Management of Completed Strokes With Dextran 40. A Community Hospital Failure

BY EDWARD V. SPUDIS, M.D., ERNESTO de la TORRE, M.D., AND LOUIS PIKULA, M.D.

Abstract: Management of Completed Strokes With Dextran 40. A Community Hospital Failure

Fifty-nine patients with onset of moderate to severe unimproving paralysis of less than 24 hours' duration were randomized into treatment (Dextran 40) and control groups, managed similarly except for the dextran. A strict effort to study a uniform cerebral process by rejecting patients with hypertension, insulin-dependent diabetes, potential emboli, and pulmonary or renal disease resulted in a small sample. Most patients considered for the study had begun to improve before the initial examination. All patients had spinal tap prior to the decision to randomize. Results were evaluated independently by the three authors over a three-week interval and tabulated after three years. A greater percentage of dextran-treated patients improved with respect to consciousness and strength in upper and lower extremities, but showed less restoration of language than the untreated patients. The differences in the two groups were not significant. One of 30 patients given dextran may have had a reaction.

Additional Key Words
restoration of language cerebral infarction randomized

Methods
Referred patients of all ages and sex were divided according to a table of random numbers into a dextran and a nondextran group. We announced in our 700-bed suburban general hospital that we wished to study patients with acute (24-hour), stable or worsening strokes who had no likely source of emboli and were not hypertensive or diabetic. In an effort to study a group with the most stereotyped lesions, we chose to eliminate all those with a known history of hypertension and those with blood pressure greater than 200 systolic and 100 diastolic over an initial two-hour period. Insulin users were rejected because of the possibility of misinterpreting the onset of symptoms. All patients with suspected intracranial hemorrhage were eliminated, and all patients with obvious renal or lung disease were rejected prior to randomization. All patients given new medications between the time of onset of symptoms or signs and the time of our first examination were rejected. The patients' usual medications were continued, e.g., digitoxin, oral diabetic agents, antacids, etc.
Basic nursing and rehabilitation measures were identical in each group. All patients were questioned and examined, and then each had a spinal tap prior to randomization. More than 200 red blood cells per millimeter$^3$ was considered excessive. Most patients had skull x-rays, brain scans, electroencephalograms, echocardiograms, and SMA-12 tests also, but these were not requirements for this study.

At the time of the initial examination the patients’ consciousness was graded into four categories: normal, lethargic, stuporous, and coma. Language was divided into normal, mild nonfluency, moderate dysphasia, and aphasia. Strength in the upper and lower extremities was graded into five categories. Notes were made concerning pupils, field defects, bruits, and proximal and distal muscle tone. These proved too variable to tabulate usefully.

After one week the patient was independently graded by a second author, and after three weeks, by the third author. We felt inter-author reliability was good. The second and third examiners never had an opportunity to see the patients while dextran was running and had little reason to try to guess which patients were controls. No new medications were added during the three-week observation period. We recognized the difficulty in simplifying language into four grades but, for purposes of this trial, doubted that dextran would selectively influence such functions as reading or verbal arithmetic. We also doubted our ability to grade such functions consistently.

The dextran patients were given 500 cc of low-molecular-weight dextran in 10% glucose in water over one hour as a “loading” dose and then 1,000 cc each 24 hours for three days. A careful effort was made to keep fluid and electrolyte balance stable. Fluids were supplemented as we thought appropriate for age, size, and fever. We did not attempt to alter the rate of flow of dextran in those few patients who made dramatic changes. Blood urea was measured daily while dextran was given.

During the first year 78 patients were examined and rejected for one or more of the following reasons: improving, 36; cardiac arrhythmia, 12; confusion only or undetectable deficit, 8; elevated blood pressure, 6; diabetes mellitus on insulin, 4; subarachnoid hemorrhage, 3; inability to do spinal tap, congestive heart failure, conversion hysteria, etc., 9. Perhaps another 50 were rejected without examination, because of pre-treatment or delay in referral.

Results

Thirty dextran patients were randomized into the treatment group. The average age was 70. Twenty-six patients had the 73-hour course of dextran. Three died at 24, 49, and 60 hours, respectively. Five more died at 4, 6, 9, 13, and 15 days. The patient dead at 49 hours probably died of congestive heart failure. The other two early deaths were in patients with dense hemiplegia and stupor and were considered “stroke” deaths. The patient dead at 13 days had severe pneumonia as a probable cause. One patient was eliminated from the study when five to eight minutes of dextran caused a severe flushing and apnea. The average duration of signs prior to randomization was 11 hours from onset of symptoms or signs. Minimum observation period prior to treatment was two hours, and the longest was overnight (24 hours) in one case in whom the improvement was questionable prior to randomization. Improvement in lower extremity strength averaged one and one-fourth grades in those patients improving; changes in other categories were less than one grade.

In the nondextran group there were 29 patients, 26 of whom also completed the 73-hour comparison period. Average age was 71 years. Three patients died (at 9, 24, and 48 hours respectively) when dextran would have been infusing had they been in the treatment group. Of the remaining 26, 23 survived the three weeks to the third examination. Others died at 4, 11, and 16 days, all classified as stroke deaths. Average time from onset to randomization was slightly over 12 hours.

In summary, the treatment group showed a greater percentage of improvement in strength in both upper and lower extremities and in consciousness than the control group, but less restoration of language. However, five patients of the 26 in the dextran group died during three subsequent weeks of observation while three of the control group died (table 1).

<table>
<thead>
<tr>
<th>TABLE 1</th>
</tr>
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<tbody>
<tr>
<td>Hospital Course of 21 Treated Survivors and 23 Controls</td>
</tr>
<tr>
<td><strong>Consciousness</strong></td>
</tr>
<tr>
<td>Dextran 11 (52%)</td>
</tr>
<tr>
<td>Control 8 (35%)</td>
</tr>
<tr>
<td><strong>Language</strong></td>
</tr>
<tr>
<td>Dextran 5 (23%)</td>
</tr>
<tr>
<td>Control 9 (39%)</td>
</tr>
<tr>
<td><strong>Strength — upper</strong></td>
</tr>
<tr>
<td>Dextran 8 (38%)</td>
</tr>
<tr>
<td>Control 6 (26%)</td>
</tr>
<tr>
<td><strong>Strength — lower</strong></td>
</tr>
<tr>
<td>Dextran 12 (57%)</td>
</tr>
<tr>
<td>Control 8 (35%)</td>
</tr>
</tbody>
</table>
Discussion

No medication for the completed stroke has been universally accepted. Because of its role in changing red cell charge and in decreasing platelet aggregation, low-molecular-weight dextran has been proposed as a useful medication in acute cerebral infarction. Our attempt to verify this usefulness in a community hospital has been unsuccessful. We have reluctantly discontinued this study after three years because we could see no definite clinical benefits prior to tabulating the results, recognizing that certain subcategories of our patient population may have benefited. A more practical reason for ending the study has been the decrease in referrals, and the current tendency to begin treatment of all acute cerebral insults with steroids.

Our two patient groups are much smaller than we anticipated because of the high incidence of cardiac arrhythmias and the remarkable percentage of patients who begin to improve spontaneously 6, 12, and 18 hours after onset of what appeared to be a catastrophic brain infarction. It is ethically stressful to withhold a potentially useful medication while the patient's illness smolders, since it is unlikely that we have an agent more useful in advanced infarction than in an incipient one. Other studies of the completed infarction also have been based on small numbers or nonuniform patients.

Our one, possibly, allergic reaction in 30 plus trials suggests that benefits from continued use in stroke management would have to be great enough to counterbalance the allergic hazards.

References

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