

Effects of Betamethasone on Rodent Erythropoiesis

J. E. Teruel, E. E. Guidi and J. L. Scaro

Instituto de Biología de la Altura. Universidad Nacional de Tucumán.
Facultad de Medicina. S. S. de Jujuy (Argentina)

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Normal, fasted and polycythemic mice were treated with high doses of betamethasone. Administration of the steroid results in a fall of splenic erythropoiesis and a diminished spleen responses to erythropoietin in fasted and polycythemic mice. The effect on bone marrow erythropoiesis varies from an increase in the normal group to a decrease in the fasted condition and no change in the polycythemic group. Bone marrow response to erythropoietin is not affected by betamethasone.

The effects of glucocorticoids on erythropoiesis of small rodents in several experimental conditions was studied (1, 3, to 9). However, the results obtained are not according as far. The relative rate of splenic and medullary erythropoiesis of glucocorticoid-treated animals were recently studied by LEVINE and CLAMAN, who demonstrated a diminished proliferative, hemopoietic and immunological capacity of mice spleen treated with cortisone acetate (10).

This study was made with the purpose of evaluate the effects of betamethasone on bone marrow and spleen erythropoiesis in normal, starved and polycythemic mice.

Materials and Methods

3 months-old female mice weighing 24-30 g were used. Groups of normal, fasted and polycythemic mice were injected daily, during four days, with betamethasone disodium phosphate* intraperitoneously (ini-

tial dose 1 mg followed of 0.4 mg on each subsequent day). Some groups were injected intraperitoneally with erythropoietin (EP) on days three and four. Normal, fasted and polycythemic groups were injected with EP solely and others were not treated and served as controls. On day five all mice were injected intravenously with 0.25 μ c of ^{59}Fe and three hours later were killed by decapitation. Mice were weighed at the time of dead. Spleen and thymus weights and hematocrit were determined. Activity of ^{59}Fe in bone marrow and spleen was determined in a scintillation counter (Nuclear Mod. EM). The amount of radioactivity in the entire spleen and two femurs was calculate as per cent of injected dose of ^{59}Fe . Total activity of bone marrow was obtained multiplying by seven the activity of the two femurs. Lymphocytolitic effect was evaluated through

* «Celestone» Schering. The doses used are expressed as pure betamethasone.

the loss of spleen and thymus weights. Erythropoietin used was contained in rabbit anemic plasma (erythropoietin activity: 1U International Reference Preparation/ml) (2). 0.20 ml were given intraperitoneally per dose. Polycythemia was induced by intraperitoneal injection of 1 ml washed red blood cells on day one.

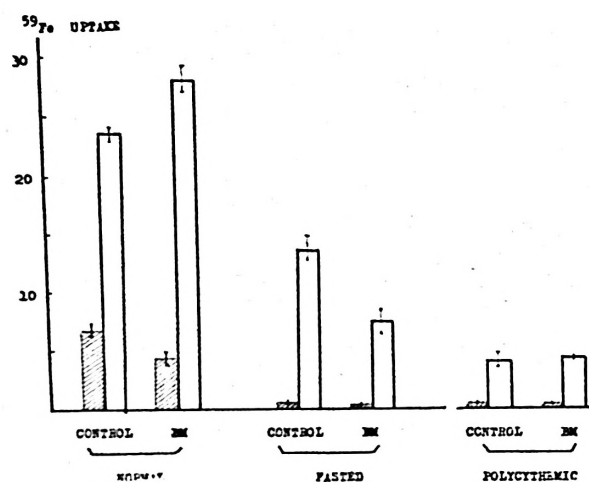


Fig. 1. Effects of betamethasone (BM) on the medullary and splenic ⁵⁹Fe uptake (%) of normal, fasted and polycythemic mice.
 ■ Spleen; □ bone marrow; vertical bars standard error.

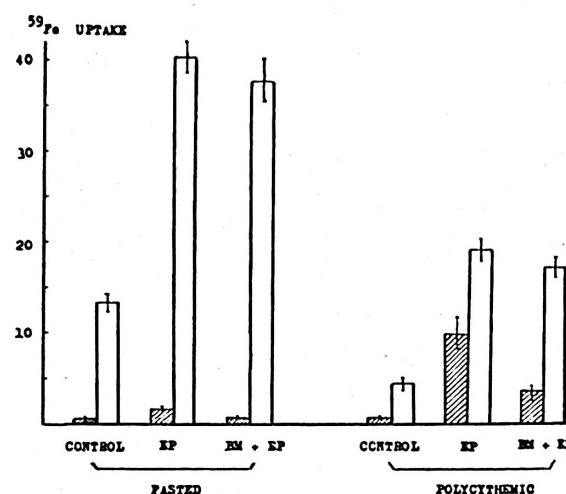


Fig. 2. Effects of betamethasone (BM) on medullary and splenic ⁵⁹Fe uptake of fasted and polycythemic mice treated with erythropoietin (EP).
 ■ Spleen; □ bone marrow; vertical bars standard error.

Results

Initial and final body weight, spleen and thymus weights and hematocrits are shown in Table I.

In normal mice betamethasone depresses splenic erythropoiesis ($P < 0.01$) and increases medullary activity ($P < 0.01$).

Table I. Effect of betamethasone (BM) and erythropoietin (EP) on the body weight lymphoid organs weights and hematocrit of the normal and polycythemic mice.
 The mean values are accompanied by the average standard error.

N.° mice	Treatment	Body weight (g)		Lymphoid organs weights (mg)		Hematocrit %
		Initial	Final	Spleen	Thymus	
19	Control	26.1 ± 0.31	26.9 ± 0.44	120.4 ± 3.60	62.4 ± 3.60	47.8 ± 0.56
19	BM	26.7 ± 0.60	27.1 ± 0.45	77.4 ± 3.56	39.0 ± 4.43	50.1 ± 0.59
11	Fasted	26.3 ± 0.05	19.5 ± 0.03	68.5 ± 3.40	29.8 ± 2.82	50.6 ± 0.62
12	Fasted + BM	26.6 ± 0.30	18.2 ± 0.36	37.9 ± 3.15	15.9 ± 2.64	51.6 ± 0.76
35	Fasted + EP	25.9 ± 0.08	18.0 ± 0.08	55.3 ± 2.26	24.7 ± 2.28	49.4 ± 0.98
20	Fasted + BM + EP	26.7 ± 0.31	17.7 ± 0.30	36.0 ± 1.74	10.0 ± 0.77	50.6 ± 0.83
11	Polycythemic	—	27.0 ± 0.92	114.1 ± 8.97	44.8 ± 3.67	64.6 ± 0.99
10	Polycythemic + EP	—	28.1 ± 0.69	159.5 ± 10.5	33.7 ± 3.21	63.7 ± 0.88
10	Polycythemic + BM	—	27.3 ± 1.05	89.8 ± 12.7	22.0 ± 4.12	67.8 ± 1.26
9	Polycythemic + BM + EP	—	27.3 ± 0.76	89.5 ± 10.6	16.0 ± 1.31	65.1 ± 1.93

Total (medullary plus splenic erythropoiesis) is not affected ($P < 0.2$). The diminished iron uptake capacity that follows starvation, in both spleen and bone marrow (11), shows a further reduction when betamethasone is given to fasted mice ($P < 0.05$). Total erythropoiesis decreases ($P < 0.01$). In polycythemic betamethasone-treated mice a fall of splenic erythropoiesis was found ($P < 0.001$) while medullary and total erythropoiesis remain unaffected. When betamethasone-treated animals were injected with EP the spleen response to EP was less than that of controls treated with EP solely. Thus, both fasted and polycythemic spleen responses to EP were prevented in part by betamethasone ($P < 0.001$ and $P < 0.02$ respectively). Medullary erythropoiesis was unaffected. Total erythropoiesis did not show difference in fasted mice whereas it was decreased in polycythemic group ($P < 0.01$).

Discussion

A relation between lymphopoietic depression and erythropoiesis has been suggested (9). Betamethasone in this study, was efficient to produce thymic and splenic involution. The lymphocytolytic effect on spleen, evaluated by changes on spleen weight, was accompanied with a diminished erythropoiesis in this organ. The effect was remarkable in fasted and polycythemic mice showing lower values of erythropoiesis than untreated animals in the same conditions. The uniformity of effects obtained on spleen area, in the three conditions above mentioned, were not observed on medullary activity. In this area betamethasone produces an increase of iron uptake in normal animals, a decrease in the fasted group and have not effect on the polycythemic group. Furthermore, the amply EP-response of medullary area in fasted mice was not modified by betamethasone.

Our data show that betamethasone have both lymphocytolytic and erythropoietic-depressive effects on spleen with variable action on medullary erythropoiesis. The concomitance of effects on the splenic area suggests a relation between lymphoid tissue and splenic erythropoiesis.

Resumen

Ratones normales, en ayunas y policitémicos, fueron tratados con dosis altas de betametasona. La administración del esteroide produjo una caída de la eritropoyesis esplénica y una disminución de la respuesta del bazo a la eritropoyetina en los ratones en ayunas y policitémicos. Los efectos sobre la eritropoyesis medular variaron desde un aumento en el grupo normal hasta una disminución en el grupo en ayunas, sin cambios en el grupo policitémico. La respuesta medular a la eritropoyetina no fue afectada por la betametasona.

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