urinary excretion rose to 2·17 l/24 h, with chloride 249 mmol/24 h and potassium 178 mmol/24 h. Mean fall in body weight was 0·29 kg/day. The patient became oedema free over two weeks.

Case 4—A 40-year-old man with severe ischaemic heart disease presented with congestive cardiac failure. Blood pressure was 170/90 mm Hg. Piretanide was used in incremental doses up to 24 mg daily. On this dose urinary excretion was 1·0 l/24 h, with sodium 39 mmol/24 h, chloride 35 mmol/24 h, and potassium 35 mmol/24 h. Mean fall in body weight was 0·3 kg/day. As oedema persisted, 5 mg metolazone was added. Urinary excretion rose to 2·48 l/24 h, with sodium 210 mmol/24 h, chloride 202 mmol/24 h, and potassium 73 mmol/24 h. Body weight fell by 0·6 kg/day. Oedema cleared over two weeks. Potassium supplements were necessary.

Comment

Adding relatively small doses of metolazone to high-dose "loop" diuretics significantly increased urine volume and excretion of sodium chloride and potassium, enabling body weight to fall and oedema to clear. The response was immediate and sustained. An initial dose of 2·5 mg metolazone is recommended. Profound natriuresis with associated kaliuresis may lead to hypovolaemia and hypokalaemia respectively. These complications should be anticipated by gradual dose titration according to urine volume and changes in body weight and adequate potassium supplementation. Ideally the patient should be treated with caution in hospital, as dangerous, uncontrolled losses of fluid and electrolytes may occur.[4]

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1 Gunstone RF, Wing AJ, Shani HGP, Njemo D, Sabuka EMW. Clinical experience with metolazone in fifty-two African patients: synergy with frusemide. *Postgrad Med J* 1971;**47**:789-93.
2 Epstein M, Lepp BA, Hoffman DS, Levinson R. Potentiation of furosemide by metolazone in refractory oedema. *Current Therapeutic Research* 1977;**21**:656-67.
3 Asscher AW. Treatment of frusemide resistant oedema with metolazone. *Clinical Trials Journal (London)* 1974;**4**:134-9.
4 Black WD, Shiner PT, Roman J. Severe electrolyte disturbances associated with metolazone and furosemide. *South Med J* 1978;**71**:380-1.

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Association between Stevens-Johnson syndrome and benoxaprofen

Benoxaprofen (Opren, Dista) is a non-steroidal anti-inflammatory agent related to naproxen and ibuprofen. Reported side effects include gastrointestinal ulceration and haemorrhage, photosensitivity, and onycholysis.[1] We report the development of severe erythema multiforme with bullous lesions affecting the lips and buccal mucosa in a patient who had recently started treatment with the drug.

Case report

A 63-year-old woman was started on benoxaprofen 600 mgs daily to relieve osteoarthritic pain of the hands and left knee. She had been treated with mefenamic acid and sulindac for several years, but these drugs were discontinued when benoxaprofen was started. Fourteen days later an erythematous papulopurpuric rash developed over the whole body surface, the thighs, forearms, and dorsum of hands being most severely affected. Bullae were present in the mouth and on the lips. She complained of severe pruritus. No other abnormalities were found on examination.

Erythrocyte sedimentation rate was 35 mm in the first hour; haemoglobin concentration 14·3 g/dl; and white cell count 7500×10^9/l with a differential count of neutrophils 74%, lymphocytes 9%, monocytes 11% and eosinophils 6%. A coagulation screen was normal, as were uric acid, urea, and electrolyte concentrations, and results of liver function tests. Electrocardiography and chest *x*-ray films were normal. A test for antinuclear factor was negative. Skin biopsy specimens were consistent with erythema multiforme, showing perivascular lymphocytic infiltrate in the dermis with spongiosis and lymphocytic infiltration of the epidermis. Direct immunofluorescence tests with labelled antihuman immunoglobulin A and G and C3 were negative.

Benoxaprofen was stopped on admission and the rash subsided over the course of 14 days. Profuse desquamation occurred, particularly on the palms of the hands. At no stage did the rash resemble a photoallergic or phototoxic drug rash.

Comment

The Stevens-Johnson syndrome is a potentially lethal condition that is often precipitated by drug treatment, sulphonamides being the drugs most commonly implicated.[2] The association of this syndrome with treatment with benoxaprofen is important, especially in view of the enthusiastic press reviews[3,4] which greeted the launch of the drug.

1 Mikulaschek Walter M. Long-term safety of benoxaprofen. *J Rheumatol* 1980;**7**, Suppl 6:100-7.
2 Bianchine JR, Macaraeg PUJ Jr, Lasagna L, *et al.* Drugs as etiological factors in the Stevens-Johnson syndrome. *Am J Med* 1969;**44**:390.
3 Anonymous. Hope for arthritics. *World Medicine* 1980;**16**:4-7.
4 *The Times*, Tucker A. Drug brings 'new era' in treatment of arthritis. The *Guardian* 1980 October 15:2.

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Failure of ejaculation with indoramin

Indoramin (3-(2-(4 benzamidopiperid-1-yl)ethyl)indole) an alpha$_1$-adrenergic-blocking agent is being investigated for the treatment of hypertension, asthma, and migraine.[1-3] While conducting a double-blind trial of indoramin in the prophylactic treatment of migraine we found a high incidence of failure of ejaculation in male patients.

Patients, methods, and results

Patients diagnosed as suffering from either common or classical migraine as defined by the World Federation Neurology Research Group on Migraine and Headache were invited to participate in the trial. Those with coexistent medical or psychiatric complaints were excluded. A double-blind procedure was followed with patients receiving placebo, clonidine 0·05 mg three times daily, or indoramin 20 mg three times daily for the first six months. Patients who had received clonidine during this time with no response were given indoramin and those who had been taking placebo without improvement were randomly allocated to clonidine or indoramin for a subsequent six months. Patients kept diary records and were reviewed monthly.

Eighteen men participated in the trial, of whom 11 received indoramin. Four men spontaneously complained of failure of ejaculation while receiving indoramin. Of the remaining seven, five were available for review, the other two defaulting from follow-up. These five men were asked specifically whether they had noted any change in sexual function, and two described failure of ejaculation. The ages of the nine patients reviewed ranged from 19 to 47 years (mean 37 years). Most of those affected had taken indoramin for at least two weeks before noting the disturbance, although in one man it had occurred on the day after starting treatment. All six affected patients described normal erections and had experienced orgasms despite total lack of ejaculation. None had noted this effect before starting indoramin, and it did not occur after the drug was stopped. No patients receiving placebo or clonidine complained of change in sexual function.

Comment

Ejaculation is a complex process affecting sympathetic, parasympathetic, and somatic pathways. Sympathetic nerves stimulate the delivery of semen to the urethra by the vas deferens, seminal vesicles, and prostate and prevent retrograde ejaculation by stimulating the internal urinary sphincter. Thoracolumbar sympathectomy from T12 to L3 abolishes seminal emission without disturbing erectile potency or the sensation of orgasm: the experience of "dry sex" as described by Kedia and Markland.[4] They also reported the same