Steroid administration and nitrogen excretion in the head-injured patient

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The effect of steroid administration on metabolic rate and nitrogen excretion was examined in 20 head-injured patients alternately assigned to receive either methylprednisolone for 14 days or no steroid treatment. Although metabolic rate, caloric intake, and nitrogen intake were not different between the two groups, the patients who received steroids had a 30% higher excretion of nitrogen during the first 6 days after injury than did the patients not receiving steroids. All patients had an increase in nitrogen excretion through the 2nd week, peaking on Day 11. By Day 21 after injury, the patients had an average cumulative nitrogen loss of 162 gm and had lost an average of 5 kg body weight regardless of whether they had received steroids. Serum albumin levels decreased in the steroid-treated patients but returned to nearly normal by Day 21 in the untreated group. Immunosuppression, evidenced by a lower initial total lymphocyte count and a higher incidence of infections, was present in the steroid group; hyperglycemia requiring insulin treatment was more common in those patients.

KEY WORDS • corticosteroid • head injury • nitrogen excretion • steroid therapy • nutrition

The catabolic state that develops after a severe head injury has been partially attributed to the use of corticosteroids. Considerable experimental evidence exists to suggest that this might be a reasonable hypothesis. Steroid administration in normal animals increases nitrogen excretion, with greater protein degradation and decreased protein synthesis in skeletal muscle. Muscle wasting and a progressive myopathy can be associated with chronic administration of steroids. However, there is scant information regarding the relative importance of endogenously secreted hormones and administered steroids following a severe head injury. A catabolic state has been described in neurologically injured patients who have never been given steroids, but it is difficult to compare these patients to patients in other studies who were given varying doses of steroids.

The present investigation was designed to examine the effect of steroid administration on nitrogen balance and the subsequent clinical course during the first 3 weeks following a severe head injury. Steroid administration could be an important treatment variable to be considered when designing nutritional studies in head-injured patients. Randomized clinical trials of steroid administration have not demonstrated a consistent improvement in mortality rate or neurological outcome from head injury. The demonstration of a significant detrimental effect might encourage individualization of the use of steroids in head-injury treatment.

Clinical Material and Methods
This series included 20 head-injured patients admitted between September 1, 1983, and September 15, 1984, to the Ben Taub General Hospital with a Day 1 Glasgow Coma Scale (GCS) score of 7 or less. The patients were alternately assigned to receive either no steroids or methylprednisolone (Solu-Medrol), 100 mg/sq m/day for 10 days, followed by tapering doses for 4 more days. In all other respects, the patients were managed by a protocol that has been described in detail previously. The principles of management emphasized intubation and controlled ventilation, early evacuation of hematomas, and monitoring of intracranial pressure (ICP), with treatment of pressures over 20 mm Hg. Treatment of intracranial hypertension included hyperventilation, sedation with morphine, paralysis with pancuronium, cerebrospinal fluid drainage, administration of mannitol, and barbiturate coma for ICP uncontrolled by mannitol. Other routine medications included antibiotics for penetrating injuries and phenytoin (Dilantin) for seizure prophylaxis. Patients
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with intracranial hypertension severe enough to require repeated doses of mannitol were dropped from the study and steroids were administered.

All patients received 5% dextrose in 50% normal saline as their only caloric source for the first 3 days after injury. On Day 4, patients were begun on enteral feedings (Magnacal or Ensure Plus) if they had adequate bowel sounds, or parenteral alimentation with 25% dextrose and 4.25% amino acids (Travasol) if they had a persistent ileus. The feedings were advanced to a goal of 3500 kcal/day and 20 gm nitrogen/day.

Metabolic studies were conducted for the first 21 days after injury. Caloric and nitrogen intake was recorded daily. Resting metabolic expenditure was measured daily for 30 minutes to 2 hours with the use of a metabolic cart.* Daily urinary nitrogen was measured by the chemiluminescence technique.† Fecal nitrogen measured in selected patients was consistently less than 2 gm/day, and total nitrogen in all other patients was estimated by adding 2 gm to measured urinary nitrogen. Weight, total lymphocyte count, and creatinine-height index were measured daily. Serum albumin was measured twice a week.

All summary data are expressed as means ± standard deviations. Data from patients who received methylprednisolone were compared by a t-test to data from patients receiving no steroids. A p value < 0.05 was considered significant.

Results

Patient Characteristics

Table 1 lists the epidemiological information of the patients studied. The 20 patients are representative of the population of head-injured patients at Ben Taub General Hospital in that there was a predominance of young men and of intracranial hematomas, 50% of patients had a favorable outcome and 20% died of their neurological injury. The two treatment groups were not different in type of injury, age, or sex distribution.

Although at least 3 days of data were collected in all 20 patients, eight patients (four in each group) were dropped from the study before the entire 21 days of information were obtained. The reasons included early awakening from coma (two patients), development of severe intracranial hypertension (three patients), or death (three patients). Both patients who awakened quickly were in the untreated group, whereas four of the six patients who developed severe intracranial hypertension or died were in the group receiving steroids. The data from all 20 patients were only analyzed for the first 3 days after injury; although this information is not contaminated by nitrogen intake, it may be biased by the presence of more severe injuries in the steroid group. In contrast, the 3-week resting metabolic expenditure and nitrogen balance data, as well as the clinical course data, were recorded only for the 12 patients (six in each group) who completed the study. These 12 patients represented a more homogeneous subset of head-injured patients who were not fatally injured, who slowly improved neurologically, and who could be consistently fed for 21 days; in addition, the two groups were comparable in severity of injury and neurological outcome.

Table 2 lists the mean values for some indicators of the baseline nutritional status in all 20 patients.

* Metabolic cart (Beckman Horizon MMC) manufactured by Beckman Instruments, Inc., Fullerton, California.
† Chemiluminescence technique developed by Antek Instruments, Houston, Texas.
were no differences in weight (expressed as kilograms or as percent of ideal body weight), creatinine-height index, or albumin levels between the two groups. Total lymphocyte count, however, was significantly lower on Day 1 in the patients who received steroids: 654 ± 417 compared to 1587 ± 719 in the no-steroid group. Corticosteroid administration is known to have a rapid lymphopenic effect in man. Since total lymphocyte count was first measured after the patients in the steroid group had received at least one dose of methylprednisolone, the difference between the groups probably reflected the steroid administration rather than preexisting nutritional status.

**Metabolic Rate and Nitrogen Excretion**

Resting metabolic expenditure on Day 1 after injury was an average of 25% greater than expected for a person of similar body size and sex, and tended to remain constant or decrease during the 1st week after injury. Thereafter, as sedative and paralyzing drugs were discontinued and as the patients improved neurologically, resting metabolic expenditure increased: there were no differences in this between the two groups at any time during the 21 days (Fig. 1 left).

As shown in Table 3, nitrogen loss during the first 3 days after injury was higher in the patients receiving methylprednisolone: 14.3 ± 4.1 compared to 11.3 ± 2.5 gm/day in the no-steroid group. As the patients received alimentation (Fig. 1 center), nitrogen excretion increased dramatically, and the differences in nitrogen loss between the two groups disappeared. By Day 7, nitrogen excretion was 16.8 ± 2.0 and 17.8 ± 8.8 gm/day in the steroid group and the no-steroid group, respectively. By Day 14, when the steroids had been tapered and discontinued, nitrogen excretion was 25.0 ± 12.6 and 23.7 ± 8.7 gm/day, respectively. During the 3rd week after injury, nitrogen excretion decreased similarly in both groups.

Although the rapidity with which feedings could be increased varied from patient to patient, by Day 8 caloric intake was sufficient to replace the measured metabolic expenditure on 96% of the 168 patient days, and after Day 9, nitrogen intake averaged between 15 and 20 gm each day in both groups. There were no differences in caloric or nitrogen intake between the two groups at any time during the 3 weeks. As shown in Fig. 1 right, cumulative nitrogen balance became progressively more negative in the patients receiving steroids during the first 6 days after injury, remained consistently about 30 gm more negative during Days 7 to 14, and then by the end of the 3rd week was no different from that of the patients receiving no steroids.

**Clinical Course**

All patients who completed the study improved neurologically during the 3 weeks. Average GCS score was 6 on Day 1, and increased to 11 by Day 21. There were no significant differences between neurological recovery in the two groups. Two patients in each group were awake, although confused, and two patients in each group remained in a vegetative condition on Day 21.

All patients gradually lost weight and muscle mass, an average of 5 kg or 7% of total body weight in both groups (Fig. 2 left). If 1 kg of lean muscle is assumed to contain 30 gm of nitrogen, then the 5-kg weight loss agrees closely with the 21-day average cumulative nitro-
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![Graphs showing weight, serum albumin, and total lymphocyte count over time after injury.]

**Fig. 2.** Comparison of anthropometric indices in the two groups of patients with complete 3-week studies. Each point represents an average of all measurements made during a 5-day period. *Asterisk* = difference between the groups (p < 0.05). Left: Weight (kg). Center: Serum albumin level (gm/dl). Right: Total lymphocyte count (TLC).

gen loss of 162 gm. Despite the similar 21-day cumulative nitrogen balance and weight loss, serum albumin decreased from 3.0 ± 0.4 to 2.6 ± 0.2 gm/dl in the patients who received methylprednisolone, while it increased from 2.9 ± 0.6 to 3.5 ± 0.8 gm/dl in the untreated group (Fig. 2 center). Since serum albumin has a lag time of approximately 10 days in response to nitrogen balance, the lower albumin level at 3 weeks in the steroid group may reflect the higher nitrogen excretion on Days 1 to 6, rather than the cumulative nitrogen balance at 3 weeks.

Total lymphocyte count was lower in patients receiving methylprednisolone in the acute phase of injury, but after Day 5 it was not different in the two groups (Fig. 2 right). The patients receiving steroid had more infections, including two with bacterial pneumonia, three with urinary tract infections, and one with disseminated candidiasis, compared to two with urinary tract infections in the no-steroid group. In addition, hyperglycemia was more common and insulin requirements were higher in the steroid-treated patients.

**Discussion**

Previous studies have shown that cortisol levels are commonly elevated in head-injured patients for 10 days to 2 weeks after the injury. The present study documents that additional steroids administered to such patients will increase fasting nitrogen excretion by about 30%. Nitrogen intake has such an impact on nitrogen excretion that the effect of steroid administration was obscured as the patients received alimentation. However, if albumin is considered a marker of visceral proteins, then the higher nitrogen loss early in the patient's course was clinically significant in producing a reduction of visceral proteins.

Exogenous steroid administration, however, is clearly not the cause of the catabolic state in the head-injured patient. Both groups of patients continued to lose weight and were in negative nitrogen balance even at the end of the 3rd week after injury, despite substantial caloric and protein intake. In contrast, metabolic rate was not affected by exogenous steroid administration. Caloric expenditure in the head-injured patient has been found to be most closely related to severity of injury, body temperature, and the amount of spontaneous motor activity. The change in resting metabolic expenditure with duration after injury demonstrated in the present study probably results from sedation and therapeutic paralysis of the patients during the 1st week after injury, and from the neurological improvement with increased motor activity after Day 7.

Future metabolic studies in head-injured patients should be controlled for steroid administration, since exogenous steroids can definitely increase nitrogen excretion. In the head-injured patient in whom ICP is monitored and the treatment of intracranial hypertension individualized, the risks of increasing catabolism, impairing immunocompetence, and producing hyperglycemia should be weighed in the decision whether to administer steroids.

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**References**


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