Effects of prednisone on ventriculoperitoneal shunt function in hydrocephalus secondary to cysticercosis: a preliminary study

ROBERTO A. SUASTEGUI ROMAN, M.D., JOSÉ LUIS SOTO-HERNÁNDEZ, M.D., AND JULIO SOTELO, M.D.

Division of Neurology and Departments of Infectious Diseases and Neuroimmunology, Instituto Nacional de Neurologia y Neurocirugia, Mexico City, Mexico

NEUROCYSTERCEROSIS is a frequent cause of hydrocephalus in endemic areas and the most common surgical intervention is cerebrospinal fluid (CSF) shunting. The clinical course of neurocysticercosis patients after shunting is variable. In some patients, especially those with subarachnoid cysticerci, chronic arachnoiditis is a progressive process. The long-term clinical outcome of patients with neurocysticercosis undergoing shunt placement was reviewed by Colli, et al., who reported that of 56 patients undergoing ventriculoatrial or ventriculoperitoneal (VP) shunting procedures for cysticercosis, 40 (71.4%) required readmission one or more times, most within the 1st postoperative year. Malfunctioning shunts were responsible for 53 readmissions and also for 51 of 75 reoperations. Sotelo and Marin studied 92 patients with hydrocephalus due to neurocysticercosis, with a mean follow-up time of 107 months. The mortality rate was 50%, with most patients dying in the 1st 2 years. Reoperation for shunt obstruction was necessary in 47% of the patients. A strong association between inflammatory changes in CSF and prognosis was observed, with higher cell counts and protein levels in patients who died. Another series reported surgical shunt revisions in 25% of 40 shunted neurocysticercosis patients at 1 year. Glucocorticoid therapy has been used in the management of diverse forms of this disease.

The objective of our study was to compare the clinical status, postoperative complications, and functional outcome between two groups of patients requiring VP shunt insertion for hydrocephalus secondary to neurocysticercosis. The control group of 30 patients underwent shunt placement and was followed routinely by the neurosurgery staff. Lumbar cerebrospinal fluid (CSF) was studied at 2, 16, and 32 weeks postoperatively in the prednisone group. At 24-month follow up two (13%) of 15 patients in the prednisone group and 18 (60%) of 30 patients in the control group required surgical shunt revisions for symptomatic shunt obstruction (p = 0.002). Follow-up studies of CSF performed at 32 weeks in the prednisone group revealed improvement of abnormal values with statistically significant differences for glucose (p < 0.02). Serial imaging studies in the prednisone group revealed persistence of cysterceral cysts with no change in size. Mean initial KPS scores were similar in both groups. At the end of the follow-up period, the mean KPS score was significantly higher in the prednisone group (p = 0.003). Prednisone and chemoprophylactic drugs were well tolerated. These results suggest that in selected patients with hydrocephalus secondary to cysticercosis, intermittent long-term prednisone therapy after VP shunting may reduce shunt malfunction and improve the functional status of the patients.

KEY WORDS • cysticercosis drug therapy • hydrocephalus • ventriculoperitoneal shunt • arachnoiditis
Clinical Material and Methods

**Patient Population**

During a 12-month period all patients admitted to the neurosurgery service with hydrocephalus secondary to neurocysticercosis and scheduled for VP shunt insertion were candidates for the study. The diagnosis of cysticercosis was established by clinical findings, by computerized tomography (CT) scans showing hydrocephalus accompanied by cysts, calcifications, or meningeal enhancement, and by CSF analysis that included positive immune reaction to cysticercal antigens by the enzyme-linked immunosorbent assay and complement fixation tests. Patients were eligible to receive prednisone if they had no medical contraindications for corticosteroid therapy, such as diabetes mellitus, high blood pressure, pregnancy, or any active infectious process and also if they were available for a close follow-up review and consented to participate in the study. All patients or a close relative signed a consent form to participate in the prednisone group after explanation of the study objectives.

Prednisone was administered orally in a single morning dose of 50 mg three times a week starting at the end of the 1st postoperative week. Most patients with neurocysticercosis lived in crowded conditions and were of low socioeconomic status; undernourishment was common. In the year previous to the start of this study, the prevalence of tuberculin skin test reactors among hospitalized patients in our institution was 32%. Considering the total dose of 150 mg of prednisone per week, we decided to administer anti-tuberculous chemoprophylaxis, with 300 mg of isoniazid and a supplement of pyridoxine given daily during the course of prednisone administration, to avoid the risk of new tuberculous infection or reactivation of endogenous tuberculosis.

Ventricular CSF was obtained during surgery for cell count, protein and sugar levels, bacterial, fungal, and mycobacterial cultures, and immunological reactions for cysticercal antigens. In the group of patients receiving prednisone, lumbar CSF was studied at 2, 16, and 32 weeks postoperatively. Preoperative chest x-ray studies, CT scans, and an early postoperative clinical evaluation were performed in all patients in the 1st week after surgery and repeated when clinically indicated. Magnetic resonance (MR) imaging studies were obtained at 6 months postoperatively. Liver function tests, white cell blood count, glucose, blood urea nitrogen, and creatinine were measured in patients in the prednisone group at 2 weeks and at 2, 4, and 8 months postoperatively. Patients in the control group were inpatients at the same time as those in the prednisone-treated group. Controls were matched to cases with respect to age and sex. Patients included as controls were those not available for close follow up (we did not know if prednisone and isoniazid would produce morbidity) and those unwilling to take the drugs or to undergo the lumbar punctures required in the protocol of the study. All patients were followed throughout their hospital stay. Patients receiving prednisone were followed monthly as outpatients by one of the authors (R.A.S.R.). Control patients were followed by the neurosurgery service staff as outpatients and their records were reviewed by us at regular intervals. In all the patients from both groups a Pudenz-type shunt system of medium pressure was used and the operation performed by the same surgical staff. No cisticidal drugs were given to any patient.

### Statistical Data Analysis

Statistical analysis was performed with chi-square or Fisher exact tests for categorical variables and Student’s t-test for continuous variables. All tests of significance were for \( p < 0.05 \).

### Results

Table 1 shows demographic data, duration of symptoms, positive neurological findings at admission, and preoperative CT findings in both groups. No statistically significant differences were found, revealing that the...
groups were comparable on entry to the study. Ventricular CSF obtained at operation was studied in 14 patients in the prednisone group and in 13 patients in the control group. Results are shown in Table 2; no significant differences between groups were found. All mycobacterial and fungal cultures of CSF were negative. Karnofsky performance status (KPS) scores were determined on admission in both groups. The prednisone group had individual scores ranging from 30 to 70 with a mean of 53.3 (± 11.1). In the control group the range was 30 to 80 with a mean of 58.6 (± 15.7).

Clinical Course
In the prednisone group most patients had symptoms during the first 4 months; dizziness, mild headaches, difficulty in walking, heartburn, and pain in surgical scars were the most common complaints. Two patients required surgery for symptomatic shunt malfunction 1 year after shunt placement. In the control group 18 patients (60%) required reoperation for symptomatic shunt obstruction at a mean of 39.5 weeks after initial surgery. Of all shunt malfunctions in this group, 72% occurred during the 1st year after shunt placement. Differences in the number of surgical procedures for symptomatic shunt obstructions between the prednisone (two (13%) of 15) and control (18 (60%) of 30) groups were statistically significant (p = 0.002).

At the end of 24 months of follow up, mean KPS scores were 93.3 (± 8.2) in the prednisone group and 77 (± 21.4) in the control group (p = 0.003, Student’s t-test). Most patients in the treatment group resumed their usual activities after 4 months of prednisone therapy.

Lumbar CSF in the Prednisone Group
Changes seen in lumbar CSF studies in the prednisone group are presented in Table 3. Mean glucose levels in CSF at 32 weeks had significantly lower values in comparison with the mean level at 2 weeks. There was a trend of improvement in abnormal values in protein levels and cell counts in CSF without achieving statistical significance.

Neuroimaging Findings
The findings of all neuroimaging studies in both groups are presented in Table 4. In the prednisone group 13 patients had cysticercal cysts, of which six were intraventricular; in two patients those cysts were not seen on MR images and subsequently were identified on admission CT scans and subsequently were identified on MR images obtained 6 months after shunting (Fig. 1). In three patients moderate degrees of ventricular enlargement persisted but patients were free of symptoms of high intracranial pressure. No reduction in size or morphological changes from intraventricular or subarachnoid cysts were seen in subsequent MR images (Fig. 2).

Tolerability of Prednisone and Complications
Five patients had gastrointestinal symptoms related to prednisone that required the administration of antacids or ranitidine for control, but prednisone was continued in all of them. Weight gain of between 3 and 5 kg was seen in most patients. No diabetes, hypertension, or liver function test abnormalities were found. No bacterial meningitis or CSF shunt infections appeared during follow up. Two patients developed upper respiratory tract infection and another had a urinary tract infection during the first 4 months of follow up. All responded without complications to orally administered antibiotics, and prednisone was continued.

Discussion
Our results indicate that a long-term intermittent regimen of prednisone reduced the need for surgery for symptomatic shunt obstruction in a group of patients with hydrocephalus secondary to neurocysticercosis. Prednisone and antituberculous chemoprophylaxis were administered under close medical supervision and the observed effect

---

**TABLE 3**

<table>
<thead>
<tr>
<th>Timing of Analysis (wks postsurgery)</th>
<th>No. of Patients</th>
<th>Mean Value (range)</th>
<th>No. of Patients at Specified Levels</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Glucose (mg/dl)</td>
<td>Protein (mg/dl)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Glucose (mg/dl)</td>
<td>Protein (mg/dl)</td>
</tr>
<tr>
<td>2</td>
<td>12</td>
<td>36.58 (3–78)</td>
<td>273 (19–1470)</td>
</tr>
<tr>
<td>16</td>
<td>11</td>
<td>42.90 (8–63)</td>
<td>101 (19–300)</td>
</tr>
<tr>
<td>32</td>
<td>12</td>
<td>53.16 (18–100)†</td>
<td>123 (18–800)</td>
</tr>
</tbody>
</table>
| * Patients received 50 mg prednisone three times a week after ventriculoperitoneal shunt placement. 
† p < 0.02 when compared with mean glucose value at 2 weeks.

**TABLE 4**

<table>
<thead>
<tr>
<th>Finding</th>
<th>Prednisone (15 patients)</th>
<th>Control (30 patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>cysts</td>
<td></td>
<td></td>
</tr>
<tr>
<td>parenchymal</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>subarachnoid</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>intraventricular</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>calcifications</td>
<td></td>
<td></td>
</tr>
<tr>
<td>parenchymal</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>subarachnoid</td>
<td>2</td>
<td>0</td>
</tr>
</tbody>
</table>

* Computerized tomography and magnetic resonance studies were obtained. All admission and follow-up studies are included.
was achieved with drugs of low cost and easy availability.

Severe hydrocephalus requiring shunting was our inclusion criterion. Nevertheless, on follow-up imaging studies only two of 15 patients in the prednisone group had only hydrocephalus with parenchymal calcifications. The other 13 patients had subarachnoid, intraventricular, or parenchymal cysts, and the functional status among these patients started to improve at 4 months of drug therapy. Although three cases showed mild ventricular enlargement, the majority of patients returned to their usual activities. The reduction of symptomatic VP shunt malfunctions requiring surgery in patients receiving prednisone and the functional improvement are possibly related to several factors: 1) absence of morbidity secondary to shunt malfunctions; 2) improvement in CSF inflammatory changes; and 3) reduction of the inflammatory host response against the parasite diminishing focal or diffuse arachnoiditis, reducing the risk of vascular complications and cranial nerve fibrous entrapment. Subarachnoid and intraventricular cysts did not undergo major changes in patients who received prednisone, in contrast with reports of spontaneous radiographic disappearance of parenchymal cysts.\

Corticosteroids in Neurocysticercosis

Previously, use of corticosteroids in neurocysticercosis has been recommended in several clinical situations. Different drugs, routes, doses, and lengths of administration have been used. Most commonly cited indications are: 1) pseudotumoral and pseudomeningeal reactions caused by basal and parenchymatous cysts; 2) prevention and treatment of cerebrovascular complications; 3) cases presenting as pseudotumor cerebri; 4) intracranial hypertension present in malignant forms of cysticercotic encephalitis in young females; and 5) amelioration of the host inflammatory response against the parasite destruction when cysticidal drugs are used. Estañol, et al., treated eight patients with neurocysticercosis who had inflammatory cells in their CSF with 25 mg per day of prednisone for a mean of 6 months. Seven of his patients had normal CSF after therapy. In a subsequent study the same author treated 15 patients with basal arachnoiditis due to neurocysticercosis with 50 mg of prednisone every other day for 6 months. Ten of 15 improved and inflammatory cells in the CSF disappeared, but five had persistent significant pleocytosis.

In our study, at 8 months of prednisone therapy inflammatory cells were still present in CSF. We consider this finding evidence of the chronic nature of cysticercotic arachnoiditis and as an argument in support of prolonged therapy. In accordance with the report by Colli, et al., patients with neurocysticercosis who undergo shunt placement and who survive for more than 2 years have a good chance for a useful life. Some questions emerge that need controlled studies to provide guidelines for management; these questions involve the time when corticosteroid ther-
Prednisone and shunting in neurocysticercosis

apy can be safely stopped or when cysticidal drugs are indicated in these patients.

Antituberculous Chemoprophylaxis

The addition of antituberculous chemoprophylaxis to the treatment regimens of patients with prolonged corticosteroid therapy is still a controversial subject. Reactivation of old tuberculous disease and development of new disease in patients previously infected has been noted. Tuberculosis developing during corticosteroid therapy tended to be disseminated or presented in unusual forms.1,2 The influence of the corticosteroid dose must be considered; 15 mg per day of prednisone or the equivalent for more than 2 to 3 weeks is the threshold suggested by the American Thoracic Society to consider chemoprophylaxis. Chronic undernourishment is also considered a special clinical situation that may increase the risk of tuberculosis.1 Tuberculin skin test reactors 35 years of age or younger are also candidates for antituberculous chemoprophylaxis. The mean age of our patients in the prednisone group was 38 years and the high prevalence of tuberculin skin reactors in our hospital along with the social milieu in which most of our patients with neurocysticercosis live supported the decision to administer chemoprophylaxis in the prednisone group.

Definitive prevention of cysticercosis requires sanitary disposition of human feces,9 and in developing countries it is an urgent need, although it is a very complex socioeconomic problem and these control measures are not possible in the short term. Meanwhile, prednisone as adjunct to CSF shunting in hydrocephalus due to neurocysticercosis under close medical follow up may be useful to reduce symptomatic shunt obstruction and to improve the functional status of the patients. These are important issues for developing countries, where medical resources and hospital beds are limited.

References


José Luis Soto-Hernández, M.D., Infectious Diseases Department, Instituto Nacional de Neurologia y Neurocirugia, Insurgentes Sur 3877, 14269, Mexico.

Address reprint requests to: José Luis Soto-Hernández, M.D., Infectious Diseases Department, Instituto Nacional de Neurología y Neurocirugía, Insurgentes Sur 3877, 14269, Mexico.