MATTERS ARISING

Long term anticoagulant treatment in the anti-phospholipid syndrome

The interesting paper recently published by Derksen et al in the Annals on the need for a long term anticoagulant treatment in patients with antiphospholipid antibodies and venous thrombosis prompts several observations. (a) The authors of the 1992 paper had venous thromboembolic episodes during pregnancy or in the immediate postpartum period. To make their conclusion more valid, could the authors specify if pregnancy-associated events were initial or recurrent thrombosis? Oral anticoagulants cannot be used at that time, where the risk of thrombosis is obviously high, so pregnancy-associated thrombosis should probably be excluded from analysis. This also applies to carrying out by Rosove et al, which included three subsequent thromboses occurring during pregnancy or post-partum. (b) An oestrogen-containing pill was used by 10 of the 19 patients at the time of 1/34 venous thromboembolic episodes. It is not clear if the pill was stopped after the initial episode, as recommended by most authors.1 If it was not, the risk of recurrent thrombosis was over-estimated in patients still receiving the pill. (c) For clinicians, the problem is to avoid recurrent thrombotic events, irrespective of their site, venous or arterial. In the study by Derksen et al, myocardial infarction had occurred in two patients despite 'adequate' anticoagulation, which demonstrates that the vascular protection provided by anticoagulants is not absolute. (d) During the past few years, growing evidence has emerged favouring the long or very long term use of anticoagulants in patients with antiphospholipid syndrome. A major problem is to determine the duration of this treatment, since it is recognised as carrying a serious risk especially at an international normalised ratio of three or more.1, 2 It is assumed that anticoagulants are required as long as antiphospholipid antibodies are present.7 To test the validity of this recommendation, could Derksen et al mention the sequential determinations of antiphospholipid antibodies in their patients, with and without relapses? At present, the prevention of recurrent thrombotic events in the antiphospholipid syndrome is still a matter of debate. Two retrospective studies favour the use of oral anticoagulants,1, 2 Conversely, antiplatelet agents have been said to be effective in patients with focal cerebral ischaemia and antiphospholipid antibodies.2 Prompt relapses may occur after aspirin or oral anticoagulant withdrawal. A clear and definitive answer, if any, requires prospective controlled trials such as the recently undertaken French cooperative study comparing aspirin to warfarin (AWAPS).


AUTHORS' REPLY: We read with great interest the letter from Drs Piette and Wechsler concerning our recent paper in the Annals on anticoagulant treatment in patients with antiphospholipid antibodies and venous thrombosis.1 We wish to make the following comments:

1) In our series four thrombotic episodes were pregnancy related. These were initial thrombosis in two patients (numbers 5 and 12) and a recurrent thrombosis in patient number 6 and 10. In 10 patients low-dose oestrogen containing pills were taken at the time of the first episode. These pills were stopped in all but one (number 17). Our data are insufficient to answer the question whether patients with antiphospholipid antibodies are at a higher risk for thrombosis in the presence of other risk factors (such as oestrogen-containing pills, pregnancy, immobilisation, cigarette smoking or hypercholesterolemia). However, our observation that additional risk factors were absent in 17/34 venous thromboses and in at least one of the episodes in 10/12 patients with recurrent thrombosis indicates that antiphospholipid antibodies itself are a risk factor, and argues against the universal need for a 'second hit' for thrombosis to occur. 2) Myocardial infarction that occurred in two patients during treatment with oral anticoagulants suggests that anticoagulant therapy does not prevent arterial thrombosis in all patients. In both patients we added low-dose aspirin to treatment with oral anticoagulants.
3) Our patients were re-tested at least every six months and all but one remained positive. The exception was patient number 4. He became negative for antiphospholipid antibodies six months before myocardial infarction and is still negative two years later. This suggests that disappearance of antiphospholipid antibodies (defined as lupus anticoagulants and anticardiolipin antibodies) does not imply disappearance of the risk for thrombosis and agrees with data showing that antibodies causing positive tests for antiphospholipid antibodies may differ from those causing thrombosis.2

We agree that the optimum therapy for patients with the antiphospholipid syndrome still has to be established. All clinical data that have been previously reported may suffer from selection bias. We need data from prospective trials on selected patients and adequate control groups. Such trials should stratify for any other underlying disease, type and titre of antiphospholipid antibodies, other risk factors for thrombosis, and type of initial event. Due to the large number of patients required and the expected rate of (re-)thrombosis they should be multicentre and have many years follow-up. Such treatment trials are complex, expensive and in the end probably easy to combat. Furthermore, in each trial only a limited number of the many possible strategies for antithrombotic treatment in patients with the antiphospholipid syndrome can be tested. We very much applaud the initiatives taken by our French colleagues collaborating in AWAPS and hope that their study will result in a safe and effective therapy of patients with the antiphospholipid syndrome. In the meantime, we advise long-term treatment with oral anticoagulants in all patients with antiphospholipid antibodies and venous thrombosis because these patients have a very high risk of recurrent venous thrombosis, and oral anticoagulants in contrast to acetylic salicylic acid, effectively prevent the recurrence of venous thrombosis.

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Evaluator:

Evaluating new physical treatments

I am grateful for the opportunity to respond to your Leader article Evaluating new physical treatments.

Let me start by describing myself as one of the author's electrotherapy "cytics", being extremely sceptical of claims made for these modalities and rarely use them. The area of controversy is large, with many studies indicating that physical treatments are ineffective, a large percentage of patients report improvement but this is probably due to the placebo effect. Therefore, I am extremely sceptical of claims made for these modalities, and rarely use them. However, the area of controversy is large, with many studies indicating that physical treatments are ineffective, a large percentage of patients report improvement but this is probably due to the placebo effect.

It is somewhat strange that the author readily advocates massage by manipulators and nurses, even though massage is poorly evaluated. Furthermore, citation of the trial performed by chiropractors was not supported by evidence. It is a common misconception that the eficacy of the treatment can be taken. Pre-empting these studies and making inferences from results of a single study would be unscientific. Moreover, electrotherapy modalities are usually applied at a higher intensity and duration than is required in the treatment setting. Therefore, the results are not applicable to clinical practice.

In summary, I would like to say that I believe physical treatments are effective in the treatment of low back pain, but that the evidence is not strong enough to support their use in clinical practice. However, I would like to see more research into the effectiveness of physical treatments, and I believe that a better understanding of the mechanisms of action is required.
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