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.

This may be submitted as a single page or as a series of small pages with a sign.

K+ channel opening: a new drug princi-ple 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 electrophysiologic aspects 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 IK,ATP by pinacidil increases dispersion of repolarisa- tion and hence ventricular tissue enough to induce extrasystolic activity (phase 2 reen-try) due to a marked abbreviation of the action potential in the epicardium. This electrical heterogeneity can be abolished by 4-aminoquinidine concentrations highly selective to block calcium independent tran-sient outward current (Ito) or by a blocker of the ATP regulated potassium channels, glyburide.2 It may also prevent development of ST segment elevation induced by pinacidil or coronary artery occlusion in dogs.3 Under conditions where the action potential is significantly abbrevi- ated, Ito is diminished or even blocked resulting in decline of contractility function and oxygen consumption. Such electrophysi-ologic modulation of the ventricular con- traction 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. Prospective studies have been obtained, however, when IK,ATP and Ito blockers have been administered simultane- ously to rats. Coronary flow was increased and fibrillatory activity decreased during acute myocardial ischaemia.4,5

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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 electrophysio- logical effects of K+ channel openers is an important issue. As stated in our review, pharmacological activation of ATP sensitive K+ channels (IK,ATP) in the heart has the potential to produce both proarrhythmic and antiarrhythmic effects. Theoretically, shortening of the action potential duration (APD) in an area of myocardial cell with low APD can result in local electrical instability, leading to reentry. This effect is likely to occur in areas of myocardial ischaemia.6,7 Hence, the opening of IK,ATP channels is expected to inhibit arrhythmias due to triggered activity (early and delayed afterdepolarisations) and abnormal automaticity. These novel drugs might be useful in the treatment of long QT related arrhythmias.8 In the setting of acute myocardial ischaemia, the contribution and interplay between different arrhythmia mechanisms is complex and incompletely understood. As a consequence, there are some reports suggesting that these proar-rhythmic and other arrhythmogenic effects of K+ channel openers may occur on species, dose, and model of ischaemia.8 The ability of K+ channel activators to reduce ischaemia injury will have to reduce the susceptibility to arrhythmias.

Although APD shortening following inhibition of Ca2+ influx, acceleration of cardiac conduction arrest, and preservation of ATP in the ischaemic myocardium is an attractive theory to explain the cardioprotec-

tive effects of K+ channel openers, the underlying mechanism is unsettled.9 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+ channel openers.10,11 Thus, the question whether K+ channel activators in clinically relevant doses might be proar-rhythmic or antiarrhythmic in general and unresolved.9 To our knowledge, there are no clinical reports of proarrhythmic effects in patients treated with K+ openers as anti hypertensive or antianginal agents. As with any new drug, we agree to observe and to report any suspected adverse effect.

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2 Wilde AM, Jane MJ. Electrophysiological effects of ATP sensitive K+ channel modulation: implications for arrhythmogene-


Prophylactic replacement of Börk-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 individual patients faced with convexo-concave prostheses. Based on admi-

tedly 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 die, if operated on in the future, is not straightforward 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. Moreover, the probability of living to the age of 65 is one thing, but when you die, if you live before then, is another. In spite of almost identical

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