Effect of Short Term Exposure to Hypoxia on Systolic Time Intervals

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Two groups of ten subjects each were studied to assess the effects of short term hypoxia on systolic time intervals (STI). One group consisted of ECG normal healthy adult volunteers and the other of adult subjects in lower medical category with the diagnosis of ischaemic heart disease (IHD) having electrocardiographic (ECG) abnormalities mainly ST-T changes. Simultaneous recordings of ECG, indirect carotid pulse tracing, phonocardiogram and apex cardiogram were taken in resting subjects in supine position at ground level and at simulated altitude of 15,000 ft in a decompression chamber at 15 minute intervals for a total duration of 45 min of hypoxia. STIs were measured.

While the QS_2 difference was non-significant between the two groups at ground level and under identical conditions of hypoxia, the ECG abnormal group showed increased PEP, decreased LVET and significantly increased PEP/LVET ratio when recorded after 45 min of hypoxia though no such difference was noted upto 30 min.

THE study of systolic time intervals (STI) has established itself as a useful non-invasive measure of myocardial performance. Weissler and co-workers[1,2] have contributed enormously in the understanding and the clinical uses of STIs. However, the applicability of STIs under hypoxia to detect early derangements of myocardial functions is relatively new.

Material and Methods

Ten healthy volunteers in the age group 19 to 32 years (mean 22.9 years) and with normal electrocardiograms (ECG) formed one group of subjects (Group A) and 10 asymptomatic subjects in the age group 22 to 44 years (mean 37.8 years) with ECG abnormalities mainly in the form of ST-T changes formed the second group (Group B).

All the subjects underwent clinical examination, pulmonary function tests and radiological and haematological investigations to exclude any cardiovascular, pulmonary, haematological and neuro-muscular disorders which might directly or indirectly increase the effects of hypoxia in any form. They were not allowed to smoke or to take any drugs during and in the 24 hours prior to the study.

Most of the subjects had previous experience in the hypobaric chamber. Their apprehension was further alleviated by a familiarisation run done for primary ear clearance test. To manage any untoward incidence, a trained observer accompanied the subjects during the chamber run.

Simultaneous recordings of ECG, indirect carotid pulse tracing (ICPT), phonocardiogram (PCG) and apex cardiogram (ACG) were made with the subject in supine position with head resting on a ring cushion to avoid any displacement of pick ups on neck during the period of study. These recordings were done first at ground level and then at 15,000 ft simulated altitude in the decompression chamber at 15 min intervals for a total stay of 45 min. The profile used for each hypobaric chamber run is given in Table I. The instrumentation and recording set up is shown in Fig. 1.

STIs were measured as follows (Fig. 2) :

a) Total electromechanical systole (QS_2) was measured from the beginning of Q wave of the ECG to the first high frequency aortic component of the second heart sound.

TABLE I

Hypobaric Chamber Profile - Short Term Hypoxia

1.	Baseline record of ECG, PCG, ICPT, and ACG simultaneously at ground level.
2.	Ascent to 8000 ft @ 3,000 ft/ min followed by descent to ground level @ 3,000 ft/min for ear clearance.
3.	Ascent to 15,000 ft @ 3,000 ft/min.
4.	Level off at 15,000 ft for 45 min.
5.	Record all parameters (at 1 above) at 0, 15, 30 and 45 min after level off.
6.	Descent to ground level @ 2,000 ft/min.

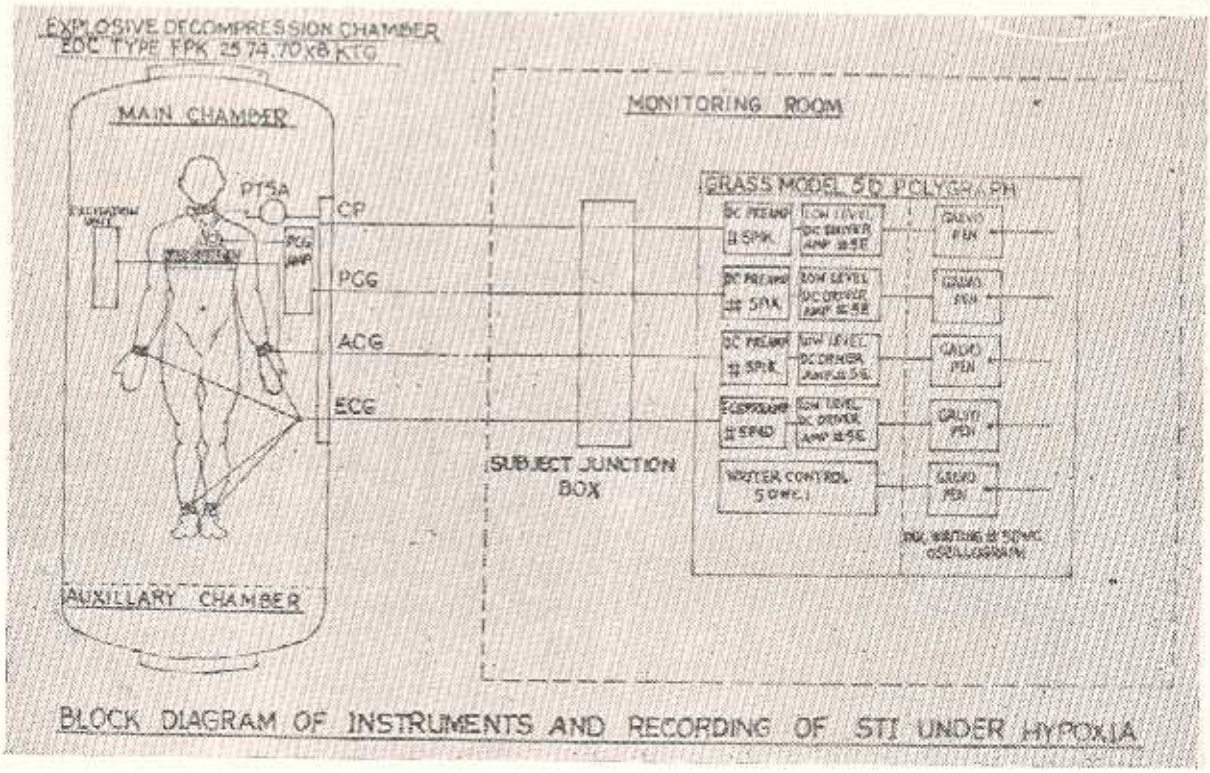

Fig. 1

b) Left ventricular ejection time (LVET) was measured from the onset of brisk rise of carotid pulse tracing to the nadir of incisura of the same wave.

c) Pre-ejection period (PEP), the interval from the onset of ventricular depolarisation to the beginning of left ventricular ejection, was calculated by subtracting LVET from QS_2 interval. PEP = QS_2 — LVET.

d) PEP/LVET ratio was calculated from (b) and (c).

(e) Heart rate (HR) was calculated from the ECG.

The indices corrected data are obtained using the regression equations suggested by Lindquist *et al*[7] for resting condition.

PEP Index (PEP I) = PEP + 0.44 HR
QS_2 Index (QS_2I) = QS_2 + 1.85 HR
LVET Index (LVET I) = LVET + 1.42 HR

To calculate PEP/LVET, no corrections are necessary and the values are put uncorrected for heart rate.

The STIs were calculated by taking an average of at least ten consecutive heart beats at a particular altitude and duration, both for normal and abnormal group. The values were processed adequately and compared for the mean difference **t** value and statistical significance for any particular class of observations between two groups of subjects.

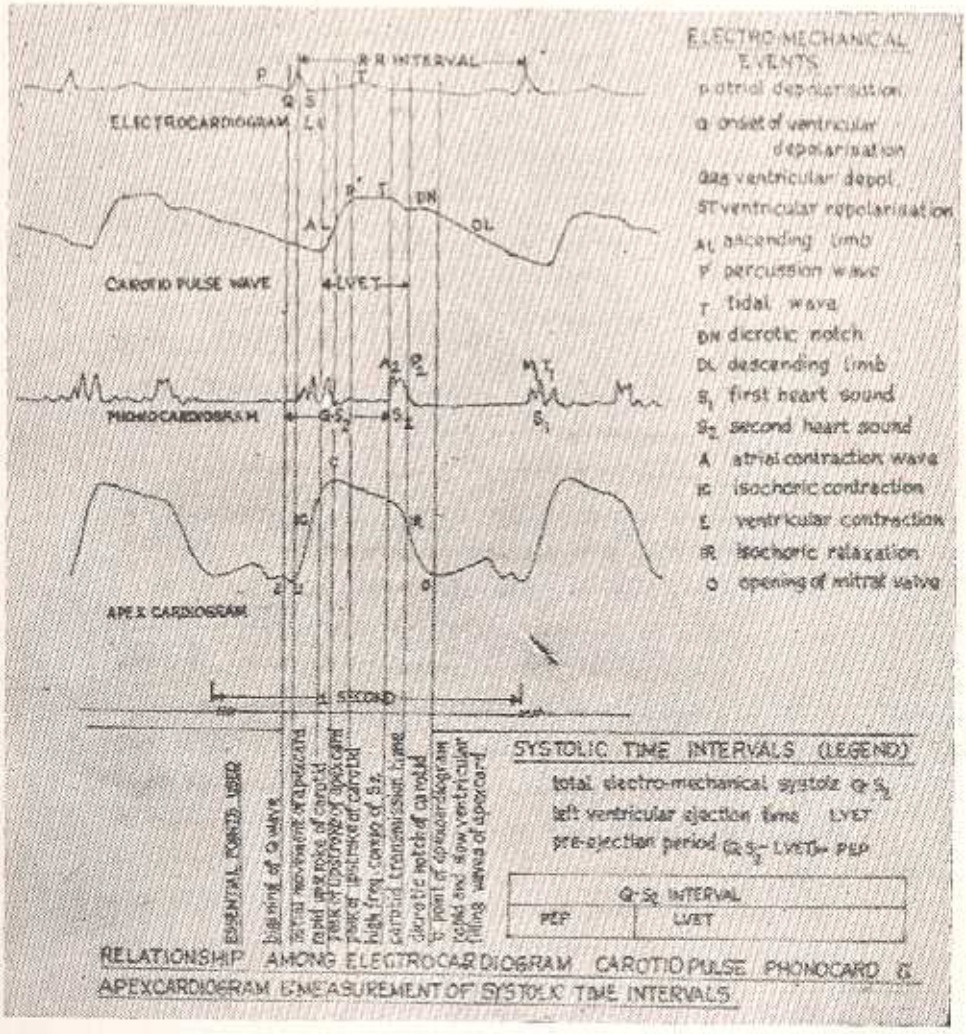

Fig. 2

Results

The mean STI values in the two groups at ground level and during varying periods of exposure to hypoxia at 15,000 ft simulated altitude are briefly depicted in Fig. 3. Table II shows the significance of mean differences in heart rate and STI parameters in the two groups when at ground level and at 15,000 ft. Table III brings out the significance of these differences in the ECG abnormal group when compared to the ECG normal group.

TABLE—II

Significance of mean differences in heart rate and STI parameters at 15,000 ft simulated altitude from ground level values in the two groups of subjects

Parameter	ECG Normal Group (Gp. A)				ECG Abnormal Group (Gp. B)			
	0 min	15 min	30 min	45 min	0 min	15 min	30 min	45 min
Heart rate	13***	13.8***	14.4***	16.5***	10·9***	11.2***	14.3***	10.4**
QS_2	-22.3**	-27.3**	-18.2*	-27.7**	-20.4***	-25.4**	-29.7***	-22.9*
LVET	-13.3*	-14.9*	-13.5*	-20**	-12.3**	-16.6**	-21.4**	-21.6**
PEP	-9*	-12.4**	-4.8	-9.7	-7.5**	-6.3	-8*	-0.2
QS_2I	-14	-2	-2	1	0	-4	-3	-2
LVETI	4	4	6*	3	3	-1	-1	-7
PEPI	-6	-9	0	-5	-3	-1	-1	-5
PEP/LVET	-0.015	-0.026	+0.001	-0.021	-0.01	0	0.002	0.036*

* $P<0.05$ ** $P<0.01$ *** $P<0.001$

TABLE—III

Significance of mean differences in heart rate and STI parameters of ECG abnormal group when compared to those of ECG normal group at ground level and at 15,000 ft simulated altitude during varying periods of exposure

Parameter	Ground Level	15,000 ft Simulated Altitude			
		0 min	15 min	30 min	45 min
Heart Rate	-3.5	-5.6	-6.1	-3.6	-9.6*
QS_2	2.2	4.1	4.1	-9.3	7
LVET	5.6	-3.4	-6.1	-12.4*	-6
PEP	6.4	8.1	12.7*	3.4	16.1*
QS_2I	-4.6	8.7	-7.4	-5.9	1.2
LVETI	-10	-11	-15*	-17*	-20*
PEPI	3.1	5.7	10.1	2	12.1
PEP/LVET	0.029	0.034	0.055*	0.031	-0.077**

* $P<0.05$ ** $P<0.01$

The mean heart rate for ECG normal group was 72/min which increased to 85/min immediately on reaching 15,000 ft altitude. The heart rate remained near this value after 15 to 30 min of exposure and then increased to 88.5 per min after 45 minutes of stay at altitude. The ECG normal group had a resting mean heart rate of 68 per min at ground level which increased to 79.4 per min and remained around this value with mild increase upto 30 minutes of exposure and then showed a gradual fall.

In the present study the heart rate between the two groups had a mean difference of — 0.6 after 45 minutes at altitude which was found to be statistically significant ($P < 0.05$).

Total Electromechanical Systole (QS_2) values showed decrease with increase of heart rate on exposure, but remained statistically insignificant with a mean difference of —7 after 45 minutes.

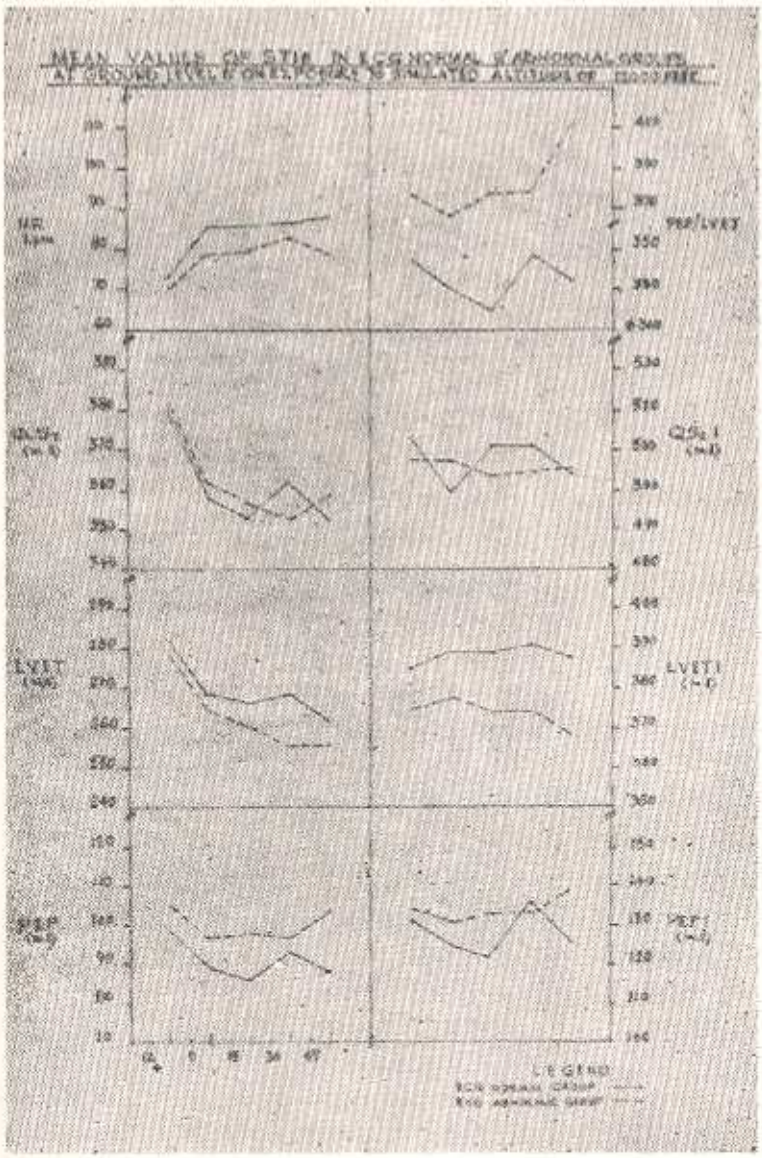

Fig. 3

The corrected values for heart rate QS_2 index (QS_2I) between the two groups remained non-significant both at ground level and at altitude.

The difference in Left Ventricular Ejection Time (LVET) between the two groups was found to be statistically significant (mean difference of 2.27, $P < 0.05$) after 30 minutes of exposure, while the corrected values (LVETI) showed statistically significant difference after 15 minutes ($P < 0.01$) and after 30 and 45 mts ($P < 0.05$) with increasing mean difference between the two groups.

Mean Pre-ejection Period (PEP) was 98 as compared to that of the abnormal group 104.6. The PEP values decreased with increase of heart rate in normal and abnormal group upto 30 minutes of exposure, after which the latter group showed increase. The mean difference between the two groups from 6.4 at ground level became 12.7 after 15 minutes and 16.1, after 45 minutes of exposure and was statistically significant ($P < 0.05$ and $P < 0.01$ respectively). The corrected PEP index for heart rate remained non-significant.

The PEP/LVET ratio was 0.346 and 0.376 for normal and abnormal group respectively at ground level. While in the normal group it reached a maximum of 0.347, in the abnormal group it reached a maximum of 0.412; with a mean difference after 45 minutes' exposure of 0.077 which was statistically significant ($P < 0.01$). This ratio also assumed significance after 15 minutes of exposure.

The mean values of HR, PEP, PEPI and PEP/LVET, when compared between the groups were found to be divergent after 45 minutes of exposure. The linear relationship of PEP/LVET ratio at 45 minutes of hypoxia at 15,000 ft reveals that while difference in the normal group shows inverse relationship the abnormal group above shows marked direct relationship.

Discussion

Systolic time intervals have been extensively used for the evaluation of left ventricular performance in cardiovascular dynamics. In various studies, PEP/LVET ratio emerges out to give the best results[12]. Other STI parameters show varying relations with heart rate under stress, e.g., exercise or hypoxia, when compared with its value in the same subject at rest on ground level.

Various endeavours to use exercise STI in the early diagnosis of coronary insufficiency and myocardial dysfunction had failed to establish its definite diagnostic value. This is because of various practical problems in making measurements, viz., interruption of upright exercise and changing to supine position or after supine exercise in supine position, disturbances during uninterrupted exercise STI etc. Apart from it, accuracies are limited with average regression coefficients, individual time intervals, respiratory phase, anxiety, wider deviations of observed values and possibility of all the factors discussed earlier. Compared to other methods of stress STI, the study under hypoxia in supine subject could provide better comparison with control values in view of the case in monitoring during any chosen period of hypoxia. In the present study the subject maintained the same resting position through out the period of test, thereby avoiding the possible sources of errors due to body movements. The ease in monitoring could also be used conveniently to determine the point where the system starts digressing from normal. As it is established that the effects of isocapnic hypoxia alone remains in agreement with those of hypobaric hypoxia using hypobaric chamber[11] the validity of this test seems more reasonable.

The differences revealed by the present study between ECG normal and abnormal groups can be explained by a number of physiological changes, which are induced by hypoxia. Hypoxia calls for an integrated action on myocardium and vascular bed by vasomotor centre, carotid body reflexes, reflexes secondary to hypoxia induced hyperpnea, direct and indirect role of sympathetic activity and stimulation of adrenal medulla. The above mechanism results in cardioacceleration under hypoxia, which affects various systolic time intervals. Initial compensation is done by an increase in heart rate and later it is effected by an increase in stroke volume.

In the present study the heart rate increased significantly in both groups immediately on exposure to hypoxia and continued to do so under longer hypoxia. The difference between the groups becomes significant after 45 minutes of exposure. Because of failure to sustain compensation, the ECG abnormal group showed a fall from initial rise, whilst the ECG normal group showed continued rise.

QS_2I is felt to be the most useful of the STI in judging the presence of positive inotropic stimulation[6]. In this study both the groups showed significant fall from ground level values, and had inverse relation with heart rate. The fall was more significant in abnormal group following 0 min and 30 min of exposure. However, the two groups showed no significant difference under identical conditions of hypoxia. The corrected QS_2 for heart rate remained non-significant at ground level in both normal and abnormal groups and did not change under hypoxia inspite of individual variations in either group. As explained later it was because of increased PEP and decreased LVET in the abnormal group in contrast to decreased PEP and increased LVET in the normal group.

When QS_2 is further evaluated in terms of its components, viz., PEP and LVET, the duration of PEP is mostly dependent upon the velocity of myocardial shortening. ECG abnormal group with IHD have reduced rate of myocardial force development, hence slow left ventricular pressure rise and increased PEP.

PEP incorporates time required for excitation contraction coupling and the period of isovolumetric contraction. Uncorrected PEP showed significant fall in both the groups due to increased inotropy. When compared, there was a significant difference between the groups following 15 min and 45 min of exposure. The corrected index (PEPI) showed no significant difference between the groups under identical conditions of hypoxia. The abnormal group showed non-significant increase following 45 minutes of exposure unlike the normal group for the reason explained above.

Both groups showed significant fall in LVET under hypoxia. Compared to ground level values, the mean difference between the two groups was not significant except that observed after 30 minutes of exposure. The normal group showed increase in LVETI in contrast to fall in the abnormal group. Acute hypoxia has been shown to cause a decrease in total peripheral resistance and an increase in stroke volume. The latter causes in increase in LVETI, a decrease in PEPI, while leaving QS_2 unaltered. The decrease in abnormal group could be as a result of impaired myocardial function and underlying reduction in stroke volume.

PEP/LVET ratio is considered to reflect left ventricular performance[9] and is a more sensitive index. Study showed progressive decrease in both groups with increasing duration of hypoxia due to beta receptor stimulation which has been shown to cause a decrease in PEP/LVET. When compared to ground level values, there was a non-significant change in normal group throughout 45 minutes of exposure to hypoxia, whereas the abnormal group showed a significant rise following 45 minutes of exposure. In other words the ratio remained within normal accepted range of 0.22 — 0.41 in normal group[4], while it exceeded this range following 45 minutes of hypoxia indicating deterioration in the abnormal group. As this ratio is inversely related to contractility, it could be correlated with already existing clinical conditions of the subjects.

The deviations in abnormal cases are possibly due to adverse effects of hypoxia on already affected myocardium and consequently deteriorating left ventricular function. Under moderate hypoxia the IHD group showed an initial normal response and deteriorated later, e.g., longer PEP, shorter LVET and increased value of PEP/LVET. It shows that after certain duration of hypoxia (45 minutes), IHD group was less effective to compensate than the normal group probably because of reduced contractility.

Conclusions

Studies of systolic time intervals under hypoxia provide valuable information of electromechanical parameters of the heart which may be used for evaluation and assessment of ECG abnormality.

Changes in STI parameters in the normal group were found to be within accepted limits, whereas in the ECG abnormal group a significant increase in PEP/LVET ratio after 45 minutes of hypoxia was observed during deteriorating myocardial function.

As the alterations were observed after 45 minutes, a longer stay at altitude (60 minutes) might help in better evaluation by making these changes more prominent.

As this method involved supine subjects without any exercise or change in posture, STI under hypoxia minimised various limitations of other methods of stress STI.

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