Drug points

Penile erection due to nifedipine

Dr H C RAYNER, Mr S MAY, and Dr J WALLS (Leicester General Hospital, Leicester LE5 4PW) write: Penile erection is caused by an increase in blood flow from the internal pudendal arteries via penile arterioles to the corpora cavernosa and spongiosum. In a survey of 165 men attending a urology clinic because of impotence vascular insufficiency was found to be the cause in 13.[1] Little is known about the role of calcium channel dependent mechanisms in the control of penile blood flow.[2] We report a case of penile erection in an otherwise impotent man caused by nifedipine, which was reproducible and dose related.

A 70 year old man attended the outpatient clinic for treatment of chronic renal impairment (creatinine clearance 41 ml/min), gout, mitral regurgitation, atrial fibrillation, and angina. Three years previously he had suffered a right retinal artery occlusion. He was not diabetic, did not suffer claudication, and did not smoke. He was being treated with digoxin, frusemide, allopurinol, warfarin, and quinine sulphate. An intravenous pyelogram had shown small kidneys bilaterally. At one visit he mentioned that he had developed painless penile stiffening unassociated with sexual arousal in the afternoons of all eight days on which he had taken 20 mg slow release nifedipine. He had previously been impotent for several years. An open study using both slow release and plain nifedipine preparations confirmed this effect, there being a graded response with increasing doses of the drug from 5 to 20 mg. A double blind trial was carried out using single doses of placebo and 5, 10, and 20 mg plain nifedipine in capsules, swallowed whole. Placebo and 5 mg caused no response; 10 mg and 20 mg doses resulted in penile stiffening, first noticeable five and three hours later and lasting four and nine hours respectively. The maximum stiffenings were graded as 20% and 60% of a complete erection respectively, the latter having been accentuated by a bath.

This is the first published report of penile erection due to nifedipine, although an unconfirmed case of priapism in a patient taking this drug has been reported to the manufacturers. Painful priapism has been associated with other vasodilator drugs, particularly prazosin but also guanethidine and hydralazine.[3] Several of these reports have also been in patients with renal insufficiency, a condition in itself associated with impotence.[4] The response to nifedipine suggests that calcium channel dependent spasm of the internal pudendal arteries or penile arterioles was important in the pathogenesis of this man's impotence. This may have been associated with atherosclerotic plaques as there was clinical evidence of atherosclerosis at other sites. The dose related nature of the response raises the possibility of therapeutic use of calcium antagonists for this condition. Such therapy should, however, be used with caution since prolonged erection may lead to complete priapism and permanent loss of erective capacity.

1 Montague DR, James RE, De Wolfe VG, Martin LM. Diagnostic, evaluation, classification and treatment of men with sexual dysfunction. *Urology* 1979;**14**:545-8.
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4 Procci WR, Goldstein DA, Adelstein J, Massry SG. Sexual function in the male patient with uraemia: a reappraisal. *Kidney Int* 1981;**19**:317-23.

Exfoliative reaction to vancomycin

Ms DEBORAH NEAL and Drs R MORTON, G R BAILIE, and S WALDEK (University of Manchester Department of Pharmacy, Hope Hospital, Salford M6 8HD) write: A 53 year old white man with end stage renal disease due to IgA nephropathy suffered his second episode of Gram positive peritonitis associated with continuous ambulatory peritoneal dialysis and due to *Staphylococcus epidermidis*. Three days earlier he had finished a course of vancomycin for an episode of *S epidermidis* peritonitis with no adverse effects. He was treated with a 1 g loading dose of vancomycin administered intraperitoneally in a four hour dialysate exchange, followed by 25 mg/l in each subsequent exchange four times a day. Ten days later he returned with a three day history of general malaise and a widespread, pruritic, maculopapular rash which was confluent on his back. He was apyrexial, his effluent contained no white cells, and there were no clinical or microbiological signs of infection; therefore the vancomycin was discontinued.

Nine days later he was readmitted with a cloudy dialysate bag from which *S epidermidis* was again isolated. The rash had resolved except for a few isolated patches and he started taking vancomycin and rifampicin because of suspected catheter colonisation. He was discharged immediately to continue his treatment as an outpatient. After seven days of treatment he returned with an intensely pruritic, red, raised rash covered by dry, flaky skin over his entire body. This had started two days after he restarted the vancomycin. He had no known allergies or history of dermatological disorders.

All his current medication was stopped and a five day reducing course of prednisolone started. The symptoms began to resolve within 48 hours, although the rash persisted and was exfoliative. Unfortunately, before complete resolution had occurred, he suffered an anterior myocardial infarction two weeks later, from which he died.

Maculopapular and urticarial rashes occur in 4-5% of patients receiving vancomycin.[1] Such a severe, exfoliating rash as that seen in our patient has not been described before. The manufacturers of vancomycin (Eli Lilly and Co Ltd) have one case on record of a 28 year old woman with renal failure who received intravenous vancomycin for a staphylococcal lung infection in 1983 and who experienced a vaguely described episode of "diffuse desquamation." She recovered after 23 days. This reaction must be differentiated from the well described red neck syndrome.[2]

It is perhaps surprising that the symptoms persisted for so long in this patient. Serum vancomycin concentrations were not determined, but it is well known that vancomycin is cleared very slowly by continuous ambulatory peritoneal dialysis with a half life of up to 90 hours,[3] allowing doses to be given as infrequently as once every seven days. Therefore appreciable serum concentrations of the antibiotic could have been maintained up to the time of death. The severity of the reaction may perhaps be explained by the fact that this was a repeated exposure to a drug to which the patient had already reacted. When a patient has experienced such an allergic reaction to a drug, rechallenge, intentional or inadvertent, may be unwise.

Other drug treatment remained unchanged throughout the event—the only concomitant medication was aluminium hydroxide capsules. We do not believe that rifampicin was implicated, since it was not administered during his previous episodes of peritonitis. Exfoliative dermatitis should therefore be added to the list of adverse effects which may be associated with vancomycin.

1 Geraci JE, Hermans PE. Vancomycin. *Mayo Clin Proc* 1983;**58**: 88-91.
2 Bailie GR, Yu R, Morton R, Waldek S. Vancomycin, red-neck syndrome and fits. *Lancet* 1985;ii:279-80.
3 Matzke GR, Zhanel GG, Guay DRP. Clinical pharmacokinetics of vancomycin. *Clin Pharmacokinet* 1986;**11**:257-82.

Systemic response to intralesional steroid therapy

Drs P DZIEWULSKI, D T GAULT, and P K B DAVIS (Department of Plastic Surgery, St Thomas's Hospital, London SE1 7EH) write: We wish to report an unusual reaction to the intralesional injection of a keloid scar. A 24 year old man with a keloid scar of his right elbow was treated with intralesional Adcortyl (0·5 ml of triamcinolone acetonide 10 mg/ml). Within five minutes he sneezed and then developed a profound rhinitis, wheezing, dyspnoea, and periorbital oedema. This lasted for one hour and then resolved spontaneously. Intralesional triamcinolone injection is an accepted treatment for keloid scars.[1] This drug has considerable anti-inflammatory and antiallergic actions. Adcortyl, however, also contains benzyl alcohol, sodium carboxymethyl cellulose, and polysorbate 80 in its formulation. Systemic reactions to benzyl alcohol have been reported[2] and this might be the causative agent. Keloid scars are very vascular, and this vascularity may facilitate rapid absorption of intralesional material.

1 Maguire HC. Treatment of keloids with triamcinolone acetonide injected intralesionally. *JAMA* 1965;**192**:325.
2 Wilson JP, Solimando DA, Edwards MS. Parenteral benzyl alcohol-induced hypersensitivity reaction. *Drug Intelligence and Clinical Pharmacy* 1986;**20**:689-91.

Delirium in a patient treated with mianserin

Drs ROBERT Z FISCH and AHARON ALEXANDROWITZ (Department of Psychiatry, Shaare Zedek Medical Center, Jerusalem 91000, Israel) write: Delirium is reported in 1-8% of patients treated with tricyclic antidepressants[1 2] and is believed to be due to their combination of anticholinergic and sedative properties.[3] Mianserin is a second generation tetracyclic antidepressant with exceptionally few anticholinergic effects.[4 5] It has been recommended as a drug of choice for elderly patients because of the lack of anticholinergic side effects.[4 6] We describe a patient who developed delirium during treatment with mianserin.

A 70 year old woman was admitted on 10 February 1987 with an initial diagnosis of suspected acute pancreatitis. She was mildly confused but during the first week in hospital her mental state recovered spontaneously. A laparotomy was performed on 11 March and two pancreatic abscesses were found and drained. After the operation the patient became mildly depressed and withdrawn and suffered from insomnia and occasional nocturnal restlessness. On 10 April a psychiatrist examined the patient. The woman had a lifelong history of "nervousness" and a few months' history of mild depression, which had been treated by her family physician with amitriptyline 25 mg. The drug had been stopped on her admission to hospital. The psychiatrist diagnosed a longlasting depression with decreased energy, constriction of interests, sadness, and lack of pleasure. There were no signs of cognitive impairment, disorientation, or forgetfulness. An organic mental disorder was anamnestically and clinically excluded. The patient was given mianserin 30 mg daily. In the next few days the woman became increasingly apathetic, drowsy, and withdrawn, with occasional periods of confusion.

On 21 April the patient was re-evaluated by the same psychiatrist and an organic mental disorder was suspected because of nocturnal agitation, daytime drowsiness, and incontinence of urine and faeces. Instructions were given to stop mianserin should the confusion worsen in the next few days. On 24 April mianserin was stopped because the patient became extremely agitated at night and had delusions. She claimed that she was bearing a child and later demanded to suckle her baby. Finally she became agitated as she thought that her child had been taken away by the nurses. Immediately after mianserin was stopped her condition improved. In a matter of days her sleep recovered, she regained continence, and she became less apathetic and withdrawn. Over the next two weeks she had no further episodes of confusion, thought disorder, or agitation.

To our knowledge there have been no prior reports of delirium caused by mianserin. This case report shows the potential of mianserin to provoke or at least worsen a confusional state. This adverse effect seems to be unrelated to an anticholinergic action. Mianserin is known to cause drowsiness and sedation and we assume that these actions were partially implicated in the genesis of the delirious state.[3 5 6]

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5 Pinder RM, Fink M. Mianserin. *Mod Probl Pharmacopsychiatry* 1982;**18**:70-101.
6 Feighner JP, Jacobs RS, Jackson RE, Hendrickson G, Merideth CH, O'Meara PD. A double-blind comparative trial with mianserin and amitriptyline in outpatients with major depressive disorders. *Br J Clin Pharmacol* 1983;**15**:227-37S.