Gastrointestinal Complication of High-Dose Corticosteroid Therapy in Acute Cerebrovascular Patients

GIAN ANDREA OTTONELLO, M.D. AND ALBERTO PRIMAVERA, M.D.

SUMMARY Corticosteroids are commonly used in the treatment of stroke, although their clinical effectiveness has not been established. Side effects, especially gastrointestinal complications, occur in patients with cerebral diseases. A necroscopy study of 124 patients investigated the occurrence of gastrointestinal lesions in patients with acute stroke treated with high-dose of corticosteroids compared to untreated patients with stroke and to patients dying from non-vascular neurological diseases. A significant relationship between the use of steroids and gastrointestinal lesion in strokes is demonstrated.

Steroids are commonly used in the treatment of stroke, but reports on their clinical effectiveness are conflicting. Dexamethasone in high doses was reported to be beneficial in the studies of Patten et al., while Spiro and Miles noted that adrenocorticosteroids, at equally high doses, caused ulcer and the recent study of Jick and Porter supported the view that corticosteroids were strongly associated with gastrointestinal bleeding.

Since upper gastrointestinal hemorrhage is a common complication of cerebral disease we investigated the incidence of gastrointestinal lesions in patients with acute stroke treated with high-dose corticosteroid therapy. They were compared with untreated stroke patients and patients with non-vascular neurological disease.

Subjects and Methods

Postmortem examinations were performed on 124 patients who died in the Department of Clinical Neurology of the University of Genoa from November 1967 to November 1975. Patients with a history of gastrointestinal disease were excluded as well as patients treated with anticoagulants.

The patients in this study were classified (table 1) and allocated to steroid or non-steroid treatment groups. Patients in the steroid group had been treated with dexamethasone, at least 6 mg/day, or other corticosteroids at equivalent dosage.

Results

Of 124 patients, 28 (22%) had evidence of upper gastrointestinal lesions at necropsy. Melena and hematemesis were observed only in 9 patients. Gastrointestinal lesions were found in 18 of 73 patients with acute stroke (24%): 7 had gastric erosion, 2 stomach ulcer, 1 duodenal ulcer and 8 multiple erosions. The frequency of these lesions in the steroid group was significantly higher ($\chi^2$-test) than in patients with cerebrovascular disease who did not receive corticosteroid therapy (37% vs 14%; table 2).

In patients with cerebral infarction, the frequency of gastrointestinal changes was significantly higher in the steroid-treated group (40%) than in the non-steroid group (10%). In patients with cerebral hemorrhage there was no significant difference (table 3) but the time of survival and the duration of corticosteroid treatment were significantly shorter ($t$-test: $p \leq 0.50$) in these patients with cerebral hemorrhage (5.8 days ± 3.7) than in patients with cerebral infarction (9.9 days ± 4.9). Upper gastrointestinal lesions among untreated patients with cerebral hemorrhage were about twice as frequent (18% vs 10%) as in untreated patients with cerebral infarction (table 3).

No statistically significant differences were found with respect to other ulcerogenic drugs, nasal-gastric tube, use of antacids or the rostrocaudal cerebral deterioration syndrome.

Among 51 patients with other neurological disease, gastroduodenal changes were found in 10 patients (18%), including 4 with gastric erosions, 1 with gastric ulcer, 5 with multiple erosions. In these patients the incidence of these complications was higher in the steroid treatment group (25%) than in non-steroid group (15%). But the relationship between frequency

<table>
<thead>
<tr>
<th>TABLE 1 Classification of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke</td>
</tr>
<tr>
<td>Cerebral ischemic infarction</td>
</tr>
<tr>
<td>Cerebral hemorrhage</td>
</tr>
<tr>
<td>Brain tumors</td>
</tr>
<tr>
<td>Meningo-encephalitis</td>
</tr>
<tr>
<td>Degenerative disease</td>
</tr>
<tr>
<td>Other</td>
</tr>
</tbody>
</table>
TABLE 2 Incidence of Gastrointestinal Lesions in Relation to Steroid Therapy (Total Sample)

<table>
<thead>
<tr>
<th>Type of disease</th>
<th>Group</th>
<th>No. patients</th>
<th>No. gastrointestinal changes</th>
<th>%</th>
<th>x²-test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebrovascular disease</td>
<td>Steroid</td>
<td>32</td>
<td>12</td>
<td>37%</td>
<td>P &lt; 0.05</td>
</tr>
<tr>
<td></td>
<td>Non steroid</td>
<td>41</td>
<td>6</td>
<td>14%</td>
<td></td>
</tr>
<tr>
<td>Other neurological disease</td>
<td>Steroid</td>
<td>24</td>
<td>6</td>
<td>25%</td>
<td>N.S.</td>
</tr>
<tr>
<td></td>
<td>Non steroid</td>
<td>27</td>
<td>4</td>
<td>15%</td>
<td></td>
</tr>
</tbody>
</table>

N.S. = not significant.

TABLE 3 Patients with Cerebral Infarction or Cerebral Hemorrhage. Incidence of Gastrointestinal Lesions Related to Steroid Therapy

<table>
<thead>
<tr>
<th>Type of disease</th>
<th>Group</th>
<th>No. patients</th>
<th>No. gastrointestinal changes</th>
<th>%</th>
<th>x²-test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebral infarction</td>
<td>Steroid</td>
<td>15</td>
<td>7</td>
<td>40%</td>
<td>P &lt; 0.05</td>
</tr>
<tr>
<td></td>
<td>Non steroid</td>
<td>19</td>
<td>2</td>
<td>10%</td>
<td></td>
</tr>
<tr>
<td>Cerebral hemorrhage</td>
<td>Steroid</td>
<td>17</td>
<td>5</td>
<td>29%</td>
<td>N.S.</td>
</tr>
<tr>
<td></td>
<td>Non steroid</td>
<td>22</td>
<td>4</td>
<td>18%</td>
<td></td>
</tr>
</tbody>
</table>

N.S. = not significant.

Discussion

Our study shows a significant relationship between the use of steroids and gastrointestinal lesions at autopsy in patients with cerebrovascular disease when compared to patients dying with non-vascular neurological diseases.

The mechanism responsible for these complications following steroid therapy can only be postulated. Fenster hypothesized a reduction of the mucosal defense mechanisms, which may be enhanced by the higher serum gastrin levels reported in patients with cerebrovascular disease.

Marshall et al. failed to demonstrate elevated gastric levels in any of 12 comatose neurosurgical patients. These differences might explain our finding of fewer gastrointestinal complications from steroid therapy in patients without cerebrovascular disease.

In addition to the studies indicating that steroid treatment is disappointing in stroke, our study demonstrates that the use of steroids may cause dangerous side effects in patients with cerebrovascular disease.

Acknowledgment

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References

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