THE ADRENAL RESPONSE TO TRAUMA, OPERATION AND COSYNTROPIN STIMULATION

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Thirty-four patients who underwent abdominal or thoracic, or both, operation for injuries were studied. Serum and urinary cortisol levels were elevated perioperatively and returned to normal levels by the fourth postoperative day. Postoperative complication was associated with persistent elevation of levels of serum and urinary cortisol. Baseline serum cortisol levels correlated with Injury Severity Scores. Cosyntropin stimulation produced a significant rise in serum cortisol to a peak level of 47.4 ± 10.2 (S.D.) micrograms per deciliter in patients after emergency operations for traumatic injury. Use of the cosyntropin stimulation test for the diagnosis of postoperative adrenal insufficiency can be extended to patients who undergo operation for traumatic injury.

The adrenal response of patients to the stress of trauma or operation has been characterized (1-5). In addition, the cosyntropin stimulation test has been performed and normal values established in patients who have undergone elective operations (3, 6, 7). Although rare, postoperative adrenal insufficiency is usually fatal if not diagnosed and treated. The recognition of adrenal insufficiency in patients operated upon for extensive traumatic injury is often difficult because of the unavailability of historical information and sometimes turbulent postoperative courses. Recognition of adrenal insufficiency in these patients would be facilitated by the establishment of the normal adrenal response to cosyntropin stimulation after operation for extensive traumatic injury. Herein, we evaluate the adrenal response to traumatic injury and operation, and we apply the cosyntropin stimulation test to patients who were operated upon in an emergency situation for traumatic injury.

MATERIAL AND METHODS

Thirty-four patients who underwent emergent abdominal or thoracic, or both, operation while receiving general anesthesia for traumatic injuries were evaluated. Injury Severity Scores (8) were calculated for all patients. All operations were at least one hour in duration. Physical findings and history, when obtainable, on admission did not suggest adrenal insufficiency in any patient. Patients were interviewed postoperatively and the hospital course was monitored for symptoms or signs of adrenal insufficiency.

Four patients had serial serum and 24 hour urine cortisol determinations from admission to the emergency room through the seventh postoperative day. Serum cortisol levels were drawn before, during and immediately after operation and at 8 A.M. and 8 P.M. for seven days. Urine was collected from the end of the operation for seven days in 24 hour aliquots.

Thirty patients underwent a cosyntropin stimulation test at 12, 24 or 48 hours after induction of anesthesia. After a baseline serum cortisol level was obtained, 200 micrograms of cosyntropin was administered intravenously. Two hours later, a "stimulated" cortisol level was obtained.

All serum cortisol levels were drawn from an intra-arterial catheter, if present, or by routine venipuncture. The blood was centrifuged and the serum stored at zero to 4 degrees C. Urine was collected by a Foley catheter, when present, and stored. All specimens from an individual patient were analyzed simultaneously by radioimmunoassay (Gammacoat I 125 cortisol radioimmunoassay kit, Clinical Assays, Travenol Laboratories, Incorporated). Serum cortisol levels were expressed in micrograms per deciliter and urinary cortisol production in micrograms per day.

In four patients studied with serial serum and urinary levels, values were plotted against time and correlated with the postoperative course of the patient. In 30 patients whose adrenal function was tested after traumatic injury and after operation, the relationship between Injury Severity Score and baseline level of serum cortisol was analyzed by linear regression analysis. The serum cortisol response to cosyntropin stimulation was compared...
with baseline values by paired Student's t tests. Similarity of degree of trauma was verified by analysis of variance of Injury Severity Scores. Adrenal response to cosyntropin was compared at different intervals after operation by analysis of variance.

In another study, 125 patients were stimulated with cosyntropin at different intervals after elective extensive operations to a mean serum cortisol level of 43.9±12.4 micrograms per deciliter (7). We compared stimulated cortisol levels from the 30 patients we operated upon after traumatic injury to the previously established normals by the two-tailed Student's t test. A new expected stimulated serum cortisol level in patients after emergent operations for traumatic injury or after elective operation was established by weighted averaging of the means.

RESULTS

Serum and urinary cortisol levels measured in four patients after operations for trauma were elevated in the perioperative period. Diurnal variation was recovered by the third postoperative day. In Figure 1, a patient who had an uncomplicated convalescence is compared with a patient who had a complicated recovery. Hepatocellular failure recognized by increased values from liver function tests and confirmed by histologic examination of specimens taken at biopsy developed in the latter patient. No cause for hepatocellular failure was found. The patient recovered from the injury, operation and hepatocellular dysfunction without further complication.

Baseline serum cortisol levels obtained 12 and 48 hours after operation for trauma correlated with Injury Severity Scores (linear regression analysis, r=0.73, p=0.017, and r=0.63, p=0.049, respectively). Twenty-four hours after trauma and operation, the baseline cortisol levels of ten patients were related to their Injury Severity Scores, but the association did not reach statistical significance (r=0.52, p=0.12).

Three groups of ten patients who received cosyntropin adrenal stimulation at different intervals after operation had suffered similar degrees of trauma. Injury Severity Scores (Table I) were similar (analysis of variance, p=0.18). Baseline cortisol levels were 28.4±12.0 micrograms per deciliter, 25.2±8.3 micrograms per deciliter and 20.4±10.2 micrograms per deciliter at 12, 24 and 48 hours after induction of anesthesia, respectively. Two hour stimulated levels were 44.7±9.4 micrograms per deciliter, 48.6±12.5 micrograms per deciliter and 48.9±8.7 micrograms per deciliter (Table II). Neither baseline levels nor stimulated levels differed significantly among the three groups (analysis of variance, p=0.23 and 0.60, respectively) (Fig. 2).

The stimulated serum cortisol levels in patients after elective extensive operation (43.9±12.4 micrograms per deciliter [7]) and in patients after traumatic injury and operation (47.4±10.2 micrograms per deciliter) were similar (Student's t test, p=0.1). The data were combined, and a normal

![Fig. 1. Serum and urinary cortisol levels in patient with an unremarkable recovery and a patient with a complicated recovery. Solid and open circles, serum and urinary cortisol levels, respectively, in a patient with an uncomplicated recovery, and solid and open triangles, serum and urinary cortisol levels, respectively, in a patient with postoperative complications.](image-url)
serum cortisol response to cosyntropin based on 155 patients treated by extensive operation electively or after traumatic injury was 44.5±12.0 micrograms per deciliter.

**DISCUSSION**

Postoperative adrenal insufficiency is rare but usually fatal if not diagnosed and treated. Incidences of one instance in 8,109 urologic surgical procedures (9) and five in 4,364 cardiac surgical procedures (10) have been reported. The actual incidence is probably higher because of a lack of diagnosis. Postoperative adrenal insufficiency is not obvious; its symptoms and signs are similar to those of many more common postoperative processes. Preoperative adrenal insufficiency is the most common cause of postoperative adrenal insufficiency. Therefore, a careful history and physical examination are critical for diagnosis of adrenal insufficiency preoperatively. When doubt exists preoperatively, formal adrenal evaluation can prevent disastrous postoperative results. In the population of patients with traumatic injury, medical history is usually unavailable and the patient is often unable to provide any history that might suggest preoperative adrenal insufficiency. Patients with traumatic injury who require surgical treatment are often taken quickly to the operating room before elaborate evaluations are undertaken.

The stress of operation has been described well in the literature. In the 1950s, serum cortisol, as a measure of adrenal function, was determined indirectly by quantitating total and free 17-hydroxycorticosteroids (11, 12). More recently, serum cortisol has been measured directly by radioimmunoassay techniques in elective extensive operations (3), operations upon the neck (5), cardiac operations (4) and surgical procedures for traumatic injury (2, 13). Serum and urinary cortisol levels were elevated immediately after operation but returned to the normal range in one to two days. Persistent or transient increases in serum cortisol corresponded to periods of postoperative complications; serum cortisol values returned to the normal range after resolution of the complications (3, 14).

Our results confirm previously described serum and urinary cortisol elevations after trauma and operation. Patients with uncomplicated recoveries had a prompt return to normal serum and urinary cortisol levels; postoperative complication was associated with persistent elevation of cortisol levels.

In one study, serum cortisol was found to be increased with severity of injury until injury was severe and cortisol levels decreased. Decreased adrenal blood flow secondary to shock was sug-

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**TABLE II.—SERUM CORTISOL LEVELS BEFORE AND AFTER COSYNTROPIN STIMULATION**

<table>
<thead>
<tr>
<th></th>
<th>12</th>
<th>24</th>
<th>48</th>
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<tbody>
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<td>n</td>
<td>10</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Base line</td>
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<td>25.2±8.3</td>
<td>20.4±10.2</td>
</tr>
<tr>
<td>Stimulated</td>
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<td>48.6±12.5</td>
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<tr>
<td>Increment</td>
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<td>23.4</td>
<td>28.6</td>
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Levels are micrograms per deciliter, mean plus or minus the standard deviation.
gested as an explanation for the reversal of this relationship (1). Our data demonstrated a correlation between the Injury Severity Score and baseline cortisol levels.

In other studies, patients were stimulated at various intervals after elective extensive operations with cosyntropin; a similar stimulated serum cortisol level was found regardless of the baseline serum cortisol or the interval between induction and stimulation (6, 7). We, too, found no correlation between baseline or stimulated cortisol values and the interval after operation for extensive trauma. However, patients demonstrated significant adrenal response to cosyntropin stimulation at 12, 24 and 48 hours after operation for trauma, which were similar to those demonstrated in patients undergoing elective extensive operations (7). The superimposition of serious trauma on operation affected the baseline but not the stimulated serum cortisol level. Therefore, we combined the two series of patients to characterize more precisely the cosyntropin stimulation test. A normal postoperative cosyntropin stimulated test defined in 155 patients required a serum cortisol level of 44.5±12.0 micrograms per deciliter two hours after intravenous administration of 200 micrograms of cosyntropin.

SUMMARY

When one is faced with a patient in extremis after trauma, elective operation or emergent operation, dexamethasone should be administered and a cosyntropin test performed. Once the stimulated serum cortisol level is drawn, hydrocortisone, which would interfere with cortisol measurement, may be substituted for dexamethasone to provide a mineralocorticoid effect not present with dexamethasone. All patients, regardless of their age and sex, duration and invasiveness of the operative procedure, the interval since operation or the presence of preoperative trauma, were stimulated to a mean serum cortisol level of 44.5±12.0 micrograms per deciliter. Therefore, a stimulated serum cortisol level of ≥20.5 micrograms per deciliter will include 97.5 per cent of normal patients. If the stimulated cortisol level is <20.5 micrograms per deciliter, adrenal insufficiency is likely and steroid therapy should be continued. If the adrenal response is adequate, then steroid therapy and its attendant risk of immunosuppression, wound healing impairment and metabolic derangement can be discontinued and the patient carefully observed.

The adrenal response to operation is not altered by antecedent trauma. The cosyntropin stimulation test can be used in patients with trauma who undergo emergent operations for the diagnosis of postoperative adrenal insufficiency.

REFERENCES