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REVERSAL OF CATABOLISM BY BETA-BLOCKADE AFTER SEVERE BURNS

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ABSTRACT

Background The catecholamine-mediated hypermetabolic response to severe burns causes increased energy expenditure and muscle-protein catabolism. We hypothesized that blockade of β -adrenergic stimulation with propranolol would decrease resting energy expenditure and muscle catabolism in patients with severe burns.

Methods Twenty-five children with acute and severe burns (more than 40 percent of total body-surface area) were studied in a randomized trial. Thirteen received oral propranolol for at least two weeks, and 12 served as untreated controls. The dose of propranolol was adjusted to decrease the resting heart rate by 20 percent from each patient's base-line value. Resting energy expenditure and skeletal-muscle protein kinetics were measured before and after two weeks of beta-blockade (or no therapy, in controls). Body composition was measured serially throughout hospitalization.

Results Patients in the control group and the propranolol group were similar with respect to age, weight, percentage of total body-surface area burned, percentage of body-surface area with third-degree burns, and length of time from injury to metabolic study. Beta-blockade decreased the heart rates and resting energy expenditure in the propranolol group, both as compared with the base-line values ($P < 0.001$ and $P = 0.01$, respectively) and as compared with the values in the control group ($P = 0.03$ and $P = 0.001$, respectively). The net muscle-protein balance increased by 82 percent over base-line values in the propranolol group ($P = 0.002$), whereas it decreased by 27 percent in the control group (P not significant). The fat-free mass, as measured by whole-body potassium scanning, did not change substantially in the propranolol group, whereas it decreased by a mean (\pm SE) of 9 ± 2 percent in the control group ($P = 0.003$).

Conclusions In children with burns, treatment with propranolol during hospitalization attenuates hypermetabolism and reverses muscle-protein catabolism. (N Engl J Med 2001;345:1223-9.)

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THE hypermetabolic response to severe burns is associated with increased energy expenditure and the release of substrate from protein and fat stores. After severe trauma, the rate of protein catabolism is increased, leading to the loss of lean body mass and muscle wasting.^{1,2} Muscle proteolysis continues for at least nine months after severe burns,³ thus increasing the likelihood of delays in rehabilitation, other complications, and death.⁴

Endogenous catecholamines are primary mediators of the hypermetabolic response to trauma or burns.^{5,6} Shortly after severe trauma or burns, plasma catecholamine levels increase as much as 10-fold.^{7,8} This systemic response to injury is characterized by the development of a hyperdynamic circulation⁹ and an increase in basal energy expenditure¹⁰ and catabolism of skeletal-muscle protein.^{3,11} Blockade of β -adrenergic stimulation after severe burns decreases supraphysiologic thermogenesis,¹² tachycardia,¹³ cardiac work,¹⁴ and resting energy expenditure.¹⁵ Decreased rates of cardiac complications and overall mortality have been documented in patients without trauma who are given beta-blockers for the control of tachycardia after major surgical procedures.¹⁶ After burns, the elevations in basal energy expenditure and muscle-protein catabolism have been found to be correlated.¹⁷ Because beta-blockade decreases energy expenditure after burns,^{6,13} we hypothesized that long-term beta-blockade with propranolol would decrease the rate of muscle-protein catabolism as well.

METHODS

Subjects

This study was approved by the institutional review board of the University of Texas Medical Branch, and written informed consent was obtained from each patient's parent or guardian. Children could be enrolled if they were less than 18 years of age, had burns on

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more than 40 percent of their total body-surface area, and had been transferred to our hospital within one week after injury. Patients with a history of asthma were excluded.

Within 48 hours after admission, each patient underwent burn-wound excision and grafting with skin autografts and allografts. The patients returned to the operating room in 6 to 10 days, when the autograft sites had healed. Sequential staged grafting procedures were performed until the wounds were closed.

The patients were fed a commercial enteral formula (Vivonex T.E.N., Sandoz Nutritional, Minneapolis) through a nasoduodenal tube. The daily caloric intake was calculated to deliver 1500 kcal per square meter of body-surface area burned plus another 1500 kcal per square meter of total body-surface area. Enteral nutrition was started at admission and continued until the wounds healed. The patients remained in bed for five days after excision and grafting procedures, after which they were allowed to walk daily until the next excision-and-grafting procedure.

Study Design

From January through December 1999, 25 patients were enrolled in this prospective, randomized trial. Thirteen received propranolol, and 12 served as untreated controls. Randomization was performed with use of a random-number-generating scheme.

On the fifth day after the first surgical procedure, all patients underwent metabolic examination. Resting energy expenditure and net protein balance across one of the patient's legs (randomly determined) were the main outcome variables. In addition, all patients underwent whole-body potassium scanning at base line to determine the fat-free mass. Immediately after the next operation, the patients in the propranolol group began to receive propranolol by nasogastric tube at a dose of 0.33 mg per kilogram of body weight every four hours (total dose, 1.98 mg per kilogram per day). This dose was adjusted to achieve a 20 percent decrease in the heart rate of each patient, as compared with the 24-hour average heart rate immediately before drug treatment. Heart rate and blood pressure were monitored continuously throughout the study. When the mean blood pressure fell below 65 mm Hg, the dose of propranolol was withheld or decreased. The dose was then increased incrementally to meet the study goal of a decrease in heart rate by 20 percent from established base-line levels as tolerated. Propranolol was given as scheduled during surgical procedures.

Two weeks after treatment was started, a second series of metabolic and protein-kinetics studies was performed. Patients who had received at least a four-week treatment course underwent a second measurement of whole-body potassium. At discharge, the patients underwent body-composition scanning with use of dual-image x-ray absorptiometry.

Measurement of Vital Signs

Temperature, heart rate, and systolic and diastolic blood pressure were measured hourly with use of a standard bladder-temperature monitor, electrocardiographic monitor, and arterial catheter, respectively. The average for each 24-hour period was determined. The heart rate was compared between groups for the duration of the study. Other analyses of changes with treatment were made between groups with data gathered on the day of the stable-isotope study.

Measurement of Serum Glucose, Potassium, and Hormone Values

Serum levels of glucose and potassium were determined (Stat-5 analyzer, Novel Biomedical, Waltham, Mass.) on the morning of the stable-isotope studies. On the same morning, serum levels of insulin-like growth factor I were determined by ethanol extraction, and serum levels of growth hormone, cortisol, and insulin were determined by enzyme-linked immunosorbent assay or enzyme immunoassay (Diagnostic Systems Laboratories, Webster, Tex.).

Determination of Infections and Energy Expenditure

Infection was defined throughout hospitalization by the presence of burn sepsis, which we have previously described.¹⁷ Between mid-

night and 5 a.m. on the day of the stable-isotope study, oxygen consumption, carbon dioxide production, the respiratory quotient, and the resting energy expenditure were determined with use of a metabolic cart (model 2900, Sormedics, Yorba Linda, Calif.) at an ambient temperature of 30°C during continuous feeding.

Kinetics Study

On the fifth day after the first and third operations, all patients underwent a five-hour protein-kinetics study, as previously described,¹⁸ while receiving a continuous feeding. Briefly, an infusion of L-[ring-²H₅]phenylalanine (Cambridge Isotopes, Andover, Mass.) was given intravenously for five hours: the initial, or priming, dose was 2 μmol per kilogram and was followed by a dose of 0.08 μmol per kilogram per minute. Biopsy of the vastus lateralis muscle of the study leg was performed two and five hours after the commencement of the infusion. To determine blood flow in the leg, indocyanine green was infused into the femoral artery. Cross-leg amino-acid kinetics were calculated according to a three-compartment model described by Biolo et al.¹⁸

The blood levels of unlabeled phenylalanine and its isotopic counterpart were simultaneously determined by gas chromatography-mass spectrometry with the use of the internal-standard approach and *N*-methyl-*N*-(tert-butyltrimethylsilyl)trifluoroacetamide, as previously described.¹⁹ Levels of indocyanine green were determined spectrophotometrically at a wavelength of 805 nm (Spectronic 1001, Bausch and Lomb, Rochester, N.Y.).

Muscle samples were stored at -70°C. Each sample was weighed, and protein was precipitated out with 5 percent perchloric acid solution. An internal standard containing 5.9 μmol of L-[ring-¹³C₆]phenylalanine per liter was added and thoroughly mixed. The level of bound-protein precipitate was determined by comparison with a set of isotopically labeled phenylalanine dilution-calibration standards, with correction for the various weights of the labeled compounds.¹⁸

We calculated the fractional rate of synthesis of skeletal-muscle protein by determining the rate of incorporation of labeled phenylalanine into protein and then measuring the level of bound protein in the intracellular pool, as previously described.¹⁹

Determination of Body Composition

The fat-free mass was determined by whole-body potassium-40 scintillation counting in a heavily shielded counting room with a low level of background noise, a ³²NaI detector array, and a computed data-analysis method that has been validated for use in children.^{20,21} The counting precision of the instrument used is within less than 1.5 percent, and it was calibrated daily by using a bottle-manikin absorption phantom (Canberra Industries, Meriden, Conn.) with simulated fat overlays. Feeding and intravenous fluids were discontinued during the studies to minimize exogenous potassium contamination.

The total-body lean mass and fat mass were measured with use of a dual-image x-ray absorptiometer (model QDR-4500W, Hologic, Waltham, Mass.) with a pediatric software package. This system has a minimal mean error rate with respect to the measurement of fat-free mass in children.²² To minimize systematic deviations, the system was calibrated daily against a spinal phantom (Hologic) in the anteroposterior, lateral, and single-beam modes for quality control of the measurements.

Statistical Analysis

Data are presented as means ±SE. The distribution of the data was normal, and the degree of variation within individual subjects was similar. We did not control for differences between the groups in sex, age, or weight. Two-sided paired t-tests were used to compare data within groups. Comparisons between groups were made by unpaired t-tests. Fisher's exact test was used for frequency data. P values of less than 0.05 were considered to indicate statistical significance.

TABLE 1. CHARACTERISTICS OF THE PATIENTS.*

CHARACTERISTIC	CONTROL GROUP	PROPRANOLOL GROUP
Age (yr)	7.8±1.4	6.6±1.5
Sex (M/F)	9/3	8/5
Weight at admission (kg)	36.7±7.1	28.1±6.0
Body-surface area (m ²)	0.95±0.14	0.83±0.11
Percentage of total body-surface area burned	47±4	57±4
Percentage of total body-surface area with third-degree burns	39±5	41±5
Time from injury to initial metabolic study (days)	10±1	12±3
Time from injury to second metabolic study (days)	24±2	29±3

*Plus-minus values are means ±SE.

RESULTS

The characteristics of the patients are shown in Table 1. One of the 25 patients chose not to participate in the stable-isotope studies. Three patients (two in the control group and one in the propranolol group) were fully healed and discharged before receiving four weeks of treatment. These subjects did not undergo a second whole-body potassium-counting study.

Propranolol decreased the heart rate by 20 percent as compared with both the patient's own base-line value ($P<0.001$) and the value in the control group ($P=0.001$) (Fig. 1A). To achieve or maintain this decrease, the dose of propranolol was increased from the initial dose of 0.33 mg per kilogram given by nasogastric tube every four hours (total dose, 1.98 mg per kilogram per day) to an average dose of 1.05 ± 0.15 mg per kilogram every four hours (total dose, 6.3 mg per kilogram per day) by the end of hospitalization. Blood-pressure (Fig. 1B), temperature, and glucose values did not differ significantly between groups. None of the patients in either the control group or the propranolol group required mechanical ventilation except for brief periods perioperatively, and none had clinically significant pneumonia. The serum potassium values at two or four weeks were higher in the propranolol group ($P=0.05$) (Table 2).

At two weeks, resting energy expenditure and oxygen consumption had increased, with a minor decrease in carbon dioxide production, from base line in the control group. In contrast, patients in the propranolol group had significant decreases in these variables (Table 2). The respiratory quotient did not change significantly in either group (Table 2).

Concurrently with the decline in energy expenditure, beta-blockade also improved the kinetics of skeletal-muscle protein. Treatment with propranolol improved the net muscle-protein balance as compared with base-line values ($P=0.002$) and with values in the

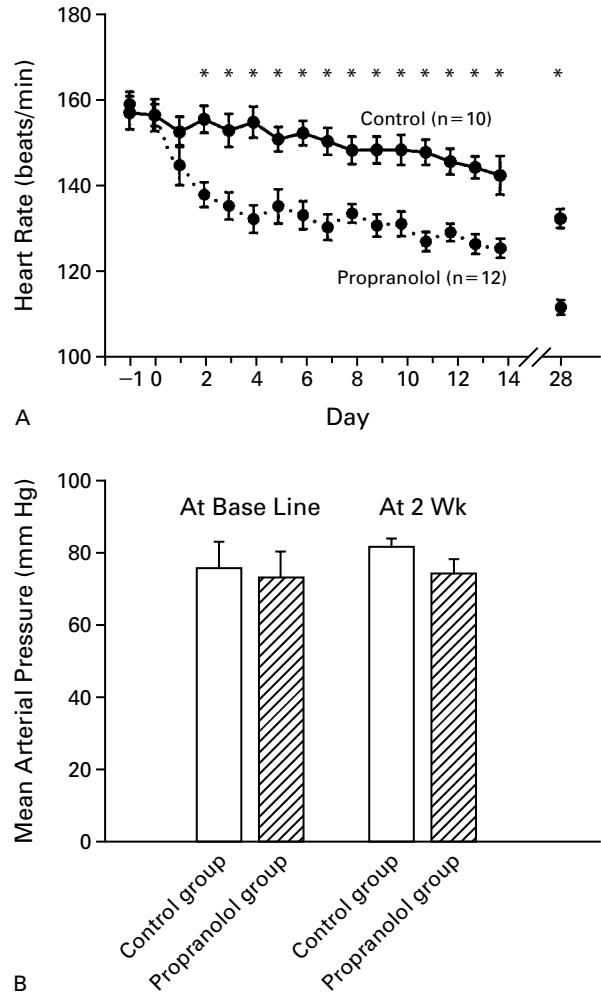


Figure 1. Mean (\pm SE) Heart Rate (Panel A) and Mean (\pm SE) Arterial Pressure (Panel B) before and during Treatment in the Two Groups.

Heart rate and blood pressure were measured hourly. Panel A shows the average heart rate before treatment (day -1), at base line (day 0), and during four weeks of treatment. Asterisks indicate significant differences ($P=0.001$) by t-test between the two groups. Panel B shows the mean arterial pressure at base line and on the day of the stable-isotope study, after approximately two weeks of treatment. There were no significant changes in arterial pressure either within or between groups.

control group ($P=0.001$) (Fig. 2). The remainder of the model-derived values for the studies comparing the propranolol group with the control group are listed in Table 3. In one of the studies in one patient, a steady state (in which the ratio of unlabeled to labeled phenylalanine was 1) was not reached, and thus this study was not included in the analysis. As a result of an increase in the efficiency of protein synthesis, there was an increase in protein synthesis, as measured by the rate of incorporation of the tracer into muscle over time, with long-term beta-blockade.

TABLE 2. CHANGES IN VARIOUS VALUES FROM BASE LINE.*

VARIABLE	CONTROL GROUP (N=12)			PROPRANOLOL GROUP (N=12)†			P VALUE‡
	AT BASE LINE	AT 2 WK	CHANGE	AT BASE LINE	AT 2 WK	CHANGE	
Systolic blood pressure (mm Hg)	110±6	112±3	1±5	111±4	108±4	-4±5	0.56
Diastolic blood pressure (mm Hg)	66±3	64±2	-2±5	64±2	58±4	-5±5	0.69
Mean arterial pressure (mm Hg)	75±8	81±3	6±9	73±7	74±4	1±8	0.70
Temperature (°C)	38.5±0.1	37.9±0.2	-0.6±0.2	38.6±0.1	38.0±0.1	-0.5±0.2	0.52
Serum potassium (mg/dl)	3.78±0.05	3.72±0.08	-0.1±0.1	3.33±0.09	3.76±0.13	0.4±0.2	0.05
Serum glucose (mg/dl)	153±16	114±4.0	-40±16	151±14	115±3	-30±13	0.67
Oxygen consumption (ml/min)	210±29	236±33	25±11	242±34	187±24	-56±22	0.002
Carbon dioxide production (ml/min)	219±32	212±26	-8±17	231±35	168±23	-64±22	0.045
Respiratory quotient	1.0±0.0	0.9±0.1	-0.1±0.1	1.0±0.0	0.9±0.1	-0.1±0.1	0.49
Resting energy expenditure (kcal/day)	1530±218	1670±221	140±67	1742±244	1321±173	-422±197	0.001
Leg blood flow (ml/100 ml of leg volume/min)	645±123	403±72	-242±308	436±75	306±78	-158±43	0.54
Insulin-like growth factor I (ng/ml)	64±9	123±16	54±12	64±11	112±19	44±13	0.56
Growth hormone (ng/ml)	1.5±0.4	2.0±0.9	0.5±1.0	1.4±0.5	1.1±0.4	-1.1±0.9	0.26
Cortisol (μg/dl)	15.2±1.7	10.2±2.3	-4.4±2.9	13.4±1.5	9.8±1.3	-2.2±2.1	0.58
Insulin (μIU/ml)	59.7±8.4	77.3±20.5	13.6±24.8	133±53	104±52	-21.0±17.3	0.29

*Plus-minus values are means ±SE. To convert values for potassium to millimoles per liter, multiply by 0.2558. To convert values for glucose to millimoles per liter, multiply by 0.05551. To convert values for cortisol to nanomoles per liter, multiply by 27.59. To convert values for insulin to picomoles per liter, multiply by 6.

†One of the 13 subjects in the propranolol group chose not to participate in any of the invasive studies.

‡P values are for the comparison between the change in the control group and the change in the propranolol group.

Twenty-two patients underwent whole-body potassium scanning a second time to evaluate changes in body composition during this period. The 10 control patients lost approximately 9 percent of their fat-free mass, whereas the 12 patients in the propranolol group lost only 1 percent ($P=0.003$) (Fig. 3). These results were independently confirmed by the results of dual-image x-ray absorptiometry, performed at the time of full healing and discharge from the hospital. Nine consecutive patients of the 25 enrolled in the study were not able to undergo dual-image x-ray absorptiometry because of technical difficulties with the scanner over a three-month period. The remaining seven patients in the control group had a lean body mass of 73.5 ± 1.5 percent, whereas the nine patients in the propranolol group had a value of 79.1 ± 1.2 percent, a difference of approximately 6 percentage points ($P=0.01$).

No adverse clinical sequelae resulted from beta-blockade. One or more doses of propranolol were withheld temporarily in 3 of the 13 patients in the propranolol group who had a mean arterial pressure between 60 and 65 mm Hg. These periods of decreased blood pressure were not related to sepsis or surgical procedures. Clinical sepsis developed during hospitalization in 3 of 12 control patients and 4 of 13

patients in the propranolol group ($P=1.0$). No other direct or indirect evidence of tissue hypoperfusion (i.e., no conversion of intermediate-thickness wounds to full-thickness wounds and no metabolic acidosis) was found at any time among the patients in the propranolol group. No episodes of wheezing were noted in any patient in the propranolol group.

DISCUSSION

During catabolism, muscle protein is degraded faster than it is synthesized, resulting in a negative net protein balance. We used stable-isotope methods and serial body-composition scanning to determine that beta-blockade with propranolol diminishes wasting of skeletal-muscle protein after severe burns. Thirteen severely burned children were given propranolol for up to four weeks and had a decrease in resting energy expenditure, without any adverse effects. Twelve of these patients had an improvement in net muscle-protein balance. Beta-blockade given over a period of weeks after severe burn led to an increase in lean body mass.

Catecholamines are the primary mediators of elevated energy expenditure after burns.^{5,6,15} Both direct^{5,6} and indirect¹⁵ calorimetry have been used to demonstrate that energy expenditure is decreased by beta-

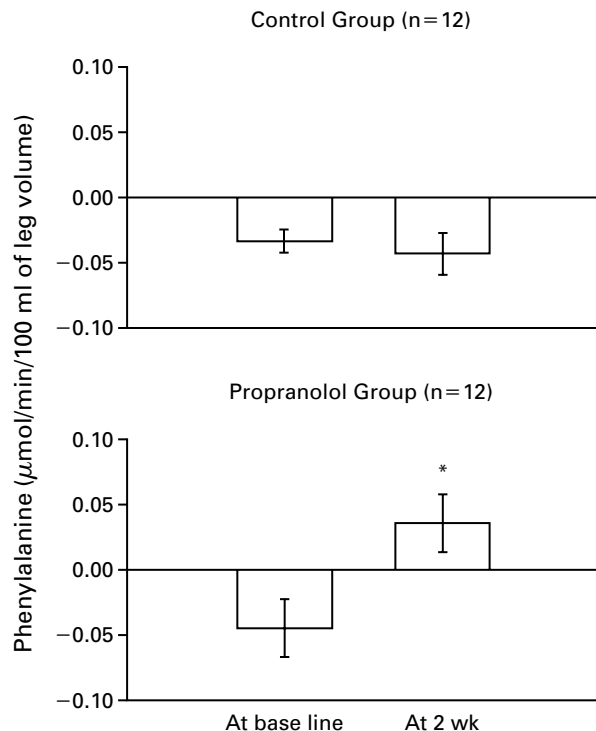


Figure 2. Mean (\pm SE) Change from Base Line in the Net Balance of Muscle-Protein Synthesis and Breakdown during Two Weeks of Treatment.

Values were obtained with use of a five-hour kinetic study that used isotopically labeled phenylalanine. The asterisk indicates a significant difference between the two groups ($P=0.001$ by *t*-test) and a significant difference between the base-line value and the value at two weeks ($P=0.002$ by paired *t*-test).

blockade after severe burns. Other studies have also demonstrated that urinary nitrogen losses²³ and whole-body urea production²⁴ are decreased by beta-blockade. Interestingly, β -agonists have been shown to stimulate muscle-protein synthesis in unstressed animals,^{25,26} although the relevance of such animal models to the physiological state of critically ill patients is unclear.

The net balance of protein synthesis and breakdown achieved anabolic levels during treatment with propranolol. Propranolol has a greater anabolic effect on muscle than other agents that have been evaluated in burn victims by methods similar to ours.²⁷⁻²⁹

To corroborate the results of our stable-isotope measurements, we used two independent body-composition tests. Fat-free mass, which corresponds to the sum of lean mass and bone mass, was measured by whole-body potassium scanning before and after four weeks of treatment. In the propranolol group, fat-free mass was preserved (the change was statistically no different from zero). In comparison, 10 control patients

lost 9 percent of their fat-free mass over this period. These results were confirmed by the results of dual-image x-ray absorptiometry, performed at the time of discharge in 16 patients.

Data derived from our stable-isotope studies provide insight into the physiological changes induced by beta-blockade at the tissue level. We found an acceleration in the rate of protein synthesis in the propranolol-treated patients. The post-traumatic increase in proteolysis is primarily the result of a large increase in protein degradation, which outweighs the increase in total protein synthesis.^{27,30,31} We found that propranolol induced an increase in the intracellular recycling of free amino acids. In the process of substrate reuse, free intracellular amino acids derived from stimulated protein breakdown were incorporated back into bound protein without leaving the myocyte.

Each of the methods we used to measure changes has limitations. For instance, we used labeled phenylalanine as the only tracer in the stable-isotope studies, assuming that since phenylalanine is neither synthesized nor degraded in the leg, any changes in the net balance reflect the total protein balance. This assumption has been verified in normal subjects but not in stressed, hypermetabolic subjects.³² Whole-body potassium scanning is based on the assumption that the ratios of potassium to nitrogen in skeletal muscle and nonskeletal muscle are constant. Wang et al. showed that this method may underestimate total lean body mass during conditions of muscle wasting.³³ A limitation of dual-image x-ray absorptiometry is that it overestimates lean body mass in patients with edema. However, all three methods demonstrated significant improvements in lean body mass with propranolol treatment, despite the different assumptions and shortcomings of each method, thus supporting the conclusion that propranolol treatment improves the accretion of lean body mass in severely burned children.

Any pharmacotherapy carries risks. Given carelessly, propranolol could cause hypoperfusion as a result of decreased cardiac output, particularly in patients with sepsis. In patients with other conditions, it could induce severe bronchospasm.

We had a specific therapeutic goal of decreasing the heart rate by 20 percent, a decrease that we have previously shown to be safe.¹²⁻¹⁴ The patients underwent continuous hemodynamic and respiratory monitoring, and there were no complications related to therapy. We found no significant decrease in blood pressure with propranolol treatment at these doses. However, propranolol was withheld temporarily from 3 of the 13 patients at some time during therapy because of a low mean arterial pressure, which indicates that patients receiving this treatment should be closely monitored. We have previously shown that propranolol treatment does not reduce the ability of patients with burns to respond to cold-induced stress.³⁴

We can only speculate on the possible mechanisms

TABLE 3. KINETICS OF SKELETAL-MUSCLE PROTEIN AFTER TREATMENT.*

VALUE	CONTROL GROUP (N=12)	PROPRANOLOL GROUP (N=11)	P VALUE
Net balance of protein synthesis and breakdown ($\mu\text{mol}/\text{min}/100$ ml of leg volume)	-0.042 ± 0.016	0.035 ± 0.011 †	0.001
Model-derived fluxes‡			
Inflow of phenylalanine into leg through femoral artery ($\mu\text{mol}/\text{min}/100$ ml of leg volume)	0.939 ± 0.175	1.085 ± 0.157	0.69
Outflow of phenylalanine from leg through femoral vein ($\mu\text{mol}/\text{min}/100$ ml of leg volume)	0.982 ± 0.180	1.034 ± 0.147	0.55
Transport of phenylalanine into myocyte ($\mu\text{mol}/\text{min}/100$ ml of leg volume)	0.145 ± 0.020	0.264 ± 0.046	0.18
Transport of phenylalanine from myocyte ($\mu\text{mol}/\text{min}/100$ ml of leg volume)	0.187 ± 0.026	0.214 ± 0.042	0.67
Arteriovenous shunt of phenylalanine past muscle ($\mu\text{mol}/\text{min}/100$ ml of leg volume)	0.795 ± 0.176	0.821 ± 0.127	0.46
Rate of disappearance of phenylalanine, approximating protein synthesis ($\mu\text{mol}/\text{min}/100$ ml of leg volume)	0.060 ± 0.013	0.157 ± 0.027	0.01
Rate of appearance of phenylalanine, approximating protein breakdown ($\mu\text{mol}/\text{min}/100$ ml of leg volume)	0.102 ± 0.015	0.107 ± 0.019	0.67
Muscle-protein synthesis of phenylalanine ($\mu\text{mol}/\text{min}/100$ ml of leg volume)	0.142 ± 0.034	0.337 ± 0.061	0.07
Muscle-protein breakdown of phenylalanine ($\mu\text{mol}/\text{min}/100$ ml of leg volume)	0.184 ± 0.030	0.287 ± 0.048	0.20
Efficiency of protein synthesis (%)§	38.7 ± 5.6	60.7 ± 3.4	0.03
Fractional synthetic rate (percentage of tracer incorporated into muscle/hr)	0.24 ± 0.03	0.34 ± 0.06	

*All values are means \pm SE. Leg volume was measured in each study; values per 100 ml of leg volume are shown, to account for different leg sizes.

†The analysis included 12 patients.

‡The model used was the three-compartment model describing protein kinetics in the muscle.¹⁸

§The efficiency of protein synthesis was calculated for each patient with use of the following equation: muscle-protein synthesis \div (transport of phenylalanine into muscle + muscle-protein breakdown).

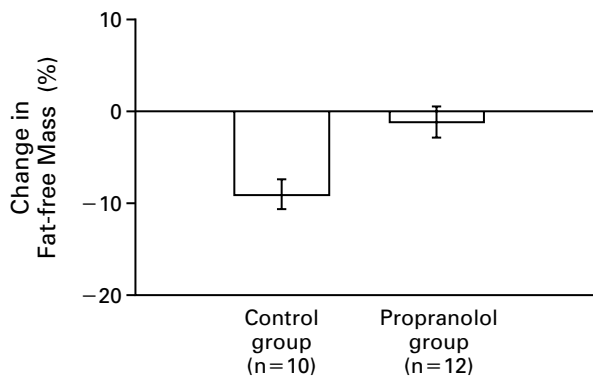


Figure 3. Mean (\pm SE) Change from Base Line in Fat-free Mass during Four Weeks of Treatment.

Values were determined with use of whole-body potassium scanning at base line and after four weeks of treatment. There was a significant difference ($P=0.003$ by t-test) between the two groups.

underlying the changes associated with propranolol treatment. Decreased catecholamine activity caused by beta-blockade could have direct effects on protein-flux machinery or could act indirectly by changing endogenous insulin responsiveness, cortisol activity, or regional blood flow. Larger studies will be required to make such determinations.

In summary, we have used indirect calorimetry, stable-isotope methods, whole-body potassium scanning, and dual-image x-ray absorptiometry to show that long-term beta-blockade decreases lean-mass catabolism in severely burned children. These changes would presumably improve the patients' strength and ability to recuperate. When it is given in doses that decrease the heart rate by approximately 20 percent from the base-line values and with careful monitoring, propranolol is safe, easily administered, and effective. This therapy may benefit a wide variety of patients who may have a negative nitrogen balance, such as those with trauma and those who are undergoing general surgery.

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