Myopathy due to mercaptopropionyl glycine

The main aim in the management of cystinuria is to reduce urinary cystine concentration and prevent cystine precipitation and recurrent stone formation. Current management achieves this by using penicillamine, which forms the water soluble thiol derivative. Because of severe toxicity treatment with penicillamine is discontinued in up to 50% of patients.[1] More recently the new drug α-mercaptopropionyl glycine has been introduced. It acts in a similar manner to penicillamine but is claimed to be free of toxic side effects. We report a patient with cystinuria treated with mercaptopropionyl glycine who developed bilateral quadriceps myopathy necessitating withdrawal of the drug.

Case report

A 38-year-old woman with known cystinuria and a long history of recurrent urinary tract calculi was treated with mercaptopropionyl glycine 600 mg daily. Before treatment was begun the urinary cystine concentration was 1461 μmol/24 hr and the drug reduced the urinary concentration to 292 μmol/24 hr (table). Seven days after beginning treatment she developed bilateral quadriceps pain, swelling, and weakness. Examination showed no neurological deficit, and the myopathy was limited to both quadriceps femori. Treatment with mercaptopropionyl glycine was discontinued, and during the next seven days the pain and swelling subsided and normal muscle power returned.

Urinary concentrations of cystine, ornithine, lysine, and arginine under normal conditions and in a patient with cystinuria before and seven days after treatment with mercaptopropionyl glycine

	Urinary concentrations (μmol/24 hr)		
	Before treatment	After treatment	Normal range
Cystine	1461	292	28–153
Ornithine	1475	769	14–170
Lysine	4295	2288	141–577
Arginine	2206	564	24–145

During the acute phase haemoglobin concentration, white cell count, and erythrocyte sedimentation rate were all within the normal range. Antinuclear factor, rheumatoid factor, lupus erythematosus cells, and antimitochondrial antibodies were all absent. Enzyme studies showed increased lactate dehydrogenase activity, but creatine kinase activity remained normal and urinary myoglobin was absent. Muscle biopsy showed no histological evidence of muscle destruction, and histochemical studies showed no abnormality. In view of these findings and the rapid improvement after treatment with mercaptopropionyl glycine had been stopped, we concluded that this was a case of drug-induced myopathy.

Comment

Cystinuria is an inherited metabolic disorder characterised by abnormalities in the renal tubular transport of cystine, lysine, ornithine, and arginine with excess excretion of any one or all four of the amino acids. The insolubility of cystine in urine results in the formation of cystine calculi which, if left untreated, will eventually result in renal failure.[2]

Treatment has been aimed at reducing cystine excretion by a low protein diet, decreasing urinary saturation by a high fluid intake, or increasing solubility by either alkalinisation of urine or by the formation of a soluble cystine thiol complex.[1] The aim of present treatment is to increase urinary cystine solubility by the formation of a soluble thiol complex using D-penicillamine and more latterly mercaptopropionyl glycine. D-penicillamine can induce serious side effects such as bone marrow depression, glomerulonephritis, and retinal haemorrhage; in 50% of patients side effects are sufficiently severe for treatment to be stopped.[1 3] Mercaptopropionyl glycine has a similar mode of action to penicillamine and was considered to be more effective in reducing urinary cystine concentrations and have a higher stone dissolution capacity and no toxic side effects. To date this drug has been used in 30 patients with cystinuria.[1 2 4] During 3-5 years of follow-up side effects have been severe enough to stop treatment in only one patient, who had a generalised rash.[2]

Myopathy due to mercaptopropionyl has not previously been reported, though with the increasing use of the drug in the treatment of cystinuria the incidence of drug-induced side effects will probably increase.

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Rapid control of recurrent ventricular tachycardia with oral amiodarone

Amiodarone is widely used in the management of serious arrhythmias unresponsive to other drugs. After oral administration its therapeutic action is said to be delayed for several days.[1] We describe two patients in whom an antiarrhythmic effect was achieved within three hours of the first oral dose of amiodarone.

Case reports

Case 1—A 70-year-old woman with a history of myocardial infarction and a myocardial aneurysm was admitted after episodes of palpitation with associated syncope. Electrocardiography showed sinus rhythm and previous anteroseptal infarction. Cardiac enzyme activity, urea and electrolyte concentrations, and liver function values were normal. Over the next seven days she had frequent episodes of symptomatic ventricular tachycardia. These were mainly self-terminating, but DC cardioversion was required on six occasions. Intravenous treatment with, in succession, lignocaine, disopyramide, and procainamide failed to suppress the arrhythmia. Verapamil given by intravenous infusion over 24 hours was similarly unsuccessful, and an infusion of mexiletine was substituted. Twelve hours later frequent symptomatic bursts of ventricular tachycardia persisted; oral amiodarone 200 mg thrice daily was then introduced and mexiletine discontinued. Within three hours of the first dose of amiodarone she reverted to stable sinus rhythm, which was maintained until her discharge from hospital 14 days later. Six months later she remained well taking amiodarone 200 mg twice daily. The QT interval increased from 0·38 s immediately before the first dose of amiodarone to 0·46 s 12 hours later.

Case 2—A 39-year-old man with a long history of paroxysmal ventricular tachycardia and with a normal coronary arteriogram and normal left ventricular function was admitted for revision of management. Previous treatment with oral mexiletine and procainamide had been ineffective, but for about a year reasonable control of the arrhythmia had been achieved with a combination of propranolol and quinidine. He gave a one-month history of increasingly frequent episodes of palpitation, occurring up to four times daily. Drugs were withdrawn 36 hours before admission. Electrocardiography on admission showed frequent runs of self-terminating ventricular tachycardia. Urea and electrolyte concentrations and liver function values were normal. Oral amiodarone 200 mg thrice daily was introduced. Within three hours of the first dose stable sinus rhythm was achieved; this was maintained until his discharge three days later and at subsequent follow-up. The QT interval increased from 0·32 s before the first dose of amiodarone to 0·44 s three hours later.

Comment

Oral amiodarone is regarded as a class 3 antiarrhythmic agent.[2] Its therapeutic effect is thought to be related to accumulation of the drug within the tissues, and this is reported to take several days.[1] After intravenous administration amiodarone has an immediate therapeutic

effect; the mechanism of this is unknown but is associated with prolongation of the QT interval.[3]

There is little doubt that in the two cases reported here amiodarone exerted an antiarrhythmic effect within a few hours of the first oral dose. Possibly previous treatment with other antiarrhythmic agents had in some way sensitised the myocardium to the effects of amiodarone. The prolongation of the QT interval suggests that in our patients oral amiodarone produced an acute pharmacological effect similar to that seen after intravenous administration.

Our observations cannot be explained on the basis of current knowledge of the pharmacokinetics of oral amiodarone and highlight the need for further investigation of its mode of action.

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Residual amblyopia in recruits to the British Army

Uniocular amblyopia is a common condition, the incidence varying between 1% and 5% depending on the population studied. Downing[1] found uniocular amblyopia of 6/12 or worse on the Snellen chart in 3·2% of military "selectees." Cole[2] reported the prevalence of amblyopia in his clinical sample as 5·3%, while Flom and Neumaier[3] reported a prevalence in children of 1%.

We carried out a study to determine whether the prevalence or depth of amblyopia in adult recruits to the British Army had fallen since the advent of intensive screening and treatment of visual defects in children.

Subjects, methods, and results

We selected a 20% random sample of recruits' medical records for the years 1965 and 1976, these being the years most separate on Army computer records. Records of visual acuity for each eye, corrected and uncorrected, were extracted for all recruits accepted for service. Potential recruits with appreciable ocular disease are not accepted for service and so were not included. Amblyopia was defined as a difference in the best recorded visual acuity between the two eyes of two or more lines on the Snellen chart, the better eye having at worst 6/9 acuity. The table summarises the results.

The results for 1965 indicated a tendency for the left eye to be the weaker of the two, but this difference was not significant and was not apparent in 1976. The prevalence of amblyopia decreased between 1965 and 1976 in both men and women, but the difference was not significant for the men and for the women was just significant in a one-sided test ($p < 0.05$). Combining the two years' results gave a mean prevalence of 0·044% (with 95% confidence limits 0·035% and 0·053%) in the men and 0·046% (confidence limits 0·031% and 0·061%) in the women. There was no significant difference in the prevalence between the men and women.

Prevalence and depth of amblyopia in military recruits in 1965 and 1976

	Men		Women	
	1965	1976	1965	1976
Total No in sample	4000	3746	499	325
No (%) with amblyopia	188 (4·7)	153 (4·1)	28 (5·6)	10 (3·1)
No (%) with two-line difference	88 (46·8)	66 (43·1)	10 (35·7)	5 (50·0)
No (%) with more than two-line difference	100 (53·2)	87 (56·9)	18 (64·3)	5 (50·0)
No (%) with left eye weaker	109 (58·0)	77 (50·3)	15 (53·6)	1 (10·0)

Comment

In this survey all subjects were aged under 30. All were volunteers for military service and needed to produce the best visual acuity possible to gain acceptance. Some with appreciable ocular disease may have been included, but the screening process ensures that these are few. Other studies of amblyopia in military personnel[1] have been criticised on the grounds that the prevalence of amblyopia was artificially high because of malingering or ocular hysteria in conscripts faced with compulsory service.[3 4] In this study the reverse is more likely, with the recorded visual acuity possibly being better than the true visual acuity, such is the motivation of non-conscripted recruits.

The sample in the survey was not particularly representative of the adult population at large since most recruits come from social classes IV and V; such people are probably more likely to have amblyopia that has not been detected and treated than people in higher social classes.

We conclude that the prevalence and depth of amblyopia in voluntary recruits to the British Army have remained the same over the years. It appears that the "final" visual acuity in the amblyopic eye of recruits born around 1959 is the same as that in recruits born around 1947 or indeed in the 1920s. Postwar efforts to detect and treat amblyopia in children seem to have produced no measurable decrease in the proportion of the adult population with "lazy eye."

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QUEEN OF THE MEADOWS, MEADOW SWEET, OR MEAD SWEET. The stalks of these are reddish, rising to be three feet high, sometimes four or five feet, having at the joints thereof large winged leaves, standing one above another at distances, consisting of many and somewhat broad leaves, set on each side of a middle rib, being hard, rough, or rugged, crumpled much like unto elm leaves, having also some smaller leaves with them (as Agrimony hath) somewhat deeply dented about the edges, of a sad green colour on the upper side, and greyish underneath, of a pretty sharp scent and taste, somewhat like unto the Burnet, and a leaf hereof put into a cup of claret wine, gives also a fine relish to it. At the tops of the stalks and branches stand many tufts of small white flowers thrust thick together, which smell much sweeter than the leaves; and in their places, being fallen, come crooked and cornered seed. The root is somewhat woody, and blackish on the outside, and brownish within, with divers great strings, and lesser fibres set thereat, of a strong scent, but nothing so pleasant as the flowers and leaves, and perishes not, but abides many years, shooting forth a-new every Spring.

It grows in moist meadows that lie mostly wet, or near the courses of water. It flowers in some places or other all the three Summer months, that is, June, July, and August, and the seed is ripe soon after.

Venus claims dominion over the herb. It is used to stay all manner of bleedings, fluxes, vomitings, and women's courses, also their whites: It is said to alter and take away the fits of the quartan agues, and to make a merry heart, for which purpose some use the flowers, and some the leaves. It helps speedily those that are troubled with the cholic; being boiled in wine, and with a little honey, taken warm, it opens the belly; but boiled in red wine, and drank, it stays the flux of the belly. Outwardly applied, it helps old ulcers that are cankerous, or hollow fistulous, for which it is by many much commended, as also for the sores in the mouth or secret parts. The leaves when they are full grown, being laid on the skin, will, in a short time, raise blisters thereon, as Tragus saith. The water thereof helps the heat and inflammation in the eyes. (Nicholas Culpeper (1616-54) *The Complete Herbal*, 1850.)