THE EFFECT OF NITRITE AND EXERCISE ON THE INVERTED T WAVE

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Received December 12, 1945

No unequivocal explanation has so far been found of the inverted T wave in the abnormal human electrocardiogram. It is likely that the deformed T wave associated with coronary disease is the outcome of cardiac ischaemia, but this does not appear to explain the mechanism of T-wave inversion in ventricular preponderance where a shift of the heart may play a part. The earlier papers dealing with temporary cardiographic changes in cardiac ischaemia and with the experimental evidence that nitrite increases the blood supply to the myocardium were reviewed by Evans and Hoyle (1933), who studied the effect of nitrite on the inverted T wave. In a series of 23 cases that showed deformity of the T in the form of flattening, diphasic change, or inversion, this component was wholly or partly corrected in 11 following the administration of the vasodilator. They concluded that elevation of the inverted T wave by nitrite in patients with angina pectoris was determined by the relief of myocardial ischaemia, and suggested that further observations might show that the fixed T wave and the one elevated by nitrite had a different significance, and that this might prove to be a measure of the collateral circulation around a damaged portion of heart muscle. Only nine of their cases, however, were of simple cardiac infarction without hypertension or aortic valvular disease, and in only three of these was the T wave corrected by nitrite. Exercising patients with coronary insufficiency will sometimes cause R-T depression or even inversion of the T wave; in others it may correct the deformity. Such changes were considered by Master, Friedman, and Dack (1942), as evidence of coronary abnormality. May (1939) observed that a lowering of the T wave, sometimes with S-T depression, as a result of the oxygen deficiency, gradually induced, is much more common in young athletic subjects than in older people. Levy, Alvan, and Bruenn (1938) agreed that oxygen want caused cardiographic alterations in healthy subjects as well as in patients with heart disease, but showed that the change was far greater when the coronary circulation was impaired. The effect of the administration of oxygen on the cardiogram of cyanosed patients was studied by Edson (1942), who found that the deformed T wave was not always corrected and especially in cases of recent coronary occlusion, while in some depression of the R-T segment or an increase in the degree of inversion of the T wave resulted. An understanding of T-wave changes in relation to myocardial nutrition is still far from complete. An explanation of the altered T wave of ventricular preponderance does not at first sight concern the relief of cardiac ischaemia. In practice, the similarity of the T I type of cardiac infarction and the inversion of T from hypertension or aortic valvular disease is a common problem in differential diagnosis. The chest lead CR₇ of Evans and Hunter (1943) may sometimes assist this differentiation, while the administration of potassium salts (Sharpey-Schafer, 1943) might help if it were a safe method. The following observations on the effects of nitrite and exercise on the inverted T wave were made to evaluate the help that such tests might afford in deciding this common clinical and cardiological problem.

THE INVESTIGATION

Forty-five cases showing deformity of the T wave in their cardiograms were selected for the tests, and were divided into four groups; 16 cases of cardiac infarction (Group I); 13 of

hypertension without clinical evidence of coronary changes (Group II), 9 of cardiac infarction with hypertension (Group III), and 7 cases of aortic valvular disease (Group IV). The criteria adopted in the separation of Groups I and III were a resting blood pressure of 170 mm. systolic at the time of the test or recorded on a previous occasion, and cardiac enlargement on cardiography. In Group I, 10 cases of infarction were of the T I type (Parkinson and Bedford, 1928) and 6 of the T III type. Of those cases of infarction with hypertension (Group III), 3 showed cardiographic changes of the T I type and 6 of the T III type. The 20 cases of "left ventricular preponderance" who gave no history of pain that would have been interpreted as indicating coronary disease were made up of 10 cases of simple hypertension, 2 of malignant hypertension, 1 of chronic nephritis with hypertension (Group II), 1 of aortic incompetence, 1 of congenital sub-aortic stenosis, and 5 of aortic stenosis and incompetence (1 rheumatic, 2 atherosclerotic with hypertension, and 2 of syphilitic origin) (Group IV). Eleven of Group II showed changes in the T wave in lead I, as did all the cases in Group IV with the exception of

FIG. 1.—The effect of amyl nitrite and of exercise on the deformed T wave of three cases of cardiac infarction. (A) At rest. (B) After nitrite. (C) After exercise.

the patient with a congenital lesion, and in none of them was the inversion of T in IVR greater than in CR₇. At the start of this investigation other leads showing inversion of the T wave were studied, but in most the lead that showed the greatest deformity was selected whether it was lead I, lead II or lead IVR except that lead III was never used.

Nitrite was administered as follows. A capsule of amyl nitrite (5 minims) was broken in a gauze swab below the nose of the patient who was previously reassured as to the safety of the procedure. Four or five deep inhalations were taken. The selected lead was then recorded at half-minute intervals and the blood pressure noted regularly. After an interval, and often on another occasion, glyceryl trinitrate was chewed. Many patients received 3/100 grain, but as a rule a dose of 1/50 or 1/100 grain was taken. Several tracings were then recorded at intervals as well as blood pressure readings.

The exercise test took the form of bending repeatedly to touch the toes, or of raising and lowering the legs with the knees straight while the subject reclined on a couch with the electrodes in position. In order to avoid any influence of drugs, this test was always performed before the administration of the nitrites, and a sufficient interval was allowed between the different procedures for the pulse rate and for the tracing to return to their resting states. Exercise was continued for a few minutes until the patient became fatigued or breathless. Standard exercise tests, such as those devised by Master, Friedman, and Dack (1942) were

not attempted owing to the variable capacity of the subjects. The performance of this test on the couch minimized loss of time before recording the tracing, for Master and his co-workers stated that occasionally the cardiographic changes produced by exercise may disappear within one minute of the cessation of exertion.

RESULTS

In Table I are analysed the effects of nitrite and exercise on the abnormal T wave. Nitrite corrected the deformity in six cases of Group I (37 per cent), in seven of Group II (54 per cent), in two of Group III (22 per cent), and in none of the seven cases of Group IV. In one case

FIG. 2.—The effect of amyl nitrite and of exercise on the deformed T wave of four cases of hypertension. (A) At rest. (B) After nitrite. (C) After exercise.

in each of the first three groups the deformity of the T wave was accentuated. Elevation of this component resulted from exercise in 9 of 16 cases (56 per cent) of simple cardiac infarction (Group I), and in but 2 of the 13 cases (15 per cent) of hypertension without apparent coronary disease (Group II). Of these two, one was a case of benign hypertension, the other of malignant hypertension. Exercise did not alter the T wave in any case of aortic valvular disease (Group IV). No change resulted from nitrite or exercise in four cases of Group I (25 per cent), five of Group II (38 per cent), six of Group III (67 per cent), and seven of Group IV (100 per cent). Only among the cases of cardiac infarction without hypertension (Group I) were found instances of correction of the T wave from exercise but not from nitrite (25 per cent). On the other hand, in Group II five cases showed an elevation with nitrite but not with exercise whereas only one in Group I met with correction from nitrite alone.

TABLE I
THE EFFECTS OF NITRITE AND EXERCISE ON THE ABNORMAL T WAVE

Diagnosis	Effect of Nitrite			Effect of Exercise		
	Deformity corrected	No change	Deformity accentuated	Deformity corrected	No change	Deformity accentuated
Cardiac infarction (16)	6	9	1	9	6	1
Hypertension (13)	7	5	1	2	11	0
Cardiac infarction and hypertension (9)	2	6	1	1	7	1
Aortic valvular disease (7)	0	7	0	0	7	0

FIG. 3.—The effect of amyl nitrite and of exercise on the inverted T wave of a case of aortic stenosis with incompetence. (A) At rest. (B) After nitrite. (C) After exercise.

After glyceryl trinitrate, in only 5 of the total 45 cases was any change in the T wave noted, of which 2 received 3/100 gr.; 2, 1/50 gr.; and 1, 1/100 gr., whereas 18 of the cases showed some change after amyl nitrite. These cardiographic changes tended to occur three to five minutes after the patient started to chew the trinitrin and half to one minute after the inhalation of amyl nitrite. The fall of blood pressure after amyl nitrite was swifter, and was generally accompanied by flushing, palpitation, and occasionally faintness, and, although it lasted only one to two minutes, was more dramatic than that which resulted from chewing the tablet. A fall of 30 to 40 mm. pressure was common in cases with resting systolic pressures within normal limits. In subjects with hypertension a fall of 60 to 80 or even 100 mm. was recorded half to one minute after the inhalation, but the original pressure was reached a minute or so later. In few cases, usually those receiving the larger doses of glyceryl trinitrate, there was a corresponding fall of the systolic pressure recorded, and the effect took two to five minutes to develop. Peripheral vasodilatation was less marked, and with the exception of one instance of collapse in an elderly woman who received 3/100 gr., the subjective discomfort was far less. From these results there would appear to be no close association between the fall in blood pressure and the incidence of cardiographic change. Tachycardia was frequent within one minute of amyl nitrite administration, but only a slight increase of pulse rate was noted after trinitrin, presumably because of the factors mentioned, namely, less subjective disturbance and smaller and more gradual fall in blood pressure after the solid preparation. Judging from the results of amyl nitrite administration, there seemed no obvious association between tachycardia and correction of the T wave, as a high pulse rate was noted as frequently with no change in the T wave as in those with an alteration of the complex; there were instances where a case of cardiac infarction, showing correction of the T wave by exercise, failed to show any cardiographic change after nitrite, in spite of a higher heart rate; also, if tachycardia were responsible for this correction, a greater number of cases might be expected to show it after exercise in Group II. Although exercise in most cases caused an increase in the blood pressure (e.g. 150/120 to 195/140, 140/90 to 180/100, and 250/120 to 280/140) there seemed no relation between the degree or frequency of changes in the blood pressure and cardiographic records in any group.

Changes in the R-T segment were also noted, although only T wave alterations have been mentioned. In three cases of cardiac infarction R-T depression occurred with exercise but the T wave became taller, and in another the T wave was unchanged in spite of slight R-T depression.

DISCUSSION

The present results with nitrite are comparable with those obtained by Evans and Hoyle (1933); 18 of a total of 45 cases showed a change in the T wave after administration of the vasodilator, whereas the figures of the previous observers were 11 of 23 cases. In the present series, in 6 of the 16 cases of cardiac infarction in Group I the deformity was corrected whereas the comparable figures in the 1933 publication were 3 out of 9 cases. Turning to Group II one finds a more frequent change in the T wave after amyl nitrite in cases of hypertension without apparent coronary lesions than in those with infarction. In 7 of the 13 cases the T wave was corrected in Group II (54 per cent) compared with 6 of 16 cases in Group I (37 per cent). If the cases of left ventricular preponderance including hypertension and aortic valvular disease (Groups II and IV) were not separated, the figures for correction by nitrite would be closer (35 per cent for Group II + Group IV). The effect of nitrite, therefore, cannot serve usefully in differentiating the cardiogram of cardiac infarction from that of left ventricular preponderance. The elucidation of cardiographic changes of the T I type occurring with hypertension and coronary pain must depend as yet on the history and on the clinical findings, while some help may be obtained from the chest lead CR₇ of Evans and Hunter.

If the relief of myocardial ischaemia is the only factor determining correction of the deformed T wave of infarction, difficulty arises in the explanation of similar cardiographic changes after exercise. An increase in the general circulation rate will lead to a greater coronary circulation rate unless the vessels are completely occluded (Peel, 1943). It is a well-known fact that patients with angina are sometimes hindered by pain at the start of a walk, but after a short distance may gain their "second wind" and complete the journey without further interruption. Anginal pain, however, accompanied the elevation of the T wave in four cases of this series, which fact does not conform to the theory of improved coronary flow with a certain amount of exertion. There is no doubt that both amyl nitrite and glyceryl trinitrate cause dilation of the coronary arteries and that these drugs will prevent the pain and also the associated R-T depression or T wave inversion, produced by exercise in some patients with angina. It is difficult to explain why glyceryl trinitrate, generally considered as powerful an antispasmodic as amyl nitrite, if not so prompt in action, does not produce comparable correction of the inverted T wave. The possibility that tachycardia induced by the volatile drug and by exercise, might influence this cardiographic alteration has already been discussed with cautious disbelief. These conclusions are in agreement with those of Evans and Hoyle.

As regards the cardiogram of left ventricular preponderance, the characteristic changes, including T-wave inversion, are presumed to depend on the anatomical configuration of the cardiac chambers in relation to each other and to the chest as a whole, and not on the condition of the heart muscle (Master, 1942). Myocardial ischaemia is not considered to be a factor. One may next look to a change in posture of the heart to explain the correction by nitrite of the hypertensive T wave deformity. A recent claim by Goldberger (1945), that such changes are similar, if not identical, with those produced by deep inspiration, requires consideration. Goldberger associates this correction with rotation of the heart and suggests that, although other factors may take part, this same mechanism underlies the effects of nitrite. The heart, which according to Scherf and Zdansky (1929) decreases in size following inhalation of this drug, is assumed by Goldberger to lie more vertically, and thus rotation would occur as in the assumption of the upright posture with deep inspiration. Hyperventilation was also often observed after amyl nitrite inhalation. From a comparison of the changes induced in the inverted T wave by deep inspiration in the upright position with those due to amyl nitrite, it would appear that the alteration of cardiac posture must play little if any part in the effects of the vasodilator (Fig. 4). Four cases of infarction and seven of hypertension were tested for such effects. When the selected lead (lead I in ten cases, lead II in one case) had been recorded with the patient lying flat, it was repeated in the upright posture during deep inspiration. Amyl nitrite was subsequently administered with the subject in the reclining position so that the effect of the vasodilator on the cardiogram could be compared with that of cardiac tilt. Only in one of the four cases of cardiac infarction and in two of the seven cases of hypertension so tested, did postural change with depression of the diaphragm cause a very slight correction of the deformed T wave. The effect of amyl nitrite on the size of the heart needs to be confirmed, but my results from varying the posture of patients with deformity of the T wave in

FIG. 4.—The effect of amyl nitrite and of deep inspiration in the upright posture on the deformed T wave of two cases of hypertension and one of anterior cardiac infarction. (A) Supine. (B) After nitrite. (C) Upright inspiration.

the cardiogram are not in agreement with those of Goldberger. Meanwhile, no satisfactory explanation is forthcoming for the correction by nitrite of the inverted T wave of hypertension.

SUMMARY AND CONCLUSIONS

The effect of nitrite and of exercise on the inverted or depressed T wave of the cardiogram was studied in 45 patients. These were divided into four groups. Group I consisted of 16 cases of cardiac infarction without hypertension, Group II of 13 cases of hypertension without clinical evidence of coronary disease, Group III of 9 cases of infarction with hypertension, and Group IV of 7 cases of aortic valvular disease.

Inhalation of amyl nitrite will often correct the inverted T wave of the cardiogram in cardiac infarction (6 of 16 cases). As often it will correct the deformed T wave of hypertension (7 of 13 cases) but no such changes resulted in any of the 7 cases of aortic valvular disease.

Exercise will give similar results in that it righted the deformed T wave in 9 of 16 patient with cardiac infarction, and in 2 of the 13 with hypertension; in none of the 7 with aortic valvular disease was there any change.

In 11 cases the T wave of the cardiogram taken when the patient was in the upright posture, with the diaphragm depressed by deep inspiration, was seldom different from the tracing in the supine posture on quiet respiration.

It is not even certain that the corrected T wave from nitrite inhalation and exercise is brought about by the relief of myocardial ischaemia since the deformed T wave of hypertension responds in the same way. Tachycardia and variation in blood pressure and of posture seem to play no part in such correction.

The tests of amyl nitrite inhalation, exercise, and change of posture will not assist in differentiating the cardiographic pattern of cardiac infarction from that of hypertension.

I am indebted to Dr. William Evans for his advice, and to Dr. E. Miles, Medical Superintendent of Oldchurch Hospital, for facilities for this investigation.

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