Letters to the Editor

Cardioversion of atrial fibrillation

Sir,

In his overview of drug-related aspects of atrial fibrillation and electrical cardioversion, Dr Lip alluded to the respective roles of digoxin, amiodarone, and warfarin,¹ a significant feature being the relationship between left ventricular dysfunction and the indications for pretreatment with these drugs. For example, notwithstanding the apparent inefficacy of digoxin for chemical cardioversion,² the fact that left ventricular dysfunction is a risk factor for atrial fibrillation^{3,4} lends support to the hypothesis that the positive inotropic action of digoxin could enhance chemical cardioversion with this drug in clinical subgroups with co-existing left ventricular systolic failure.⁵ A provisional validation of this hypothesis comes from the documentation of a significant association between cardioversion success with low energy shocks, and pretreatment with drugs such as digoxin and amiodarone,⁶ which share the ability to improve left ventricular performance even in the presence of sinus rhythm.^{7,8} Atrial fibrillation is itself a risk factor for left ventricular systolic failure,⁹ and the latter is, in turn, a predisposition to left atrial thrombogenesis.¹⁰ The prevention of *de novo* thrombogenesis (whilst allowing pre-existing thrombi to resolve) appears to be the basis for the success of warfarin-related prophylaxis against post-cardioversion embolism.¹¹ So long as risk factors for thrombogenesis, such as left ventricular systolic failure and spontaneous echo contrast, persist, the risk of postcardioversion thromboembolism, will not be eliminated even if the left atrium and its appendage test negative for thrombosis by transoesophageal echocardiography,^{12,13} hence the justification for universal anticoagulation prior to electrical cardioversion. This caveat might be equally applicable to atrial flutter, following the documentation of a 21% prevalence of left atrial thrombi in 24 patients with atrial flutter, in some of whom left ventricular systolic failure again appeared to be a significant risk factor for left atrial thrombogenesis.¹⁴

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This letter was shown to the author who responded as follows:

Sir,

I thank Dr OMP Jolobe for his interest in my review of cardioversion of atrial fibrillation.¹ His letter raises several points that merit further discussion. Control of the ventricular response in chronic atrial fibrillation has traditionally been attempted with digoxin, although this drug is ineffective during exercise or when catecholamine levels are high, or in attempting cardioversion to sinus rhythm.^{2,3} Digoxin may also make paroxysmal atrial fibrillation worse, resulting in an increased frequency of paroxysms, which occur at higher heart rates.⁴ These effects are related to the mechanisms of action of digoxin. Firstly, digoxin has some direct effect on atrioventricular nodal conduction, but the degree of control of the ventricular response due to this is modest and may require oral doses in excess of those generally used to control the resting heart rate, hence increasing the risk of toxicity.⁵ The predominant negative chronotropic effect of digoxin, however, is to increase vagal tone at rest which, in turn, decreases atrioventricular nodal conduction and probably increases the number of fibrillating wavelets in the atria.^{6,7} The increase in vagal tone also reduces the atrial refractory period, and thus paradoxically renders the atrium more susceptible to fibrillation. Therefore, digoxin alone is unlikely to be successful in the pharmacological cardioversion of atrial fibrillation or in maintenance of sinus rhythm.

Beneficial clinical effects of digoxin in heart failure have recently been demonstrated in digoxin withdrawal studies, although some authorities advise caution until results from

prospective studies are available.⁸ In the study by Dalzell *et al*,⁹ an association between electrical (direct current) cardioversion success and prior treatment with digoxin was found only on univariate analysis, with the duration of atrial fibrillation being the only independent predictor of cardioversion success in multivariate analysis. Pretreatment with amiodarone, by contrast, is well-known to be effective in achieving cardioversion and sustaining sinus rhythm.¹⁰ Whether or not treatment of heart failure alone (with or without digoxin) allows cardioversion to sinus rhythm remains to be demonstrated. However, beneficial haemodynamic effects of treating heart failure, such as the reduction of intra-atrial pressures may be one mechanism. It should also be remembered that many patients with new-onset atrial fibrillation spontaneously revert to sinus rhythm, especially if an acute precipitating factor were present.^{1,3}

Finally, Dr Jolobe comments on the relationship between left ventricular systolic failure and thrombogenesis. It has long been recognised that thromboembolism is a frequent cause of death in patients with congestive heart failure, whether or not in sinus rhythm, occurring in up to 30% of patients.¹¹ In the pooled analysis of the atrial fibrillation trials, cardiac impairment was also a recognised contributory risk factor to stroke risk in atrial fibrillation.¹²

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