The Electrocardiographic Effects of Intravenous Veratrum Viride

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Previously unnoted T-wave inversions in the precordial leads resulting from the intravenous injection of veratrum viride are described. Evidence is presented that these changes are not caused either by the hypotensive action of the drug or by myocardial anoxia or by hypopotassemia. The T-wave inversions probably result from vagal stimulation which cause altered ventricular repolarization.

EXCELLENT articles have appeared on the hypotensive effects of the drug veratrum viride. There have been no systematic studies, however, of the electrocardiographic effects of the veratum alkaloids. In four out of eight patients given protovatrine intravenously, Meilman and Krayer found a temporary return to normal of a flat or inverted T wave in lead I, but they studied only the limb leads. Fries and Stanton also reported reversal of the strain pattern of hypertensive heart disease after treatment with oral veratrum viride. While the hypotensive actions of intravenously administered veratum alkaloids were being investigated in our laboratory, certain electrocardiographic changes which have not been reported were observed; these changes are the basis of this report.

Patients and Materials

When this investigation was begun three years ago, the purified alkaloids of veratrum were not available; Veratroine* was therefore used. This preparation is an alcoholic solution of the mixed alkaloids of veratum viride, each cubic centimeter containing 2.5 mg. of the alkaloids. A dose of 0.3 to 0.5 mg. was measured with a tuberculin syringe, diluted with physiologic saline to 1.0 cc. and given intravenously in two to three minutes. This dose was used irrespective of weight or age since we found that it uniformly produces a significant vaso-depression.

Eighteen patients from 29 to 66 years of age were selected from the clinic and hospital for study; 15 were men and 3 were women. All these patients had a blood pressure over 150/100, most of them for more than five years; one patient had a blood pressure of 150/90 with a previously established diagnosis of chronic essential hypertension.

Electrocardiographic changes were observed at frequent intervals on a Sanborn Visocardette. In two patients only standard limb leads were recorded, and in one, only the standard and CF leads. In the remaining patients, standard and unipolar limb leads and precordial leads were recorded.

Results

In eight of the patients, a control injection of 1.0 cc. of normal saline given intravenously one half hour before the veratrum had no effect on the blood pressure or electrocardiogram. The electrocardiographic effects observed following the intravenous administration of veratrum viride may be divided into two main groups.

1. Rhythmity, Conductivity, and Irritability Effects

Three patients developed ectopic rhythms after receiving 0.5 mg. of veratrum. In one patient nodal rhythm occurred and persisted for about one minute. The other patient developed second degree A-V block, accompanied by ventricular premature systoles of eight minutes' duration. This was soon followed by complete A-V dissociation with idioventricular rhythm of variable rate, during which time the blood pressure dropped rapidly. Atropine

*Veratroine is marketed by Parke, Davis and Company.
(1.3 mg.) was given by vein and a normal sinus rhythm was restored within five minutes. The third patient developed ventricular premature systoles of brief duration.

2. T-Wave Changes

The T-wave alterations were of several types and are grouped as follows: (a) change from upright to inverted T, observed four times; (b) inversion of ascending or descending limb of T, seen three times; (c) increase of inversion of control inverted T, seen four times; (d) decrease of inversion of control inverted T, seen twice; (e) change from inverted to upright T, seen once; (f) no change, observed in one patient.

Of 15 patients studied with precordial leads, 11 exhibited some of the six changes just stated. The T-wave changes in the precordial leads varied in type and degree in different electrocardiographic positions. Inversion of the T waves was most pronounced in leads V4 and V5. Inversion of the terminal portion of the descending limb of the T wave was usually seen in V2 and V3; occasionally, the descending limb of T was inverted in V1 and V2, and the ascending limb in V4 to V6.

The most marked increase in inversion of the T wave was from a control negativity of 2 mm. to a negativity of 4 mm. in leads V4 to V6 (fig. 1); this lasted for 90 minutes. As shown, the initially upright T wave in leads I, V5, and V6 became inverted, while the T wave in lead II decreased in amplitude and the T wave in lead III became taller. Other T-wave inversions after veratrum viride are shown in figures 2 and 3. One patient showed a change from an inverted T in lead III to an upright T...
without T-wave changes in precordial leads. T-wave changes in limb and precordial leads, therefore, are not always correlated.

Nitroglycerin, oxygen, Neosynephrine, and atropine were given to several patients in whom the veratrum preparation produced T-wave changes. In two patients, nitroglycerin, 0.4 mg. sublingually, did not influence the inverted T waves (fig. 1). In two subjects, 100 per cent oxygen administered for 5 to 15 minutes by mask caused no change (fig. 2).

As seen in figure 3, the vasopressor effect of 1.0 mg. of Neosynephrine given intravenously was associated with a reversal of the inversion of the T waves. In three other patients similar effects in leads V₄ and V₅ followed Neosynephrine administered intravenously in doses of 0.3 to 0.7 mg.

Atropine in doses of 0.65 mg. to 2.6 mg. was given intravenously to three patients 10 to 30 minutes before the injection of Veratrone. It was also administered in the same doses intravenously to three other patients 15 to 40 minutes after the injection of Veratrone, at a time when maximum electrocardiographic changes had developed. In one patient illustrated in figure 2, atropine, 1.2 mg. given 15 minutes after the administration of Veratrone, changed the inverted T waves in the precordial leads to the upright configuration seen in the control record. When, on a different occasion, the same patient was given 1.2 mg. of atropine 30 minutes prior to Veratrone, inversion of the T waves in the precordial leads did not occur. Comparable findings were noted in another patient who received atropine both before and after veratrum viride. In one subject, atropine given 20 minutes prior to veratrum...
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Veratrum viride prevented inversion of the T waves in V3 and V4, and in another patient atropine given 20 minutes after veratrum viride altered the inverted T wave in V4 to upright.

In one patient veratrum viride elevated rather than inverted the precordial T waves: the left ventricular strain pattern, best seen in leads V5 and V6, disappeared five minutes after the injection of 0.3 mg. of the drug and did not reappear for at least 20 minutes.

DISCUSSION

The observations in the present experiments that, following the administration of veratrum, upright T waves, especially in the precordial leads, became inverted suggest the possibility that myocardial anoxia developed as blood pressure fell. This concept seems to be supported by the resemblance of the inverted T waves to those seen in myocardial anoxia. The appearance of these changes during the drop in blood pressure, and their disappearance after the blood pressure was elevated by pressor drugs, suggests the presence of anoxia. Although it is well known that myocardial anoxia can be produced when the blood pressure is reduced to low levels, it has not been demonstrated that this necessarily exists during relative hypotension, or a drop from hypertensive to normal levels. Many factors other than anoxia, such as drinking cold water,5 thermal alteration of ventricular repolarization,6 and drugs and other agents, have been shown to cause inversion of the T waves in the electrocardiogram.

None of the patients developed abnormal Q waves, although the T-wave inversion persisted as long as one and one-half hours and the

![Image of electrocardiogram](http://circ.ahajournals.org/)

Fig. 3. T-wave inversions resulting from 0.5 mg. of veratrum viride apparently reversed by the pressor effect of 1.0 mg. of Neosynephrine. Discussed in text.
blood pressure was reduced to subnormal levels. Anginal symptoms did not occur during these experiments; this is in accord with the observations of Meilman and Krayer that the administration of protoveratrine by vein to two patients with a history of angina did not aggravate the symptoms.

Nitroglycerin and oxygen had no effect on the T-wave alterations; this suggests that veratrum does not cause coronary vasoconstriction. The T-wave inversions appeared at normal or subnormal blood pressure levels in some patients, before the hypotensive effect had developed, and persisted after the major hypotensive effect had subsided. In several patients these changes had disappeared before the blood pressure rise (due to diminution of veratrum effect) had started. Since the T-wave inversions may occur independently of the blood pressure changes, the latter do not necessarily cause the former.

The duplication of the T-wave alterations by the application of carotid sinus pressure (fig. 4), either before or after the injection of veratrum, is a most interesting finding and suggests that vagal stimulation can influence repolarization of the myocardium. However, the blood pressure lowering effect of carotid sinus pressure noted in figure 4 cannot be separated from its vagal stimulating action, except by the fact that hypotension caused by carotid sinus pressure (fig. 4) occurred within at least four seconds after the application of pressure, whereas the hypotension resulting from veratrum did not develop for 8 to 15 minutes after the administration of the drug. If hypotension causes myocardial anoxia, it would seem that more than four seconds would be required for it to develop. Furthermore, Levine has reported that carotid sinus pressure relieves angina by virtue of the decreased demand for coronary flow during a slower heart rate. This relief of angina would hardly support the concept of myocardial anoxia.

With regard to the parasympathomimetic action of veratrum, it is of interest that the one patient who developed A-V dissociation had been on digitalis for several weeks prior to the experiment, so that veratrum probably accentuated the vagal and/or cardiac action of digitalis. There is evidence that other parasympathomimetic drugs, such as Mecholytl, can invert T waves, although these effects have been studied only in limb leads.

The disappearance of the left ventricular strain pattern in one patient is difficult to explain. Since coronary vasoconstriction does not occur in these experiments, it is suggested that veratrum alters ventricular repolarization by reason of its vagal stimulating action. This idea gains some support from the work of Hellerstein and Liebow who found T-wave changes as a result of thermal alterations of the properties of the endocardium and/or epicardium. They reported that when an electrode is near an area of retarded repolarization, the T wave becomes negative and vice versa. It is possible that the veratrum-induced vagal stimulation caused retarded epicardial repolarization and, thereby, produced reversal of the T-wave changes discussed above. In the case of the patient with normalization of left ventricular strain pattern, it is possible that there occurred relatively greater delay in subendocardial repolarization, thereby producing upright T waves.

A further possibility suggests itself. Bellet has shown in both animals and man that inverted precordial T waves without QRS changes can occur as a result of hypopotassemia. There is a close resemblance between the inverted T waves in our experiments and

FIG. 4. Effect of carotid sinus pressure before veratrum viride (1) and after administration of the drug (2) in patient T. H. Also illustrated in figure 3. Discussed in text.
in those of Bellet's experiments. The possibility of a relationship between veratrum and hypopotassemia was tested by comparing the plasma potassium levels before and after the injection of 0.5 mg. of veratrum in eight patients (table 1). The plasma potassium concentration was not significantly changed after veratrum. Despite the occurrence of vasodepression in these patients, inverted precordial T waves were seen in only two patients. The possibility is not excluded that in a larger series plasma potassium may be found to be altered. Furthermore, plasma potassium determinations were done only during the maximum hypotensive response, but not after that period. This facet of the investigation indicates that intravenous veratrum viride does not alter plasma potassium during the maximum fall of blood pressure.

The concept of reflex vasodepression via the vagus has arisen largely on the basis of experimental work with this drug. Von Bezold and Hirt11 and Jarisch and Richter12 observed in animals a vasodepression and bradycardia which was abolished by sectioning the vagi; this is known as the Bezold effect. It has been shown, notably by Dawes,13 that the left ventricle is the most important receptor site for the afferent arc of the Bezold reflex; the efferent pathways for this reflex are incompletely known. It was noted in our experiments that the precordial T-wave inversions usually occurred in complexes of left ventricular origin. This lends indirect support to the idea that the left ventricle is a site of the efferent arc of the Bezold reflex.

**Summary and Conclusions**

1. Veratrum viride in doses of 0.3 to 0.5 mg. was administered intravenously to 18 hypertensive patients and electrocardiographic effects were studied.

2. Two patients developed ectopic arrhythmias and one patient had second degree A-V block and A-V dissociation.

3. Hitherto unnoted T-wave inversion, chiefly in leads V₄ and V₆, are described. These changes are not necessarily related to the hypotensive effect of the drug and are not affected by oxygen or nitroglycerin. The pressor effect of Neosynephrine and atropine abolished these T-wave changes. In one patient, vagal stimulation by carotid sinus pressure reproduced the T-wave inversions. Although the latter resemble the T-wave inversions of hypopotassemia, no alterations in blood potassium were found during the period of maximum hypotensive action of the drug.

4. The parasympathomimetic action of veratrum viride can cause T-wave changes which very likely are not the result of myocardial anoxia, but rather of altered ventricular repolarization.

**Sumario Español**

Inversiones de las ondas T previamente no notadas en la derivaciones precordiales resultado de inyeccion intravenosa de veratrum viride se describen. Evidencia se presenta de que estos cambios no son causados por la accion hipotensa de la droga ni por la anoxia del miocardio o hipopotassemia. Las inversiones de las ondas T probablemente resultan debido a estimulación vagal que causa repolarización ventricular alterada.

**References**


