Anticoagulants and the Björk-Shiley prosthesis

Sir,

We read this paper with great interest (British Heart Journal, 1978, 40, 558–562). Long-term anticoagulation is associated with the risk of bleeding and to an extent enforces restriction on the quality of life of the patient (British Medical Journal, 1978). In addition there is a risk, though small, of thrombosis in spite of adequate anticoagulation. In view of this we feel that it is important to look for alternatives to long-term oral anticoagulants. However, there are several important points in your study that require careful consideration before drawing any conclusions. Dipyridamole has been started on day 3; it is well documented that platelets become 'stickier' in the immediate postoperative period, and by day 3 platelets may have already become attached to the valves. In the absence of anticoagulation the platelet plugs may be stabilised by thrombin generation and clot formation.

We have shown that dipyridamole when used clinically has to attain an optimum blood level of 3.5 μmol/l (range 2 to 5 μmol/l) to produce an adequate antiplatelet effect (Rajah et al., 1977). There is no indication in the study that any blood level or platelet functions had been done on any of the patients in the dipyridamole group before discharge from hospital. It has been our experience that on a dose of 150 mg daily most patients did not attain optimum blood levels and platelet functions were not inhibited. This implies that in your study most of the patients in the dipyridamole group were in no way protected after valve replacement.

Before embarking on the use of antiplatelet drugs alone in this clinical situation we feel that it is necessary to extend the findings of Sullivan et al. (1971). Here it was clearly shown that the dipyridamole and warfarin group combined was superior to warfarin alone, but the limitation of that trial was that a number of patients dropped out of the trial because of the side-effects of dipyridamole. We have been conducting a similar trial to that of Sullivan et al. for the past 4 years; the dose of dipyridamole is determined by its blood level and/or platelet functions routinely. We confirm the superiority of dipyridamole and warfarin over warfarin in patients with the Starr-Edwards, Björk-Shiley, and Lillehei-Kaster valves, and in addition the drop-out of patients because of the side-effects of dipyridamole is negligible.

If dipyridamole alone is to be used in a trial, we suggest starting it before operation, giving it intravenously in the immediate postoperative period, and orally when the patient can swallow. It may be relevant to point out that dipyridamole has been shown not to prolong bleeding time and hence increase the risk of bleeding; however, intravenous dipyridamole is to be used with caution in patients with hypotension. We also suggest that the dosage be titrated against either blood level or platelet function or both. Further, it may be more reasonable to consider a combination of platelet inhibitory drugs like dipyridamole and acetylsalicylic acid, than a single agent in the prophylaxis of arterial thrombosis especially with disc valve prosthesis in the mitral position.

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References


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

Sir,

It is well documented that anticoagulation is associated not only with the risk of bleeding but also with thrombosis even when the prothrombin ratio is carefully controlled. Because of this unsatisfactory situation it remains important to investigate alternatives to long-term anticoagulants.

Platelets have been shown to be 'stickier' in the immediate postoperative period, but there are no data to support the conjecture that because of this they become attached to the prosthetic valve within the first 3 days. Thromboembolism occurred a mean period of 6 months after operation in both groups, whereas one might have expected in the absence of anticoagulation that platelet plugs would be stabilised by thrombin generation and clot
formation with earlier evidence of systemic embolisation in the group of dipyridamole treated patients.

We noted with interest the important data reported by Rajah et al. (1977), showing that to obtain adequate antiplatelet effects with dipyridamole blood levels of between 2 and 5 μmol/l needed to be attained. However, these data were not available during the period of our clinical trial, since the significantly greater incidence of thromboembolism in the dipyridamole treated group was appreciated in November 1974, after which new arrangements were made for all patients to be treated with warfarin. In addition, allocation of patients to warfarin or dipyridamole treatment groups was non-random and the majority of patients in the latter group were those returning overseas in whom dipyridamole was used, because there were no facilities available for prothrombin time estimation, let alone estimation of dipyridamole blood levels or platelet function tests.

We were aware that Sullivan et al. (1971) showed that dipyridamole and warfarin combined were superior to warfarin alone in the prevention of thromboembolism, but we were concerned about the number of patients dropped from the trial because of undesirable side-effects of dipyridamole. We were interested to learn that the Leeds group had confirmed the findings of Sullivan et al. (1971) in patients with varying types of prosthetic valves and await this publication.

We note the recommendation that if dipyridamole is to be used alone it should be started preoperatively and continued intravenously immediately postoperatively. However, do this group have trial data regarding groups of patients treated with dipyridamole pre- and perioperatively compared with dipyridamole started postoperatively to support their recommendation, and also their suggestion that platelets become adherent to prosthetic valves in the first 3 days postoperatively? We acknowledge the caution concerning the intravenous use of dipyridamole in patients with hypotension and add that a considerable number of patients undergoing valve replacement return to the Intensive Care Unit conspicuously hypotensive.

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Notice

References

Contributors should note that, in future, references in the text of papers submitted to this journal and in the bibliography should be prepared in the new format, as outlined briefly in the Notice to contributors.

Full details of this new, uniform style, which was agreed at a meeting of the International Steering Committee of Medical Editors held in Vancouver, were published in the Br Med J (1979; 1: 532-35) and Ann Intern Med (1979; 90: 95-9). Reprints of this article are available from the Br Med J (price 50p).