Review Article:

QUINIDINE IN THE TREATMENT OF AURICULAR ARRHYTHMIAS

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Preface

The clinical efficacy of a drug is determined by weighing the anticipated benefits from its use against the danger of toxic effects. Lack of appreciation of this fact has led to misunderstanding relative to the value of quinidine. When properly employed, quinidine is a safe and effective drug in the treatment of certain auricular arrhythmias. Increasing interest in the cardiac arrhythmias in recent years warrants a review of the toxic and therapeutic effects of quinidine.

Physiologic Action, Dosage, and Toxic Effects of Quinidine

Quinidine prolongs conduction recovery in the auricular muscle and slows the rate of discharge from ectopic foci. It raises the threshold in experimental production of auricular arrhythmias. The importance of decrease in vagal tone secondary to the use of the drug is not known.

It has been demonstrated that the maximum level of concentration in the blood after oral administration of quinidine is attained in about two hours. For this reason, when quinidine is used in the treatment of important auricular arrhythmias, it should be given at intervals of two hours, usually in a dosage of 0.4 Gm. of quinidine sulfate for five doses. Quinidine has cumulative action, so that gradually increasing concentrations in the blood are achieved. Even 12 hours after the last dose, the blood level remains about 40 per cent of the maximum level; for this reason, the same dosage schedule on the second day may be of therapeutic benefit. If the arrhythmia persists, the dosage may be increased to 0.6 Gm. every two or three hours for four or five doses, and subsequently a dosage of 0.8 to 1.0 Gm. or more every three hours for four doses may be tried if toxic manifestations have not occurred. The total daily dosage should not exceed 4 to 6 Gm. Quinidine may be given intramuscularly or intravenously, but indications are rare for parenteral therapy of auricular arrhythmias.

Fear of toxic reactions has limited the use of quinidine. Because it is an isomer of quinine, symptoms of cinchonism may occur. Nausea, vomiting, and diarrhea are common. Nausea and vomiting may necessitate discontinuance of therapy. Diarrhea may be controlled by symptomatic measures. Skin eruptions, purpura, and fever are rare and are indications for termination of treatment. Electrocardiographic changes and ventricular arrhythmias may result from
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The earliest electrocardiographic effect is prolongation of the Q-T interval (fig. 1A), and this is not a contraindication to continued use of the drug. Auriculoventricular conduction disturbances may occur and if severe are an indication for termination of therapy. Prolongation of intraventricular conduction may result when large doses of quinidine are employed (fig. 1B). If the duration of the QRS complex exceeds the normal for the individual by more than 50 per cent, the drug should be discontinued. Ventricular premature contractions occur occasionally and may lead to the development of ventricular tachycardia. This serious arrhythmia is seen most frequently after the intravenous use of quinidine and probably accounts for the majority of the fatalities reported. It rarely develops if other electrocardiographic and clinical warnings of toxicity have been heeded. Cardiac arrest may occur but it is extremely rare. Daily electrocardiograms should be taken during treatment, and when large doses of quinidine are used, records should be made and interpreted before each successive dose of the drug is given. If electrocardiographic evidence of serious toxicity is seen, treatment should be terminated. Since hypotension is common during the administration of quinidine, the
patient should remain in bed each day during treatment and for several hours thereafter.

Treatment of Auricular Arrhythmias

Auricular premature contractions rarely require the use of quinidine and are often better controlled by other measures, such as reassurance, rest, and mild sedation. When disturbing symptoms accompany the premature contractions, quinidine may be helpful. Moderate dosages are required in most cases, and in some instances the irregularity may not be eliminated even though large dosage is employed.

Auricular paroxysmal tachycardia is a common arrhythmia, and most attacks are of brief duration. Prolonged episodes require some therapeutic measure. Carotid sinus pressure should be tried initially. Frequently neostigmine, 0.5 to 10 mg. subcutaneously, will terminate the attack, particularly if carotid sinus pressure is applied about 15 minutes after administration of the drug. If this treatment is not effective, digitalis intravenously, usually in the form of 0.8 mg. of lanatoside C, should be tried. In some instances, carotid sinus pressure is required after the patient has received digitalis, the maneuver being tried 15 to 30 minutes after completion of the intravenous injection. Quinidine is not a very potent drug in the treatment of auricular paroxysmal tachycardia. Occasionally it may be useful in the prevention of recurrent attacks. A dosage of 0.4 Gm. four times daily is employed in most instances.

Auricular paroxysmal tachycardia with auriculoventricular block is a relatively rare arrhythmia and is resistant to treatment. In some cases it may be due to digitalis intoxication and can be eliminated by the use of potassium salts orally administered. Quinidine therapy may be effective in cases not caused by digitalis intoxication.

Auricular flutter is a serious arrhythmia that usually occurs in patients with organic heart disease. Quinidine is frequently employed in treatment, but the arrhythmia can be terminated more often and safely by adequate digitalization. Digitalis in a dosage of 0.1 Gm. three times daily for as long as three weeks may be required before the auricular mechanism is converted to auricular fibrillation. Cessation of digitalis therapy after development of auricular fibrillation will result in restoration of sinus rhythm in many instances. If auricular fibrillation persists, it can then be terminated by the use of quinidine. Occasionally it is necessary to use quinidine in the treatment of auricular flutter if symptoms of digitalis intoxication occur.

Auricular fibrillation is the most frequent important auricular arrhythmia. It may exist in patients who have organic heart disease or it may occur in the absence of other clinical evidence of cardiovascular disease. Auricular fibrillation is usually present in patients who have systemic emboli in the absence of acute myocardial infarction. Pulmonary emboli may also occur. The increased
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risk of embolization in patients with auricular fibrillation constitutes one of the major reasons for restoration of sinus rhythm. Rarely, emboli may occur when auricular fibrillation has been converted to sinus rhythm, and for this reason it formerly was believed that a history of embolization constituted a contraindication to quinidine therapy. However, embolic complications are frequent in patients who have auricular fibrillation and in whom no attempt has been made to restore sinus rhythm. Sokolow\textsuperscript{2} considers a history of previous emboli an indication for treatment. He found that in patients who had had previous embolic accidents, further embolization at the time of re-establishing sinus rhythm was less frequent than in patients who had experienced no previous embolic episodes. The cardiac output is reduced in persons who have auricular fibrillation associated with organic heart disease, and restoration of sinus rhythm usually results in an increased output.\textsuperscript{4,5}

An attempt to restore normal sinus rhythm should be made in most cases of auricular fibrillation. Long-standing auricular fibrillation, a history of embolization, the presence of cardiac enlargement, a past history of congestive heart failure and mild conduction disturbances are not contraindications to treatment. In the presence of mitral stenosis it is more difficult to restore sinus rhythm, and auricular fibrillation is likely to recur even though prophylactic quinidine is employed. If the arrhythmia is not well tolerated and there is some contraindication to operative treatment of mitral stenosis, quinidine therapy may be tried. Angina pectoris may disappear after the development of auricular fibrillation, and if it does, restoration of sinus rhythm should not be attempted. Subacute bacterial endocarditis and severe conduction defects constitute contraindications to the use of the drug. Aged persons often tolerate auricular fibrillation well, and there seems to be a higher incidence of toxic effects from the use of the drug in the aged. In elderly patients, therefore, quinidine should not be employed if auricular fibrillation has not resulted in congestive heart failure or embolization. Quinidine is not effective in the treatment of auricular fibrillation due to thyrotoxicosis until after the thyroid disease has been controlled. Acute myocardial infarction may result in the development of auricular fibrillation. The ventricular rate should be reduced by the administration of digitalis. In many cases sinus rhythm will return spontaneously within a few days. Quinidine therapy may be used after recovery from the myocardial infarction if the arrhythmia persists.

Anticoagulants have been used prophylactically to decrease the risk of embolization on restoration of sinus rhythm. It is doubtful that such treatment is helpful, and it is not recommended. Congestive failure should be eliminated, if possible, before quinidine is employed. Lewis\textsuperscript{6} emphasized the need for digitalis to control the ventricular rate before the administration of quinidine, and this remains an important principle. Quinidine slows the auricular rate and has a vagal blocking effect. These factors tend to increase the ventricular rate, sometimes to an alarming degree if 1:1 conduction is established. Therapeutic doses of digitalis do not decrease the effectiveness of quinidine and do not "fix" the heart in fibrillation.
Fig. 2. Continuous strip of lead II that shows variable auricular mechanisms resulting from the therapeutic effect of quinidine.
The auricular rate decreases gradually during quinidine treatment of auricular fibrillation and may reach levels below 200 per minute before sinus rhythm is restored. The electrocardiographic appearance may resemble that of auricular flutter, but the auricular complexes are not perfectly regular. In some instances, typical auricular flutter may occur. By taking a continuous electrocardiogram it can be shown that restoration of sinus rhythm is not always a single, sharply defined phenomenon. Figure 2 shows a record of lead II taken during quinidine treatment of auricular fibrillation. The rhythm first returned to normal about two and one-half hours after the drug was first taken, but recurrent periods of auricular fibrillation or flutter of decreasing duration alternated with sinus rhythm until finally normal sinus rhythm had become established. Sinus rhythm may be restored during the night, five to ten hours after the last dose of quinidine. For this reason, the cardiac mechanism should be determined before quinidine is given each day.

In about 75 per cent of cases quinidine therapy for chronic auricular fibrillation is successful. After restoration of normal rhythm, prophylactic quinidine is employed to decrease the likelihood of reversion to auricular fibrillation. Usually 0.4 Gm. is given four times daily. If large amounts of drug have been required in treatment, prophylactic doses of 0.6 or even 0.8 Gm. may be required, but this is unusual. The drug should be administered for about one month, because auricular fibrillation is most likely to recur during the first few weeks after treatment. If the arrhythmia recurs after termination of prophylactic quinidine, restoration of sinus rhythm should be followed by permanent quinidine prophylaxis.

Paroxysmal auricular fibrillation is best treated by digitalization. The duration of the paroxysms is self-limited. Quinidine is often effective prophylactically. It is given in a dosage of 0.4 Gm. four times daily, though larger doses may be required occasionally.

**SUMMARY**

The use of quinidine in the treatment of auricular arrhythmias is reviewed. Beneficial results and toxic effects, methods of administration, and clinical indications are presented.

**References**


