Effects of propranolol in a case of orthostatic hypotension

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SUMMARY In a hypertensive patient with orthostatic hypotension, the changes in several haemodynamic indices with respect to posture were evaluated. In the upright position, systemic blood pressure was reduced as compared with the supine position, and peripheral vasodilatation was present, as shown by an increase in Jantsch's index of the impedance plethysmographic tracings. Systolic time intervals remained unchanged with changes in posture. Propranolol 10 mg intravenously brought the response to normal. In fact, after beta-blockade in the standing position the blood pressure remained unchanged and normal peripheral vasoconstriction was observed. Similar results were seen during atrial pacing at a constant heart rate of 130 beats/minute. In this patient, propranolol appears to normalise the response to the posture change, by restoring normal vasoconstriction in the upright position.

Orthostatic hypotension has been classically defined as a reduction in arterial pressure on standing. This uncommon disorder is probably related to sympathetic nervous dysfunction induced either by certain diseases, such as diabetes mellitus (Sharpey-Schafer and Taylor, 1960), hypertension (Drenick, 1957; Lewis and Dunn, 1967; Božović *et al.*, 1970) and other disorders (Ibrahim *et al.*, 1975), or by different drug treatments (Parra and Vidrio, 1969; Ibrahim *et al.*, 1975). An idiopathic form of orthostatic hypotension, sometimes associated with tachycardia, is also known (MacLean *et al.*, 1944; Scherba, 1954). Propranolol has been suggested (Miller *et al.*, 1974) in the treatment of orthostatic hypotension on the assumption that beta-blockade, by reducing orthostatic tachycardia, would increase cardiac output and stabilise arterial pressure.

The present study was designed to assess the effects of propranolol administration in a hypertensive patient affected by orthostatic hypotension, with no pronounced tachycardia.

Case report and methods

A 62-year-old man was admitted to hospital because of hypertension and increasing weakness and light-headedness on standing. Supine arterial pressure ranged between 170/110 and 180/120 mmHg; on standing, the arterial pressure decreased to levels as

low as 130/100 mmHg. Heart rate showed only a minimal increase in the upright position. A detailed evaluation, including thyroid and adrenal gland functions, disclosed no abnormality. Plasma renin values were 198 ng/100 ml. No significant amounts of catecholamines or their metabolites were found in urine samples. The patient did not take hypotensives or any other drug before or during his stay in hospital.

According to Ibrahim (1975), a preliminary study was performed to verify the integrity of each of the individual components of the baroreceptor reflex arch. This was done by testing changes in systemic blood pressure during hyperventilation, mental arithmetic, and cold pressor tests.

Thereafter, in the supine position, electrical impedance plethysmography was carried out on both legs of the subject, to derive a noninvasive index of blood flow. This plethysmographic method, described elsewhere (Nyboer, 1970; Nyboer *et al.*, 1974), was chosen because, by surface impedance electrodes the segmental volumic conditions can be best defined without abnormal segmental compression, or crude air or water-tight encasement, always required for mechanical plethysmography. Electrocardiogram, phonocardiogram, and carotid pulse were recorded on an Electronics for Medicine photographic recorder; this was done in order to obtain systolic time intervals (STI), which cor-

relate well with invasive indices of cardiac performance (Weissler *et al.*, 1961; Metzger *et al.*, 1970). Arterial pressure was measured simultaneously by a cuffed manometer and heart rate was derived from the electrocardiogram. All these recordings were then repeated with the patient in the standing position.

Subsequently, propranolol (10 mg) was administered intravenously and the entire procedure was repeated both in the supine and upright position.

Finally, 3 hours after the administration of the drug, when heart rate and arterial pressure had returned to previous values, a temporary transvenous cardiac pacemaker was implanted and the procedure was repeated at a constant heart rate of 130 beats/min before and after a new dose of propranolol 10 mg intravenously. Left ventricular ejection time (LVET), LVET corrected for heart rate (LVETc) (Weissler *et al.*, 1969), pre-ejection period (PEP), and isometric contraction time (ICT) were calculated according to the methods of Py and Meurin (1971); in order to quantify the changes in the plethysmographic waves, the Jantsch index was calculated for each tracing (Jantsch, 1958). In order to assess the reproducibility of the results, the study was repeated after 48 hours.

Written consent was obtained from the patient before the study.

Results

The preliminary tests indicated that the lesion was at the periphery of the baroreceptor reflex arch, since abnormal responses were measured during all of the tests (Table).

SINUS RHYTHM

Before propranolol

Arterial pressure, which was 175/115 mmHg in the supine position, decreased to 130/100 mmHg when

Table Effect of tests of autonomic function on arterial pressure in a patient with orthostatic hypotension

	Blood pressure (mmHg)		
	Systolic	Diastolic	Mean
Supine	175	115	135
Tilt up	130	100	110
Cold pressor test	165	110	128.3
Mental arithmetic	160	100	120
Hyperventilation	165	100	121.5

upright, while heart rate rose from 95 to 98 beats/min (Fig. 1). The LVETc decreased from 392 to 386 ms on standing. PEP and ICT remained unmodified (100 and 20 ms, respectively). The postural change induced an increase in Jantsch's index in both legs, from 0.70 to 0.94 in the right and from 0.76 to 0.95 in the left limb (Fig. 1).

After propranolol

Arterial pressure showed minimal change from supine (170/110 mmHg) to standing position (175/110 mmHg) and heart rate increased from 82 to 92 beats/min (Fig. 1). LVETc was prolonged from 371 to 377 ms. No change was seen in PEP and ICT (110 and 30 ms, respectively). The Jantsch index decreased in both legs, from 0.66 to 0.55 and from 0.70 to 0.60 in the right and left leg, respectively (Fig. 1).

DURING ATRIAL PACING

Before propranolol

Arterial pressure decreased from 180/120 to 130/100 mmHg on standing (Fig. 2); LVETc decreased from 408 to 393 ms and PEP and ICT were unchanged (130 and 30 ms, respectively). The Jantsch index rose in both legs in the erect position from 0.63 to 0.75 in the right leg and 0.70 to 0.87 in the left leg (Fig. 2).

Fig. 1 Effects of standing on heart rate (HR), mean arterial pressure (MAP), and Jantsch index (JI) in the left and right leg, before (solid line) and after (dotted line) propranolol (10 mg i.v.).

Fig. 2 Effects of standing on mean arterial pressure (MAP) and the Jantsch index (JI) in the left and right leg, before (solid line) and after (dotted line) propranolol (10 mg i.v.) during atrial pacing at 130 beats/min.

After propranolol

Arterial pressure was 150/110 mmHg in the supine position and on standing (Fig. 2). LVETc was prolonged from 408 to 418 ms while PEP was 130 ms in the supine and upright position and ICT was 30 ms in both positions. The Jantsch index decreased from 0.70 to 0.63 in the right leg and 0.74 to 0.66 in the left (Fig. 2). The entire procedure was repeated after 48 hours and very similar results were obtained.

Discussion

Propranolol has recently been suggested for treating orthostatic hypotension since its effects on heart rate could normalise cardiac output impaired by orthostatic tachycardia (Miller *et al.*, 1974).

The patient studied in this report showed distinct hypotension on standing. This was accompanied by a modest increase in heart rate. Moreover, in the upright position there was an increase in flow in the peripheral vascular bed, as reflected by a rise in the Jantsch index.

The change in posture was not accompanied by any discernible change in stroke volume, as shown by the minimal change in LVETc. This observation rules out the possibility that the observed hypotension is dependent on a decrease in cardiac output. It indicates that the increase in the Jantsch index could be related only to peripheral vasodilatation, which takes the place of the normal postural vasoconstriction.

During atrial pacing at 130 beats per minute similar results were obtained, thus showing that an increase in heart rate will not modify this response.

Propranolol administration can inhibit the decrease in arterial pressure on standing. This event

is accompanied by a small increase in LVETc and normal postural vasoconstriction as shown by the decrease in the Jantsch index. Similar results were observed during atrial pacing, thus showing that the stabilising effects of beta-blockade on arterial pressure are not related to reduced heart rate. Propranolol administration modified the vasodilatation induced by posture change, restoring the normal vasoconstrictive response. As a consequence, the abnormal reflex response in the peripheral vascular bed seems to be the haemodynamic factor responsible for the reduction in arterial pressure with upright posture. This conclusion is in agreement with a previously reported hypothesis (Ibrahim *et al.*, 1974), as well as recent studies suggesting that lesions in the efferent sympathetic pathways are the predominant findings in orthostatic hypotension (Ibrahim *et al.*, 1975). On the other hand, other studies have shown the participation of both alpha- and beta-receptors in the regulation of posture related arterial reflexes (Rengo *et al.*, 1976). Accordingly, the orthostatic hypotension in this patient could be the result of a disturbance of balance in the peripheral sympathetic nervous system, caused by peripheral beta-receptor hypersensitivity, or by alpha-receptor fatigue (Luria *et al.*, 1964).

In conclusion, the beta-receptor blockade induced in this patient seems to allow the action of catecholamines mainly on the alpha receptors, thus restoring the normal postural vasoconstriction.

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