Evaluation of the Effect of Vitamin D on the Length of Hospital Stay in Children with Gastroenteritis Aged 3 Months to 14 Years Admitted to the Pediatric Hospital of Bandar Abbas

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Abstract

Background: Acute gastroenteritis is one of the major causes of pediatric hospitalization and mortality worldwide. Vitamin D can improve the immune system, and its deficiency may exacerbate the severe symptoms of any infectious disease. Thus, the aim of this study was to investigate the effect of vitamin D on children admitted to a hospital due to acute gastroenteritis.

Methods: In this double-blind randomized placebo-controlled trial, 100 children aged 3 months to 14 years old hospitalized due to acute gastroenteritis in Bandar Abbas pediatric hospital, Iran, were enrolled. The participants were divided into two groups of case and placebo (n = 50 per group). Patients were excluded from the study if they met the exclusion criteria. After obtaining parental (or guardian) consent, in addition to the conventional treatment of gastroenteritis, the placebo group received 2 cc of olive oil (as placebo) and the cases received 100000 IU of vitamin D (ZAHRAVI Vit D3). Discharge criteria included reduction of fever and defecation and improvement of the patient’s general condition. The required data including age, sex, baseline serum vitamin D level, level of dehydration, axillary temperature, and length of hospital stay were recorded in a checklist by a physician. Descriptive statistics, chi-square test, and Student’s t-test were used to compare the recorded data in SPSS, version 24.

Results: The mean lengths of hospital stay were 3.46 and 2.54 days in the placebo and case groups, respectively, indicating a significant difference between the two groups in this regard (P < 0.001). However, there were no significant age and sex differences between the two groups regarding hospital stay (P = 0.09 and P = 0.14). Furthermore, there was no significant relationship between length of hospital stay and the level of dehydration in either group (P = 0.15). We found that axillary temperature at discharge was significantly lower in the vitamin D group than the placebo group (P = 0.017). In general, length of hospital stay was shorter in the vitamin D group, and there was no difference between patients with baseline vitamin D level of < 30 ng/mL and those with vitamin D level of ≥ 30 ng/mL in the vitamin D group regarding length of hospital stay (P = 0.057). On the contrary, in placebo group, hospital stay was significantly longer in those with vitamin D level of < 30 ng/mL (P = 0.039).

Conclusions: This prospective study demonstrated that vitamin D supplementation is significantly related to the reduction of hospital stay in pediatric acute gastroenteritis patients aged 3 months to 14 years old. This finding was achieved after unification of the confounding variables such as socioeconomic status. We also noted that the effect of vitamin D on hospital stay was not associated with age, sex, and level of dehydration.

Keywords: Gastroenteritis, Vitamin D, Hospital Stay, Pediatrics

1. Background

Gastroenteritis is a technical term denoting a diarrheal disease that can be accompanied by other clinical presentations such as nausea, vomiting, fever, and abdominal pain. This disease is one of the most serious infectious diseases in human beings in underdeveloped and developing countries (1). Moreover, it is the fourth leading cause of mortality in children aged less than five years old (2-4). Viruses and bacteria can both be responsible for acute gastroenteritis (5). The World Health Organization (WHO) has reported that Rotavirus, Escherichia coli, Campylobacter jejuni, and Shigella species are respectively the most important causes of gastroenteritis in Third World countries, while Campylobacter jejuni and Rotavirus are of greater importance in the developed countries (3).
Currently, Rotavirus is the most common cause of severe gastroenteritis in infants and children worldwide (6). Signs and symptoms of gastroenteritis are caused by the pathogenic and inflammatory effects of the aforementioned microorganisms on intestinal epithelial cells.

The most common nutritional deficiency around the world is vitamin D deficiency, and since only less than 10% of it is supplied by dietary sources, either supplementation or adequate exposure to sun is required to fulfill the needs of an individual (7, 8). Generally, vitamin D can boost the activity of the immune system; therefore, vitamin D insufficiency or deficiency in children can exacerbate the symptoms of an infectious disease, many of which occur due to inflammatory responses of the immune system (9). A quite recent study demonstrated that vitamin D deficiency can increase the rate of diarrheal diseases among school-age children (10). Vitamin D can affect both innate and adaptive immune systems. As a matter of fact, vitamin D functions through binding to a nuclear receptor (vitamin D receptor [VDR]), which is present in many tissues including the immune system (11). It has been shown that all immune system cells express VDR, especially T cells which play an important role in the process of inflammation (12). It has been demonstrated that vitamin D inhibits the proliferative and secretory functions of T cells (13, 14).

Diarrheal diseases fundamentally develop and progress in a way that diagnosis or prediction of their causative agent solely based on clinical manifestations is almost impossible; thus, in order to reduce the mortality rate of the disease, we must investigate the effect of possible treatment strategies including vitamin D supplementation. Therefore, we conducted the current study to evaluate the effect of vitamin D supplementation on hospitalized children with acute gastroenteritis.

2. Methods

2.1. Participants

This prospective double-blind randomized placebo-controlled trial was conducted in Bandar Abbas pediatric hospital from March 2017 to March 2018. Overall, 100 children with gastroenteritis who were admitted to the hospital due to acute gastroenteritis confirmed by a pediatrician during this period were enrolled in the study using the convenience sampling method. The standard sample size was determined with the confidence interval of 95% (α = 0.05) and power of 80% (β = 0.2) based on the previous studies. The inclusion criterion was age of 3 months to 14 years. The exclusion criteria were as follows: immunosuppression, use of immunosuppressive drugs, history of cystic fibrosis, malnutrition, consumption of large doses of vitamin D due to previous diseases, contraindications for vitamin D including hypercalcemia, hypervitaminosis D, biliary diseases associated with malabsorption of vitamin D, and hypersensitivity to vitamin D, and lack of parental cooperation or consent to participate in the study. Parental (or guardian) written informed consent was obtained from all parents.

2.2. Study Design

The study received ethics approval from the Ethics Committee of Hormozgan University of Medical Sciences, Hormozgan, Iran. The patients were randomized into two groups of case and placebo by means of random allocation software. Fifty patients in the placebo group received the conventional treatment plus 2 cc of olive oil as placebo, and 50 patients in the vitamin D group received the conventional treatment plus 100000 IU of vitamin D (ZAHRAVI Vit D3). Both patients and their parents and the study physician were blinded to group allocations. Two 50000 IU vitamin D pearls were cracked open and given to the patients orally so that cases and controls could not perceive the difference between olive oil and vitamin D.

Length of hospital stay was measured in days. Discharge criteria included reduction of fever and defecation and improvement of the patient’s general condition. The required data including age, sex, baseline serum vitamin D level, level of dehydration, axillary temperature, and length of hospital stay were recorded in a checklist by a physician. Vitamin D was measured by means of the enzyme immunoassay (EIA) method and using a DRG kit (DRG, Marburg, Germany). We considered a baseline vitamin D level of < 20 ng/mL deficient, 20 ≤ vitamin D level < 30 ng/mL insufficient, and vitamin D ≥ 30 ng/mL normal. The level of dehydration was determined by the attending physician according to the WHO manual for the treatment of diarrhea and was categorized into minimal or no dehydration, mild to moderate, and severe dehydration based on physical findings including mental status, thirst, heart rate, quality of pulses, breathing, eyes, tears, mouth and tongue, skin turgor, capillary refill, extremities, and urine output (9). Axillary temperature was measured using a standard mercury thermometer.

2.3. Data Analysis

Statistical analysis of the data was performed using SPSS, version 24. Chi-square test and Student’s t-test were run to compare the variables between the groups. P value less than 0.05 was considered significant.
3. Results

This study was performed on 100 patients (50 cases per group). Thirty patients in the case group and 19 patients in the placebo group were boys (60% and 38%, respectively). Also, 34% of the cases and 34% of the controls had minimal or no dehydration, 58% of the cases and 48% of the controls had mild to moderate dehydration, and 22% of the cases and 18% of the controls had severe dehydration. In general, 27%, 53%, and 20% of the patients had minimal or no dehydration, mild to moderate dehydration, and severe dehydration, respectively (Table 1).

The mean lengths of hospital stay were 3.46 and 2.54 days in the placebo and case groups, respectively, showing a significant difference between the two groups in this regard (\( P < 0.001 \)); hospital stay was longer in the placebo group. Meanwhile, as can be noted in Table 2, there were no significant age and sex differences between the groups regarding hospital stay (\( P = 0.09 \) and \( P = 0.14 \); Table 2).

Although hospital stay was longer in the placebo group with any level of dehydration, the difference between the two groups was not statistically significant (\( P = 0.15 \)); the level of dehydration did not alter the effect of vitamin D on hospital stay. Generally, hospital stay was shorter in the case group with any baseline vitamin D level compared to the placebo group (\( P = 0.000 \)); however, within the case group, hospital stay was slightly longer in those with baseline vitamin D level of \( \geq 30 \) ng/ml, but the difference was not significant (\( P = 0.057 \)). Thus, baseline vitamin D level did not affect the length of hospital stay. On the contrary, within the placebo group, hospital stay was significantly longer in those with vitamin D < 30 ng/ml (\( P = 0.039 \); Table 3).

In addition, although axillary temperature on admission was not significantly different between the two groups (\( P > 0.05 \)), axillary temperature at discharge was significantly lower in the case group compared to the placebo group (\( P = 0.017 \); Table 4).

<table>
<thead>
<tr>
<th>Groups</th>
<th>Vitamin D</th>
<th>Olive Oil</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boys</td>
<td>30 (60)</td>
<td>19 (38)</td>
<td>49 (49)</td>
</tr>
<tr>
<td>Girls</td>
<td>20 (40)</td>
<td>31 (62)</td>
<td>51 (51)</td>
</tr>
<tr>
<td>Minimal or no dehydration</td>
<td>10 (20)</td>
<td>17 (34)</td>
<td>27 (27)</td>
</tr>
<tr>
<td>Mild to moderate dehydration</td>
<td>29 (58)</td>
<td>24 (48)</td>
<td>53 (53)</td>
</tr>
<tr>
<td>Severe dehydration</td>
<td>II (22)</td>
<td>9 (18)</td>
<td>20 (20)</td>
</tr>
</tbody>
</table>

*Values are expressed as No. (%).

4. Discussion

The results of this study showed that vitamin D supplementation reduces the length of hospital stay (improvement of signs and symptoms), and this effect is not associated with age, sex, and level of dehydration. However, baseline vitamin D level was effective on hospital stay; thus, the lower the baseline vitamin D level, the longer the length of hospital stay. Previous studies have evaluated the effect of vitamin D on diseases other than gastroenteritis, most commonly respiratory infections.

In a randomized clinical trial conducted by Somnath et al. on 154 children with acute lower respiratory infection, it was demonstrated that a single oral dose of 100000 IU of vitamin D₃ did not shorten the duration of hospital stay.
Table 3. Evaluation of the Length of Hospital Stay with Respect to Baseline Vitamin D Level

<table>
<thead>
<tr>
<th>Group, Baseline Vitamin D</th>
<th>Mean Length of Hospital Stay (Days)</th>
<th>Standard Deviation</th>
<th>Number of Patients</th>
<th>F</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case</td>
<td></td>
<td></td>
<td></td>
<td>3.93</td>
<td>0.057</td>
</tr>
<tr>
<td>&lt; 30 ng/mL</td>
<td>2.52</td>
<td>0.90</td>
<td>19</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 30 ng/mL</td>
<td>2.55</td>
<td>1.09</td>
<td>31</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>2.54</td>
<td>1.01</td>
<td>50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td></td>
<td></td>
<td></td>
<td>4.172</td>
<td>0.039</td>
</tr>
<tr>
<td>&lt; 30 ng/mL</td>
<td>3.94</td>
<td>1.10</td>
<td>21</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 30 ng/mL</td>
<td>3.11</td>
<td>0.87</td>
<td>29</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>3.46</td>
<td>1.05</td>
<td>50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td></td>
<td>23.55</td>
<td>0.000</td>
</tr>
</tbody>
</table>

Table 4. Evaluation of Axillary Temperature at Discharge in the Two Groups

<table>
<thead>
<tr>
<th>Groups</th>
<th>Mean Temperature on Admission</th>
<th>Standard Deviation</th>
<th>P Value</th>
<th>Mean Temperature at Discharge (°C)</th>
<th>Standard Deviation</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case</td>
<td>36.8</td>
<td>2</td>
<td>&gt; 0.05</td>
<td>36.34</td>
<td>0.35</td>
<td>0.017</td>
</tr>
<tr>
<td>Placebo</td>
<td>37.3</td>
<td>1</td>
<td></td>
<td>36.52</td>
<td>0.37</td>
<td></td>
</tr>
</tbody>
</table>

(15). Also, Amrein et al. reported that among critically-ill patients with vitamin D deficiency, administration of high-doses of vitamin D did not reduce the length of hospital stay, hospital mortality, or 6-month mortality (16). Additionally, Langlois et al. found that vitamin D supplementation did not reduce hospital stay. They also found that daily vitamin D doses of >300000 IU did not improve mortality and length of intensive care unit (ICU) stay in critically-ill patients (17). These results were contrary to our findings since we found that vitamin D supplementation reduced the length of hospital stay. This discrepancy in results might be attributed to different sample sizes, different causes of hospital admission, different doses of vitamin D administration, different baseline levels of vitamin D, and different demographic features of the studied samples.

In a study performed by Sankar et al. on 101 children aged 1 month to 17 years admitted to ICU, it was demonstrated that the median duration of ICU stay was significantly longer in vitamin D-deficient children than those with no vitamin D deficiency. The association between length of ICU stay and vitamin D deficiency remained significant, even after adjusting for key baseline variables, diagnosis, illness severity, need for fluid boluses, ventilation, inotropes, and mortality (18). Similarly, we found that the length of hospital stay was longer in children with baseline vitamin D level < 30 ng/mL.

Our results suggest that timely administration of adequate vitamin D can have positive impacts on children with gastroenteritis, including reduction of hospital stay and prevention of exposure to nosocomial infections.

4.1. Conclusions

Our results revealed that vitamin D supplementation reduces the length of hospital stay; however, the factors that influence the efficacy of vitamin D remain to be further studies upon. One of the limitations of our study was the short duration of the study; therefore, we could not investigate the long-term effects of vitamin D supplementation. Thus, future studies should be performed during a longer period of time so that the prognosis and long-term outcomes of patients receiving vitamin D supplementation can be evaluated.

Supplementary Material

Supplementary material(s) is available here [To read supplementary materials, please refer to the journal website and open PDF/HTML].
Acknowledgments

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Footnote

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References


