EFFECT OF PROPRANOLOL ON WORK CAPACITY AT SIMULATED HIGH ALTITUDE

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Summary : Studies have been carried out on 11 soldiers in an altitude chamber (Barometric pressure 480 mm Hg) to find out the effect of Propranolol on work capacity at simulated altitude. Oral administration f 40 *mg* Propranolol hydrochloride, thrice daily for five days, did not affect the work capacity for prolonged physical effort as judged by the measurement of maximal oxygen uptake capacity. The drug caused a significant reduction in the resting heart rate ($P<0.001$), but the maximum hear trate attained during maximal work rate was not significantly different.

Key words : adrenergic beta-receptor block high altitude work capacity

INTRODUCTION

Propranolol has been shown to be an effective beta adrenergic blocking agent (8). The activities of the sympathoadrenal system play an important role in cardiovascular regulation under various pathophysiological conditions. Many of the changes in cardiac performance that take place during exercise, resemble those resulting from sympathetic stimulation of the heart. It has been postulated that an increase in sympathetic activity occurs during exercise and is important in the mediation of the associated cardiac response (2, 9, 24). Epstein et al (19) reported a significant reduction in heart rate, cardiac output and mean arterial pressure during sub-maximal and maximal exercise after administration of Propranolol. At sub-maximal levels of work $\dot{V}O_2$ was unchanged, the fall in cardiac output being compensated for by an increase in arteriovenous oxygen difference. At maximal levels of work, the cardiac output was incompletely compensated for and the maximal $\dot{V}O_2$ achieved was, therefore, reduced. They also observed a 40% reduction in endurance time for a particular work. Donald and Samueloff (16) administered a test of exercise of considerable severity in dogs but could not find any change in the ability to exercise after the adrenergic blockade. Cronin (13) reported that administration of Propranolol prior to moderate exercise completely abolished the rise in plasma-free fatty acids and lactate, and also reduced heart rate and cardiac output. Cain (10), and Barnard and Foss (7) observed reduction in exercise oxygen consumption and oxygen debt in dogs during sub-maximal exercise both at sea level and at altitude. Studies were, therefore, conducted to get precise information about the effect of beta block on work capacity at simulated altitude.

MATERIALS AND METHODS

The study was conducted on 11 soldiers. Their physical characteristics and selected physiological functions are given in Table I. Throughout the study, the subjects were detained in a hospital and were under medical supervision. Three sets of observations were made — (a) at ambient pressure of Delhi (about 745 mm Hg); (b) at a pressure of 480 mm Hg in a low-pressure chamber; and (c) at 480 mm Hg in the low-pressure chamber after administration of the drug. The programme of the study was as follows :—

The subjects reported at the laboratory at 9 A.M. every day after a light breakfast and, after one hour's rest on a chair, the following parameters were estimated. They abstained from smoking or taking any food as long as they were in the laboratory.

(i) *Resting heart rate*—Recorded by palpating the radial artery.

(ii) *Resting blood lactate level*—Concentration of lactic acid was determined from blood drawn from a finger tip (the hand was pre-warmed in water of 40-45°C) and analysed according to Strom's modification of Barker and Summerson method.

(iii) *Maximum oxygen uptake capacity* ($\dot{V}O_2$ *max*)—$\dot{V}O_2$ max was estimated on a mechanically-braked bicycle ergometer using a continuous test. The subjects pedalled at a rate of 60 rpm and, to start with, the work load was adjusted to 450 *kpm/min*. At the end of the third minute, the work load was raised to 600 *kpm/min*. Subsequently, after every two minutes, the work load was increased by 150 *kpm/min* until the subject terminated the work on the basis of subjective exhaustion. The working time ranged from 9 min to 13 min at ambient pressure, and 7 min to 11 min in the decompression chamber. This procedure was found to be satisfactory to elicit the $\dot{V}O_2$ max for similar subjects. Six of the subjects were studied twice at ambient pressure on subsequent days. Their $\dot{V}O_2$ max values for the first day and second day did not differ by more than 100 *ml/min*. Expired air was measured during the last minute of each work load, using a Kofranyi-Michaelis respirometer and the aliquots of expired air was analysed in a Scholander micro gas analysis apparatus. $\dot{V}O_2$ was calculated by standard formulae for the open-circuit method and expressed as *ml/kg/min* STPD. A minimal collection period of 30 seconds was arbitrarily selected for calculating the max $\dot{V}O_2$. Thus, for those subjects who were unable to complete 30 seconds during the final minute of the work, the previous reading was used to calculate the max $\dot{V}O_2$.

(iv) *Maximum exercise ventilation* (V_E *max*)—Pulmonary ventilation during maximal exercise on the bicycle ergometer was recorded and the values were expressed as *litres/min*. BTPS.

(v) *Maximum heart rate* (*Max HR*)—E.C.G. was recorded during the last 15 seconds

of each work load and the maximum heart rate reached during the exercise was noted. One electrode was fiitted over the manubrium sterni and the other was placed in the space between the fifth and sixth ribs where the apex beat of the heart is most readily palpated. The third (neutral) electrode was placed on the back of the chest.

(vi) *Maximum blood lactate* (*Max LA*)—Blood lactate was estimated five minutes after the maximal exercise, by the method of Barker and Summerson modified by Storm. The blood was collected from a pre-warmed finger tip.

The above parameters were recorded again after four days in a decompression chamber at a barometric pressure of 480 *mm* Hg. The subjects rested in the chamber for an hour before any measurement was made.

The subjects were administered 40 *mg* of Propranolol hydrochloride (Inderal), I.C.I., England, 3 times a day for 5 days. The last dose was taken on the morning of the fifth day and the final testing in the chamber was done within three hours of the last dose.

Results

The results are summarised in Tables I and II. The mean resting heart rate was 74.0 at the ambient pressure which was significantly increased to 82.2 ($P < 0.01$) at 400 *mm* Hg.

Table I : *Physical characteristics and selected physiological functions of the subjects*

Subject	*Age* (*yr*)	*Height* (*cm*)	*Weight* (*kg*)	*Resting heart rate* (*beats/min*)	*Resting lactic acid* (*mg%*)	$\dot{V}O_2$ *max* (*ml/kg/min in STPD*)	$\dot{V}_E$ *max* (*l/min BTPS*)	*Max HR* (*beats/min*)	*Max LA* (*mg%*)
RK	30	171.5	54.5	72	9.5	40.2	71.0	176	56.6
MS	30	169.5	54.1	78	24.5	38.7	84.3	180	78.4
BRS	29	174.0	66.9	68	13.6	38.3	94.2	192	54.3
PS	28	180.0	64.5	60	24.5	30.0	60.4	150	60.9
HS	35	175.0	52.6	72	19.6	41.6	85.4	196	63.4
RKS	29	175.0	62.0	84	13.6	30.3	81.8	192	78.4
BS	35	182.5	69.1	66	23.7	29.2	66.8	180	61.0
SS	30	168.0	54.4	74	16.7	39.9	73.8	184	58.7
TS	35	168.5	78.0	80	9.4	32.3	92.5	188	93.4
AS	32	174.0	58.7	72	27.9	31.9	68.4	176	104.4
US	30	170.5	59.6	88	6.8	39.6	60.3	180	61.2
Mean	31.2	173.5	61.3	74	17.2	35.6	76.3	181.3	70.1
SD±	2.6	4.6	7.8	8.1	7.2	4.8	12.1	12.4	16.5

Table II : *Mean, S.D. and level of significance of various physiological responses.*

		atmospheric pressure 750 *mm Hg*	480 mm *Hg*	480 *mm Hg* + *Propranolol*
		I	II	III
Resting heart rate	Mean	74.0	82.2†	70.2**
	SD ±	8.1	8.3	7.5
Resting lactic acid	Mean	17.2	23.5	19.5
	SD ±	7.2	7.7	9.2
VO_2 max	Mean	35.6	28.5††	27.5
	SD ±	4.8	3.6	4.3
VE max	Mean	76.3	74.7	76.8
	SD ±	12.1	19.4	20.9
Max HR	Mean	181.3	175.3	170.8
	SD ±	12.4	13.4	13.5
Max LA	Mean	70.1	69.8	65.5
	SD ±	16.5	13.9	17.1

Students' t test employed for statistical analysis.
†P<0.01, †† P<0.001 (Comparison of II with I)
** P<0.001 (Comparison of III with II)

Similarly, the resting blood lactic acid acid level was increased from 17.2 *mg%* at ambie pressure to 23.5 *mg%* at 480 *mm* Hg. However, this increase was statistically not significa The mean values for $\dot{V}O_2$ max, $\dot{V}_E$ max, HR max and max LA were 35.6 *ml*, 76.3 l., 18 and 70.1 *mg%* at ambient pressure, and values for these parameters at 480 *mm* Hg press were 28.5 *ml*, 74.7 l., 175.3 and 69.8 *mg%* respectively. Only the change in $\dot{V}O_2$ max w significant (P <0.001).

When the mean values for the above parameters, without and with administration of P pranolol at 400 *mm* Hg pressure, were compared the following changes could be observed :–

The mean resting heart rate decreased significantly from 82.2 before to 70.2 with t drug (P <0.001). The resting lactic acid level was 23.5 *mg%* without the drug and 19 *mg%* after the administration of the drug. The mean values for $\dot{V}O_2$ max, max HR and m LA decreased 28.5 *ml*, 175.3 and 69.8 *mg%* without beta block to 27.5 *ml*, 170.8 a 65.5 *mg%* with beta block, respectively. $\dot{V}_E$ max was increased to 76.8 l. with the dr compared to 74.7 l. without. These changes in $\dot{V}O_2$ max, max HR and max LA and V max are not statistically significant. The mean work rate at the last minute of the exer test 1065 was *kpm* before and 1015 *kpm* after the drug. These values were not significan different.

Discussion

The mean resting heart rate increased significantly when the subjects were in the low-pressure chamber. This well-known effect of hypoxia has been reported by many authors (6, 17). No definite cause of this cardiac acceleration is known. Assmusen and Chiodi (3), and Dripps and Comroe (17) suggested that the change in heart rate during hypoxia is initiated at the chemoreceptors of aortic and carotid bodies. This was challanged by Daly and Scott (14) who showed that hypoxic stimulation of the carotid bodies produced bradycardia in dogs. Wright (29) has written that the cardiac acceleration produced by hypoxia is due to direct effect of oxygen lack on the sinoauricular node, and furthermore, this is coupled with effects due to the reflex secretion of the adrenaline from the adrenal glands. After administration of Propranolol, the resting heart rate was reduced when the subjects were tested in the low-pressure chamber. The decrease was highly significant ($P < 0.001$). But these values were not different from the heart rate values at ambient pressure. This observation suggests that the cause of the cardiac acceleration during hypoxia is the increased sympatho-adrenal activity. When the sympatho-adrenal activity was blocked by the drug, the cardiac accelerator response to hypoxia was abolished.

The mean resting blood lactate level was increased in accute hypoxia. But this increase was not statistically significant. Similar increase was reported also by Hansen *et al* (21). The drug caused a reduction in the resting lactate level which approached the values at ambient pressure. The increase in resting blood lactate observed in the low-pressure chamber also may be due to the increased adrenergic activity. When the adrenergic activity was blocked by the drug, this increase also was not observed.

The values for $\dot{V}O_2$ max observed was found to be lower than the reported values of $\dot{V}O_2$ max for Indian soldiers (18, 25). Sen Gupta *et al* (26) reported $\dot{V}O_2$ max values of 45 ± 6.13 *ml/kg/min* for active soldiers (belonging to infantry and artillery) and 36.1 ± 6.46 *ml/kg/min* for sedentary group (belonging to supporting services like medical ordinance and supply corps). The values for the present subjects are comparable to the figure for sedentary group studied by Sen Gupta *et al* (26). The subjects of the present study were Reservists and hence were not leading a very active life. However, these values were higher than the values reported for Indian miners and laboratory workers (11). At simulated altitude, $\dot{V}O_2$ max averaged about 80% of its sea-level value. This reduction in the aerobic capacity was highly significant ($P < 0.001$). Stenberg *et al* (27) reported that in their subjects the $\dot{V}O_2$ max averaged about 72% of that at sea level, when they were tested in simulated altitude of 13,115 ft(PB 462). Consolazio (12) observed a 17% decrease in $\dot{V}O_2$ max at 11,400 ft on a group of army volunteers. Our data is comparable to the above two studies. There was a slight non-significant decrease of 1 *ml/kg/min* in $\dot{V}O_2$ max after the drug.

Epstein *et al.* (19) reported decrease ($P < 0.05$) in oxygen uptake during maximal

exercise after the administration of Propranolol. The discrepancy between our data and that of Epstein *et al* may be due to the fact that there was a gap of only 45 min between their control test and the test after drug. This short interval probably was insufficient for the complete recovery from the effect of the first exercise, even though they have shown in four of their subjects that there was no significant differences between the circulatory measurements during the two successive periods of exercise without the administration of any drug. The other possibility of disagreement in finding may be due to the different mode of administration of the drug and the difference in dosage. Epstein *et al* (19) administered the drug intravenously (0.15 *mg* per *kg* body weight) just before the exercise, whereas our subjects were given the drug orally.

On maximal work load, the heart rate decreased by 6 beats at simulated altitude. Similar results are reported by others (12, 28). Max LA remained unchanged. This is in agreement with the finding of Stenberg *et al* (27) and Hermansen and Saltin (22). The HR max was reduced insignificantly by about 5 beats after the drug. This is in contrast to the findings of Epstein *et al* (19) who reported a significant reduction in heart rate during maximal exercise at sea level after the administration of the drug. This discrepancy may also be due to the difference in dosage and the different mode of admlnistration of the drug, as discussed earlier. The blood lactate level after the maximum exercise, also decreased though not sinificantly, after the drug. This is in agreement with Furberg (20) who observed a reduction in blood lactate concentration during work and also after three minutes of the exercise as a result of the beta blockade.

Maximal oxygen uptake capacity has been widely used as a measure of the capacity for prolonged work (1, 4, 15, 23, 28). Since the present study did not show any significant decrease in aerobic capacity after administration of the drug, we conclude that oral administration of Propranolol did not affect the aerobic capacity of the individual for prolonged work.

Epstein *et al* (19) found a significant fall (about 40%) in the endurance time. They estimated the endurance time, with and without beta blockade, by giving a work rate that produced exhaustion in 3-6 minutes. The criterion for the exhaustion in the objective feeling of the test subjects. The test would have been more meaningful if physiological criteria like heart rate or blood lactate level at the end of the exercise, were used. The activities of such duration depend to a large extent on the anaerobic capacity of the individuals. For a maximal effort which could be maintained for 4 minutes, the anaerobic processes contribute about 30% of the total energy need (5). It is possible that Propranolol interfered with the anaerobic processes which, in turn, decreased the endurance time. An indication for the decrease in anaerobic energy release can be seen by the decrease in blood lactate level in our subjects after the administration of Propranolol and from the data of Furberg (20) and Barnard and Foss (7), who reported lower blood lactate levels during exercise following Propranolol administration.

Cain (10) reported a significant decrease in oxygen debt in dogs after Propranolol both at altitude and at sea level which also indicates an impairment in the anaerobic metabolism.

ACKNOWLEGMENT

Authors' sincere thanks are due to Maj Gen Inder Singh, Senior Consultant (Medicine), Office of the DG, AFMS, New Delhi, and to Surg Capt M.S. Malhotra, I.N., Director, Defence Institute of Physiology and Allied Sciences, Delhi Cantt. for valuable suggestions and encouragement for the work. Thanks are also due to Shri Nand Kishore for statistical analysis of the data and to Sarvashri N. Srinivasulu, T. Sampathkumar and B.S. Arora, for teachnical assistance.

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