Atabrine in Ventricular Tachycardia

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The therapeutic efficacy of Atabrine in ventricular tachycardia has not yet been clearly demonstrated. In this case report, Atabrine stopped ventricular tachycardia and restored normal sinus rhythm following the fifth two-hourly oral dose of 0.30 Gm. Nausea and vomiting were the only toxic effects noted. Ventricular tachycardia, in this case, occurred as a complication of acute myocardial infarction. The latter's characteristic electrocardiographic picture became obvious as the arrhythmia was corrected.

In recent years several reports have been published indicating the therapeutic value of Atabrine for the correction of cardiac arrhythmias, particularly the supraventricular types. Very few cases of ventricular tachycardia have been treated with Atabrine and in none was a successful result obtained. The following case is therefore reported to point out the potentialities of Atabrine in ventricular tachycardia and to stimulate further studies with this drug in the ventricular arrhythmias.

Case Report

When first seen, A. G., a married Spanish male, 60 years of age, complained of "pain in the throat" which radiated to the epigastrum and was of approximately 24 hours' duration. The condition started suddenly while he was playing billiards after a heavy dinner. The pain was soon followed by palpitation, difficulty in breathing, nausea and vomiting.

Previous to this illness, the patient had had slight exertional dyspnea but never accompanied by any chest pain or discomfort. To his knowledge, his blood pressure had always been normal.

Physical examination revealed a markedly dyspneic, moderately cyanotic, anxious patient bathed in cold clammy perspiration. The pulse was imperceptible, the blood pressure unobtainable, and the heart sounds very faint and rapid. The electrocardiogram (fig. 1) revealed ventricular tachycardia at a rate of 200 per minute.

The patient was immediately placed under oxygen. Caffeine sodiobenzoate was given intramuscularly, 0.50 Gm. every three hours. The blood pressure was soon recorded at 110/80. Procaine amide, 200 mg., (Pronestyl) was next given intravenously under blood pressure and electrocardiographic control. During the Pronestyl administration the blood pressure fluctuated between 110/80 and 94/80, but the ventricular tachycardia persisted. Following the intravenous dose, Pronestyl was also given orally in a dose of 1.0 Gm. every two hours for two doses and afterward at six-hour intervals. In addition, 100 mg. of khellin (Kelicorin) was given intramuscularly once daily. The heart rate remained between 110 and 130 per minute and the blood pressure between 110/90 and 95/80.

On the second hospital day, 400 mg. of Pronestyl in 500 cc. of 5 per cent dextrose in water were given by slow venoclysis in addition to the oral doses. The arrhythmia still persisted as disclosed by the daily electrocardiograms. In two days the total dose of Pronestyl given was 11.6 Gm.

On the third day, quinidine sulfate (Quinidor) was given instead of Pronestyl in a dose of 0.40 Gm. every hour for three doses and then the same dose every three hours. Later, this was increased to 0.60 Gm. every three hours and finally every two hours. The pulse rate slowed down slightly to between 110 and 115, while the blood pressure fluctuated between 110/86 and 90/70. With a total dose of 5.6 Gm., the patient complained of tinnitus. The drug was finally discontinued when a total dose of 11.2 Gm. had been given in two and one-half days. The patient became nauseated and began to sweat profusely with consequent general weakness. He refused to take any more of the medicine. The pulse rate then rose to 140 and the blood pressure remained between 118/70 and 86/72. The serial electrocardiograms showed no change in the arrhythmia.

On the sixth hospital day, quinidine was stopped. Then, about four hours after the last dose of quinidine, the patient was started on Atabrine in a dose of 0.30 Gm. every two hours. When next seen, after five doses of Atabrine, the patient exhibited for the first time a pulse rate of 92 per minute. Similarly,
the electrocardiogram disclosed the first instance of normal sinus rhythm with only occasional ectopic ventricular complexes. At the same time, the tracing finally revealed the underlying cardiac pathology, myocardial infarction of anteroposterior location with septal involvement (fig. 2). From then on, the pulse rate remained in a normal range, between 80 and 90, and the blood pressure remained between 112/86 and 90/60. Subsequent electrocardiograms showed the progressive changes resulting from the infarction, as well as the total disappearance of the ectopic rhythm. Two hours after the last dose of Atabrine, the patient vomited and then refused to take the next dose. The drug was, therefore, tapered off and discontinued after two additional days. During the rest of his stay in the hospital the patient improved steadily, in spite of a mild pneumonic process which was promptly checked with antibiotics. When discharged, after 39 days in the hospital, his electrocardiogram still showed the evidences of infarction but there was no trace of the ventricular tachycardia. The clinical course in relation to the cardiac arrhythmia and the drugs employed is illustrated in figure 3.

Two and one-half months later, the patient was re-examined. He stated that, since leaving the hospital, he continued to improve. He had had no chest pain. The heart rate was 82 per minute and the blood pressure was 140/96. The heart sounds were clear, regular and of good quality. The standing treatment consisted of Kelcorin, one tablet three times a day and one ampule once a week. The electrocardiogram then revealed some improvement in the S-T and T configuration in the extremity leads.

**Fig. 1.** Electrocardiograms of patient taken on the second day (first hospital day).

**Fig. 2.** Electrocardiograms of patient taken on the seventh hospital day.

**Fig. 3.** Clinical course of patient in relation to the cardiac arrhythmia and the drugs employed.

$V. T.$ = Ventricular Tachycardia; $S. R.$ = Sinus Rhythm.

**DISCUSSION**

In 1945 Babkin and Ritchie$^1$ demonstrated that quinine partially paralyzed the vagal inhibitory fibers of the dog's heart. Two years later, Gertler and Karp$^2$ observed that Atabrine possessed an identical property. This parallelism of pharmacologic effect and the established efficacy of quinidine, an isomer of quinine, in restoring regular sinus rhythm to hearts in auricular fibrillation and other cardiac arrhythmias suggested that Atabrine would be similarly effective. This hypothesis was soon verified in experimentally produced arrhythmias in dogs by Gertler and Karp$^3$ as well as in clinical trials on hospitalized patients by Gertler and Yohalem.$^4$

Following closely these initial encouraging clinical results, Vega Diaz$^5$ in 1948 reported a small series of six patients, four with paroxysmal auricular fibrillation, one with paroxysmal nodal tachycardia and one with paroxysmal...
auricular flutter. In four of the six patients, the author obtained very spectacular results with the return to sinus rhythm occurring in from 20 seconds to 10 minutes following the intravenous or intramuscular administration of Atabrine.

In 1949 Gertler and Yohalem reported a more extensive study on 26 patients with auricular fibrillation, two with nodal tachycardia, two with auricular flutter, and two with ventricular tachycardia. In those with auricular fibrillation, Atabrine gave successful results in 13 of 27 trials. Of added interest was the fact that quinidine, administered before Atabrine was given, was ineffective in 16 trials. Moreover quinidine and/or digitalis failed also in those patients in whom Atabrine, too, failed to restore a normal rhythm. In the other six cases with arrhythmias other than auricular fibrillation, Atabrine yielded successful results in three. The remaining unsuccessful ones included the two cases of ventricular tachycardia.

These authors concluded that the best results with Atabrine seemed to occur in older patients with arteriosclerotic heart disease and in younger patients in whom the arrhythmia was of less than 48 hours duration. The time of disappearance of the arrhythmias occurred at the time when the maximum blood levels of Atabrine had been reached following intramuscular injections of the drug. The only toxic effects noted were nausea and vomiting.

It would seem, therefore, that our single case of ventricular tachycardia treated with Atabrine, while not the first case so treated, could very well be the first reported case in which successful results were obtained with Atabrine in this type of arrhythmia. The literature would readily suggest that the therapeutic use of Atabrine as an antiarrhythmic should perhaps be limited to supraventricular arrhythmias. Nevertheless, the fact that we failed to restore normal sinus rhythm with more than adequate doses of Pronestyl first and quinidine later presented a situation in which we were forced to try any other known antiarrhythmic measure. Unlike the cases previously reported, Atabrine was administered orally rather than parenterally; however, the dose at which reversion to sinus rhythm occurred paralleled closely that which other authors found to be therapeutically effective.

The conclusion that Atabrine was responsible for the correction of the arrhythmia in this case seems very reasonable because such correction occurred at the time when the desired blood concentration must have been reached. That Pronestyl was not the effective measure in the control of the arrhythmia is very obvious. That control was not due to quinidine is also quite evident for two main reasons: First, the arrhythmia persisted in spite of clinical signs of quinidine toxicity; second, the reversal to sinus rhythm occurred not at the time when the plasma quinidine concentration was highest but rather about 16 hours after the last dose of quinidine.

This case also corroborates the observations of others regarding the lack of serious toxic effects of Atabrine even with such high doses as were given. Similarly, nausea and vomiting were the only side effects produced.

Incidentally our experience in this case further demonstrates the value of serial electrocardiograms not only for the study of the arrhythmia but for the disclosure of the underlying cardiac pathology. The electrocardiographic alterations of the latter may be significantly masked by the complicating arrhythmia, especially in ventricular tachycardia. The latter produces so much distortion in the ventricular complexes that most other conditions may not be sufficiently exhibited in the tracing. As soon as the normal mechanism is reestablished following correction of the ventricular tachycardia, the electrocardiographic features of myocardial infarction become evident.

Considering the gravity of ventricular tachycardia as a complicating arrhythmia in myocardial infarction and the success obtained in this case with Atabrine, after vain attempts with Pronestyl and quinidine, this single experience should reawaken interest in further studies on Atabrine in ventricular tachycardia. While this report is not intended to indicate that Atabrine is superior to either Pronestyl or quinidine, it nevertheless adds additional clinical evidence of the antiarrhythmic properties
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of Atabrine not only in supraventricular arrhythmias, but in ventricular tachycardia as well.

SUMMARY

The abolition by Atabrine of ventricular tachycardia in a 60 year old male patient is reported. Atabrine restored normal sinus rhythm after Pronestyl and quinidine failed to do so.

Atabrine was given orally in doses of 0.30 Gm. every two hours. Reversal to sinus rhythm was noted after the fifth dose. The only toxic effects produced were nausea and vomiting, which occurred once following the fifth dose.

The underlying disease, myocardial infarction, became obvious as sinus rhythm was restored. This illustrates the value of serial electrocardiographic studies particularly in the presence of ventricular tachycardia which in this case masked the electrocardiographic features of myocardial infarction.

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