Home sodium monitoring in patients with diabetes insipidus

Rebecca P. Green, MD, PhD, and Michael Landt, PhD

Objective: To determine whether home care givers can accurately measure plasma sodium in children with diabetes insipidus (DI) by using an I-STAT portable clinical analyzer (PCA) and to collect preliminary data on home PCA use.

Study design: Care givers of 4 children with DI and impaired thirst or inability to access water freely were instructed in PCA use. During an initial preclinical phase, the accuracy of sodium concentration measured by care givers was assessed by comparison to simultaneous analysis in a clinical laboratory. Participants were subsequently randomly assigned to daily home PCA monitoring or routine care. All participants crossed over from their original randomized group assignment to the alternate group.

Results: After a single education session, all care givers were able to perform PCA testing. There was good correlation between PCA and laboratory sodium ($r = 0.92$). On the basis of Error Grid Analysis, use of the PCA sodium would have resulted in treatment decisions identical to those made based on the laboratory sodium value in 62 of 66 instances. Four minor differences in treatment would have occurred. There was no statistically significant difference in clinical outcome during daily monitoring versus routine care.

Conclusions: Results obtained by care givers using the PCA are sufficiently reliable for assessment of fluid status and making treatment decisions. (J Pediatr 2002;141:618-24)
serum sodium concentration in children with DI and an impaired thirst mechanism or inability to access water freely. The device was designed for point-of-care hospital use but was amenable to home use. We hypothesized that caregivers could learn to use the device accurately. In addition, we speculated that having access to the device in the home could reduce the number of clinically significant episodes of fluid imbalance and improve care for these patients.

**Methods**

**Subjects**

Ten children met the inclusion criteria of central DI, with either impaired thirst or age or disability resulting in inability to access water freely. Caregivers were contacted regarding participation. Three children were excluded on the basis of lack of access to a phone (1) or inability to attend all of the study visits (2). The other 7 were enrolled, and 4 completed the study (Table I). Reasons for lack of completion were withdrawal from the study (1) and failure to return for necessary study visits (2). No participants failed to complete the study because of inability to use the device.

The protocol was reviewed and approved by the Washington University Medical School Human Studies Committee. Parents or legal guardians signed written consent for participation. When appropriate, children provided written assent.

**The Monitoring Device**

The Portable Clinical Analyzer (I-STAT Corp, East Windsor, NJ) is a hand-held analyzer that simultaneously performs multiple assays on whole blood. The device is approved for in-hospital use by trained personnel. The I-STAT system requires a CLIA certificate for in-hospital use but may be prescribed for home use by a physician. It is composed of two main components, the hand-held analyzer (20 × 6.5 × 5 cm, 539 g, battery powered) and single-use reagent cartridges (2.7 × 4.5 cm). For point-of-care testing, care givers lanced the participant’s finger (Tenderlett, Baxter #B4277-IJA) and collected 65 µL of blood into a glass capillary tube containing lithium heparin (Clinitube Heparinized Glass Capillary Tube, D-957G-70-125 or I-STAT 65 µL Capillary Tubes, Abbott List No. 06P21-02). The blood was transferred from the capillary tube into a reagent cartridge, and the cartridge was inserted into the analyzer. The analyzer reported results in 2 minutes. The analyzer was programmed to run an internal Electronic Simulator each day that a sample was analyzed. In addition, the analyzer runs a series of control checks throughout the testing cycle. Study nurses did cartridge quality control testing with liquid control solutions when the cartridges were received. Care givers were instructed in appropriate storage of the cartridges. For the venous analysis done during the preclinical phase, blood specimens were collected into lithium heparin–evacuated tubes, and a small sample was dispensed into the cartridge with the use of a disposable bulb pipette. The device has been previously tested in nonlaboratory hospital settings on venous specimens and has been shown to have excellent reliability for measuring sodium when compared with results obtained on simultaneously obtained heparinized plasma on a standard laboratory analyzer. The device had not been tested in the home setting with the use of capillary blood.

### Table I. Baseline characteristics of study participants

<table>
<thead>
<tr>
<th>Patient Number</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>10</td>
<td>7.5</td>
<td>4</td>
<td>2.5</td>
</tr>
<tr>
<td>Age at Dx with DI</td>
<td>2 mo</td>
<td>3 y</td>
<td>1 y</td>
<td>15 mo</td>
</tr>
<tr>
<td>Sex</td>
<td>M</td>
<td>M</td>
<td>F</td>
<td>M</td>
</tr>
<tr>
<td>Cause of DI</td>
<td>Meningitis</td>
<td>Holoprosencephaly</td>
<td>Hydrancephaly</td>
<td>Holoprosencephaly</td>
</tr>
<tr>
<td>Other diagnoses</td>
<td>Congenital hypothyroidism, seizure disorder, asthma</td>
<td>Central hypothyroidism, choanal atresia</td>
<td>Seizure disorder, hypopituitarism, Nissen and G-tube</td>
<td>Possible fetal alcohol syndrome, cleft lip and palate, s/p meningitis</td>
</tr>
<tr>
<td>Developmental delay</td>
<td>Severe</td>
<td>Mild to moderate</td>
<td>Severe</td>
<td>Moderate</td>
</tr>
<tr>
<td>Oral Nutrition</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Ambulatory</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Communication</td>
<td>None</td>
<td>Speech</td>
<td>None</td>
<td>Signing</td>
</tr>
<tr>
<td>DI Hospitalizations*</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Care givers</td>
<td>Foster mother, employed, sibling</td>
<td>Both parents, employed</td>
<td>Foster parents, one employed</td>
<td>Children’s home</td>
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<td></td>
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</tbody>
</table>
*In the last 6 months.
Study Design

After enrollment, all care givers were educated in the appropriate analysis techniques. Each then took part in a 3-month preclinical (accuracy) phase. During this period, sodium concentration was measured at a minimum frequency of every 2 weeks at a clinical laboratory. At the time the venous specimen was obtained for laboratory testing, the care giver independently collected a capillary specimen and analyzed it by using the PCA (total of 46 events). In addition, a second venous specimen was obtained by laboratory personnel for analysis on the PCA whenever possible (85% of the time). The care giver tested this specimen with the use of the PCA. The result of each PCA test was recorded by the care giver and transmitted to the study physician. All clinical decisions during this period were based on the reference laboratory sodium concentration.

During the second phase of the study, patients were randomly assigned to receive “routine care” (defined below) or daily home monitoring. After random assignment, the study groups crossed over at 3, 6, and 9 months, completing the second phase 12 months after random assignment. Each patient completed two 3-month intervals in the daily home PCA monitoring group and two 3-month intervals in the routine care group. At initiation of random assignment, before each crossover in therapy and at completion of the study, the patient and their care giver(s) were seen in the pediatric GCRC of Washington University Medical Center. Each visit included a complete physical examination and endocrine assessment, a review of monitoring techniques, and measurement of PCA capillary sodium concentration obtained by the care giver, as well as PCA venous sodium concentrations and laboratory chemistries. To assess differences in clinical outcome, at each GCRC visit care givers were asked to fill in a brief questionnaire pertaining to doctor and hospital visits, laboratory studies not ordered by the study physician, and missed work over the preceding 3 months.

During “routine care” periods, laboratory sodium assessment was done on the basis of each patient’s routine before enrollment in the study, with a recommended frequency of weekly to monthly. Additional testing was done when clinically indicated. Care givers were instructed to contact the study physician by phone for any DI-related concerns, during periods of illness, or during an unexpected response to dDAVP (such as failure to urinate when expected or inappropriately large urine volume). During the 3-month intervals of home PCA monitoring, care givers were asked to analyze the patient’s sodium concentration daily, independent of the clinical status of the patient. More frequent monitoring was recommended when clinically indicated. In addition to clinical indications for physician contact identical to those used during routine care, care givers were instructed to contact the study physician in the event of a sodium value <135 mmol/L or >150 mmol/L. There were no scheduled endocrine physician visits for either group outside the study visits, which occurred every 3 months. To minimize interpatient differences in management, consistent management guidelines were utilized by the study physician to direct care during both daily monitoring and routine care. The target range for sodium was defined as 135 to 150 mmol/L. When a sodium concentration outside the target range was reported, the management plan was designed to correct sodium concentrations at a rate of −5 mmol/L in a 24-hour period. In otherwise well participants, sodium values between 125 and 165 mmol/L were managed at home without in-person evaluation by a health care provider. After completion of the study, a brief phone interview was conducted to further assess outcome.

Statistics

SAS version 8 was used for all statistical analysis. Linear regression modeling was used to calculate the correlation coefficient, slope (± SE), and intercept (± SEM), comparing capillary PCA sodium concentration with venous specimen sodium concentration. A paired t test or Wilcoxon signed rank
test was used to compare clinical outcome differences between the monitoring and routine care. A paired t test was used to compare the percentage of out-of-range values from the first PCA use period and second PCA use period for daily monitoring. Pooled standard deviation and coefficient of variance were calculated using the root-mean-square average technique.

RESULTS

Comparison of PCA and Laboratory Results

After a single education session, all care givers were able to obtain and test capillary specimens with the PCA. To determine the accuracy of sodium concentrations measured with the PCA by using capillary specimens collected by care givers (PCA capillary sodium), these results were compared both with sodium concentrations measured on venous plasma at reference laboratories (laboratory sodium) and with venous results from the PCA by using specimens collected by laboratory personnel (PCA venous sodium) (Fig 1). Values obtained during the 3-month preclinical period and values obtained during GCRC visits were analyzed together (total of 66 sets). Correlation between PCA capillary sodium and laboratory sodium was good ($r = 0.92$, slope = 0.857 [± 0.047], intercept = 20.6 [± 6.9], $P < .0001$). Because testing was performed at various laboratories, there was concern that between-laboratory variation, introduced by the use of different analytic systems to determine sodium, might increase the observed differences between care giver-collected results and laboratory results. To address this issue, whenever possible (85% of tests) the laboratory personnel collecting the specimen provided a second venous specimen to the care giver, to be tested on the PCA. The correlation of the care giver-collected capillary sodium concentrations with results with the specimens collected by the laboratory personnel, both analyzed with the PCA, was similar ($r = 0.93$, slope = 0.882 [± 0.047], intercept = 17.2 [± 6.9], $P < .0001$).

Clinical Accuracy

In Error Grid Analysis,13 laboratory and monitor values are compared on the basis of whether they are clinically accurate, inaccurate but resulting in benign or no changes in treatment, or inaccurate and leading to unnecessary or potentially dangerous corrective therapy. Because evaluation of the clinical utility of the PCA in the home set-
ting was amenable to similar analysis, a modification of the Error Grid principle was applied to the accuracy data (Fig 1). The assumptions behind the PCA sodium error grid were (1) the target sodium was between 135 and 150 mmol/L and sodium concentrations in this range required no additional intervention; (2) a sodium level <135 initiated therapy with the goal of increasing sodium 5 mmol/L over the next 24 hours; (3) a sodium level >150 initiated therapy with the goal of reducing sodium 5 mmol/L over the next 24 hours; (4) values <125 or >165 result in referral to a medical facility for evaluation, even if the patient appeared otherwise well; and (5) the laboratory sodium concentrations reflect the “true” sodium concentration. In the error grid, the graphic representation of PCA capillary versus venous results was divided into zones. The significance of each zone was defined by how the management decision based on the PCA capillary value would differ from the decision, based on a specimen collected by the reference laboratory.

Sixty-two of 66 comparisons between laboratory sodium concentration and PCA capillary sodium concentration are in the error grid zone reflecting clinically accurate measurements (Fig 1, zone A). In two comparisons, reliance on the capillary PCA sodium concentration would have resulted in treatment to reduce sodium when the sodium was in the target range when measured by the reference laboratory (Fig 1, zone D). In two comparisons, use of the capillary PCA result would have resulted in failure to provide treatment to reduce sodium when sodium measured by the reference lab was above the target range (Fig 1, zone C). No treatment recommendations made based on PCA results would have resulted in a significantly different or erroneous treatment. To address the potential effect of interlaboratory analyzer differences, comparisons (n = 56) between the care giver-collected capillary specimens and the laboratory personnel-collected venous specimens analyzed on the PCA were also subjected to error grid analysis. All of these comparisons are in zone A. This may support the initial hypothesis that some of the apparent differences between the PCA capillary results and the laboratory determinations could be due to variation in sodium determinations between reference laboratories.

**Daily Home Monitoring**

In the second phase of the study, all patients alternated between daily home PCA sodium monitoring by the care giver or routine care at 3-month intervals for 1 year. Compliance with daily home PCA monitoring ranged from 51% to 99% and compliance with the physician contact criteria based on sodium ranged from 27% to 93% (Table II). We compared the number of calls to the physician, DI-related hospitalizations, emergency room visits, physician office visits, and DI-related laboratory testing during daily home PCA monitoring and routine care (Table III). Calls based on the
Table III. Clinical outcome comparison of daily monitoring compared with routine care

<table>
<thead>
<tr>
<th>Outcome variables†</th>
<th>Daily monitoring</th>
<th>Routine care</th>
<th>P value‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of calls to study physician</td>
<td>29.75 (23–41)</td>
<td>10.75 (0–22)</td>
<td>.028</td>
</tr>
<tr>
<td>DI-related hospital admissions</td>
<td>0</td>
<td>0.25 (0–1)</td>
<td>1</td>
</tr>
<tr>
<td>DI-related ER visits</td>
<td>1.25 (0-5)</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>DI-related PMD visits</td>
<td>0.5 (0-2)</td>
<td>0.5 (0-1)</td>
<td>1</td>
</tr>
<tr>
<td>DI-related Lab work</td>
<td>3.5 (0–7)</td>
<td>14.5 (2–30)</td>
<td>.147</td>
</tr>
<tr>
<td>Hours off work†</td>
<td>13.33 (0–40)</td>
<td>24 (0–72)</td>
<td>1</td>
</tr>
</tbody>
</table>

†Mean (and range) per patient during daily monitoring and routine care periods (6 months each). †Hours off work includes only 3 of the 4 persons. The 4th participant moved from a group home to a single-child foster care setting late in the 3rd crossover period. Time off work reported for this participant is not included here because the change in environment was believed to be a significant confounder that was relevant to that participant only.‡P values were determined by paired t test or Wilcoxon signed rank test as appropriate.

Despite the absence of statistically significant differences in outcome, all the care givers in the study believed that access to the PCA improved their ability to care for their children. Three of the four participating families specifically requested continued home use, and all four stated during a follow-up interview that they would continue to use the device if it were available. Three of the four believed that the improvement was due solely to immediate access to sodium information. One thought that both increased physician access and immediate access to sodium information had contributed. All care givers believed that they had a good understanding of how to manage moderately abnormal sodium results, without contact with a physician. Care givers reported no or infrequent technical problems with testing and believed that the PCA results were reliable. Participants believed that access to the PCA for sodium monitoring increased their comfort level while caring for their child with DI, particularly during times when the child’s clinical status was changing, such as illness, unexpected breakthrough, or during dDAVP and fluid intake adjustment.

Reproducibility of Measurements Made in the Home

Because repeat testing involved lanc- ing the participant’s finger a second time, duplicate measurements were not made routinely. However, during the daily home PCA monitoring phase, when PCA sodium results were >155, <130, or not congruent with the clinical situation, care givers were asked to repeat the sodium determination. Compliance with obtaining repeat measurements was highly variable. The average number of repeated tests per subject was 8.5 in 6 months (range, 5-15). By comparing sodium results obtained twice within a 2-hour period, we were able to estimate the precision of the PCA sodium determinations in the setting of home monitoring. The pooled standard deviation for repeat sodium was 2 mmol/L, with a pooled coefficient of variance of 1.3%.

Qualitative Outcomes

Despite the absence of statistically significant differences in outcome, all the care givers in the study believed that access to the PCA improved their ability to care for their children. Three of the four participating families specifically requested continued home use, and all four stated during a follow-up interview that they would continue to use the device if it were available. Three of the four believed that the improvement was due solely to immediate access to sodium information. One thought that both increased physician access and immediate access to sodium information had contributed. All care givers believed that they had a good understanding of how to manage moderately abnormal sodium results, without contact with a physician. Care givers reported no or infrequent technical problems with testing and believed that the PCA results were reliable. Participants believed that access to the PCA for sodium monitoring increased their comfort level while caring for their child with DI, particularly during times when the child’s clinical status was changing, such as illness, unexpected breakthrough, or during dDAVP and fluid intake adjustment.

DISCUSSION

Current trends in health care reflect a move to home-based care. Home glucose monitoring and self-management instruction is now a routine part of diabetes care. Similar approaches are being studied for other laboratory measures, in particular anticoagulation therapy. Blood pressure monitoring in the home is becoming
commonplace, resulting in international consensus guidelines for self-blood pressure monitoring. Plasma sodium concentration is strongly correlated with fluid status in individuals with DI and can be measured in the home setting. This makes it an ideal candidate for home-based monitoring and management in this patient population. In individuals with DI and impaired thirst or inability to access free water, episodes of severe hypernatremia and hyponatremia occur because of gradual shifts in fluid balance, acute illnesses limiting fluid intake, or acute and unexpected changes in dDAVP response. Severe hypernatremic dehydration with encephalopathy, central nervous system injury, and venous thrombosis are potential complications of undertreated DI. Water intoxication during dDAVP therapy, with associated hyponatremia and seizures, occurs at the other extreme. Recently Rizzo et al reported significant hyponatremia-related morbidity and death associated with dDAVP therapy in children with DI. Their findings led them to suggest that changes in dDAVP dose or fluid administration be managed in a hospital setting. Our results suggest that home monitoring could provide an alternative, allowing changes in dDAVP and fluid administration to be safely undertaken at home.

One concern for physicians interested in having patients use home monitoring devices is the possibility of increased physician burden caused by increased patient-to-physician phone contact. Although an increase in physician calls was seen during daily home sodium monitoring in this study, much of this was related to the study design, as instructions were provided to contact the study physician whenever the sodium was <135 or >150. In a follow-up interview, all care givers believed that they would be comfortable making management decisions about moderate- to- ly abnormal sodium values without contacting a physician. Home management guidelines similar to those used by the study physician during this study could potentially be utilized by care givers to strengthen their self-management decision-making skills. Therefore, it seems likely that the physician phone call burden related to home monitoring could be significantly reduced.

Because this is a rare disease, the study involved too few patients to determine if there is an association between daily monitoring and clinical improvement. In addition, experience with other point-of-care testing would suggest that with larger patient populations, we are likely to encounter some care givers who are unable to utilize the device. Studies of long-term use in a larger number of subjects will be necessary to address these issues and evaluate the cost-effectiveness and feasibility of home monitoring and self-management programs for DI.

We thank Dr. Louis Muglia for assistance with developing the DI management guidelines used during this project, as well as his thoughtful comments on the study design and manuscript. Thanks also to Dr. Kathleen Betbin, Dr. Neil White, and Dr. Abby Holland for their review and comments on the manuscript and Dr. William Shannon for his helpful discussions about appropriate statistical tests. Ms Gayle Chipman at I-STAT was instrumental in assuring access to all supplies needed for the duration of the study.

REFERENCES