Evaluation of sodium deficit in infants undergoing intestinal surgery

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A B S T R A C T

Background: Sodium is a critical growth factor for children. Severe deficits cause growth impairment and cognitive dysfunction. Both the diagnosis and risk of sodium depletion in children undergoing intestinal surgery are poorly understood.

Methods: With IRB approval, children undergoing intestinal surgery (2009–2012) who had a urine sodium measurement were retrospectively reviewed. Sodium deficits were defined: urine sodium <30 mmol/L and ~10 mmol/L were deficient and severely deficient, respectively. Demographics, weight changes, and intake (sodium, fluid, and nutritional) were tabulated. Data were analyzed using regression analysis and Mann Whitney U tests.

Results: Thirty-nine patients, 51.3% female, with a gestational age of 32.2 weeks and weight of 1.43 kg were identified. The most common diagnoses were NEC (38.5%), intestinal atresia (20.5%), and isolated perforation (10.3%). Sodium deficiency was documented in 36/39 (92%) and 92.9% for those in continuity. Severe deficiency occurred in 64%. Urine sodium was significantly correlated with weight gain (p = 0.002). Weight gain in patients with urine sodium <30 mmol/L was significantly decreased vs. those ≥30 mmol/L (+0.58 g/d vs. +21.6 g/d, p = 0.016).

Conclusion: In this population, sodium depletion is common in children undergoing intestinal surgery, even when the colon is in continuity. Correction of the sodium deficit to achieve urine sodium >30 mmol/L is associated with improved weight gain.

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Small bowel intestinal resection may pose a significant nutritional risk with associated fluid and electrolyte deficits in patients. Infants with small bowel stomas, particularly premature infants, are known to be at an increased risk of sodium and water loss [1,2]. Dehydration accompanied by a sodium deficit may profoundly impact not only the infant’s ability to gain weight, but to grow [3,4]. Unless specifically monitored, sodium depletion may become severe even in the context of a normal serum sodium as well as apparent normal fluid balance. Traditionally infants with short bowel syndrome, with or without small bowel stomas, were felt to be the population at highest risk of sodium depletion secondary to intestinal loss [5–7]. Literature evaluating the risk of sodium depletion in infants with distal small bowel stomas, but without short bowel syndrome has been sparse [1,2]. In addition, to our knowledge, no literature exists which evaluates sodium depletion in post-surgical patients without short bowel syndrome who are in continuity.

When patients are in a positive sodium balance, normal urine sodium is ≥30 mmol/L and measurements <30 are considered to represent total body sodium depletion; <10 mmol/L is felt to indicate a severe deficit [6]. Unfortunately, most literature in this area is over 20 years old [1,2,4–8] and the majority of studies which describe the intestinal handling of sodium were performed in animals or adults [8,10,12,13]. The primary aim of this study was to evaluate the occurrence of sodium deficit in infants undergoing intestinal surgery. The secondary aim was to determine the effects of a sodium deficit and the impact on infant growth. Our hypothesis was that the severity of sodium deficit correlates to impaired growth in infants after intestinal surgery and that the correction of sodium depletion resulted in improved weight gain.

1. Methods

With IRB approval (REB#: H12-0224) a retrospective cohort study from 2009 to 2012 was undertaken. Infants 12 months of age and under who underwent intestinal surgery and who had measurement of a random urine sodium were reviewed. All patients initially underwent emergency surgery and a subgroup of patients had subsequent elective stoma closure. The data around these events were utilized. In 2009, a clinical practice guideline (Fig. 1A & B) for sodium monitoring and supplementation in the intestinal failure population was developed. Patients with short bowel syndrome and/or intestinal failure who were managed by the institutional intestinal rehabilitation team had urine sodium measurements. Starting in 2011, selected post intestinal surgery patients (without short bowel syndrome) were included.
A

Sodium Supplementation Guideline

1. Deficit states:

Measure Urine Na (UNa) just prior to initiation of enteral feeds

**<10 mmol/L**

- Add sodium to feeds†:
  - Achieve total* intake of: 6 mEq/kg/d
  - repeat UNa weekly

- If repeat UNa <10 mmol/L:
  - supplement to achieve total* of at least 8 mEq/kg/d
- If UNa <10 mmol/L & growth failure:
  - supplement with to achieve total* of at least 10 mEq/kg/d

**10-30 mmol/L**

- Add sodium to feeds†:
  - Achieve total* intake of: 4 mEq/kg/d
  - repeat UNa weekly

- If <10mmol/L: follow 1
  - If 10-30 mmol/L & growth:
    - continue 2
- If 10-30 mmol/L & growth failure:
  - follow 1
- If >30mmol/L**:
  - continue with 2

**> 30 mmol/L**

- monitor urine sodium

Fig. 1. (A) Guideline for sodium measurement and supplementation in deficit states. (B) Guideline for sodium measurement and supplementation in balance/excess states.
There were nine infants who had <50% predicted small intestinal bowel length.

Data following the initial emergent operation demonstrated a sodium deficiency and severe deficiency in 92% and 64% respectively (Table 2). The majority of patients had stoma creation at the initial operation and severe sodium deficiency was most frequently documented in infants with a jejunostomy. For patients who received a Bishop Koop anastomosis or were in continuity after initial operation, 100% had a sodium deficiency. For the 3 patients in whom urine sodium measurements were ≥30 mmol/L after the first intestinal surgery, all patients had only a single measurement performed when patients were on 100% parenteral calories.

There were 14 patients in continuity that had a urine sodium measurement; 92.9% had a sodium deficiency and for 57.1% the deficit was severe (Table 3). In this group, 7 had >50% predicted small bowel length with full-length colon and of these, 85.5% had a sodium deficit (Table 3). For the eleven patients who had urine sodium measurements after elective stoma closure, 90.9% had a sodium deficit. All eleven patients had sodium depletion on at least one occasion while they had a stoma.

Urine sodium was measured an average of 3.5 times per patient during the study period (11 patients had 5 measurements after the initial surgery and 9 patients had 3 measurements after elective stoma closure). There were 3 patients who had more than 20 urine sodium measurements (the data after the maximum number of 8 urine sodiums were not used).

With the evaluation of the entire data set (range of enteral feeding 0%–100%), urine sodium was not significantly correlated with weight gain, with fluid intake, stoma output, or urine output. Urine sodium was correlated with serum sodium (p = 0.05) as well as total intake of sodium (p < 0.001). Additionally, changes in weight were not found to be statistically related to total sodium intake, fluid intake, stomal output, urine output or serum sodium. On subgroup analysis,
Table 3
Patients in continuity after initial operation or stoma closure.

<table>
<thead>
<tr>
<th>Pt</th>
<th>Dx</th>
<th>Small intestine length (cm), [GA (weeks)]</th>
<th>Intact full length colon?</th>
<th>Lowest UNa (mmol/L)</th>
<th>Total Na intake (MEq/kg/d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NEC</td>
<td>35 [28]</td>
<td>no</td>
<td>&lt;5</td>
<td>6.7</td>
</tr>
<tr>
<td>2</td>
<td>NEC</td>
<td>5 [28]</td>
<td>no</td>
<td>&lt;5</td>
<td>4.4</td>
</tr>
<tr>
<td>3</td>
<td>NEC</td>
<td>53 [27]</td>
<td>yes</td>
<td>&lt;5</td>
<td>1.8</td>
</tr>
<tr>
<td>4</td>
<td>NEC</td>
<td>56.5 [27]</td>
<td>yes</td>
<td>&lt;5</td>
<td>1.9</td>
</tr>
<tr>
<td>5</td>
<td>NEC</td>
<td>17 [27]</td>
<td>yes</td>
<td>4</td>
<td>4.9</td>
</tr>
<tr>
<td>6</td>
<td>jejunal atresiaa</td>
<td>95 [34]</td>
<td>yes</td>
<td>8</td>
<td>0.6</td>
</tr>
<tr>
<td>7</td>
<td>jejunal atresia</td>
<td>150 [34]</td>
<td>yes</td>
<td>29</td>
<td>5.4</td>
</tr>
<tr>
<td>8</td>
<td>ischemia</td>
<td>83 [52]</td>
<td>yes</td>
<td>21</td>
<td>6.8</td>
</tr>
<tr>
<td>9</td>
<td>ischemia</td>
<td>37 [39]</td>
<td>yes</td>
<td>26</td>
<td>5.1</td>
</tr>
<tr>
<td>10</td>
<td>meconium ileus</td>
<td>175 [40]</td>
<td>yes</td>
<td>10</td>
<td>5.9</td>
</tr>
<tr>
<td>11</td>
<td>isolated perforation</td>
<td>65[25]</td>
<td>yes</td>
<td>10</td>
<td>2.8</td>
</tr>
<tr>
<td>12</td>
<td>volvulus</td>
<td>125 [36]</td>
<td>yes</td>
<td>38</td>
<td>0.4</td>
</tr>
<tr>
<td>13</td>
<td>Hirschsprung</td>
<td>50 [41]</td>
<td>no</td>
<td>6</td>
<td>0.9</td>
</tr>
<tr>
<td>14</td>
<td>colonic atresia</td>
<td>104 [40]</td>
<td>no</td>
<td>5</td>
<td>4.9</td>
</tr>
</tbody>
</table>

a Mean sodium intake 1 week prior to lowest urine sodium measurement.
b Patients in continuity at initial operation.

Comparing total sodium intake to achieve weight gain of >20 g/day, median values for patients with a jejunostomy, ileostomy, jejunocolic and ileocolic anastomosis were 5.9, 5.45, 4.81 and 3.25 MEq/kg/d respectively. There were no statistically significant differences between these anatomic subgroups.

For the nine infants with <50% predicted small bowel intestinal length, the median total sodium intake to gain weight of < or ≥ 10 g/d and < or ≥ 20 g/d was 2.8 vs. 5.4 MEq/kg/d (p < 0.001) and 3.95 vs. 5.4 MEq/kg/d (p = 0.04). The range of total sodium intake associated with weight gain for the 10 g/d was 2.9–12.7 MEq/kg/d. For the weight gain threshold of 20 g/d, the range of sodium intake was 2.5–7.3 MEq/kg/d.

For the patients who were receiving >50% of their calories enterally, urine sodium was positively associated with weight gain (p = 0.002). In this subgroup, weight gain in patients with urine sodium ≥ 30 mmol/L was +21.6 g/day vs. +0.6 g/d in those with urine sodium <30 mmol/L (p = 0.02). There was no significant difference in weight changes when a threshold of 20 mmol/L of urine sodium was used. On multiple regression analysis, the only independent predictor of weight gain was a urine sodium measurement when the patient had >50% of total calories delivered enterally (Table 4).

3. Discussion

By day 7 of life, neonatal kidneys conserve sodium to maintain a positive sodium balance [14]. Integrity and function of the intestine are key to allow infants to achieve this sodium conservation; in healthy states, 97% of the sodium entering the colon is absorbed [13]. A positive sodium balance is critical to allow DNA synthesis, stimulate cell proliferation, nutrient absorption and ultimately, growth [3,4]. In deficit states, excretion falls to very low levels with minimal decreases in tissue concentration. When severe sodium depletion occurs, wasting, growth impairment and cognitive function deficits have been documented in children [3,4]. Supplementation of sodium has been shown to increase growth velocity, however it does not induce “catch up” growth [3]. It is therefore critical to monitor the at-risk infants’ sodium status carefully and provide supplementation prior to the development of growth impairment.

In the current study, sodium depletion was documented in 92% of the study population. Impaired weight gain was significantly correlated with decreased urine sodium. Significant differences in weight gain occurred above and below the threshold urine sodium of 30 mmol/L. Supplementation was positively associated with increased urine sodium and weight gain.

The evaluation of the subgroup of patients with >50% enteral calories was anticipated to better reflect those who had stabilized postoperative fluid shifts and would typically be anticipated to be gaining weight. Prior to establishing enteral tolerance (when feeds are started and stopped or very low in volume), stomal output and subsequent losses may be minimal. At >50% enteral calories, it could be expected that infants would have additional sodium losses via their stomas and thus be at increased risk for sodium deficit. Following the clinical practice guideline for sodium supplementation for infants with functioning stomas would be expected to result in both increased sodium intake and increased total body sodium which may be reflected in increased urine sodium. This may be the explanation as to why total sodium intake correlated to urine sodium and to weight gain in this subgroup. The reason that there was not a significant association found for the entire study population (0%–100% enteral calories) between total sodium intake and weight may be that before patients reached 50% enteral feeds, weight changes were influenced more by fluid shifts, not just growth, particularly postoperatively or during episodes of sepsis. Sepsis episodes were not recorded in the current study.

On multiple regression analysis, once patients had achieved >50% of their calories enterally, of the variables measured in the current study, only urine sodium independently predicted weight gain or loss. This suggests that the importance of the mucosal absorptive function for sodium has a greater impact on weight for infants receiving >50% of calories enterally, than sodium intake. This is felt to be of practical significance as it emphasizes the importance of functional sodium absorption in directing sodium supplementation needs.

For those with short bowel syndrome (less than 50% of predicted small intestinal length) there was a significant difference in the total intake sodium associated with weight gain over the range of 0%–100% enteral intake, consistent with previously reported results [2]. The difference was more pronounced at the 10 g/day (compared to the 20 g/day) threshold. This observation may be due to one patient with a proximal jejunostomy who, despite supplementation

### Table 4
Multiple regression analysis of factors vs. weight change for patients on >50% enteral calories.

<table>
<thead>
<tr>
<th></th>
<th>95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>total sodium intake</td>
<td>−4.67–7.038</td>
<td>0.93</td>
</tr>
<tr>
<td>cal/kg/day</td>
<td>−1.07–0.98</td>
<td>0.2</td>
</tr>
<tr>
<td>total fluid (ml/kg/d)</td>
<td>−1.39–0.175</td>
<td>0.26</td>
</tr>
<tr>
<td>ostomy output (ml/kg/d)</td>
<td>−0.93–0.98</td>
<td>0.94</td>
</tr>
<tr>
<td>urine sodium</td>
<td>−0.42–0.68</td>
<td>0.02</td>
</tr>
</tbody>
</table>

a CI = Confidence Interval.
(5–12.7 MEq/kg/day) was unable to gain more than 20 g/day for 6 of 8 measurements.

In the current study, there was wide variation in the amount of sodium supplementation related to weight gain. Although median values of total sodium supplementation associated with weight gain of ≥20 g/day indicated a trend to increased values for jejunostomy patients compared to ileostomy, jejunocolic and ileocolic anatomy patients, the differences were not statistically significant. This may reflect the heterogeneous intestinal absorptive function of our patient population. These heterogenic intestinal anatomy and function are a possible explanation for the current study's discrepant findings to those of Bower who demonstrated a direct relationship between sodium intake and growth in patients with NEC or meconium ileus who had stomas (9/11 patients had an ileostomy) [2].

For the three patients who had normal urine sodium measurements, all had only one measurement taken. In addition, these patients had not initiated on any enteral feeds postoperatively and were on 100% parenteral nutrition. None of these patients had any stoma output in the week prior to the urine sodium measurement and thus development of a sodium deficit at the time would not have been anticipated. Whether any of these patients eventually developed sodium deficiency is unknown.

The finding of sodium deficits in patients without short bowel syndrome and who have intestinal continuity has, to our knowledge, not been previously described. Traditionally, it was believed that for patients with sufficient length of small bowel and an intact colon, sodium would be efficiently absorbed [12,13]. In the study subgroup who was in continuity after initial operation or after stoma closure, 7 had > 50% of expected small bowel length (with a full-length colon) when compared to published norms [15]. A possible explanation for the finding of sodium depletion in 6 of 7 of these patients may be related to an impaired ability to absorb sodium secondary to the villous atrophy that occurs in the distal bowel even prenatally (intestinal atresia) or after stoma creation. Wang observed experimentally in animals that the defunctioned colon was found to have villous atrophy [16]. With time, normal intestinal absorption would be anticipated, but the exact duration is unknown.

There are several limitations in our study. First, given its retrospective nature, many factors were not controlled for including the criteria for obtaining a urine sodium, the timing and the frequency of measurement. In addition, the number limit of urine sodium measurements was arbitrary to try and more accurately capture the results from the entire group of patients. This may have resulted in loss of important data especially as the patients get further out from postoperative fluid shifts. Also, despite a clinical guideline available to direct sodium supplementation during states of presumed deficit or excess, the guideline was inconsistently followed. As well, calculations of total fluid and sodium intake were made by including only the amounts administered via parenteral or enteral nutrition. Other sources of sodium and fluid may have been substantial in some patients (particularly in the immediate postoperative period) and were not included in the data collected. Furthermore, dehydration is a confounding factor and some of the observed low urine sodium values may have been related more to dehydration rather than to sodium deficiency. In the current study, urine specific gravity was not routinely obtained. Urine output was used as a surrogate for dehydration, but this is difficult to interpret without the specific gravity or the fractional excretion of sodium. Finally, renal conservation of sodium is known to be decreased in infants less than 32 weeks, thus the validity of defining deficiency states for premature infants when the urine sodium <30 mmol/L is in question.

Nearly all infants undergoing intestinal surgery in which urine sodium was measured had a sodium deficit and the majority developed a severe deficiency. Impaired weight gain was significantly associated with urine sodium <30 mmol/L and sufficient supplementation to achieve urine sodium ≥30 mmol/L significantly improved weight gain. Whether the findings of this study represent the high-risk group or only a portion of a larger group of patients at risk is not clear. However, the finding of sodium deficiency in patients who are in continuity and who do not have short bowel syndrome has important implications for all infants undergoing intestinal surgery. The results of the current study need to be interpreted with caution as the information was obtained retrospectively and factors were not controlled. It is clear a prospective study is needed to better understand the population at risk of sodium deficiency, the timing of deficit occurrence and the intestinal adaption with respect to sodium handling. Until such study results are available however, it would seem prudent to monitor urine sodium in infants undergoing intestinal surgery to ensure deficits do not develop in this fragile patient population.

Acknowledgment

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References