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Quinidine before direct current countershock
A controlled study

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One hundred and twenty-four patients with chronic atrial fibrillation were subjected to a controlled study on the effect of quinidine treatment upon the incidence of postconversion arrhythmias.

Digitalis medication was stopped 2 to 4 days before the electroconversion. For the same period the quinidine series was treated with a long-acting quinidine sulphate. The mean serum level of quinidine on the day of electroconversion was 3·6 mEq/l.

Arrhythmias related to the DC shock occurred at an equal rate in the quinidine and in the control series. Of 3 cases with ventricular fibrillation, 2 were observed in the control series. No deaths were recorded.

The study shows that quinidine treatment before direct current countershock does not affect the incidence of postconversion arrhythmias.

Quinidine treatment before electroconversion has three obvious advantages. Firstly, recognition of drug intolerance is made possible. Secondly, spontaneous restoration of sinus rhythm occurs in more than 10 per cent of the patients. Thirdly, quinidine dosage can be adjusted to give the correct serum level.

In spite of this, the procedure has partly fallen into disrepute, because some authors (Castellanos *et al.*, 1965; Åberg and Cullhed, 1968; Åberg, 1969) have provided evidence that quinidine pretreatment is responsible for the occurrence of serious and even lethal postconversion arrhythmias. In contrast, other studies (Lemberg *et al.*, 1964; Rossi and Lown, 1967; Hall and Wood, 1968) have shown it to possess a protective action against the same dysrhythmias.

It is hard to reconcile the conflicting views thus presented, because most of the available reports suffer from an obvious lack of uniformity as regards quinidine dosage and from a corresponding lack of control groups.

The problem is at present of notable clinical interest, because recent controlled studies (Byrne-Quinn and Wing, 1970; Härtel *et al.*, 1970; Hillestad *et al.*, 1971) have proved quinidine to be effective in maintaining sinus rhythm after electroconversion. It, therefore, seemed justified to undertake the present work.

The report is a controlled study of 124 consecutive patients with chronic atrial fibrillation exposed to direct current countershock. The study shows that treatment with quinidine before electroconversion does not exert any significant effect on the incidence of postconversion arrhythmias.

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Patients and methods

The patients were randomly allocated into two groups, one receiving quinidine therapy before electroconversion and the other not. Placebo tablets were not used.

Digitalis medication was regularly stopped 2 to 4 days before electroconversion and quinidine treatment simultaneously started. A long-acting preparation containing 0·2 g quinidine sulphate was used and given twice daily aiming at a serum quinidine level of between 4 and 6 mg/l. For estimation of the latter the method of Balatre, Lefevre, and Merlen (1960) was employed. All the patients were under adequate anticoagulant treatment during electroconversion. Regular measurements were made of the serum levels of quinidine and the blood electrolytes. On the day of attempted conversion these measurements were always repeated.

Direct current countershock was given in the ordinary way under light general anaesthesia (Hillestad *et al.*, 1971). Postconversion arrhythmias were defined as those that occurred in direct relation to the application of the synchronized DC shock.

Results

It can be seen that the quinidine series and the corresponding control group compare favour-

TABLE 1 *Clinical details of patients given quinidine before DC shock and of controls*

	Quinidine series			*Control series*		
	Women	*Men*	*Total*	*Women*	*Men*	*Total*
No. of patients	35	28	63	36	25	61
Age (yr), mean	51	54	52	54	56	55
range			22–77			35–75
Duration of atrial fibrillation (mth)						
0–6	15	13	28	14	7	21
7–24	12	5	17	12	6	18
>24	7	10	17	10	12	22
Heart size (ml/m² body surface)	610	620	614	600	684	634
range			270–1050			320–945

ably with regard to most clinical data (Table 1).

The various heart disorders underlying the arrhythmias are also evenly distributed in the two experimental series (Table 2). The predominant disorder in each group is rheumatic heart disease which accounts for more than half of the diagnoses. A majority of the patients with rheumatic heart disease had recently undergone one or other type of heart surgery, from commissurotomy to insertion of artificial valves. And with regard to operative procedure, no significant difference between the two series could be found.

The results of the trial (Table 3) show that sinus rhythm was restored at an equal rate in both groups provided the spontaneous conversions are included. The difference between the frequency of spontaneous conversion in the two groups is significant in favour of quinidine. This indicates that the serum concentration of quinidine was satisfactory during the trial. This is further corroborated by the fact that the five spontaneous conversions of the quinidine series occurred on serum quinidine levels varying from 2·8 to 3·4 mg/l., with a mean value of 3·1 mg/l. The latter figure is less than the mean quinidine level for the total series. Of the 5 patients who underwent spontaneous reversion, 4 suffered from rheumatic valve disease, while only one suffered from lone fibrillation. Their atrial fibrillation had lasted from 4 to 9 months, with an average of 6 months. Their rhythm disorder had thus persisted for less than the average for the total series. The energy level required by electroconversion to obtain sinus rhythm in the quinidine series was 140 joules against 150 joules in the control series. The difference is insignificant. Application of DC shock in the patient with a quinidine level of 7·4 mg/l. did not produce any arrhythmia.

Ectopic rhythms occurred with the same incidence in both series. Atrial ectopic beats were usually of short duration and of little significance. Nodal rhythm with acceptable ventricular rates persisted for some days or up to three weeks without causing any symptoms. Ventricular premature beats appeared as single or coupled or in short bouts from two to three beats. These ventricular

TABLE 2 *Aetiology of atrial fibrillation in two series*

	Quinidine series	*Control series*
No. of patients	63	61
Rheumatic heart disease		
Mitral valve disease	38	33
Aortic valve disease	8	9
Atherosclerotic heart disease	7	6
Lone fibrillation	4	4
Thyrotoxic cardiopathy	2	2
Congenital heart disease	2	2
Chronic myocarditis	2	4
Myxoma cordis	0	1

TABLE 3 *Occurrence of arrhythmias in response to DC shock in quinidine series and in control series*

	Quinidine series	*Control series*
No. of patients	63	61
Sinus rhythm obtained		
Spontaneously	5	1
By DC shock	52	53
Quinidine level (mg/l.)	3·6	0
range	0·7–7·4	
Potassium level (mEq/l.)	4·2	4·0
range	3·4–4·8	3·6–4·5
Atrial premature beats	2	1
Nodal rhythm	1	2
Ventricular premature beats	4	3
Ventricular fibrillation/ tachycardia	1	2

extrasystoles were regarded as contraindications for further attempts at electroconversion at the time. For all the mentioned arrhythmias the highest quinidine level noted was 4·1 mg/l. and in no case was the potassium level abnormal.

Serious ventricular arrhythmia occurred in 3 patients who are to be considered in more detail. One was a 74-year-old man suffering from a postinfarction heart insufficiency. Atrial fibrillation had been present for 24 months. His general condition was good despite a heart volume of 720 ml/m^2 body surface. Digitalis therapy had been omitted 6 days before the conversion, and he had not received quinidine. On the day of conversion all his blood values were normal. Ventricular fibrillation occurred in response to the first shock with 100 joules. Two successive shocks with 200 joules produced nodal rhythm, which within a couple of minutes changed to atrial fibrillation. No further attempts were made to restore sinus rhythm.

A 57-year-old woman with a lone fibrillation of 6 years' duration had not used digitalis for some months. She got no pretreatment with quinidine. Blood pressure and heart size were both normal as were the electrolytes. At the first shock with 100 joules ventricular fibrillation appeared. Successive shocks with increasing energy levels up to 400 joules were rapidly administered without result. Resuscitation became necessary, while sodium bicarbonate and lignocaine were given intravenously. 20 minutes after the start of the ventricular arrhythmia a shock with 400 joules produced a few seconds asystole, which was followed by regular sinus rhythm. The patient was discharged without any sequelae, and sinus rhythm persists after 26 months of observation.

Another 57-year-old woman suffered from chronic myocarditis with atrial fibrillation of 30 months' duration. The relative heart volume was 740 ml/m^2 body surface. Digitalis medication was stopped three days before electroconversion and quinidine treatment instituted. On the day of electroconversion the serum concentration of quinidine was 3·2 mEq/l. The electrolytes were normal. A shock with 100 joules was ineffective. The next one with 200 joules produced ventricular fibrillation which did not respond to a further increase in the energy level to 400 joules. Lignocaine 100 mg was given intravenously, and a subsequent electroshock with 400 joules restored sinus rhythm. The normal cardiac rhythm is present after 21 months of observation.

The only complication encountered during the pretreatment period was syncope in a 52-year-old woman suffering from mitral stenosis. No signs of hypotension, ventricular fibrillation, or asystole could be shown during the attack. A test of the serum concentration of quinidine, taken simultaneously showed the latter to be 2·9 mg/l. Quinidine was therefore not considered responsible for the syncope, and the treatment was continued without further complications.

Discussion

The present study shows that the incidence of postconversion arrhythmias is unaffected by pretreatment with quinidine. The study is controlled and the series large enough to draw this conclusion. The results may serve to explain the contrasting views put forward by other reports.

Quinidine treatment before cardioversion has been termed a medical hazard by Åberg (1969). His statement refers to 8 cases of serious postconversion arrhythmias of which 6 had received quinidine treatment before the shock (Åberg and Cullhed, 1968). Though the statement is based upon a large experience, the lack of control series is apparent.

In the study by Castellanos *et al.* (1965), the patients were given 1·2 g quinidine hours before cardioversion. This is a large dose. Among the 111 patients 4 got serious ventricular arrhythmias. Only one of these occurred in direct relation to the shock. Moreover the clinical data indicate that the observed arrhythmias were toxic reactions to quinidine and thus unrelated to cardioversion itself. In another study (Radford and Evans, 1968) quinidine treatment was discontinued because of complications which occurred at a distance from the cardioversion and could be ascribed to quinidine. However, real postconversion arrhythmias were not seen in this study among the 34 patients who got quinidine pretreatment.

A favourable effect of quinidine on the incidence of transitory postconversion rhythm disturbances was observed by Lemberg *et al.* (1964) and Hall and Wood (1968). The latter authors undertook a controlled study of 94 patients with rheumatic heart disease. Quinidine was given in the amount of 1 g in divided doses, in the 24 hours before the shock and reduced the frequency of postconversion arrhythmias from 43 to 14 per cent. The mean serum quinidine level was 2·2 mg/l., determined by the method of Brodie and Udenfriend, which should correspond to 4 mg/l. by the method of Balatre *et al.*, a method which we are using.

Rossi and Lown (1967) carried out a controlled study of 50 consecutive patients, who received 1·2 g quinidine in divided doses in the 24 hours before cardioversion. Serum concentration of quinidine was only determined in 15 of 25 patients in the quinidine group and showed a mean level of 2·2 mg/l., determined by the method of Brodie and Udenfriend. Quinidine treatment gave effective protection against all postconversion arrhythmias, except for those of nodal origin. Rhythm disturbances were more serious and lasted longer in the control group, and the energy level required for conversion was greater in this group. The study is notable for its high rate of ectopic rhythms. Furthermore the series was small.

Similar objections can hardly be maintained with regard to the present study which did not show any influence of quinidine upon the incidence of postconversion arrhythmias or upon the energy level required to obtain sinus rhythm. It may, therefore, be concluded from the present study that treatment with quinidine before electroshock can safely be given provided the serum concentration of quinidine is under control.

References

Åberg, H. (1969). Quinidine prior to direct current countershock – a medical hazard. *Acta Medica Scandinavica*, **186**, 157.

Åberg, H., and Cullhed, I. (1968). Direct current countershock complications. *Acta Medica Scandinavica*, **183**, 415.

Balatre, P. H., Lefevre, C., and Merlen, J. F. (1960). Dosage fluoriscimétrique de la quinine et la quinidine dans le sérum sanguin et dans les urines. *Annales de Biologie Clinique*, **18**, 228.

Brodie, B. B., and Udenfriend, S. (1943). Estimation of quinine in human plasma, with a note on the estimation of quinidine. *Journal of Pharmacology and Experimental Therapeutics*, **78**, 154.

Byrne-Quinn, E., and Wing, A. J. (1970). Maintenance of sinus rhythm after DC reversion of atrial fibrillation. A double-blind controlled trial of long-acting quinidine bisulphate. *British Heart Journal*, **32**, 370.

Castellanos, A., Lemberg, L., Gilmore, H., and Johnson, D. (1965). Countershock exposed quinidine syncope. *American Journal of the Medical Sciences*, **250**, 254.

Hall, J. I., and Wood, D. R. (1968). Factors affecting cardioversion of atrial arrhythmias with special reference to quinidine. *British Heart Journal*, **30**, 84.

Härtel, G., Louhija, A., Konttinen, A., and Halonen, P. I. (1970). Value of quinidine in maintenance of sinus rhythm after electric conversion of atrial fibrillation. *British Heart Journal*, **32**, 57.

Hillestad, L., Bjerkelund, C., Dale, J., Maltau, J., and Storstein, O. (1971). Quinidine in maintenance of sinus rhythm after electroconversion of chronic atrial fibrillation. A controlled clinical study. *British Heart Journal*, **33**, 518.

Lemberg, L., Castellanos, A., Swenson, J., and Gosselin, A. (1964). Arrhythmias related to cardioversion. *Circulation*, **30**, 163.

Radford, M. D., and Evans, D. W. (1968). Long-term results of DC reversion of atrial fibrillation. *British Heart Journal*, **30**, 91.

Rossi, M., and Lown, B. (1967). The use of quinidine in cardioversion. *American Journal of Cardiology*, **19**, 234.

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