Cardiovascular effects of phenothiazines

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Abstract

Phenothiazines have significant electrophysiologic and cardiocirculatory effects. The electrophysiologic effect of these drugs is similar to that reported for quinidine. Phenothiazines decrease the rate of rise of phase 0 of the action potential, decrease the duration and amplitude of phase 2, and prolong phase 3. The surface ECG changes produced by phenothiazines are lengthening of the QTC interval, ST-T wave changes, increased size of U waves, and prolongation of the PR interval. The degree of repolarization abnormalities secondary to phenothiazines seems to be dose-related.

Various arrhythmias have been attributed to the effect of phenothiazine therapy and numerous cases of sudden death as a result of fatal arrhythmia have been described. Paradoxically, phenothiazines such as chlorpromazine and thioridazine also have been shown to have significant antiarrhythmic properties. Chlorpromazine shows a powerful vasodilatory effects which is caused by alpha-adrenergic receptor blockade, a central action, and a direct effect on the vascular wall. In addition, the drugs also have a direct depressant effect on the myocardium. As a result of peripheral vasodilatation and negative inotropic effects, hypotension is the most common adverse reaction of phenothiazines in patients with no evidence of congestive heart failure.

Experimental studies have demonstrated significant reductions in systemic and pulmonary vascular resistance as well as systemic blood pressure following intravenous administration of chlorpromazine. These hemodynamic changes were accompanied by significant increase in cardiac output in one study and by no change in cardiac output in
another study. The vasodilatory effect of chlorpromazine resulted in increased renal and mesenteric blood flow and prolongation of survival time in dogs following hemorrhagic hypotension. Chlorpromazine was found effective in relieving abnormal vascular tonus and improving the circulation in patients undergoing cardiopulmonary bypass surgery. In patients with myocardial infarction complicated by congestive heart failure, intravenous administration of chlorpromazine caused significant hemodynamic improvement and a considerable degree of sedation. The drug was found effective in reducing the vasoactive response in patients with cardiogenic shock which resulted in improved tissue perfusion and metabolism.

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*1 Supported in part by a grant No. CHL-00653-11 from the National Institutes of Health.

* Dr. Frishman is a “Teaching Scholar” of the American Heart Association.

American Heart Journal
Volume 100, Issue 3, September 1980, Pages 397-401