Effects of beta-receptor blocking agents propranolol and practolol on ST-T changes in neurocirculatory asthenia

Eliana Wolf, Karl Braun, and Shlomo Stern

From the Department of Physical Medicine and Rehabilitation, and the Cardiovascular Laboratory, Hadassah University Hospital and Hebrew University - Hadassah Medical School, Jerusalem, Israel

In 10 patients with neurocirculatory asthenia the effect of two adrenergic beta-blocking drugs, propranolol and practolol, were studied on the ST-T changes observed in the resting electrocardiogram and on those occurring under orthostatic conditions. The drugs were administered intravenously on different occasions. Propranolol improved the ST-T abnormalities in the resting electrocardiogram in all 10 patients and in 6 even restored the tracing to normal. In the same 10 subjects, practolol improved the abnormalities in 8, restored them to normal in 4, while in 2 patients no change occurred under the influence of this drug. Propranolol resulted in complete disappearance of orthostatic ST-T changes in 6 out of 9 patients and improved the tracing in the others; practolol improved the orthostatic electrocardiogram in 6 subjects, but in none was a complete return to normal observed.

'Neurocirculatory asthenia' is characterized by praecordial symptoms, dyspnoea, palpitation, and sometimes sweating, tremor, and fatigue, in subjects without signs of organic heart disease. Recently, a better understanding of the autonomic nervous system and its alpha- and beta-subdivisions led to the use of the terms 'hyperkinetic heart' or 'hyperdynamic beta-adrenergic circulatory state' to describe this entity (Gorlin, 1972; Fröhlich, Tarazi, and Dunstan, 1969). Neurocirculatory asthenia is usually accompanied by a normal electrocardiogram (White, Cohen, and Chapman, 1947; Kannel, Dawber, and Cohen, 1958). In some rare cases the electrocardiogram of such patients in the resting state may, however, disclose changes in the ST-T segment (Holmgren *et al.*, 1959; Levander-Lindgren, 1962). The beneficial effect of the beta-receptor blocking drug propranolol on various haemodynamic variables, as well as on the clinical manifestations of neurocirculatory asthenia seems to be well established (Bollinger *et al.*, 1966; Schweitzer, Pivoňka, and Gregorová, 1968; Rosenblum and Delman, 1970; Marsden, 1971). The effect of this drug on the ST-T abnormalities occasionally observed in these patients has, however, not been fully investigated, and no data are

available on the effect of the newer and more selective beta-blocking drug, practolol, in this respect. Orthostatic electrocardiographic abnormalities and tachycardia are other interesting features of neurocirculatory asthenia, and the effect of propranolol on these changes has been studied by Nordenfelt (1965).

In this study we describe the influence of two beta-receptor blocking drugs, practolol and propranolol, administered intravenously, in 10 patients with neurocirculatory asthenia who exhibited ST-T changes in their resting electrocardiogram. We also studied the effect of these drugs on the orthostatic electrocardiographic abnormalities in the same patients.

Patients and methods

Ten patients with neurocirculatory asthenia were investigated in the course of this study (5 women, aged 16 to 35, and 5 men, aged 20 to 37). All suffered from palpitation, fatigue, shortness of breath, and some of them from chest pain not induced by effort. In all of them consistent ST-T abnormality was found in the resting electrocardiogram or in serial tracings recorded weeks apart, in the standard or chest leads or both. None of the patients had received any medication for at least 10 days before the test. A multistage bicycle test was performed on a Quinton bicycle with heart rate, blood

pressure, and electrocardiogram monitoring. The initial load of 200 kg m/min was increased by increments of 200 kg m/min, and every work load was performed for 5 minutes with a subsequent rest period. The exercise was continued until the heart rate rose to 170 a minute. Severe general or leg fatigue was also an indication to discontinue the test. An orthostatic electrocardiogram test was done in the following manner: after recording pulse rate, blood pressure, and resting electrocardiogram, these measurements were repeated in the erect position after 1 minute of standing, and again after 8 more minutes of standing. Propranolol, 5 mg, or practolol, 15 mg, diluted in 15 ml normal saline was then injected intravenously during 5 minutes. Pulse rate, blood pressure, and electrocardiogram were recorded every 5 minutes for a period of 60 minutes after the injection. An electrocardiogram in the supine position was again recorded, and the orthostatic test was then repeated, as before. On another occasion, but within 14 to 21 days of the first test, the same procedure was repeated in the same subjects but with the injection of the drug not used the first time. No medication of any sort was given to the patients between the two tests. In 5 of the patients propranolol was used in the first test and practolol in the second, while in the other 5 the order was reversed.

Results

The results of the exercise tests are summarized in Table 1. It can be seen that a normal exercise tolerance was observed in only 4 of the patients; it was reduced in 3 and much reduced in the other 3 patients. Table 2 details the resting electrocardiographic abnormalities and shows that 7 of the patients had persistent sinus tachycardia in the resting supine position. Both propranolol and practolol reduced the heart rate to more or less the same extent. The abnormalities after propranolol

improved in all 10 patients and in 6 of them even returned to normal. The injection of practolol improved the ST-T abnormalities in 5 patients, but only in 4 did the electrocardiogram become completely normal; in 2 patients practolol had no effect at all on the ST-T abnormalities. The blood pressure was much more reduced after propranolol than after practolol. An illustrative figure showing an electrocardiogram at rest and after propranolol and practolol is shown in Fig. 1.

In all 10 patients there was pronounced acceleration of pulse rate up to 105 to 140 a minute in the standing position (Table 3). Orthostatic ST-T changes, additional to those observed in the resting record, occurred in 9 of the 10 patients. These were mainly T wave changes and in only two patients was slight ST depression observed. The injection of propranolol and practolol induced a significant reduction of the heart rate in the standing position in all patients, but propranolol had a slightly greater influence in this respect. During administration of both of these drugs, we observed a slight but definite decrease in the systolic and diastolic blood pressure in the standing position, again slightly more so after the infusion of propranolol. Propranolol resulted in complete disappearance of the orthostatic electrocardiographic abnormalities in 6 of the 9 patients. In the remaining 3, slight T wave abnormalities prevailed in the standing position. Practolol, on the other hand, improved the orthostatic ST-T abnormalities in 6 of the 9 patients, but in none was a complete return to normal electrocardiogram observed. Two illustrative figures showing the electrocardiogram in the standing position and after propranolol and practolol are given (Fig. 2-3).

TABLE 1 Results of multistage bicycle exercise test in 10 patients with neurocirculatory asthenia

Case No.	Sex	Age (yr)	Bicycle test			
			Submaximal effort (kg m/min)	Heart rate	Exercise tolerance	Electrocardiographic abnormalities (in addition to those present in supine position)
1	M	28	800	165	Normal	No change
2	F	24	300	175	↓↓	No change
3	F	19	200	175	↓↓	No change
4	M	20	600	175	↓	Negative T in III, aVF
5	F	30	500	170	↓	Negative T in III, aVF
6	F	16	500	165	Normal	No change
7	M	37	600	170	↓	No change
8	F	35	600	170	Normal	No change
9	M	21	500	175	↓↓	ST depression of 1 mm and negative T in V ₄
10	M	27	800	140	Normal	Negative T in III, aVF, V ₄

↓ = Reduced.

↓↓ = Very reduced.

TABLE 2 *Electrocardiogram, heart rate, and blood pressure in supine position in 10 patients with neurocirculatory asthenia before and after intravenous injection of practolol and propranolol*

Case No.	Before injection			After injection of propranolol			After injection of practolol		
	Electrocardiogram in supine position	Heart rate	Blood pressure (mmHg)	Electrocardiogram in supine position	Heart rate	Blood pressure (mmHg)	Electrocardiogram in supine position	Heart rate	Blood pressure (mmHg)
1	Flat T in III, aVF, V4-6	75-85	130/85	Normal	52	90/70	T positive in V4-6	55	110/40
2	Flat and negative T in V3-6	115-125	120/80	Normal	55	105/60	Flat and slightly positive T in V3-6	65	110/60
3	Flat T in III, aVL; ST depression 1 mm in V4-5	115-125	130/80	Normal	75	105/70	Normal	70	110/60
4	Biphasic T in III, III, aVF	70-80	130/80	Normal	65	130/80	Normal	65	130/80
5	Flat T in all leads	90-100	110/80	Normal	67	110/80	Normal	70	110/80
6	Flat T in III, aVF	70-80	110/70	Normal	58	100/60	Normal	60	110/70
7	Flat T in all leads	85-95	140/90	Positive T in I, II, aVL, V2-4	60	110/80	No change	60	120/80
8	Flat T in V2-3	90-100	120/80	T more positive in V2-3	65	105/70	Slightly positive T in V2-3	75	100/80
9	Flat and biphasic T in I, II-III, aVL, aVF	95-105	110/80	Positive T in II, aVL	75	100/70	No change	72	110/70
10	Biphasic T in II-III, aVF, V4-6	95-105	120/85	T slightly positive in all leads	60	110/70	T slightly positive in V4-6	60	110/70

Discussion

The purpose of the present study was to compare the effects of the two beta-blocking agents propranolol and practolol on the electrocardiographic abnormalities at rest and after an orthostatic test in patients with neurocirculatory asthenia. We demonstrated that propranolol improved the ST-T abnormalities in the resting electrocardiogram in all these patients, whereas practolol did so in only 8 of the 10. The number of tracings that returned to normal was also higher after propranolol than after practolol. Because of this effect these drugs appear to be useful for the differentiation of the benign electrocardiographic abnormalities of neurocirculatory asthenia from those induced by organic heart disease. Earlier reports have shown an improvement in ST-T abnormalities in patients with neurocirculatory asthenia after a single oral dose of propranolol (Noskiewicz and Chrzanowski, 1968; Furberg, 1967) and in patients with anxiety (Jackson, 1971).

Orthostatic electrocardiographic abnormalities are not an unusual finding in the younger age group (Kemp and Ellestad, 1968). Maksud *et al.* (1971) and Nordenfelt (1965) described how such ST-T abnormalities disappeared in subjects without organic heart disease after intravenous injection of

propranolol. Our results with propranolol are similar to theirs. The comparison of the effect of this drug and that of practolol shows that though the bradycardiac effect of the two drugs in the supine position was similar, in the standing position the response to the intravenous injection of practolol was less than to propranolol. The ST-T abnormalities during orthostatic stress in all subjects diminished, and in many even disappeared after propranolol, but the improvement after practolol was less pronounced.

The mechanism mediating the regression of the ST-T changes after propranolol and practolol is not yet clear, but the acutely reduced beta-sympathetic tone, the reduced heart rate, and/or reduced blood pressure are probably the factors involved. In our experiments both these drugs reduced blood pressure slightly, though careful inspection of the results disclose that propranolol reduced the systolic and diastolic pressures slightly more than did practolol. This is not in disagreement with the results of Prichard, Aellig, and Richardson (1970), who found that oral propranolol and practolol, in doses equivalent to ours, had no effect on blood pressure in patients with angina pectoris, since it is plausible that blood pressure in neurocirculatory

FIG. 1 *Electrocardiogram at rest and after injection of propranolol and practolol. Note improved pattern I, aVF, V₄, and V₅, especially after propranolol.*

asthenia reacts more readily to beta-blocking drugs than in patients with angina pectoris.

The difference between the effect of the two drugs may possibly be caused by different physicochemical properties, distribution, metabolism, and excretion. These differences may be explained by the presence of the acetoamino group in the *P*-position in prac-

tolol and its absence in propranolol. This most probably leads to their different haemodynamic effects, as shown by Gibson (1971), who demonstrated that in the presence of an equally reduced heart rate, propranolol reduced the cardiac output and blood pressure, while practolol left these unaltered. Our results support the assumption that

FIG. 2 Same patient as in Fig. 1. Note pronounced abnormalities in the standing position, as compared to the resting electrocardiogram. The tracing improved considerably, especially after propranolol.

propranolol normalizes or improves sympathicotonic changes better than practolol. In our opinion, both drugs can be very useful in the differential diagnosis of electrocardiographic abnormalities in doubtful heart disease, but propranolol appears to be superior to practolol in this respect. Unless a specific reason for preferring practolol exists, as in patients with asthma, propranolol seems to be the drug of choice in this condition.

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FIG. 3 Electrocardiogram in the standing position, demonstrating tachycardia and ST-T changes. Note improvement after both propranolol and practolol.

TABLE 3 Results of orthostatic test in 10 patients with neurocirculatory asthenia before and after intravenous injection of propranolol and practolol

Case No.	Standing position	Standing position After injection of propranolol			After injection of practolol				
	Electrocardiographic abnormalities (in addition to those present in supine position)	Heart rate	Blood pressure (mmHg)	Electrocardiogram	Heart rate	Blood pressure (mmHg)	Electrocardiogram	Heart rate	Blood pressure (mmHg)
1	Biphasic T in V4-6	105	120/80	No orthostatic abnormalities	60	90/70	No influence on orthostatic abnormalities	65	80/70
2	Major inversion in chest leads	140	115/80	No orthostatic abnormalities	80	110/60	Flat and slightly positive T	80	110/60
3	Negative T in V3-6	120	110/80	No orthostatic abnormalities	60	110/80	No influence on orthostatic abnormalities	60	120/80
4	Flat and biphasic T in II-III, aVF, aVL, and V2-6	120	110/80	No orthostatic abnormalities	75	100/70	No influence on orthostatic abnormalities	70	100/80
5	Major T inversion in V2-6, ST depression of $\frac{1}{2}$ m in V4-5	135	120/80	No orthostatic abnormalities	77	100/65	Very slight orthostatic abnormalities	88	110/80
6	High P waves	140	125/80	No orthostatic abnormalities	90	100/60	No orthostatic abnormalities; normal P waves	95	120/75
7	Major T inversion in III, aVF, T biphasic in II; high P waves, ST depression $\frac{1}{2}$ mm V4	135	140/90	Almost without orthostatic abnormalities	95	130/80	Better; orthostatic abnormalities still present	105	130/80
8	Major T inversion III, aVF, V4-6; high P waves	135	120/80	Orthostatic abnormalities still present but less than after practolol	100	110/70	Better; orthostatic abnormalities still present V4-V6; normal P waves	100	120/80
9	Major T inversion in III, aVF, V4-5	140	105/80	Almost normal electrocardiogram	92	105/80	Better, but electrocardiogram still abnormal	100	105/80
10	Deep inversion of T wave in III, aVF, V4-5	100	110/70	No orthostatic abnormalities	72	100/60	Better, orthostatic abnormalities still present, aVF, III	75	110/70

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Requests for reprints to Dr. Shlomo Stern, Hadassah University Hospital, Jerusalem, Israel.