LETTERS TO THE EDITOR

Scope
Heart welcomes letters commenting on papers published in the journal in the previous six months. Topics not related to papers published earlier in the journal may be introduced as a letter; letters reporting original data may be sent for peer review.

Presentation
Letters should be:
- not more than 600 words and six references in length
- typed in double spacing (fax copies and paper copy only)
- signed by all authors.

The text should be as brief as possible, not more than two small or a single figure. Please send a copy of your letter on disk. Full instructions to authors appear in the January 1997 issue of Heart (page 89).

K⁺ channel opening: a new drug principle in cardiovascular medicine

Sir,—Nielsen-Kudsk JE et al recently reviewed K⁺ channel openers, addressing their clinical usefulness as vasodilatory and cardioprotective drugs.1 They eluded to electrical factors of these drugs and stated that two of them, pinacidil and nicorandil, had been given to thousands of patients without reports of adverse arrhythmias. They also mentioned that repolarisation abnormalities in terms of ST segment and T wave changes were a common finding in the electrocardiogram following administration of pinacidil. However, we feel there is cause for some concern regarding the potential proarrhythmic effects of these drugs, and we encourage prescribers to be very observant regarding arrhythmias in their patients.

It is known that augmentation of ATP regulated potassium current I_{ATP} by pinacidil increases dispersion of repolarisation in canine ventricular tissue enough to induce extrasystolic activity (phase 2 reentry) due to a marked abbreviation of the action potential in the epicardium. This electrical heterogeneity can be abolished by 4-aminoypyridine administration, which selectively inhibits calcium independent transient outward current (I_{to}) or by a blocker of the ATP regulated potassium channels, glyburide.2 3 Pinacidil may also prevent development of ST segment elevation induced by pinacidil or coronary artery occlusion in dogs.4 Under conditions where the action potential is significantly abbreviated, I_{to} is diminished or even blocked resulting in decline of contractility function and oxygen consumption. Such electrophysiological modulation of the ventricular contraction is most likely the effect underlying the cardioprotective mechanism of K⁺ channel openers. The question is, however, whether a desired cardioprotective benefit from K⁺ channel openers could lead to arrhythmic events? Until more information is available, we would hesitate to accept that repolarisation abnormalities induced by pinacidil are benign in all patients. As we have seen with many drugs in the past, the initial experience may look very promising but extended use may later disclose serious side effects. Promotion of these drugs has been obtained, however, when I_{ATP} and I_{to} blockers have been administered simultaneously to rats. Coronary flow was increased and fibrillatory activity decreased during acute myocardial ischaemia.5 6

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This letter was shown to the authors, who reply as follows:

Sir,—We agree with Drs Gussak and Bierregaard that the cardiac electrophysiological effects of K⁺ channel openers is an important issue. As stated in our review, pharmacological activation of ATP sensitive K⁺ channel (I_{ATP}) in the heart has the potential to produce both proarrhythmic and antarrhythmic effects. Theoretically, shortening of the action potential duration (APD) in an epicardiac myocardial cells, induced by K_{ATP} channel openers would pre-dispose to reentry ventricular tachyarrhythmias, resulting from a reduction in the refractory period of myocardial action potentials. This reduction of APD is of critical importance for the onset of reentry arrhythmias.7 8 In the setting of acute myocardial ischaemia, the contribution and interaction between different arrhythmia mechanisms is complex and incompletely understood. As a consequence, there are some experimental data showing proarrhythmic and other arrhythmogenic effects of K_{ATP} openers depending on species, dose, and model of ischaemia.9 The ability of K_{ATP} channel activators to reduce ischaemic injury will not reduce to the susceptibility to arrhythmias. Although APD shortening followed by inhibition of Ca²⁺ influx, acceleration of diastolic contractile arrest and preservation of ATP in the ischaemic myocardium is an attractive theory to explain the cardioprotective effects of K_{ATP} channel openers, the underlying mechanism is unsettled.1 Recent studies indicate that cardioprotection can be achieved at doses which do not reduce APD and that there is a lack of correlation between the APD shortening and cardioprotective effect of K_{ATP} openers.4 Thus, the question whether K_{ATP} channel activators in clinically relevant doses might be proarrhythmic or antiarrhythmic remains open.6 To our knowledge, there are no clinical reports of proarrhythmic effects in patients treated by K_{ATP} openers as antiarrhythmic or antiischaemic agents. As with any new drug, we agree to be observant and to report any suspected adverse effect.

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Pharyngeal replacement of Björk-Shiley convexo-concave heart valves: an easy-to-use tool to aid decision-making in individual patients

Sir,—Steyerberg et al1 presented an attractive model to facilitate decision-making in patients in whom Björk-Shiley convexo-concave prostheses. Based on admitted idealised risks for surgical and non-surgical strategies, they have indicated how patients can maximise their chances of living a normal life span, that is, life expectancy if the valve prosthesis were not prone to breaking up. The example given, briefly, is of a 40 year old man who would be expected to have a Björk-Shiley convexo-concave prosthesis. Maximising his odds of reaching the age of 65 should, according to the authors, direct the decision-making process. This is, in my opinion, not correct, and they are stepping back with their admission that “Most patients are risk averse and attach more value to nearby than to years in the distant future” is not strong enough to negate their thesis. Certainly the quality of life to be expected between the ages of 40 and 50 is greater than that to be expected between the ages of 55 and 65. More importantly, the probability of living to the age of 65 is one thing, but when you die, if you die before then, is another. In spite of almost identical

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