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Matthew Churchill, Sean Grimm, and Michael Reding

Objective. To assess the effects of diuretic use on hydration status following stroke. Methods. Admission serum hydration markers and neurologic assessments were prospectively recorded for 296 stroke rehabilitation inpatients with stable renal function. Dysphagia was defined by bedside dysphagia evaluation and subsequent modified barium swallow, if necessary. Serum hydration markers were checked at approximate 10-day intervals. Analysis of variance was used to test the effects of clinical variables on serum markers for hydration during the rehabilitation hospital stay. Odds ratios were used to quantify the risks of developing a blood urea nitrogen value ≥ 45 mg/dl. Results. The mean peak blood urea nitrogen associated with each of the following were diuretic usage yes/no (33 mg/dl ± 18/26 ± 17, P < 0.01), dysphagia yes/no (32 ± 21/25 ± 14, P < 0.001), and need for thin-liquid restriction yes/no (34 ± 20/25 ± 15, P < 0.001). The odds ratio for developing a peak blood urea nitrogen ≥ 45 for patients taking a diuretic with evidence of penetration or aspiration documented by modified barium swallow was (19.8, P < 0.001). The odds ratio for developing a peak blood urea nitrogen ≥ 45 for those taking a diuretic who needed thin-liquid restriction was (4.8, P = 0.004). Conclusions. Diuretic usage was associated with a significant increase in peak blood urea nitrogen across the entire stroke study sample. The highest odds ratio for developing a peak blood urea nitrogen ≥ 45 was 19.8 for patients taking a diuretic who had dysphagia plus modified barium swallow evidence of penetration-aspiration.

Key Words: Diuretic—Cerebrovascular disease—Dysphagia—Dehydration.

Diuretics are effective and widely used in the treatment of hypertension. They are an essential component of managing congestive heart failure. Both of these disorders are common comorbidities in patients following stroke. Based on our experience, physicians frequently continue prescribing diuretics after stroke. We are not aware of previous studies assessing their effects on maintenance of adequate hydration in this population. A computerized literature review using Ovid software to search the MEDLINE database from 1966 to August 2003 failed to identify any relevant articles using a variety of keywords including diuretic, cerebrovascular disorder, dehydration, and dysphagia.

Stroke may affect one’s level of alertness, perception of thirst, ability to access liquids, and ability to swallow them when offered. Stroke victims with such impairments may be at increased risk for diuretic-induced dehydration. Dysphagia evaluation and treatment might be expected to obviate some of the effects of dysphagia on diuretic-induced dehydration. We are, however, unaware of studies that have specifically addressed the effects of dysphagia or dysphagia treatment strategies on diuretic-induced dehydration. We therefore reviewed our stroke rehabilitation data bank to assess the effects of diuretic use on hydration, length of rehabilitation hospital stay, and functional outcome. Relevant stroke sequelae were chosen as covariables: dysphagia, dietary liquid consistency modifications, somnolence, cognitive impairment, impaired self-care, and mobility function. Our test hypothesis was that diuretic usage following stroke is associated with an increased risk of dehydration, that the risk is greatest for dysphagic patients, and that the risk is not obviated by aggressive dysphagia management.

METHODS

Admission blood urea nitrogen (BUN) and neurologic assessments were prospectively recorded over a 12-month interval for consecutively admitted stroke rehabilitation inpatients without significant underlying renal dysfunction. The diagnosis of stroke was based on clinical history, neurologic examination, and compatible neuroimaging studies in each case. Level of alertness (alert versus

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somnolent), Mini-Mental Status Examination (MMSE), and language function (no aphasia versus presence of receptive, expressive, or mixed expressive-receptive language deficit) were scored by the neurologist at the time of rehabilitation hospital admission.

At the time of rehabilitation hospital admission, the Burke Dysphagia Screening Test (BDST), based on the neurologic history and examination, was used to identify patients requiring bedside dysphagia evaluation (BDE) by a speech-language pathologist. The BDST assesses 7 risk factors for dysphagia and includes a 3-oz water swallow test. This screening tool has been previously described and has been shown to identify patients at risk for developing dysphagia-related medical complications.

Dysphagia sufficient to place the patient at risk for dehydration was defined as evidence of suspected pharyngeal dysfunction based on the bedside dysphagia evaluation. Patients passing the BDST and not referred for BDE were defined as not dysphagic. If pharyngeal phase swallowing deficits were suspected at the time of BDE, a video fluoroscopic modified barium swallow (MBS) study was performed usually within 4 to 7 days of rehabilitation hospital admission. Evidence of laryngeal penetration or evidence of aspiration (any amount or any consistency) were scored as aspiration. If pharyngeal penetration or evidence of aspiration was present, patients were instructed in the use of various compensatory swallowing techniques, as appropriate, based on results of the MBS evaluation: head turn, chin tuck, supraglottic swallow, Mendelsohn maneuver, and so on.

Functional Independence Measure (FIM) scores were recorded within 72 h of rehabilitation hospital admission and within 72 h of discharge from the rehabilitation unit. FIM scores assess the patient’s ability to feed, dress, groom, bathe, toilet, transfer, walk and climb stairs, speak, comprehend speech, interact socially, problem solve, and remember. FIM scores were recorded by rehabilitation team members unaware of the patient’s serum hydration parameters.

Markers for state of hydration were serum BUN, serum creatinine (Cr), BUN/Cr ratio, and serum sodium (Na⁺). These values were checked at the time of admission to the rehabilitation unit and subsequently at approximate 10-day intervals. To facilitate comparisons over time and across treatment and comorbidity groups, the peak values of each of the above hydration markers were recorded over the course of the rehabilitation hospital stay.

The prescription for a diuretic was usually initiated at the acute-care hospital and reflected the practice patterns of physicians at more than 100 referral institutions. Following admission to the stroke rehabilitation unit, medications were maintained and changed only if needed.

Analysis of covariance (ANCOVA) was used to compare admission demographic variables for those with versus without use of a diuretic. Two-factor analysis of variance (ANOVA) with Fisher’s protected least significant difference (PLSD) correction for multiple comparisons was used to assess interactions between diuretic use and other nominal independent variables of interest (presence or absence of dysphagia, need for thin-liquid restriction, level of alertness, MMSE score < 25, and presence or absence of aphasic language deficit). Dependent variables were serum hydration markers: peak BUN, peak BUN/Cr ratio, and peak Na⁺. Odds ratios were used to quantify the risks associated with each of the independent variables and development of significant dehydration, indicated by peak BUN values ≥ 35 or ≥ 45 mg/dl. Statistical inferences were said to be significant if the 2-tailed probability statistic was less than 0.05. All variances are listed as standard deviations. Statistical analyses were computed using StatView for Windows, version 5.0.1 (SAS Institute, Inc., Cary, NC, 1998).

RESULTS

Table 1 shows the demographic features of our study sample consisting of 296 consecutively admitted stroke rehabilitation inpatients over a 12-month period. The mean age, interval poststroke, admission FIM values, and gender ratios are not
significant different for those with versus without use of a diuretic. The demographic features of our study sample are similar to those reported by other acute inpatient stroke rehabilitation units in the United States.

Of the 55 patients receiving a diuretic, 26 (47%) received it for management of hypertension, 27 (49%) for congestive heart failure with or without hypertension, and 2 (4%) for other indications (i.e., dependent edema, etc.). Hydrochlorothiazide was prescribed for 20 patients and furosemide was ordered for 35. Diuretic usage was either reduced or discontinued in 38 of 55 (69%) patients during the course of their rehabilitation hospital stay.

Table 2 shows the mean peak serum hydration values associated with each of the following variables: use of a diuretic, dysphagia with BDE evidence of pharyngeal phase dysfunction, need for thin-liquid restriction, level of alertness, cognitive function as assessed by MMSE, and presence or absence of aphasic language deficit. Two-factor ANOVA was used to correct for interactions between use of a diuretic and each of the other independent variables. Fisher’s PLSD was used to correct for multiple comparisons. All study variables except the presence or absence of an aphasic language deficit were associated with significantly increased mean peak BUN values. Many of the study variables were also associated with significantly increased peak BUN/Cr ratios and peak Na⁺ values.

Table 3 shows individual odds ratios and 95% confidence intervals for developing a peak BUN ≥ 35 or ≥ 45, respectively, for each of the primary study variables. Odds ratios are also shown for the combined effects of using a diuretic plus each of the other study variables. Use of a diuretic alone was not sufficient to increase the risk of dehydration. Dysphagia as assessed using the BDE or MBS was a marker for increased risk for dehydration. The highest odds ratios for developing dehydration were for patients with MBS evidence of laryngeal penetration or aspiration with or without the use of a diuretic. The next highest odds ratio was for those who required an NTL restriction plus use of a diuretic. An MBS was performed on 45 patients. Laryngeal penetration or aspiration was seen in 38 of these 45 patients. Of the 38 patients with documented laryngeal penetration or aspiration, 7 were taking a diuretic.

The clinical significance of a peak BUN ≥ 35 or a peak BUN ≥ 45 was assessed by comparing the change in FIM scores and length of rehabilitation hospital stay for those who did versus did not reach these target values. The change in FIM score from rehabilitation hospital admission to discharge was not significantly different for those who did versus did not reach the two target BUN values, respectively: 21 ± 12 versus 21 ± 11, \( P = 0.60 \), and 20 ± 14 versus 21 ± 11, \( P = 0.43 \). The length of rehabilitation hospital stay needed for patients to reach their rehabilitation goals was, however, significantly longer for those who did versus did not reach either of the target BUN values respectively: 38 ± 16 versus 30 ± 15, \( P < 0.001 \), and 39 ± 15 versus 31 ± 15, \( P = 0.004 \).

DISCUSSION

Our results support the clinical impression that diuretics must be used with caution in stroke victims with dysphagia. This caution has, however, not been previously documented or quantified in the existing medical literature. As mentioned in the introduction, a computerized literature review using Ovid software to search the MEDLINE database from 1966 to August 2003 failed to identify any relevant articles using a variety of keywords including diuretic, cerebrovascular disorder, dehydration, and dysphagia. The fact that 20% (11/55) of patients admitted to our stroke rehabilitation unit taking a diuretic were dysphagic underlines the general inattention to this problem by referring physicians in the New York City area.

Given the number of antihypertensive medications currently available, our data argue for the avoidance of diuretics for stroke victims with dysphagia, somnolence, or cognitive impairment. When diuretics are used for management of congestive heart failure in such patients, a need for reduction in diuretic dosage should be expected.
As shown in Table 2, stroke-related impairments such as somnolence and cognitive impairment with MMSE scores < 25 were also associated with elevated mean peak BUN and mean peak BUN/Cr ratios. This may reflect impaired ability to maintain sufficient alertness to consume adequate liquids or to impaired perception of thirst. The presence of an aphasic language deficit was not associated with a significant rise in peak serum hydration markers. This implies that maintenance of adequate hydration is not merely due to an inability to express one’s need for liquids.

Odds ratio analysis shows that the greatest risk of diuretic-induced dehydration is experienced by patients with evidence of aspiration or penetration of liquid barium during video fluoroscopic MBS. The odds ratio for such patients developing a peak BUN greater than 35 was 9.0, \(P = 0.002\). The odds ratio for such patients developing a BUN greater than 45 was 19.8, \(P < 0.001\). MBS evidence of aspiration or penetration of liquid barium is objective evidence of significant difficulty managing liquids. Our data indicate that these patients are often unable to increase their fluid intake to compensate for the use of a diuretic.

Odds ratio analysis also shows that the risk of diuretic-induced dehydration is increased by dysphagia severe enough to warrant thin-liquid restriction. The odds ratio for such patients developing a peak BUN greater than 35 was 4.8, \(P = 0.004\). Thin-liquid restriction is an attempt to maintain hydration by giving thickened liquids. The goal is to maintain as normal a liquid consistency intake as possible. The thicker the liquid, the easier it is to maintain bolus control during the pharyngeal phase of swallowing. Thicker liquids flow more slowly and are less likely to penetrate into the laryngeal vestibule above the vocal folds or be aspirated past the vocal folds into the trachea. Liquids may be thickened using commercially available starch-based thickeners to the consistency of fruit nectar or to honey consistency.

It is apparent from Table 3 that diuretic usage adds only a moderate amount to the significantly elevated odds ratio for developing dehydration seen with dysphagia alone. Our results were obtained using BDE- or MBS-based compensatory swallowing strategies and dietary liquid consistency modifications designed to optimize the safety and efficiency of oral hydration. The odds

### Table 2. Effects of Clinical Variables on M ± SD Peak Serum Hydration Values

<table>
<thead>
<tr>
<th></th>
<th>(n)</th>
<th>Peak BUN</th>
<th>Peak BUN/Cr Ratio</th>
<th>Peak Na⁺</th>
</tr>
</thead>
<tbody>
<tr>
<td>Taking diuretic</td>
<td>55</td>
<td>33 ± 18**</td>
<td>27 ± 10</td>
<td>141 ± 4</td>
</tr>
<tr>
<td>No diuretic</td>
<td>241</td>
<td>26 ± 17**</td>
<td>24 ± 9</td>
<td>141 ± 3</td>
</tr>
<tr>
<td>Dysphagia⁺</td>
<td>61</td>
<td>32 ± 21***</td>
<td>27 ± 11**</td>
<td>142 ± 3**</td>
</tr>
<tr>
<td>No dysphagia⁺</td>
<td>234</td>
<td>25 ± 14***</td>
<td>25 ± 8**</td>
<td>141 ± 3**</td>
</tr>
<tr>
<td>No thin liquids⁺</td>
<td>85</td>
<td>34 ± 20***</td>
<td>28 ± 11***</td>
<td>142 ± 4**</td>
</tr>
<tr>
<td>All liquids allowed⁺</td>
<td>210</td>
<td>25 ± 15***</td>
<td>23 ± 9***</td>
<td>141 ± 3**</td>
</tr>
<tr>
<td>Somnolent</td>
<td>33</td>
<td>44 ± 25***</td>
<td>33 ± 13***</td>
<td>143 ± 4**</td>
</tr>
<tr>
<td>Alert</td>
<td>263</td>
<td>25 ± 15***</td>
<td>24 ± 8***</td>
<td>141 ± 3**</td>
</tr>
<tr>
<td>MMSE &lt; 25⁺</td>
<td>172</td>
<td>30 ± 19**</td>
<td>26 ± 10*</td>
<td>141 ± 3</td>
</tr>
<tr>
<td>MMSE ≥ 25⁺</td>
<td>82</td>
<td>23 ± 10**</td>
<td>23 ± 9*</td>
<td>141 ± 3</td>
</tr>
<tr>
<td>Language deficit</td>
<td>91</td>
<td>27 ± 15</td>
<td>25 ± 10</td>
<td>141 ± 3</td>
</tr>
<tr>
<td>No language deficit</td>
<td>205</td>
<td>28 ± 18</td>
<td>24 ± 9</td>
<td>141 ± 3</td>
</tr>
</tbody>
</table>

BUN, blood urea nitrogen; Cr, serum creatinine; Na⁺, serum sodium; MMSE, Mini-Mental Status Examination. ANCOVA with Fisher’s protected least significant difference correction for multiple comparisons.

a. Count for these variables < 296 due to incomplete data.

*\(P < 0.05\). **\(P < 0.01\). ***\(P < 0.001\).

### Table 3. Odds Ratios (ORs) and 95% Confidence Intervals (CIs) for Reaching Blood Urea Nitrogen (BUN) End Points Based on Presence or Absence of Different Study Variables

<table>
<thead>
<tr>
<th>Study Variable</th>
<th>Peak BUN ≥ 35</th>
<th></th>
<th>Peak BUN ≥ 45</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR 95% CI</td>
<td>OR 95% CI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diuretic</td>
<td>1.5</td>
<td>0.7-3.1</td>
<td>1.5</td>
<td>0.5-3.6</td>
</tr>
<tr>
<td>Dysphagia⁺</td>
<td>2.2</td>
<td>1.2-4.0</td>
<td>4.2</td>
<td>2.1-8.3</td>
</tr>
<tr>
<td>MBS(PA)b</td>
<td>3.5</td>
<td>1.9-6.3</td>
<td>7.2</td>
<td>3.6-14.3</td>
</tr>
<tr>
<td>NTLc</td>
<td>2.2</td>
<td>1.2-4.1</td>
<td>5.6</td>
<td>1.7-7.8</td>
</tr>
<tr>
<td>Diuretic + dysphagia⁺</td>
<td>2.0</td>
<td>0.6-6.7</td>
<td>4.3</td>
<td>1.3-14.0</td>
</tr>
<tr>
<td>Diuretic + MBS(PA)b</td>
<td>9.0</td>
<td>1.4-95.6</td>
<td>19.8</td>
<td>3.0-211</td>
</tr>
<tr>
<td>Diuretic + NTLc</td>
<td>2.2</td>
<td>0.5-7.9</td>
<td>4.8</td>
<td>1.2-17.8</td>
</tr>
</tbody>
</table>

a. Abnormal bedside dysphagia evaluation suggesting evidence of pharyngeal phase dysfunction.

b. MBS(PA), modified barium swallow evidence of laryngeal penetration or aspiration.

c. NTL, order written for “no thin liquids.”

As shown in Table 2, stroke-related impairments such as somnolence and cognitive impairment with MMSE scores < 25 were also associated with elevated mean peak BUN and mean peak BUN/Cr ratios. This may reflect impaired ability to maintain sufficient alertness to consume adequate liquids or to impaired perception of thirst. The presence of an aphasic language deficit was not associated with a significant rise in peak serum hydration markers. This implies that maintenance of adequate hydration is not merely due to an inability to express one’s need for liquids.

Odds ratio analysis shows that the greatest risk of diuretic-induced dehydration is experienced by
ratios observed in Table 3 show that current dysphagia management strategies are not sufficient to normalize the risks of dehydration among dysphagic stroke victims. Use of a diuretic by such patients is potentially avoidable and is only likely to further compromise the patient’s hydration status.

We do not interpret our data to indicate that thickened liquids cause an increased risk of dehydration. The more rational interpretation is that dysphagia, which is improved by prescribing thickened liquids, is the primary cause of the increased risk of diuretic-induced dehydration. This interpretation is supported by a previous study from this institution that showed no significant difference in hydration parameters for dysphagic patients prospectively randomized to various levels of thickened liquid intake.10

Our results were obtained from a rehabilitation unit aware of the consequences of diuretic usage following stroke. Initial prescription of diuretics reflected the practice patterns of physicians at more than 100 referring acute-care hospitals. Transfer medications were maintained and changed only as indicated following admission to the stroke rehabilitation unit. It is assumed that the diuretic effects reported here would be even more significant if studied at other rehabilitation facilities that do not perform routine serial screens for diuretic-induced dehydration.

Patients were transferred from acute-care hospitals to our inpatient acute stroke rehabilitation unit a mean of 16 ± 13 days poststroke. The mean length of stay on the inpatient unit was 32 ± 15 days. Stroke-related neurologic and functional deficits show an exponential recovery curve with maximum rate of recovery experienced in the first 1 to 3 months following stroke. It is reasonable to assume that the diuretic effects observed on our inpatient stroke rehabilitation unit were also extant prior to transfer during the acute-hospital stay. It is also reasonable to assume that our observations are also applicable to stroke victims with persistent neurologic deficits requiring placement in skilled nursing facilities. Patients with minor strokes who did not require inpatient rehabilitation were not studied. The adverse effects of diuretics in such patients are unknown.

CONCLUSIONS

Diuretic usage is associated with a significant increase in peak BUN and peak BUN/Cr ratio during the rehabilitation phase following stroke. Diuretics should be prescribed with caution in stroke victims with evidence of dysphagia. Diuretic usage in patients with dysphagia requiring thin-liquid restriction or with MBS evidence of liquid barium penetration-aspiration carries an odds ratio of 4.8 or 19.8, respectively, for developing a peak BUN ≥ 45.

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