Prophylactic Phosphate Supplementation for the Inpatient Treatment of Restrictive Eating Disorders

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Keywords: Anorexia nervosa; Refeeding syndrome; Hypophosphatemia; Eating disorder

ABSTRACT

Purpose: The medical stabilization of adolescent patients with restrictive eating disorders can be associated with refeeding syndrome, a potentially fatal complication preceded by refeeding hypophosphatemia (RH). Whether RH can be prevented by routine prophylactic phosphate supplementation has not been previously examined. This study sought to determine the safety and efficacy of a refeeding strategy that incorporates prophylactic phosphate supplementation to prevent RH.

Methods: Retrospective chart data were collected for patients aged younger than 18 years with restrictive eating disorders admitted to a tertiary pediatric inpatient ward between January 2011 and December 2014. All patients were refed with a standardized protocol that included prophylactic oral phosphate supplementation (1.0 ± 0.2 mmol/kg/day).

Results: During the 4-year study period, 75 admissions (70 patients) were included for analysis. The mean age and percent median body mass index of included patients were 15.3 years and 83.5%, respectively. Seven out of 75 (9%) had percent median body mass index of <70% and 26 out of 75 (35%) had percent body weight loss >20%. All patients were normophosphatemic at the time of admission (mean serum phosphate 1.24 ± 0.2 mmol/L). Serial laboratory evaluation revealed that all supplemented patients maintained serum phosphate levels >1.0 mmol/L during the initial 7 days of refeeding. Eleven patients became mildly hyperphosphatemic (range 1.81–2.17 mmol/L) with no associated clinical consequences. Additional analysis of 11 patients presenting with hypophosphatemia before refeeding revealed that with supplementation, phosphate values normalized by Day 1, and this group experienced no further RH episodes during initial refeeding.

Conclusions: Prophylactic oral phosphate supplementation appears safe, and no episodes of RH occurred in patients with restrictive eating disorders undergoing inpatient refeeding.

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Original article

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Anorexia nervosa (AN) is a complex, potentially life-threatening illness frequently affecting adolescents. The condition can be associated with complications such as cardiac dysrhythmias, hypotension, decreased bone mineral density, and growth arrest [1]. Affected individuals may necessitate hospital admission for medical stabilization and nutritional rehabilitation to prevent serious or fatal complications. Guidelines for the management of AN have been published by various organizations including the Society for Adolescent Health and Medicine [2], the Canadian Pediatric Society [3], and the American Academy of Pediatrics [4]. There is general consensus on indications for hospital admission; however, there remains significant clinical equipoise regarding the approach to inpatient management.

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The primary goal of a medical hospitalization for patients with AN is physiologic stabilization through weight restoration. The need to correct weight loss must be balanced against the potentially fatal risk of refeeding syndrome (RS). RS is defined as fluid and electrolyte shifts secondary to insulin surges brought on by refeeding severely malnourished patients [1]. These electrolyte abnormalities can result in muscle weakness, delirium, cardiac dysrhythmias, and failure. An early sign of RS is a drop in serum phosphate or refeeding hypophosphatemia (RH). The depletion of total body phosphate stores during malnutrition coupled with increased cellular influx of phosphorus during refeeding places AN patients at risk for profound extracellular hypophosphatemia. Low serum phosphorus is thought to cause a deficiency of intracellular phosphorylated compounds (i.e., adenosine triphosphate, 2,3-diphosphoglycerate) necessary for normal cellular metabolism, which, in turn, produces the cardiac, neuromuscular, hematologic, and respiratory dysfunction seen in full RS [5,6].

RH typically develops during the initial 3–7 days of nutritional refeeding [7]. For hospitalized adolescents with AN, a drop in serum phosphate level <1 mmol/L (<3 mg/dL) is considered significant [8]. The factors predisposing to RH remain poorly understood, but it is believed that severe malnutrition is thought to portend the highest risk [7–10]. Recent guidelines from the Society of Adolescent Health and Medicine propose using a combination of percent median body mass index (%mBMI) <70%, body mass index (BMI) z score >−3 or % body weight loss (%BWL) of >20% in 1 year to define severe malnutrition [2]. Studies reporting that the frequency of RH among adolescents hospitalized with AN is limited, and estimates of this complication vary widely. A recent systematic review reported a 14% mean incidence of RH among 17 studies from 1980 to 2012 which included 1,039 patients (mean %mBMI = 78%) [9]. One of the studies included in this review observed a rate of RH as high as 38% [10].

At present, it is unclear whether refeed patients should receive prophylactic phosphate to prevent RH or receive phosphate treatment only once laboratory-confirmed RH has been detected. Some authors advocate daily phosphate supplementation for all hospitalized patients being refeed [11,12], whereas others recommend close early monitoring and supplementation only when phosphate levels begin to decline [7,13]. Since 2010, the Montreal Children’s Hospital has followed a standardized, short-term, continuous nasogastric (NG) refeeding protocol for all patients admitted with restrictive-type eating disorders [14]. This protocol incorporates the determination of baseline electrolyte values and immediate daily prophylactic phosphate supplementation beginning at the time of admission for all patients, including those that are normophosphatemic. Electrolytes are monitored daily for the first week.

To our knowledge, no study has assessed the impact and outcomes of a refeeding strategy that utilizes prophylactic oral phosphate supplementation during refeeding. We hypothesized that oral phosphate supplementation could safely be used to prevent RH among at-risk, normophosphatemic adolescents hospitalized for nutritional rehabilitation. We undertook a 4-year retrospective chart review with the specific aims of (1) determining the efficacy of prophylactic phosphate supplementation to prevent RH and (2) reporting on any harms associated with prophylactic phosphate supplementation among our inpatient population.

Methods

Study design setting and participants

Ethical approval for this study was obtained from the Montreal Children’s Hospital Research Ethics Board. A retrospective chart review was conducted among patients admitted to the Montreal Children’s Hospital for restrictive eating disorders during the 4-year study period between January 1, 2011, and December 31, 2014. The Montreal Children’s Hospital is a tertiary pediatric referral center that admits eating disorder patients aged younger than 18 years for medical stabilization. Patients are treated via a standardized continuous NG tube refeeding protocol as described previously [14]. Admitted patients are prescribed an initial daily caloric intake of 1800 kcal/day. All patients have electrolytes drawn within the first 24 hours of admission and are started on prophylactic phosphate supplementation, regardless of initial phosphate values. Supplementation is administered for a minimum of 7 days, and electrolytes are monitored daily during this period. After 7 days, phosphate supplementation is tapered over 2–3 days and subsequently discontinued at the discretion of the admitting physician. Phosphate supplementation is provided in the form of an oral phosphate solution, containing 1.5 mmol (48 mg) of elemental phosphorous per mL, administered at a dose of 1 mmol/kg/day (31 mg/kg/day) divided in four daily doses. A multivitamin (Centrum, Pfizer Inc.; 125-mg elemental phosphorous) is prescribed at the time of admission at the discretion of the admitting physician.

The study population was identified using the International Classification of Diseases, Ninth Revision (ICD-9) and discharge summary coding for the terms anorexia nervosa, atypical anorexia nervosa, bulimia nervosa, vomiting associated with other psychological disturbances, other eating disorder, eating disorders un-specified, and specified eating disorders. Patients were included if they were between the age of 10 and 18 years, admitted for protocol-based NG refeeding, and met criteria for AN or a restrictive form of eating disorder based on the DSM-5 criteria. For patients with multiple admissions, each admission was analyzed separately. Patients admitted with the diagnosis of bulimia nervosa, pre-existing medical comorbidities affecting phosphate metabolism (e.g., kidney disease, malabsorption, thyroid dysfunction) or patients with a restrictive eating disorder admitted for reasons other than nutritional rehabilitation (e.g., depression or suicidality) were excluded.

Hospital chart data were extracted to determine baseline patient characteristics at the time of admission and included: gender, age, temperature, BMI, and percent median BMI (%mBMI; current BMI/50th percentile BMI for age and sex × 100), %mBMI was calculated utilizing World Health Organization standardized growth curves [15]. %BWL was obtained from the hospital nutritionist consultation when available and was based on premorbid growth curves or self-reported weight loss during the preceding year. Patient self-reported duration of symptoms was also noted.

Refeeding protocol treatment parameters and daily laboratory values were collected. The normophosphatemic range was defined as a phosphate level between 1.0 mmol/L (3.1 mg/dL) and 1.8 mmol/L (5.6 mg/dL). Adverse events were defined as clinical symptoms requiring medical intervention (i.e., imaging, pharmacological treatment, hydration) that occurred concomitant to an episode of either hypophosphatemia (<1.0 mmol/L) or hyperphosphatemia (>1.8 mmol/L). Hypokalemia was defined as...
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