Methylprednisolone and the Size of Myocardial Infarcts

In 1972, Barzilai and co-workers[1] reported in *Chest* that treatment with hydrocortisone decreased mortality in patients with myocardial infarction. That report generated considerable controversy, and the role of therapy with corticosteroids in patients with myocardial infarction has remained controversial. Morrison and associates[2] have reported a decrease in the size of infarcts after treatment with corticosteroids, based on cumulative activity of creatine phosphokinase in the plasma, but the studies by Roberts and co-workers[3] and the work by Peters et al reported in this issue of *Chest* (see page 483) failed to demonstrate any beneficial effects. The discrepancies among these three studies are not readily explained. The hemodynamic status of the patients, the methods used to measure the size of infarcts, the time from onset of symptoms until administration of the drug, and the doses of steroid used are all similar. What, then, explains the differences in results among these studies?

One wonders whether the two smaller studies of Roberts et al[3] and Peters et al might have demonstrated a beneficial effect from therapy with steroids had the number of patients been greater. Thus, the question arises, "Is another large clinical study of therapy with steroids and the size of infarcts warranted at this time?" Results to date suggest that a large clinical trial of therapy with steroids should not be undertaken. The practicability of such a study conflicts with the justifiably conservative viewpoint of many clinical researchers that a pharmacologic trial should be halted in the absence of an obvious beneficial effect if there is a possibility that administration of the drug can be deleterious. In the case of the corticosteroids the possibility exists for impaired healing of the infarct and increased severity of arrhythmias.[3,4] In both clinical and animal studies with the corticosteroids, a clear-cut impairment of healing of wounds has been reported after multiple large doses.[3,5] It is clear that such a regimen is contraindicated in patients with acute myocardial infarction. The effect of one or two large doses of corticosteroid on the healing of a myocardial infarct remains unclear and will continue to generate doubts over therapy with steroids until clear beneficial effects can be proven. Increased severity of arrhythmias after treatment with corticosteroids is also more prominent after multiple doses of steroid.[3] Nevertheless, increased severity of arrhythmias has been reported after single large doses of corticosteroids,[4] and it may be noteworthy that three out of the four patients who suffered severe arrhythmias in the study by Peters et al were in the drug-treated group. It is unfortunate that often arrhythmias are not carefully quantified in clinical and animal studies.

To clarify the discrepancies in results obtained with therapy with corticosteroids in patients with myocardial infarction, further studies in animals are needed in which the size of the completed infarct is measured anatomically or by completed washout curves for serum creatine phosphokinase. Since many studies in animals have focused only on the first several hours after experimentally induced myocardial ischemia, there is no reported experiment in dogs in which therapy with corticosteroids has been shown to reduce the measured size of the infarct 24 or more hours after ischemia. Another priority in future clinical and experimental animal studies should be an attempt to identify specific subgroups in which therapy with the steroids is effective. Studies with digitalis and nitrates, for example, indicate that these drugs may decrease the size of an infarct when left ventricular end-diastolic pressure is elevated but are otherwise ineffectual.[6,7] The steroids, by virtue of their vasodilator effect, may act in a similar manner. Another possibility is that therapy with the steroids is more effective in patients with an extension of infarction than in uncomplicated cases. The positive study of Morrison et al[2] included a higher percentage of patients with extension of infarction than did the negative studies of Roberts et al[3] and Peters et al.

Finally, due to the limitations of all of the methods now available to estimate the size of infarcts in man, it may be wise to continue refining such measurements, but when studying the effect of any agent proposed to reduce the size of infarcts, to place more stress on other clinical observations, such as mortality, functional class, and incidence of arrhythmias. After all, the ultimate goal in reducing the size of an infarct is to reduce mortality and morbidity in patients with myocardial infarction.

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References

1 Barzilai D, Plavnick J, Hazani A, et al: Use of hydrocortisone in the treatment of acute myocardial infarction: Summary of a clinical trial in 446 patients. Chest 61:488-491, 1972

2 Morrison J, Reduto L, Pizzarello R, et al: Modification of myocardial injury in man by corticosteroid administration. Circulation 53 (suppl 1):200-204, 1976

3 Roberts R, DeMello V, Sobel BE: Deleterious effects of methylprednisolone in patients with myocardial infarction. Circulation 53 (suppl 1):204-206, 1976
4 Vogel WM, Zannoni VG, Abrams GD, et al: Inability of methylprednisolone sodium succinate to decrease infarct size or preserve enzyme activity measured 24 hours after coronary occlusion in the dog. Circulation 55:588-595, 1977
5 Maclean D, Maroko PR, Fishbein MC, et al: Effects of corticosteroids on myocardial infarct size and healing following experimental coronary occlusion. Am J Cardiol 39:280, 1977, (abstract)
6 Watanabe T, Covell JW, Maroko PR, et al: Effects of increased arterial pressure and positive inotropic agents on the severity of myocardial ischemia in the acutely depressed heart. Am J Cardiol 30:371-377, 1972
7 Epstein SE, Borer JS, Kent KM, et al: Protection of ischemic myocardium by nitroglycerin: Experimental and clinical results. Circulation 53 (suppl 1):191-197, 1976

Respiratory Maneuvers in Electrocardiographic Diagnosis

There are three conditions in which respiratory maneuvers may be of assistance in electrocardiographic diagnosis: (1) the analysis of a Q wave in leads 3 and aVF especially if there is no Q in lead 2; (2) the definition of a true left anterior fascicular block (LAFB) which is based upon the degree of left axis deviation; this intraventricular conduction defect produces a negative deflection, an S wave, in lead 3; and (3) the diagnosis of pericarditis as opposed to myocardial infarction.

In the first condition, the decision regarding the presence of an *abnormal* Q wave in inferior leads 3 and aVF in the resting routine electrocardiogram often rests upon the size of this initial negative deflection, as its duration may be borderline (between 0.03 and 0.04 sec). If there is a large Q in the inferior leads and it is due to an old inferior myocardial infarction, the respiratory maneuver of recording leads 3 and aVF *during* deep inspiration and expiration will not cause it to become smaller or disappear entirely. If the Q_3 is due to cardiac position, then, with descent of the diaphragm in inspiration, the heart rotates in the mediastinum and its frontal plane axis shifts. With this shift the initial negative deflection in the QRS alters radically and is seen to be clearly an S and not a Q or there will be no negative deflection at all. Thus, an error of diagnosis—namely citing the tracing as showing an old inferior myocardial infarction—can be avoided.

In the second condition, the definition of the presence of LAFB as opposed to a left axis deviation (LAD) not due to an IV conduction defect, has been predicated upon the degree of LAD. Between minus 30° and minus 45° there is an area of uncertainty as to diagnosis, while LAD of minus 45° or greater is usually due to left anterior fascicular block.[1] Again, if there is a true intraventricular conduction defect and not a positional cause for the left axis deviation, the frontal plane axis of the QRS complex will not shift with the inspiration-expiration maneuver. Hence, recording of these maneuvers in the three limb leads (1, 2, 3), preferably simultaneously inscribed, will demonstrate no change in the degree of left axis deviation with left anterior fascicular block even when the axis lies between minus 30° and minus 45°. If the left axis deviation is not due to LAFB, the axis will shift as much as 30-40 degrees during these exercises.

In acute and subacute (or healing) pericarditis, it is often difficult to rule out the diagnosis of myocardial infarction on clinical grounds. It is true that in pericarditis the ST and T abnormalities are widespread in the ECG leads, and not localized as in myocardial infarction. However, during the initial phases of the illness it is useful to have diagnostic reinforcement, if possible, to the diffuse T wave abnormalities. It has been found[2] that in patients with pericarditis, the T wave abnormalities can *alter their form* during inspiration and expiration maneuvers monitored by the ECG leads. As the acute process subsides into a healing stage, these respiratory fluctuations in T wave form decrease and once the process has healed the maneuver no longer induces the T wave changes. Presumably[2] the fibrin strands secondary to pericardial inflammation tug at various sites on the epicardium during the subacute stage, and when these break or are absorbed, the pericardial fluid is absorbed and tissues heal. Such strands no longer pick at the epicardium as the heart swings in the mediastinum. Even when the resting ECG has no T abnormalities, they may be provoked by the maneuver in the healing phase. Such T alterations with breathing are not seen in myocardial infarction.

The three conditions cited thus can be assisted by the respiratory maneuvers mentioned, and while not definitive in a strict sense, are of considerable clinical value.

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References

1 Criteria Committee of New York Heart Association: Nomenclature and Criteria for Diagnosis of Diseases of the Heart and Great Vessels (7th ed). Boston, Little, Brown and Company, 1973, p 242
2 Ferrer, MI: A new electrocardiographic test for pericarditis. JAMWA (in press)