was poor so she was treated with soluble insulin; she immediately developed a weal at the injection site and six hours later complained of generalised pruritus. Similar symptoms and signs, together with angioneurotic oedema, occurred with both Actrapid MC insulin (Novo) and monocomponent beef insulin (Wellcome).

The patient had no history of allergy, her eosinophil count was normal, and complement concentrations were normal before and after challenge with Actrapid MC insulin.

Intradermal skin tests using 4 units each of Actrapid MC, Leo neutral, and soluble insulin produced weals of 5-6 cm diameter at all three sites, injections of 0.2 ml each of 0.1% methyl hydroxybenzoate and 0.3% cresol (both preservatives in Actrapid and Leo neutral insulins) caused weals of only 1 cm diameter. There was no reaction to an injection of normal saline.

Total IgE was measured by the paper radioimmunosorbent test (PRIST: Pharmacia) before and after challenge with Actrapid MC insulin and both values were raised at 132 U/ml and 165 U/ml respectively (normal values for non-atopic adults: 122 U/ml).

Specific anti-insulin IgE was detected in appreciable concentrations against soluble, Actrapid MC, and Leo neutral insulins using a radio allergosorbent test (RAST: Pharmacia) (table), and subsequently specific IgE antibody was demonstrated against monocomponent beef insulin by RAST and also by an indirect immunofluorescence technique using fluorescein labelled anti-IgE as described.³

IgG insulin antibodies were also present in high concentrations against highly purified beef and pork insulins but not against pro-insulin or other pancreatic hormones.

Specific IgE insulin antibodies (detected by RAST)

Insulin	0.05% human albumin (counts per minute)	Reported patient				Patient positive for insulin antibody	
		Before challenge		After challenge		for insulin antibody	
		Counts per minute	Ratio	Counts per minute	Ratio	Counts per minute	Ratio
Soluble	400	826	2.1	1064	2.7	225	0.6
Leo neutral	418	2253	5.4	1902	4.6	277	0.7
Actrapid MC	309	3916	12.7	3158	10.2	347	1.1

Counts per minute are expressed as mean of duplicate samples.

Ratio is cpm allergen/cpm 0.05% human albumin.

Patient positive for insulin antibody is a patient with insulin resistance and high concentrations of IgG antibodies but no evidence of allergy.

Comment

Allergic reactions to insulin are mediated by IgE antibodies, and while these have been found in many patients with allergy to standard insulins they were not demonstrated in the only reported case of allergy to monocomponent insulin.² Intermittent insulin treatment, as occurred in our case, is an important predisposing cause of insulin allergy, and Davidson *et al*⁴ found that 30% of their patients with local reactions and 51% of those with systemic reactions had such a history. In addition they found that 10% of these patients also had insulin resistance; certainly our patient's IgG antibody concentrations were well in the range normally found in such patients.

Zinc has been incriminated as a cause of allergy,⁵ but, as with protein impurities in standard insulins, it is thought to cause only local reactions while systemic allergy is due to the insulin molecule itself. Another difference from our patient is that allergy due to zinc is cured by changing to zinc-free insulin. Hormonal contaminants in insulin preparations may stimulate antibody formation but these have not been linked with allergy and, in any case, were not found in appreciable concentrations in this patient.

Insulin allergy is normally managed by changing to a less antigenic