Recurrent and incessant pericarditis: intrapericardial triamcinolone therapy

In my experience the largest individual group of sufferers from recurrent and especially incessant pericarditis have been those without recurrent effusions who are presumed, though rarely firmly demonstrated (as here), to have an immunopathy, and especially those who are ‘steroid hooked’[1]. Indeed, there is some evidence that corticosteroid treatment has been necessary to initiate the cycle of recurrences[7–9]. Moreover, recurrent episodes appear to be more frequent when corticosteroid therapy is prescribed during the first attack of pericarditis compared to patients not so managed[7–9]. It is here that one hopes that either a thoracoscope or the specialized instrument for penetrating the ‘dry’ pericardium (PerDUCER[2]) can be used to approach this problem. Since the patients almost uniformly respond to systemic corticosteroid there is every hope for the success of an agent like triamcinolone safely deposited in the wet or dry pericardium in a concentration that would be unreachable with oral or parenteral therapy and usually without detectable side effects, which, in any case, could not become chronic. Professor Maisch and colleagues[3] have established the efficacy and safety of intrapericardial triamcinolone for autoreactive effusive pericarditis and myopericarditis. It is to be hoped that in appropriate clinical trials they and other investigators can broaden its indications.

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References


Homocysteine and vascular disease

See doi:10.1053/euhj.2002.3161 for the article to which this Editorial refers

Although case control studies remain robust in linking an elevated plasma homocysteine concentration to the development of premature atherosclerosis and thrombosis, prospective studies have been less convincing. On balance, however, it is generally accepted that an elevated level of this amino acid, common in patients with atherosclerosis, constitutes a weak but independent risk factor for the development of vascular disorders and may also be a determinant of prognosis. The concentration of plasma homocysteine is inversely related to that of folate as well as plasma vitamins B12 and B6[1]. Inadequate concentrations of B vitamins are common among those with high homocysteine levels. Hence vitamin therapy has received much attention as a possible treatment option in patients with vascular disorders.

Treatment studies — a perspective

Early intervention studies by Wilcken et al.[2], Boers et al.[3] and Brattstrom et al.[4] showed the usefulness of folic acid treatment in patients with vascular
diseases. A later meta-analysis of randomized trials showed that homocysteine levels could be reduced by about 25% with folic acid supplements in doses ranging from less than 0.5 mg to 5 mg per day [5]. Other studies have explored the value of lower doses. Ward et al [6] administered folic acid supplements in doses of 100 μg, 200 μg and 400 μg. Of the three doses, 200 μg appeared to be as effective as 400 μg, while 100 μg was not optimal. Wald et al [7] randomized patients with ischaemic heart disease to one of five dosages of folic acid (0.2, 0.4, 0.6, 0.8, and 1.0 mg.d⁻¹) and concluded that a dosage of folic acid of 0.8 mg.d⁻¹ was necessary for a maximum reduction in homocysteine level.

Diet studies

A dietary strategy may also be pursued as folic acid is found abundantly in green leafy vegetables. In one study, Chait et al [8] randomly assigned 491 adults to either a prepared vitamin-fortified meal plan or a self-selected diet. With the prepared meal, the circulating concentration homocysteine fell by about 10–15%. In another study, Appel et al [9] fed subject participants a control diet, low in fruits, vegetables, and dairy products, with a fat content typically seen in the U.S. One of three diets was then randomly assigned: the control diet, a diet rich in fruits and vegetables but otherwise similar to control, or a combination diet rich in fruits, vegetables, and low-fat dairy products and reduced in saturated and total fat. Homocysteine concentration fell in the combination diet and was inversely associated with change in serum folate. Malinow et al [10] assessed the effects of cereals fortified with three levels of folic acid in men and women with coronary artery disease. The cereal providing 127 μg of folic acid decreased homocysteine by only 3.7%, while cereals providing 499 and 665 μg of folic acid decreased plasma homocysteine but only by 11.0% and 14.0%, respectively. At a population level, fortification of grain products with folic acid was mandated here in the United States by the Food and Drug Administration in 1996. This measure was designed to reduce the risk of neural-tube defects and was essentially complete by mid-1997. Following this, the mean homocysteine concentration in the population decreased from 10.1 to 9.4 μmol.l⁻¹ and the prevalence of high homocysteine concentrations (>13 μmol.l⁻¹) decreased from 18.7 to 9.8% [11].

Non-homocysteine effects of folic acid

While folic acid may reduce the concentration of homocysteine, possibly reducing the risk of vascular disease, it is now appreciated that this vitamin has other, perhaps beneficial, effects on endothelial function independent of homocysteine. Doshi et al [12] investigated the effect of folic acid on endothelial function and homocysteine in patients with coronary disease. Folic acid increased plasma folate, lowered homocysteine, and improved FMD but improvement did not correlate with homocysteine reduction.

The PACIFIC study

In the PACIFIC study, the authors determined the effect of low dose folic acid on homocysteine levels [13]. Mostly men over the age of 65 years were enrolled and only two doses of folic acid were used, 0.2 and 2.0 mg. Both doses resulted in a decrease in homocysteine levels but the larger dose produced a greater fall of 1.8 μmol.1⁻¹ compared with 1.2 μmol.1⁻¹, a statistically significant difference. As with previous studies, the higher the pretreatment homocysteine concentration, the greater the reduction following the commencement of therapy with folic acid. As the authors point out, the effect of folic acid was somewhat less than in previous studies where a reduction of 25% in homocysteine concentrations is often seen. This finding could have been due to the relatively low baseline homocysteine concentrations of 11 μmol.1⁻¹, possibly attributable to dietary interventions as part of secondary prevention and/or the use of multivitamin pills which were being taken by about 10% of the patients.

The authors also noted a 5–10% elevation in homocysteine concentrations associated with the use of the vasopeptidase inhibitor omapatrilat. It remains unclear if this was dose-dependent. It does not seem to have been due to a reduction of folic acid or vitamin B12 levels although creatinine concentrations rose in the patients, suggesting a possible effect on the renal handling of homocysteine. Many drugs commonly used in patients with coronary disease may potentially increase homocysteine levels and omapatrilat may be added to the list. It is unknown, however, if this will adversely affect prognosis and outcomes in these patients.

The large, randomized and well-designed PACIFIC study is important as it shows a modest reduction in homocysteine concentrations by low dose folic acid although this is not as marked as 2 mg.day⁻¹. In the U.S.A., these lower doses of folic acid are readily available in fortified foods and in Europe and Asia by vitamin supplementation. Through the SEARCH study, the clinician will now be aware of yet another drug with potential for altering the metabolism of homocysteine.
There are still many important unresolved issues: 0.2 mg day⁻¹ may reduce the homocysteine concentration, as in this study, but is this optimal, since 2 mg has a greater effect? Does this low dose improve vascular function in patients with atherosclerosis? And is the dose of folic acid which produces the maximum reduction in homocysteine the same as that which produces optimal improvement in vascular function? The effects of these lower doses of folic acid on endothelial function deserve further exploration.

The use of folic acid in highly selected groups of patients with vascular disease has already been evaluated in small intervention studies with encouraging results[14]. Results of several large secondary prevention trials involving thousands of patients with vascular disorders, which are now ongoing, are eagerly awaited[15].

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References

Point-of-care echocardiography: small, smart and quick

See doi:10.1053/euhj.2002.3162 for the article to which this Editorial refers

Echocardiography is currently the most widely used and cost-effective diagnostic imaging tool in cardiology. Since it is often the best or even the only applicable method, it has largely replaced other imaging modalities in a wide variety of health care environments. Generally, echocardiographic laboratories use ‘high-end’ instruments that have advanced features.

Miniaturization represents a recent revolutionary advance in echocardiography. Although a hand-held ultrasound imager was already proposed in the early 1970s[1], the concept was ahead of its time and technical limitations, image quality and reimbursement issues led to the interruption of its further development. Recently, improvements in microcomputer technology have led to the development of ultrasound machines easily carried to the bedside and capable of providing two-dimensional image quality comparable to that seen on full service...