# EFFECT OF PROPRANOLOL AND PHENOXYBENZAMINE ON MUSCLE STRENGTH AND PHYSICAL ENDURANCE, AND ON EXERCISE-INDUCED CHANGES IN MUSCLE GLYCOGEN AND BLOOD LACTIC ACID LEVELS IN RATS

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**Summary :** Propranolol and phenoxybenzamine (PBZ) had no major effect on swimming-endurance performance and skeletal muscle pulling-strength in rats. Propranolol, like exercise itself diminshed the resting skeletal muscle glycogen (SMG) content, but the drug did not lower the resting blood lactic acid (BLA) levels. Propranolol significantly antagonised the 25-min exercise-induced BLA elevation, indicating that lactacidaemia is possibly a $\beta$-receptor response. However, propranolol did not exhibit an overall beneficial effect on swimming endurance. PBZ had a negligible effect on maximal swimming time (MST) and had no major effects on the SMG content and BLA levels.

**Key words :** propranolol, phenoxybenzamine, swimming endurance, pulling strength, blood lactic acid, skeletal muscle glycogen

## INTRODUCTION

Physical performance is analysed mainly in terms of exercise (work), strength and endurance. Bowman and Nott (3) explained the biphasic defatiguing action of adrenaline, on basis of a direct effect on the muscle fibre, as well as a facilitatory action on neuromuscular transmission.

The glycogenolytic and lactacidaemic responses of adrenaline involve $\alpha$-and/or $\beta$-adrenoceptors. The calorigenic, hyperglycaemic, fatty acid mobilising and lactic acid producing effects of exercise are antagonised by $\beta$-blocking agents (2, 9). Furberg (7) observed decreased endurance after propranolol, though the rate of rise of blood lactic acid (BLA) was lower during heavy work. However, in addition Furberg (6) found a

rapid depletion of muscle glycogen with propranolol. Thus in the ergogenic action, the participation of sympathetic nervous system and psychomotor stimulation is fairly clear, but the role of adrenoceptors is rather controversial (8, 20).

This study was undertaken to elucidate the role played by the adrenoceptors during exercise by using suitable adrenoceptor blocking agents, and by carrying out, simultaneously, the estimations of skeletal muscle glycogen and blood lactic acid.

## MATERIALS AND METHODS

Albino rats (Haffkine strain), of either sex, weighing between 100 and 250 *g* were used throughout the study.

*Rota-rod test ;*

The method of Dunham and Miya (5) was employed to determine the doses that produce no neurological deficit, and the peak activity time(s) for propranolol and phenoxybenzamine (PBZ). The test was done at fixed RPM (5 revolutions per min). The dose with which 50% of the animals fell from the rod within one min ($ED_{50}$) was determined by the method of Miller and Tainter (14). If the rat failed to remain on the rota-rod for a 1–min period, more than once, the neurological motor deficit was assumed to be present.

The $ED_{50} \pm$ SE of propranolol and PBZ was 12.88 $\pm$ 2.45 and 10.04 $\pm$ 2.24 *mg/kg* (ip), with peak activity time(s) as 30 and 80 min respectively, as determined by the rota-rod test. For further work the dose selected for propranolol was 9.75 *mg/kg*, ip (3/4 $ED_{50}$), and for PBZ, 5.00 *mg/kg*, ip (1/2 $ED_{50}$).

*Swimming-exercise test ;*

The method of Molinengo and Orsetti (15) was used. The rats were made to swim to exhaustion for the determination of maximal swimming time (MST), and the animals were removed from the bath when they were unable to surface on three repeated attempts. Naive rats were exercised, and no training preceded the experimental sessions. The MST was determined both before and after drug treatment.

*Muscle-pull test ;*

The method of Porter *et al.* (16) was followed in essential details. The "grip" reflex was exhibited by the animal while pulling on the mesh. Rats were made to pull a

wire mesh against a spring calibrated in grams. In an attempt to escape the tail restraint they pulled the sliding platform till they lost the grip.

*Estimations ;*

Blood lactic acid (BLA) was determined by the method of Barker and Summerson (1) and skeletal muscle glycogen (SMG) was estimated by the method of Kemp and Kits van Heijningen (12). For the post-exercise estimation of BLA and SMG, the animals were made to swim for 3 or 25 min and were sacrificed immediately after the swimming session.

Statistical analysis of data was done using Student's t-test for unpaired and t-test for paired means. A significant difference was assumed to exist with P values $< 0.05$.

The drugs used were propranolol hydrochloride (I.C.I., Macclesfield, Cheshire) and phenoxybenzamine hydrochloride (S.K. & F., Montreal). Control groups received normal saline (ip volume, 1.0 *ml/kg* body weight). The drugs, in dose(s) selected by rota-rod test, were dissolved in 0.9 % sodium chloride and were administered ip keeping in view their peak activity time.

## RESULTS

*Swimming-exercise test and muscle-pull test ;*

In the swimming-exercise test, it was observed that propranolol somewhat reduced the MST. The difference, however, was not significant. In a lower dose (6.5 *mg/kg*, ip), it had no effect on MST at all. PBZ also was found to have no effect on MST (Table I).

In the muscle-pull test, the pulling strength of rats was not significantly affected by either of the two drugs (Table I).

*Muscle glycogen and blood lactic acid levels ;*

Exercise itself significantly reduced SMG at 3 and 25 min. Propranolol decreased

TABLE I : Effect of porpranolol and phenoxybenzamine on the maximal swimming time (MST) and skeletal muscle pulling strength of albino rats.

| Drug (mg/kg, ip) | n | Swimming–Exercise Test: Maximal swimming time (min, Mean±S.E.M.) | | | Muscle–Pull Test: Pulling strength (g, Mean±S.E.M.) | | |
|---|---|---|---|---|---|---|---|
| | | Before drug | After drug | | Before drug | After drug | |
| Propranolol hydrochloride (9.75) | 6 | 17.5±6.71 | 7.9±3.29 | NS | 1241.7±102.00 | 1200.0±93.09 | NS |
| Phenoxybenzamine hydrochloride (5.00) | 6 | 33.8±5.76 | 34.2±5.99 | NS | 1258.3±91.67 | 1233.3±70.32 | NS |

NS : Value does not differ significantly from 'before drug value' (paired t-test)

the SMG content in the resting muscle ($P < 0.05$), but it had no further effect on the exercised (3 and 25 min) muscle. PBZ had no significant effect on the resting SMG content, or on the exercise-induced reduction in SMG content. BLA levels were affected peculiarly with propranolol. While exercise (3 or 25 min) significantly increased BLA, propranolol had no significant effect on the resting BLA level, or on 3 min-exercise induced rise of BLA, whereas it decreased significantly ($P < 0.01$) the BLA levels of 25 min exercise (Table II). PBZ did not alter the exercise–induced rise in BLA level at 3 or 25 min : neither was the resting BLA level affected (Table II).

TABLE II : Effect of propranolol and phenoxybenzamine on skeletal muscle glycogen (SMG) and blood lactic acid (BLA) levels of albino rats, after 3 and 25 min of swimming exercise sessions.

| Group(s)* | n | Skeletal Muscle Glycogen (mg/100 g) | | | Blood Lactic Acid (mg/100 ml) | | |
|---|---|---|---|---|---|---|---|
| | | Mean±S.E.M. | P** | | Mean±S.E.M. | P** | |
| *Propranolol hydrochloride (9.75 mg/kg, ip)* | | | | | | | |
| I (N-Ex) | 6 | 584.72±39.41 | — | | 11.17±0.97 | .. | |
| II (N-Ex+D) | 6 | 439.30±38.12 | <0.05 | (I/II) | 9.72±2.28 | NS | (I/II) |
| IIIa (Ex-3) | 6 | 353.51±38.75 | <0.01 | (I/IIIa) | 51.66±5.96 | <0.001 | (I/IIIa) |
| IIIb (Ex-25) | 6 | 382.76±14.91 | <0.001 | (I/IIIb) | 50.00±4.93 | <0.001 | (I/IIIb) |
| IVa (Ex-3+D) | 6 | 286.71±65.14 | <0.01 | (I/IVa) | 50.08±3.13 | <0.001 | (I/IVa) |
| IVb (Ex-25+D) | 6 | 336.33±58.46 | NS<br><0.01<br>NS | (IVa/IVb)<br>(I/IVb)<br>(IIIb/IVb) | 24.83±4.43 | <0.001<br><0.02<br><0.01 | (IVa/IVb)<br>(I/IVb)<br>(IIIb/IVb) |
| *Phenoxybenzamine hydrochloride (5.00 mg/kg, ip)* | | | | | | | |
| I (N-Ex) | 6 | 584.72±39.41 | — | | 11.17±0.97 | — | |
| II (N-EX+D) | 6 | 528.92±58.23 | NS | (I/II) | 21.67±4.68 | NS | (I/II) |
| IIIa (Ex-3) | 6 | 353.51±38.75 | <0.01 | (I/IIIa) | 51.66±5.96 | <0.001 | (I/IIIa) |
| IIIb (Ex-25) | 6 | 382.76±14.91 | <0.001 | (I/IIIb) | 50.00±4.93 | <0.001 | (I/IIIb) |
| IVa (Ex-3+D) | 6 | 446.80±60.30 | NS | (I/IVa) | 48.88±4.94 | <0.001 | (I/IVa) |
| IVb (Ex-25+D) | 6 | 464.56±65.35 | NS | (I/IVb) | 48.05±3.98 | <0.001 | (I/IVb) |

* I (N-Ex) non-exercised animals; II(N-Ex+D) non-exercised animals+selected dose of drug; IIIa(Ex-3) animals exercised for 3 minutes; IIIb(Ex-25) animals exercised for 25 minutes; IVa(Ex-3+D) animals exercised for 3 minutes+selected dose of drug; IVb(Ex-25+D) animals exercised for 25 minutes+selected dose of drug.

** Student s t-test for unpaired means applied (groups compared in parentheses).

NS : Value does not significantly differ from the control.

## DISCUSSION

Swimming, which is a submaximal muscular stress, affects general metabolism, haemodynamics, and the hormonal balance of the body (10). The compensatory and regulative forces function mainly through the autonomic nervous system. In our study propranolol caused a small, insignificant diminution in swimming time. In contrast, Thoren (19) observed a better performance by children subjected to submaximal and maximal exercise following $\beta$-blockade, although the total work capacity remained unchanged. Further, both propranolol and PBZ, exerted no effect on the pulling strength of rats.

Propranolol reduced the SMG levels, both in the resting and exercised muscle. Cronin (4) observed that $\beta$-blockade resulted in a diminished oxygen consumption (anoxia), and the overall efficiency of the skeletal muslce was not increased, which is in agreement with our findings. PBZ had no significant effect on the resting SMG levels and insignificantly antagonised the exercise-induced SMG fall. This is in agreement with the findings of Schwartz (18), who is of the opinion that PBZ has no major effect on adrenaline-induced glycogenolysis. On the contrary, Hornbrook and Brody (11) found that PBZ potentiates the metabolic effects of catecholamines.

In the present study a profound rise in BLA levels was registered after a 3 min spell of submaximal exercise, while on prolonged submaximal exercise (25 min) no further increase in BLA level was observed. This may be explained by a physiological shut down of anaerobic glycogenolysis, once a steady state is reached as suggested by Mathews and Fox (13). Another possibility could be that the utilization of lactate by the organism on prolonged exercise is greater than its production. Propranolol was found to significantly antagonize the 25 min-exercise-induced rise in BLA, when the lactic acid was in the phase of paying off the oxygen debt. Root and Hofmann (17) have indicated that lactacidaemia is a $\beta$-adrenergic response, and is effectively antagonised by $\beta$-blockers. Reports by Barnard and Foss (2) and Harris *et al.* (9) also support this finding. These workers have reported that propranolol clearly prevented the exercise-induced rise in arterial lactate and lactic acid-pyruvic acid ratio.

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