Short report

A comparative study of disopyramide and procainamide in the treatment of myotonia in myotonic dystrophy

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SUMMARY Ten patients with myotonic dystrophy were allocated at random to treatment with disopyramide and procainamide in a cross-over trial. Disopyramide was found to be at least as effective as procainamide in the relief of myotonia; and two patients who could not tolerate procainamide both tolerated disopyramide.

Myotonic dystrophy was first described by Steinert¹ and the clinical features have been reviewed by Thomasen² and others. There have been many attempts to elucidate the underlying pathophysiology. The basic abnormality has been ascribed to hypersensitivity of the muscle membrane,³ increased membrane fluidity⁴ and impairment of normal neurotropic influences exerted by motor neurones on muscle fibres.^{5,6} Quinine, steroids and procainamide have all been used for treatment of the myotonia with variable success. In 1959, Leyburn and Walton⁷ carried out a controlled trial comparing quinine, prednisolone and procainamide. They found reduction of myotonia with each drug in most cases, quinine being the least effective. There was little to choose between prednisolone and procainamide but with the latter some patients developed troublesome side-effects. Munsat³ achieved some slight improvement of myotonia with sodium phenytoin, which was well tolerated. The similarity in pharmacological properties of procainamide and disopyramide suggested that a trial of this drug was warranted.

Methods

Subjects

Ten patients, all of whom had suffered from myotonic dys-

trophy for between 4 and 21 years were included in the trial. There were seven men and three women aged between 31 and 59 years. All complained of weakness of their hands and the majority had noticed difficulty in relaxation of grip. Eight had also experienced impairment of gait. All exhibited bilateral ptosis, weakness and wasting of the masseters, temporalis, facial and sternomastoid muscles and wasting and weakness of the forearms and hands. The seven men had similar distal wasting and weakness of the legs but in two women the lower limbs were symptomatically normal; in the other woman, there was proximal weakness without wasting. Percussion myotonia was elicited in eight patients over the thenar eminence or tongue or both, and in two others myotonia was revealed by electromyography. Initial assessment was made without modification of current treatment. Two patients were taking procainamide and one of these was also receiving quinine; three were taking disopyramide, one diltiazem, and four were without medication. The patients were then asked to sustain maximum hand grip for three minutes, and afterwards to open the hand fully with fingers extended. The time taken to accomplish the latter task was recorded. In addition, an estimate of grip strength was made using an RAF Gripometer.

Trial design

Patients were divided at random into two groups; Group A received procainamide (250 mg 6 hourly for the first week, then 500 mg 6 hourly for the second week), Group B were given disopyramide (100 mg 8 hourly for the first week, then 200 mg 8 hourly for the second week). After 14 days treatment, patients were re-assessed, treatment reversed between the two groups and a re-assessment made after a further 14 days. Procainamide hydrochloride (Pronestyl) was supplied in 250 mg tablets and disopyramide base (Rythmodan) in 100 mg capsules. Patients were allowed to recognise differences between the medications. Thus where procainamide or disopyramide had been taken pre-

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viously, the patients knew when they were allocated to their usual medication. Otherwise, the patients were unaware of the nature of the medication prescribed. Treatment was coded and the code known only to the dispensing pharmacist.

Results

Of the five patients who had not received procainamide or disopyramide previously, two were initially treated with procainamide followed by disopyramide (Table). On procainamide one patient (NT) had an improvement in grip strength of 10% but when changed to disopyramide, this reverted to its former level; nevertheless, whilst taking disopyramide he felt that his thumbs were less stiff, although hand opening was normal throughout. In the other patient (AH) hand opening was also normal throughout and grip strength was unaffected by either medication. When the two patients who had been taking procainamide before the trial were changed to disopyramide, grip strength was unchanged in both but in one (GB), there was an improvement in hand opening of eight seconds and he felt generally less stiff whilst taking disopyramide.

Of the patients who had not received procainamide or disopyramide previously, three were initially treated with disopyramide followed by procainamide. On disopyramide, one patient (MR) had an improvement in grip strength of 5% and retarda-

tion of hand opening detected before commencement of treatment was restored to normal. In a second patient (AM), however, grip strength was unchanged and moreover, retardation of hand opening increased by 5 seconds. The third patient (DP) had no change in either parameter but her legs felt stronger. When changed to procainamide, the first patient (MR) maintained the improvement in grip strength and hand opening. The second patient whose hand opening deteriorated on disopyramide (AM) showed a return to normal on procainamide. The third patient (DP) preferred disopyramide although neither medication affected her grip strength or hand opening. When the three patients who had been taking disopyramide before the trial were changed to procainamide, one (JP) felt more stiff on the smaller dose of procainamide and although she improved when the dose was increased, she generally preferred disopyramide. There was a slight deterioration in grip strength on procainamide but hand opening remained normal throughout. The other two patients could not tolerate procainamide, whilst treatment with disopyramide was well-tolerated and in one case (WS) had reduced stiffness although in the other (MP) no benefit had been noticed.

In general, apart from the one case referred to above, no difference was found in the response to the different doses used. In all, five patients developed side-effects on procainamide ranging

Table Results in the two patient-groups

(a) Results in patients who had received neither procainamide nor disopyramide previously and were initially allocated to procainamide.				
(b) Results in patients who had received procainamide previously.				
Patient	Treatment sequence	Hand opening	Grip strength	Subjective comments
(a) NT	1. Procainamide	Normal throughout	+10%	Thumbs less stiff on disopyramide
	2. Disopyramide		-10%	
AH	1. Procainamide	Normal throughout	No change	No benefit from either drug
	2. Disopyramide			
(b) GB	1. Procainamide	15 seconds	No change	Generally less stiff on disopyramide
	2. Disopyramide	7 seconds		
AW	1. Procainamide	Normal throughout	No change	No benefit from either drug
	2. Disopyramide			
(a) Results in patients who had received neither procainamide nor disopyramide previously and were initially allocated to disopyramide.				
(b) Results in patients who had received disopyramide previously.				
(a) MR	1. Disopyramide	10 s → normal	+5%	Improved by both drugs
	2. Procainamide	Normal		
AM	1. Disopyramide	10 s → 15 s	No change	Preferred procainamide
	2. Procainamide	15 s → normal		
DP	1. Disopyramide	Normal throughout	No change	Preferred disopyramide
	2. Procainamide			
(b) JP	1. Disopyramide	Normal throughout	No change	More stiff on smaller dose of procainamide
	2. Procainamide			
WS	1. Disopyramide	Could not tolerate procainamide		Greatly benefited by disopyramide
	2. Procainamide			
MP	1. Disopyramide	Could not tolerate procainamide		No benefit from disopyramide
	2. Procainamide			

from abdominal pain and diarrhoea in the above two cases to sore throat, mild dyspepsia, constipation and transient facial swelling in four others. Six patients developed side-effects on disopyramide, five having either dryness of the mouth and blurring of vision or both. These symptoms were mild and principally noted on the maximum dose used.⁶ One other patient experienced mild heartburn.

Discussion

A cross-over trial of disopyramide and procainamide in the treatment of myotonic dystrophy has shown that disopyramide is as effective as procainamide and that it may be better tolerated. The response to treatment was nevertheless variable but the most striking improvements were seen where myotonia was more evident, as in delayed hand opening. Leyburn and Walton⁷ suggested that the individual variation in the response to drugs in patients with myotonic dystrophy was probably dependent on whether myotonia or weakness were the dominant disorder. It would seem likely that the best response would be obtained in the paramyotonias and in myotonia congenita in which myotonia predominates.

The precise mode of action of drugs that benefit myotonia remains obscure. Roses *et al*⁴ showed that sodium phenytoin may correct membrane fluidity which is increased in myotonia. Munsat³ pointed out that various agents used successfully in the treatment of myotonic dystrophy including quinine, quinidine, procaine, procainamide, ACTH and steroids shared the property of membrane stabilisation, altering ratios of intracellular to extracellular ions or by some direct physicochemical effects. The site of action of phenytoin was similarly concluded to be the muscle itself by virtue of its effect on ion balance. Stabilisation of the polarised membrane of the muscle fibre preventing the repetitive firing of cardiac muscle is suggested to underlie the antiarrhythmic properties of quinine and procainamide. In a similar fashion, the fast repetitive action potentials associated with the after-contraction of

myotonic muscle may also be prevented by membrane stabilisation.⁸ Disopyramide resembles these agents in its effects on cardiac muscle, its mechanism of action being explained in part by a quinidine-like effect on action potential duration.⁹ This latter property is thus one shared by agents which are both effective in the treatment of myotonia. It is therefore tempting to ascribe the effect on myotonic muscle to membrane stabilisation through such modification of action potential. Nevertheless, differences between the properties of cardiac and skeletal muscle must be borne in mind in reaching such a conclusion.

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