THE CATABOLIC EFFECT OF CRANIOTOMY AND ITS INVESTIGATIVE TREATMENT WITH TESTOSTERONE PROPIONATE

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The catabolic effect of various types of trauma and surgical procedures on body protein is well documented.1,2,5,7,9 Several reports have appeared recently which indicate that in certain instances trauma to the brain or spinal cord may be followed by marked catabolic activity.3,8,10 This study was undertaken in an attempt to evaluate the average catabolic activity, as reflected in urinary excretion of nitrogen which occurs after craniotomies that involve removal of intracranial tumors or cerebral tissue. We also have investigated the use of testosterone propionate as an anti-catabolic agent in such cases.

MATERIAL AND METHODS

Ten consecutive patients who were to be subjected to craniotomy and removal of an intracranial tumor or cerebral tissue or both, and who were in a reasonably good nutritional state, were selected as subjects for this investigation. During the first 5 days after operation daily estimations were made of the total nitrogen, creatine nitrogen and preformed creatinine nitrogen excreted in the urine. The day of operation was counted as the 1st postoperative day. The fecal excretion of nitrogen was estimated, inasmuch as there is no more than a normal amount of nitrogen in the stools during the posttraumatic catabolic period.7 The nitrogen and caloric intake were accurately charted, but a special attempt was not made to regulate this intake. During the 5-day period of observation the concentrations of serum chloride, sodium and potassium were determined daily in each case. The first 5 consecutive patients (control group) were treated with the measures routinely employed by us during the postoperative period. In addition to these routine measures, the second 5 consecutive patients received 50 mg. of testosterone propionate intramuscularly for 6 days, commencing the day prior to operation. Inasmuch as we do not routinely employ tube feeding or the use of intravenous protein supplements during the immediate period after craniotomy, the intake of nitrogen of these patients during the first 48 hours after operation was practically zero. The average intake of nitrogen

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for the next 3 days was 6 to 7 gm. daily, while the average daily intake of nitrogen for the 5-day period of observation was 4 to 5 gm. in both the control group and the group receiving testosterone propionate.

**RESULTS**

*Control Group of Patients.* Each of the 5 patients in the control group demonstrated a negative nitrogen balance during each of the first 5 postoperative days. The average daily urinary excretion of nitrogen was 13.5 gm., while the average nitrogen balance was minus 9.2 gm. daily. The peak urinary excretion of nitrogen was reached on the 2nd and 3rd postoperative days. The highest urinary excretion of nitrogen in 24 hours was 18 gm., noted in Case 1 on the 2nd and 3rd postoperative days. The daily urinary excretion of creatine nitrogen averaged 129 mg. The highest excretion of creatine

### TABLE 1

*Average daily urinary excretion of nitrogen and creatine nitrogen, and average daily nitrogen balance of 5 control patients during first 5 days after craniotomy*

<table>
<thead>
<tr>
<th>Case Number</th>
<th>Sex and Age, Yrs.</th>
<th>Diagnosis</th>
<th>Operation</th>
<th>Averages</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Urinary Excretion of Nitrogen, gm. in 24 hr.</td>
</tr>
<tr>
<td>1</td>
<td>M 45</td>
<td>Bilateral olfactory groove meningioma</td>
<td>Bilateral frontal craniotomy (Soutar flap); subtotal removal of tumor</td>
<td>15.5</td>
</tr>
<tr>
<td>2</td>
<td>M 49</td>
<td>Chromophobe adenoma of pituitary</td>
<td>Left transfrontal craniotomy; intracapsular removal of tumor</td>
<td>15.0</td>
</tr>
<tr>
<td>3</td>
<td>M 39</td>
<td>Acoustic neurofibroma</td>
<td>Right suboccipital craniotomy; total removal of tumor</td>
<td>12.8</td>
</tr>
<tr>
<td>4</td>
<td>M 47</td>
<td>Oligodendroglioma of right frontal lobe</td>
<td>Right frontal craniotomy; radical resection for glioma</td>
<td>13.5</td>
</tr>
<tr>
<td>5</td>
<td>M 60</td>
<td>Meningioma of right sphenoid ridge</td>
<td>Right transfrontal craniotomy; total removal of tumor and involved dura; removal of osteoma</td>
<td>11.0</td>
</tr>
</tbody>
</table>
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nitrogen in 24 hours was 31± mg., noted in Case 3. None of the patients in the control group had achieved a positive nitrogen balance by the 5th postoperative day. Concentrations of sodium, potassium or chlorides in the serum were not significantly abnormal during the period of observation. Important data concerning excretion of nitrogen in the control group appear in Table 1.

**TABLE 2**

**Average daily urinary excretion of nitrogen and creatine nitrogen, and average daily nitrogen balance of 5 patients who received testosterone propionate during first 5 days after craniotomy**

<table>
<thead>
<tr>
<th>Case Number</th>
<th>Sex and Age, Yrs.</th>
<th>Diagnosis</th>
<th>Operation</th>
<th>Averages</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Urinary Excretion of Nitrogen, gm. in 24 hr.</td>
</tr>
<tr>
<td>6</td>
<td>M 43</td>
<td>Malignant glioma left frontal lobe</td>
<td>Left frontotemporal craniotomy; radical resection of tumor</td>
<td>9.7</td>
</tr>
<tr>
<td>7</td>
<td>M 42</td>
<td>Astrocytoma (grade 3) right temporal lobe</td>
<td>Right temporoparietal craniotomy; radical resection of tumor</td>
<td>9.3</td>
</tr>
<tr>
<td>8</td>
<td>F 52</td>
<td>Chromophobe adenoma of pituitary</td>
<td>Right transfrontal craniotomy; resection of right frontal lobe with subtotal removal of tumor</td>
<td>5.1</td>
</tr>
<tr>
<td>9</td>
<td>F 44</td>
<td>Suprasellar meningioma</td>
<td>Right transfrontal craniotomy; subtotal removal of tumor</td>
<td>5.6</td>
</tr>
<tr>
<td>10</td>
<td>M 47</td>
<td>Meningioma sphenoid ridge</td>
<td>Left temporal craniotomy; subtotal removal of meningioma</td>
<td>6.5</td>
</tr>
</tbody>
</table>

**Patients Receiving Testosterone Propionate.** Although each of the 5 patients in this group demonstrated a cumulative negative nitrogen balance during the first 5 postoperative days, 2 of these patients demonstrated a slightly positive nitrogen balance by the 4th day. The urinary excretion of nitrogen averaged 7.2 gm. daily, while the average nitrogen balance was minus 4.8 gm. The highest concentration of nitrogen excreted in the urine in 24 hours was 15.7 gm., noted in Case 6 on the 2nd postoperative day. The daily urinary excretion of creatine nitrogen averaged 110 mg. The highest concentration of creatine nitrogen excreted in 24 hours was 244 mg., noted
in Case 10. Concentrations of sodium, potassium or chloride in the serum were not significantly abnormal during the period of observation. Table 2 shows significant data concerning excretion of nitrogen in the group of patients who received testosterone propionate.

DISCUSSION

The results in our control group of patients generally confirm the report of Drew and associates\(^6\) concerning loss of nitrogen after craniotomy. Although the wastage of nitrogen after craniotomy is not as severe nor as prolonged as that after burns, fractures of long bones, some gastro-intestinal operations, or severe injuries to the spinal cord,\(^1,3,5,7,9\) this loss of nitrogen can constitute a critical problem in some malnourished patients undergoing intracranial surgical procedures. Inasmuch as the degree of nitrogen wastage appeared to be significantly less for patients receiving testosterone propionate than for patients in the control group, it is concluded that the administration of this drug in adequate amounts lessens the catabolism of body protein which is induced by the surgical procedure of craniotomy. Inasmuch as testosterone may produce retention of electrolytes and water,\(^4\) the possibility that this drug might cause an increase of postoperative cerebral edema must be evaluated. Retention of electrolytes was not evident during these short periods of observation.

Profound loss of nitrogen, and other bizarre metabolic sequelae, have been associated with some intracranial lesions, particularly certain lesions affecting the frontal regions of the brain.\(^8,10\) Marked catabolic activity is also the rule after severe injury to the spinal cord.\(^3\) Inasmuch as the average loss of nitrogen after removal of intracranial tumors or cerebral tissue is neither extremely large nor prolonged, it seems reasonable to speculate as to whether injury to specific fiber tracts in the brain or spinal cord may be instrumental in inducing excessive catabolic activity. Such speculation has been advanced by Sweet and co-workers,\(^10\) and McLardy\(^8\) has presented evidence that bilateral injury to the subcallosal fasciculus of the brain may produce metabolic sequelae of sufficient magnitude to result in death from malnutrition. The fact that injury to a small segment of the spinal cord may induce a greater catabolic reaction than the resection of a large volume of cerebral tissue also invites inquiry into the possibility that qualitative rather than quantitative factors determine the degree of catabolic activity after trauma to, or operation on the central nervous system.

SUMMARY

Patients undergoing craniotomy for brain tumor were observed to undergo a moderate catabolic reaction which was reflected in the increased excretion of nitrogen in the urine and a negative nitrogen balance for the first 5 days after operation.

The degree of nitrogen wastage that occurred after craniotomy was less
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marked for the 5 patients who received testosterone propionate than for the 5 control patients who did not receive this drug.

REFERENCES