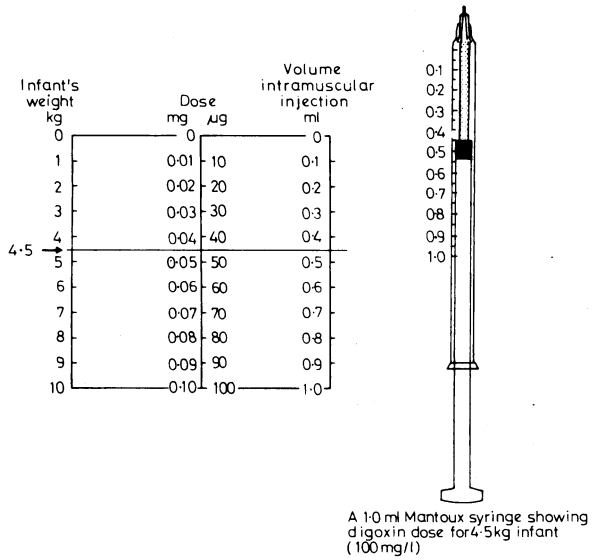
40-60 μg/kg depending on the clinical response. It is important to reassess the child's response before each subsequent dose is given—for example, if the child vomits or the pulse rate falls below 120 beats/min, then the next dose is omitted. If urgent digitalisation is thought necessary the first two doses can be given together. Subsequent maintenance treatment should be 10 μg/kg once or twice daily, or digoxin elixir paediatric *BPC* 50 mg/l by mouth once or twice daily.

For example, a baby weighing 4500 g will require a dose of 45 μg, or 0·45 ml, of intramuscular digoxin injection paediatric, *BP*, every four hours for four to six doses, with careful clinical reassessment before each dose. The same dose—that is, 0·9 ml of Lanoxin-PG Elixir—can then be given once or twice daily by mouth as maintenance treatment. A simple nomogram (see figure) acts as an aide mémoire to this regimen, and the use of a Mantoux syringe allows accurate and simple preparation and administration.



Dosage nomogram for the use of digoxin injection paediatric, *BP* (100 mg/l).

Comment

We have already shown that the initial phase of this regimen results in satisfactory plasma concentrations[1] in both preterm and full-term infants, although the wide variability found underlines the need for repeated clinical evaluation during initial loading. Our subsequent experience with this regimen suggests that it makes both drug prescribing and administration simple.

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Allopurinol hypersensitivity

Allopurinol (4-hydroxypyrazolo(3,4-D)pyrimidine) is the mainstay of treatment for gout. A common side effect is rash or gastrointestinal upset, but xanthine stones,[1] hepatic granulomas,[2] agranulocytosis,[3] reversible leucopenia, and alopecia may occur. Hypersensitivity with vasculitis has been reported, mostly in patients with hyperuricaemia secondary to diuretic treatment—usually thiazides for hypertension—and often with mild renal impairment.[4] The following case probably occurred in primary gout, though secondary hyperuricaemia cannot be excluded.

Case report

A West Indian aged 34 was diagnosed by his general practitioner as having gout with nephropathy because of acute pain in the first metatarsophalangeal joint, a serum urate concentration of 0·52 mmol/l (8·7 mg/100 ml), and a serum urea concentration of 8·5 mmol/l (51·2 mg/100 ml). Results of urine analysis are not available. Blood count was normal but erythrocyte sedimentation rate (ESR) was 41 mm in the first hour. On 4 August 1978 he began allopurinol 300 mg daily. On 13 September he noticed an intensely pruritic rash in the groins, which progressed over the next week associated with fever, sweats, lethargy, and anorexia. He was admitted on 21 September.

Examination showed an ill man with fever (38·5°C), generalised maculopapular rash, and cervical and axillary lymphadenopathy. Blood pressure was 120/70 mm Hg. Haemoglobin concentration was 13·4 g/dl; white cell count $13·1 \times 10^9$/l (13 100/mm^3), 15% eosinophils; ESR 42 mm in first hour; serum albumin concentration 29 g/l; serum aspartate aminotransferase activity 2778 IU/l; serum alanine aminotransferase activity 2222 IU/l; serum lactate dehydrogenase activity 6213 IU/l; serum alkaline phosphatase activity 133 IU/l; serum bilirubin concentration 16 μmol/l (0·9 mg/100 ml); serum urea concentration 22 mmol/l (133 mg/100 ml); serum creatinine concentration 280 μmol/l (3·2 mg/100 ml); and serum urate concentration 0·54 mmol/l (9·1 mg/100 ml). Urine contained 60×10^6 red cells and 60×10^6 white cells/l with granular casts; 24-hour collection yielded 3 g protein. Chest radiograph and electrocardiogram were normal. Blood cultures grew no pathogens. Serum IgA concentration was raised (6·5 g/l); IgG and IgM concentrations were normal. Serum C3 concentration was 1·60 g/l (normal 0·70-1·61) and C4 concentration 0·73 g/l (0·15-0·45). Antinuclear factor was not detected. Tests for soluble immune complexes and allopurinol sensitivity by lymphocyte transformation and migration inhibition were negative. Biopsy showed dermal vasculitis, and immunofluorescence staining disclosed granular deposits of IgG and IgM with complement around small dermal blood vessels.

Prednisolone 60 mg daily was instituted on 25 September. The patient improved, but on 13 October, when the dose was reduced to 20 mg daily, rash and fever recurred. He was discharged on 23 October taking 30 mg daily. Blood count and liver enzyme values were normal. ESR was 26 mm in first hour; serum albumin concentration 28 g/l; serum urea concentration 9·0 mmol/l (54·2 mg/100 ml); and serum creatinine concentration 190 μmol/l (2·1 mg/100 ml).

Renal biopsy performed in February 1979 (Dr B H B Robinson) because of persistent renal impairment (creatinine clearance 36 ml/min) demonstrated glomerular fibrosis with extensive tubular atrophy and chronic inflammation of the interstitium consistent with an "allergic" glomerulonephritis.

Comment

The syndrome of allopurinol hypersensitivity consists of maculopapular rash, nephritis, hepatitis, fever, and eosinophilia. Although probably mediated by immune complexes, its precise mechanism is not understood. Allopurinol has a serum half life of 1·25 hours but its active metabolite oxypurinol has a half life of 18-30 hours. Oxypurinol is handled in a similar way to uric acid, being retained in patients taking thiazide diuretics and with renal impairment; thus sensitivity to this metabolite or possibly allopurinol ribonucleotide, whose fate is unknown, may be the cause. Alternatively, a persistent immunological reaction, sometimes necessitating prolonged steroid treatment, may reflect cross-reaction with normal purines, ribonucleotides, or nucleic acids.

In other reported cases symptoms occurred four to six weeks after starting allopurinol 200-400 mg daily, and in one case after only seven days.[5] Over a third of these patients died from renal failure, infection, and gastrointestinal haemorrhage. Treated promptly most patients recover, although prolonged steroid treatment may be required. The hazards of allopurinol should be considered, particularly before prescribing for secondary hyperuricaemia without clinical gout, as both thiazides and renal impairment appear to be predisposing factors.

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