Effects of Propranolol on the ECG Changes During Positive Acceleration (+G_z)

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Electrocardiographic monitoring of 20 healthy subjects was carried out at + 2.5 and 3.5 Gz before and one hour after oral administration of 40 mgm of Propranolol, a Beta adrenergic blocking agent and the results compared. The sue of Propranolol resulted in a significant bradycardia and caused reversal of P and T wave changes seen on positive G exposure. It is, therefore, likely that the ECG changes are mainly the result of increased sympathetic tone that occurs due to haemodynamic changes on exposure to +Gz.

Introduction

Accelerative forces acting from head to feet direction (+Gz) result in significant and profound alterations in cardiovascular physiology. Although the genesis of cardiovascular reactions produced by +Gz have been studied by various workers and well appreciated, [2, 4, 5, 17, 18] the electrocardiographic changes resulting from these accelerations have been the subject of considerable controversy and discussion. Critical analysis of these electrocardiographic manifestations ([1, 2, 3, 4, 6, 9]) have revealed certain consistent changes which include :-

(a) Significant increase in the heart rate.
(b) Peaking of 'P' wave.
(c) Flattening and inversion of T wave or reduction in its amplitude.

The ST-T changes are normally indicative of myocardial ischaemia, therefore considerable emphasis has been laid on these electrocardiographic findings during +Gz.

The present study has been carried out using Propranolol, a Beta adrenergic blocking agent to ascertain the mechanism of these ECG changes.

Material and Methods

Twenty healthy subjects in the age group of 21-37 years were used for our studies. Clinical examination including an electrocardiogram was routinely done on every subject to exclude any pre-existing clinical disorder or electrocardiographic abnormality.

The subjects were instrumented for ECG recording from the centrifuge using special electrodes. The special electrodes used were of the floating type which do not come in direct contact with the skin.

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The contact is established only through the conducting jelly. The records comprised of the bipolar leads I, II & III only.

The conventional method of limb electrode placement, i. e., Right Arm (RA), Left Arm (LA), Left Leg (LL) and Right Leg (RL), were replaced by positioning the electrodes at new sites without jeopardising the characteristics of the ECG records. Keeping in view the isopotential map of the human body[8] the sites chosen were as follows :-

RA — Right deltoid region

LA — Left deltoid region

LL — On anterior axillary line midway between costal margin and iliac crest.

RL — Junction of the right mid clavicular line with the costal margin.

The records of leads I, II and III by this method were nearly identical with those obtained with the standard lead placement system.

These leads were used as the input for triple ECG amplifiers model E-33 and recorded on a 6-channel jet recorder with paper speed at 25 mm/sec. Base line ECG records were taken for every subject from the Human Centrifuge Gondola. Then the subjects were exposed to the following G profiles (Fig. 1.).

(a) Peak 2.5 and 3.5 g for 15 secs each.

(b) Constant rate of rise of 0.5 g/Sec.

(c) Rate of decay 0.1 g/Sec.

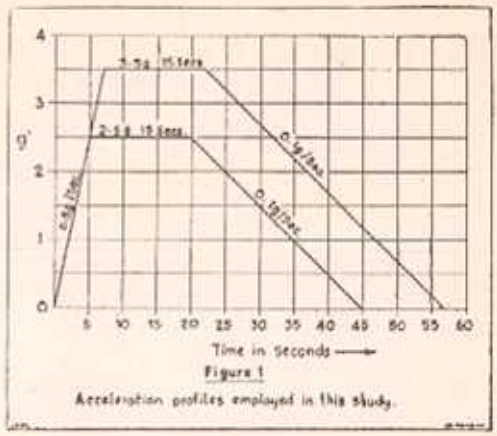

Figure 1

Acceleration profiles employed in this study.

The subjects were administered one tablet of Propranolol (40 mgm) orally, and after one hour basal record was taken prior to repeating the G profiles as mentioned above. All records were analysed for changes in heart rate, rhythm, electrical axis, P wave, QRS, T and ST segment contours.

Results

Typical ECG records before and after Propranolol are given in Figs. 2, 3, 4, & 5. The mean heart rate values pre and post drug are given in Fig. 6, and Fig. 7 gives the T wave changes seen before and after administration of the drug. Table I gives the mean ranges of ECG parameters before drug and Table II shows these changes after drug administration. Tables III and IV give the T wave changes seen before and after drug.

The important changes noted are :—

a. (i) A linear and proportionate increase in the heart rate with increasing+ Gz loads.

(ii) A significant decrease in the resting heart rate after propranolol.

TABLE—I

Mean and range of the various parameters of ECG at rest and at different levels of positive G without Propranolol.

(Figures within the brackets represent range)

Phase	Rate (Per Min)	Rhythm (%)	Electrical Axis (degrees)	P Amplitude (mm)	T Contour	%
Resting	82 (68—92)	Regular Sinus	60 (0–60)	1.5 (1–2)	Upright	100
		Sinus Arrythmia (5)				
+ 2.5G	110 (92—132)	Regular Sinus (100)	60 (0–90)	2.4 (1–3)	Inverted Flat Upright	55 15 30
+ 3.5G	118 (92—144)	Regular Sinus (100)	60 (0–90)	2.5 (1–4)	Inverted Flat Upright	55 25 20

(iii) A less marked increase in the heart rate in the post drug exposures.

b. A significant increase in amplitude of P wave with exposure to +Gz both before and after propranolol, though the mean increase in P wave amplitude in the post drug phase is relatively less marked.

c. (i) Flattening and inversion of T waves in 70–75% of subjects during +Gz exposures.

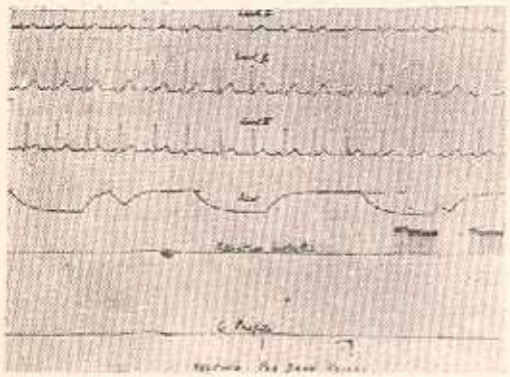

Fig. 2. Pre Drug Resting Record

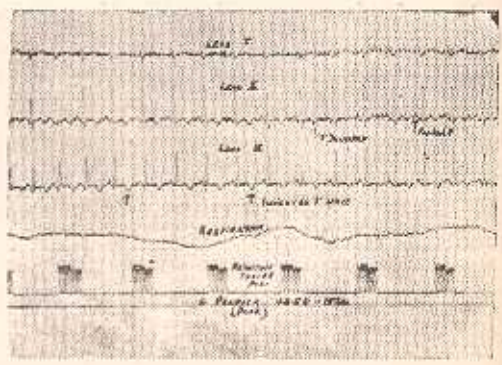

Fig. 3. Pre Drug Peak 3.5 g Record.

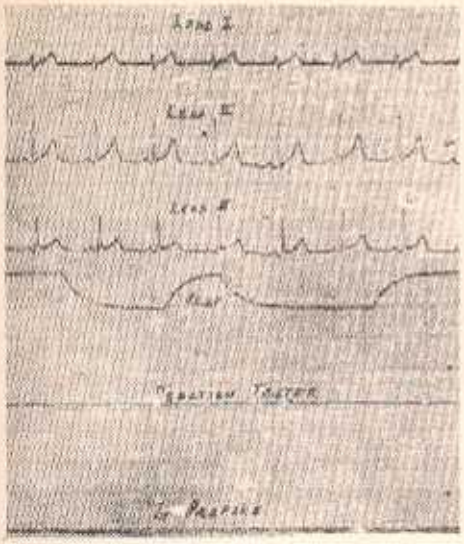

Fig. 4. Post Drug Resting Record

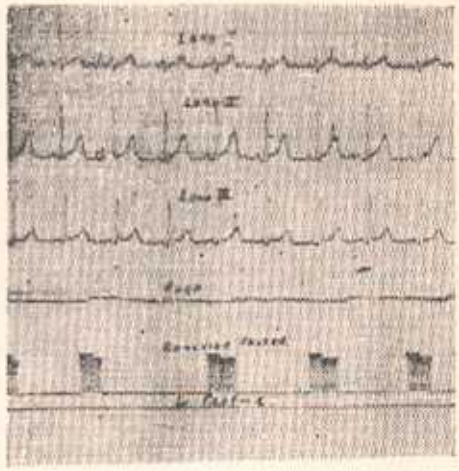

Fig. 5. Post Drug Peak 3.5g Record

TABLE — II

Mean and range of the various parameters of ECG at rest and at different levels of positive G after one hour of Propranolol.

(Figures within the brackets represent range)

Phase	Rate (per min)	Rhythm (%)	Electrical Axis (Degrees)	P Amplitude (mm)	T Contour	%
Resting	68 (60—82)	Regular Sinus (85)	60 (0–80)	1.5 (1–2)	Upright and tall	100
		Sinus Arrythmia (15)				
+2.5G	84 (72–96)	Regular Sinus (95)	65 (0–90)	1.9 (1–3)	Upright	95
		Sinus Arrythmia (5)			Flat to Inverted	5
+3.5G	91 (84–104)	Regular Sinus (100)	65 (0–90)	2.17 (1–3)	Upright Inverted	95 5

(ii) Significant increase in the T wave amplitude at rest after propranolol.

(iii) Complete abolition of T wave changes noted in (a) above, except in one case, after the drug.

d. Sinus Arrythmia present in one subject (5%) at rest disappeared during +Gz exposure. After propranolol sinus arrythmia is seen in 15% of cases (3 cases) which disappeared on exposure to + 3.5 G.

e. Electrical Axis did not show any significant alteration during +Gz before and after propranolol.

f. No changes of any significance are noted in other ECG parameters, viz. QRS complexes and ST segment.

Discussion

The haemodynamic changes seen during positive G are well understood and documented. These changes can be compared

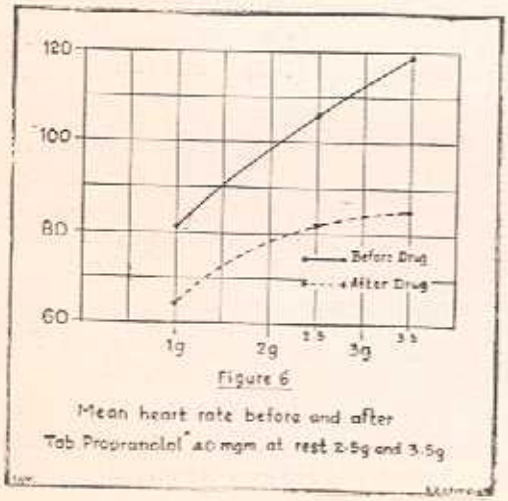

Figure 6

Mean heart rate before and after Tab Propranolol 40 mgm at rest 2.5g and 3.5g

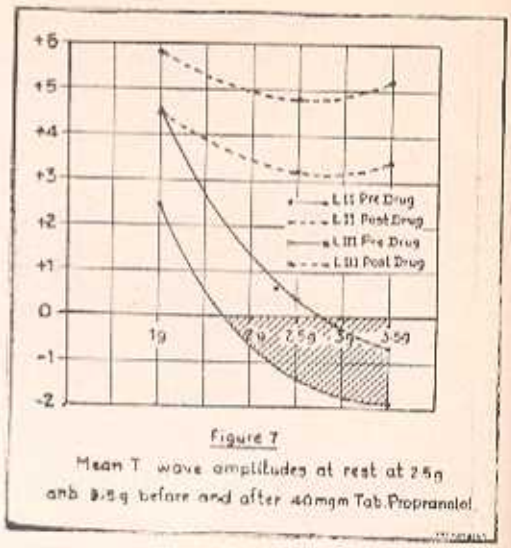

Figure 7

Mean T wave amplitudes at rest at 2.5g and 3.5g before and after 40mgm Tab Propranolol

with a situation of "Exaggerated Orthostasis [3, 10]. The head level arterial pressure falls during positive G exposure[5], the magnitude of which is proportional to the length of the hydrostatic column between the head and the heart, and the amount of positive G stress. The fall of BP at the carotid sinus level results in increased sympathetic tone leading to reflex tachycardia and vasoconstriction.

The effects of of Beta adrenergic blockade on the functions of cardio-vascular system and ECG [3, 7, 10, 11, 13, 14, 15, 16] include:

(a) A decrease in cardiac output, heart rate, systolic BP and left ventricular work.

(b) An increase in the end diastolic pressure.

(c) Decreased myocardial oxygen consumption secondary to decreased mechanical demands on the myoca-

TABLE — III

Distribution of T wave changes in Leads II and III at rest and at different levels of +Gz before and after Propranolol.

	PHASE	LEADS	INVERTED No.	%	FLAT No	%	UPRIGHT No.	%
Pre Drug	Resting	II	—	—	—	—	20	100
		III	—	—	1	5	19	95
	+ 2.5G	II	3	15	2	10	15	75
		III	11	55	3	15	6	30
	+ 3.5G	II	6	30	2	10	12	60
		III	11	55	4	20	5	25
Post Drug	Resting	II	—	—	Nil	—	20	100
		III	—	—	—	—	20	100
	+ 2.5G	II	1	5	—	—	19	95
		III	1	5	—	—	19	95
	+ 3.5G	II	1	5	—	—	19	95
		III	1	5	—	—	19	95

rdium and due to depression of synthesis of free fatty acids which is the major metabolic fuel of the myocardium[16].

(d) An increase in the height of T wave and decrease in the QT interval.

The significance of the ECG changes during positive G is uncertain and disputed particularly in relation to T-ST segment alterations. Divergent views have been put forward by various workers to explain the mechanism of T wave alterations. Whereas Gauer[4] and Zuidema at el[18] considered the ST-T changes to be indicative of myocardial ischaemia, Browne & Fitzsimons[1] attributed these changes to descent of Diaphragm during +Gz. Bjaurtedt et al cited by 3, correlated the T wave changes during positive G to alterations in heart rate only. But Nordenfelt[9] in another study was unable to reverse these changes using rate slowing carotid massage. Cohen and Brown[2] feel that T and ST segment changes are reflex mediated and are an exaggeration of the changes seen in Orthostasis and during stimulation with Epinephrine and other sympathomimetic drugs. In a later study[3] the same authors using Beta adrenergic blocking agent (Propranolol) were able to completely normalise the ECG changes during +Gz.

The present study has demonstrated the following significant changes during positive G with propranolol.

(a) Heart Rate : The lowered heart rate response to acceleration after propranolol is consistent with the rate of reduced sympathetic tone at rest and under stress.

TABLE — IV

Mean T wave amplitude in Leads II and III at different levels of +Gz in cases showing inversion, flat and upright T waves compared before and after Propranolol.

(Figures in brackets are ranges)

T Wave Characteristic	No. of cases	Lead	RESTING			+ 2.5 G			− 3 5 G		
			Pre Drug	Post Drug	Diff.	Pre Drug	Post Drug	Diff.	Pre Drug	Post Drug	Diff.
Inversion	11	II	4.0 (+1 to +6)	5.9 (+1.5 to +9)	*	0.5 (−3 to +3)	4.8 (−1.5 to +8)	★	−0.6 (−3 to +2)	5.2 (−1 to +8.5)	★
		III	2.4 (0 to +5)	4.0 (+1 to +7)	NS	−1.2 (−3 to +2)	3.4 (−1 to +5.5)	★	−2.0 (−3 to −1)	3.4 (−1 to +6)	★
Flat	4	II	4.6 (+3 to +7)	5.2 (+3 to +8)	NS	1.9 (0 to +2.5)	6.2 (+4 to +11)	NS	2.5 (0 to +5)	6.2 (+4 to +12)	NS
		III	3.0 (+2 to +4)	3.2 (+2 to +5)	NS	0 (Nil)	4.0 (+2 to +7)	*	0 (Nil)	3.9 (+2 to +8)	NS
Upright	5	II	4.3 (+3 to +5)	6.7 (+4 to +9)	*	3.4 (+1.5 to +5)	6.9 (+4.5 to +9)	★	4.0 (+1.5 to +6)	6.3 (+5 to +8)	*
		III	2.4 (+1.5 to +3.5)	4.7 (−2 to +7.5)	NS	1.7 (+1 to +3)	5.2 (+2 to +8)	*	2.1 (+1 to +3.5)	5.0 (+2.5 to +7)	★
Entire Group	20	II	4.2 (+1 to +7)	6.0 (+1.5 to +9)	★	1.5 (−3 to +5)	5.6 (−1.5 to +11)	★	1.2 (−3 to +.6)	5.7 (−1 to +12)	★
		III	2.5 (0 to +5)	4.1 (+1 to +7.5)	★	−0.2 (−3 to +3)	4.0 (−1 to +8)	★	−0.6 (−3 to +3.5)	3.9 (−1 to +8)	★

(★ = Significant at P = 0.01; * = Significant at P = 0.05; NS = Not significant)

(b) P Waves : Peaking of P waves in Lead II was consistent in the predrug exposures to +Gz. There was a significant reduction in the amplitude of P waves in the post-drug exposures, thus proving their reflex nature. Complete normalisation of P waves after the use of propranolol has also been noted by Cohen and Brown[3]

(c) T waves: Flattening and inversion of T waves in leads II and III was seen in most of the subjects and reduction of amplitude in a few cases. The T wave flattening/inversion noted in 15 subjects (75%) were completely normalised after propranolol in all except one subject (5%). This shows that increased sympathetic tone was the dominant factor responsible for the T wave changes. The total absence of ST segment depression in these cases also excludes the possibility of myocardial ischaemia. Also, the dose of propranolol used in this study is considerably less than that required to abolish the effects of coronary insufficiency.

(d) Rhythm : The sinus arrythmia at rest noted in 3 cases (15%) after propranolol is indicative of relative increase in vagal tone consequent to the blockade of Beta adrenergic effect. No other conduction defects or arrythmias were noted in this study.

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