Hypoparathyroidism: Hyperphosphatemia and Treatment

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Abstract

Treatments for hyperphosphatemia in hypoparathyroidism were identified as a low-phosphorus diet, phosphate binders, diuretics, and parathyroid hormone replacement (PTH 1-34 and PTH 1-84). The treatments that have proven considerable promise for the hypoparathyroid patient were the parathyroid hormone replacement therapies. The author recommended PTH 1-84 as the mainstay of hormone replacement therapy as it had already been granted FDA orphan drug status. The author also recommended more research on the effectiveness of the low-phosphorus diet and phosphate binders on lowering phosphate levels in hypoparathyroidism. Although there was sufficient literature and studies involving hyperphosphatemia in ESRD, little research has been reported in the treatment for hypoparathyroidism. The purpose of this study was to identify the treatments and their effectiveness for hyperphosphatemia in hypoparathyroidism. There was a definite gap in the knowledge needed for evidence-based practice of hyperphosphatemia in hypoparathyroidism. Using Josephine and Loretta Zderad’s humanistic theory, the author concluded that nurses have the opportunity to support hypoparathyroid patients by educating, assisting, and providing more evidence-based practice.
Hypoparathyroidism: Hyperphosphatemia and Treatment

Hypoparathyroidism is a rare disorder affecting 65,000 people in the United States, and 120,000 people outside of the United States (Public Radio (PR) Newswire, 2010). The most common cause of hypoparathyroidism is inadequate secretion of parathyroid hormone after interruption of blood supply to the parathyroids or surgical removal during thyroidectomy, parathyroidectomy, or radical neck dissection (Smeltzer, Bare, Hinkle, & Cheever, 2008, p. 1472). In the case where the parathyroids are accidentally removed, without hormone replacement therapy or treatment, a rapid decline in blood calcium level leads to fatal tetany within 3 or 4 days (Saladin, 2007, p. 668). But with others, it is caused by a rare genetic disorder or an autoimmune disorder as with my son. Our experience with hypoparathyroidism has put us in the hospital many times, at the Annual Hypoparathyroidism Patient Conference in Washington D.C., and experimentally treating his hypercalcuria and hyperphosphatemia with injectable parathyroid hormone (PTH) 1-34, otherwise known as Forteo, at the Mayo Clinic. Of all our experiences of being “chained to a pill box” or middle of the night blood draws or trips to the ER, the diet prescribed to my son has been the most difficult, leaving my son staring at his food and anorexic. The “no-phosphorus diet,” as our endocrinologist described it, is one way to treat hyperphosphatemia. This low-phosphorus diet, among other therapies, is used to treat hyperphosphatemia, and is the focus of this research report. More research is needed on this disease and its treatments. The significance of this literature review is to generate knowledge on hypoparathyroidism and hyperphosphatemia for nursing practice.

**Background**

The parathyroid glands are located in the neck and embedded in the posterior aspect to the thyroid gland. There are usually four, each about the size of a pea. Parathyroid hormone
(PTH) is the protein hormone produced by the parathyroid glands. This hormone regulates calcium and phosphorus metabolism and homeostasis.

As serum calcium decreases, PTH is secreted, which increases calcium absorption from the gastrointestinal tract by stimulating calcitriol synthesis; increases calcium reabsorption from the renal tubule, therefore reducing urinary calcium excretion; and releases calcium from the bone by stimulating bone resorption (Saladin, 2007, p. 653). This increase in serum calcium suppresses PTH secretion (Smeltzer et al., 2008, p. 325), making a negative feedback system (Smeltzer et al., 2008, p. 1470). If calcium levels increase too much, another mechanism of control is activated as calcitonin is secreted from the thyroid gland.

When in the body, elemental phosphorus exists as the phosphate anion (Schucker & Ward, 2005). Serum phosphorus levels and phosphate may be terms used interchangeably in this paper.

Renal excretion of phosphate lowers serum phosphate levels, and is the only means for lowering total body phosphate (Schucker & Ward, 2005). As renal function declines as in renal failure, or in this case, the loss of the PTH, the result is hyperphosphatemia.

Calcium levels are inversely related to phosphorus levels (Smeltzer et al., p. 327). Serum phosphate readily binds to serum calcium, thus lowering total serum calcium levels, and vice versa. In normal bodies, PTH would be secreted as calcium levels decrease (Schucker & Ward, 2005), but in hypoparathyroidism, PTH is not secreted, thus lowering calcium levels without control. Figure 1 shows the action of PTH in a body with intact parathyroids.
Hypoparathyroidism is diagnosed by the combination of hypocalcemia, hyperphosphatemia, normal or low parathyroid hormone (PTH) and with normal plasma creatinine (Husebye, Perheentupa, Rautemaa, & Kampe, 2009). Magnesium levels are also often low. Hypoparathyroidism is considered a rare disease by the National Institute of Health. A rare disease has a prevalence of fewer than 200,000 affected individuals in the United States (Office of Rare Diseases Research).
With the absence of PTH, hyperphosphatemia and hypocalcemia result, decreased intestinal absorption of dietary calcium and decreased resorption of calcium from bone and through the renal tubules. Decreased renal excretion of phosphate causes hypophosphaturia, and low serum calcium levels result in hypercalcuria. The degree of hypocalcemia and hyperphosphatemia can be highly variable from patient to patient, and within an individual patient can fluctuate over time (Levine, nd).

**Hypocalcemia**

Hypocalcemia is the main symptom of hypoparathyroidism causing a myriad of symptoms. Irritability of the neuromuscular system causes the main symptom of tetany, but the list of symptoms is exhausting: tremor, numbness, tingling, aches and pains, cramps in the extremities, stiffness in the hands and feet, bronchospasm, laryngeal spasm, carpopedal spasm, dysphagia, photophobia, cardiac dysrhythmias, ECG changes, hypotension, and seizures. The most troubling perhaps for the patient are the psychiatric symptoms of anxiety, irritability, depression, psychosis, intellectual impairment, and delirium (Smeltzer et al., 2008, p. 1473; Velasco, Manshadi, Breen, & Lippman, 1999).

**Hyperphosphatemia**

Although hyperphosphatemia is mostly asymptomatic, it may cause tetany, tachycardia, anorexia, nausea and vomiting, muscle weakness, hyperactive reflexes, and soft tissue calcifications (Smeltzer, 2008, p. 317). Severe hypocalcemia is one of the most serious results of hyperphosphatemia, producing the signs and symptoms of hypocalcemia. An elevated calcium-phosphorus product is also a problem, which can lead to calcifications of the myocardium, coronary arteries, cardiac valves, basal ganglia, kidneys, and cornea (Smelter, 2008, p. 317).
High phosphate concentrations are also predictors of cardiovascular mortality in end-stage renal disease (ESRD) patients (Friedman, 2005). Patients with chronic phosphorus levels above 6.5 mg/dL have an 18% to 39% higher death rate (Robb, 2008).

Figure 2 shows the causes and effects of hyperphosphatemia on the body. Hypoparathyroidism is not listed as a cause, and the effect of increased PTH secretion in response to hyperphosphatemia is not relevant in hypoparathyroidism.

Figure 2. Causes and Effects of Hyperphosphatemia

\[ \text{Figure 2. From Tonelli, Pannu, \\& Manns, 2010.} \]
Treatment

The goal in treatment of hypoparathyroidism is to maintain serum calcium at a level that requires the minimal amount of calcium and vitamin D to achieve symptom relief without causing hypercalcuria (Horwitz & Stewart, 2008). This puts the serum calcium range for hypoparathyroid patients at 8.0-9.0 mg/dl (2.00-2.25 mm) (normal range is 9.0-10.5 mg/dl (2.25-2.63 mm)) (Horwitz & Stewart, 2008). Vitamin D and dietary supplements of calcium are used in conjunction to treat hypocalcemia in hypoparathyroidism. Calcitriol (Rocaltrol) is the most commonly used form of vitamin D (Karch, 2008, p. 590).

The conventional approach to maintaining normal serum calcium levels in hypoparathyroid patients consists of oral calcium and 1,25-dihydroxyvitamin D in relatively large amounts (Rubin & Bilzekian, 2010). The large doses of calcium are given to augment intestinal calcium absorption, and the large doses of vitamin D are given to mimic the intestinal effects of the missing 1,25(OH)2D (Horwitz & Stewart, 2008). This combination goal is to overwhelm the kidneys ability to excrete the large calcium dose, so that serum calcium will increase (Horwitz & Stewart, 2008). With this substitution therapy, phosphate levels usually normalize as well, but not in some (Husebye et al., 2009).

This treatment is a challenge as patient’s calcium levels fluctuate from hypercalcemia and hypocalcemia, and are sensitive to these “biochemical swings.” Also, this treatment can lead to worsening hypercalciuria, putting the patient at risk of nephrocalcinosis, nephrolithiasis or renal insufficiency, which are all common in hypoparathyroid patients (Rubin & Bilzekian, 2010).

According to Smeltzer, Bare, Hinkle, & Cheever, a diet high in calcium and low is phosphorus should be prescribed with oral tablets of calcium salts to supplement the diet (2008,
A phosphorus binder also is administered after meals to bind phosphate and promote its excretion through the gastrointestinal tract (Smeltzer et al., 2008, p. 1473).

Table 1.

*Methods for controlling hyperphosphatemia in hypoparathyroidism*

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<tr>
<th>Method</th>
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<tr>
<td>Restrict dietary phosphorus intake</td>
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<td>Minimize phosphate absorption by the intestine (phosphate binders)</td>
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<tr>
<td>Increase active vitamin D to facilitate calcium absorption (calcitriol)</td>
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<tr>
<td>Replace missing parathyroid hormone (PTH 1-34 and PTH 1-84)</td>
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</table>

Adapted from Friedman (2005)

The goal to control hyperphosphatemia is to keep normal serum phosphorus level at 2.5 to 4.5 mg/dL (0.8 to 1.45 mmol/L), and may be higher in children (Smeltzer et al., 2008, p. 331). The treatment of hyperphosphatemia is to decrease dietary intake phosphorus and to administer phosphate binders when necessary (Blokker, 2008).

To control phosphate levels in chronic kidney disease, the first line therapy is the use of a phosphate-restricted diet (Eddington & Heaf, 2009). Foods high in phosphorus are avoided. These foods are hard cheese, cream, nuts, meat, whole-grain cereals, dried fruits, dried vegetables, kidneys, sardines, sweetbreads, and dairy (Smeltzer et al., 2008, p. 333). Processed foods and dark colas are also avoided, as preservatives are high in phosphorus as well.

Many patients, especially the young find this diet restrictive and interfering with their lives, as Eddington and Heaf state, then phosphate binders are introduced (2009). Binders work to bind with phosphorus while it’s in the stomach, therefore preventing it from entering the bloodstream. It then leaves the body in the stool (Robb, 2008).

Calcium-containing binders are the most common phosphate binders used in practice. When applied to hypoparathyroid patients, the use of calcium needs to be regulated with serum calcium levels. Two other phosphate binders are newer including sevelamer hydrochloride.
(Renagel), a resin-based binder, and lanthanum carbonate (Fosrenol) (Eddington and Heaf). Renagel is the second most common used phosphate binder in clinical practice (Friedman, 2005).

Diuretics are also used to increase calcium levels as an adjunct to therapy. Thiazide and thiazide-like diuretics, specifically, work to decrease calcium excretion by stimulating calcium reabsorption at the distal convoluted tubule (Horwitz & Stewart, 2008).

There is no PTH replacement therapy FDA approved at this time, but there is an orphan drug status for PTH 1-84 of rDNA origin given by subcutaneous injection. NPS Pharmaceuticals is currently running clinical studies to determine its safety and effects on bone (PR Newswire, 2010). It is given subcutaneously once or twice daily with calcium supplementation as needed.

There are two different PTH replacement therapies currently used and in trials. The whole PTH has 84 amino acids, therefore PTH 1-84 is dubbed the whole protein. PTH 1-34 is considered half the protein, consisting of the first sequence of 34 of the amino acids of the hormone.

Although both PTH therapies are not FDA approved, hypoparathyroid patients are using PTH 1-34. PTH 1-34 is FDA approved for the treatment of osteoporosis with the brand name of Forteo. With it on the market, hypoparathyroid patients are able to use it off-label.

Because of the lack of information regarding hypoparathyroidism and treatment, I am conducting this review of literature to acquire more information on the effectiveness of calcium and vitamin D supplementation, the low-phosphorus diet, phosphate binders, diuretics, and PTH 1-34 and 1-84 in treating hyperphosphatemia.

**Research Problem Statement**

Although there is a quantity of literature and studies involving hyperphosphatemia in ESRD, little research has been reported in the treatment for hypoparathyroidism. There is a
definite gap in the knowledge needed for evidence-based practice of hyperphosphatemia in hypoparathyroidism.

**Research Purpose**

The purpose of this study was to identify the treatments and their effectiveness for hyperphosphatemia in hypoparathyroidism.

**Research Questions**

In patients with hypoparathyroidism, how effective are calcium and vitamin D supplementation, the low-phosphorus diet, diuretics, phosphorus binders, and parathyroid hormone 1-34 and 1-84 in treating hyperphosphatemia?

**Theoretical Framework**

The nursing theory I applied to my research problem is Josephine Paterson and Loretta Zderad’s humanistic theory. This theory was created to offer a way of responding to the call of human needs. A call can be “as a subtle murmur of pain, sorrow, anxiety, desperation, joy, laughter, even silence” (Parker & Smith, 2010, p. 338). This call is answered by a nurse’s response of the human touch.

Drs. Paterson and Zderad explained five phases to their study of nursing, which are interwoven with a constant flow between, in all directions, and all-at-once emanating toward a center that is nursing (Parker & Smith, 2010, p. 343). These phases of humanistic nursing inquiry are:

- Preparation of the nurse knower for coming to know
- Nurse knowing the other intuitively
- Nurse knowing the other scientifically
- Nurse complementarily synthesizing known others
- Succession within the nurse from the many to the paradoxical one
By using three concepts basic to this theory, bracketing, angular view, and noetic loci, nurses are able to open themselves up to the unknown and possibly different. Later in the process, a nurse is able to make sense of and give meaning to the phenomena being studied. The consciousness and angular view are bracketed so to not superimpose our own thoughts, experiences, and beliefs unto the lived experience of the other. “Bracketing prepares the inquirer to enter the uncharted world of the other without expectations and preconceived ideas. It helps one to be open to the authentic, to the true experience of the other” (Parker & Smith, 2008, p. 343).

The concepts of empathy, comfort, and presence innate in applying the humanistic nursing theory are applicable to the nursing interactions with the hypoparathyroid patient. A greater understanding of the symptoms of hypocalcemia and hyperphosphatemia, the burden of “being chained to a pill box,” the constant dismissal of “calls” for help, and the healthcare fields lack of understanding and treatment options for hypoparathyroid patients leaves them feeling, alone, desperate, and depressed. To give the patient the support that interacting with the patient in this humanistic, open approach gives an answer to their “call.” The ability to be with and endure with a patient in the process of living and suffering is what makes all the difference to those calling for help.

**Research Utilization Model**

For this study, the ACE Star Model of Knowledge Transformation was used as a guide to determine the knowledge about hyperphosphatemia treatments in hypoparathyroidism. Evidence was collected using CINAHL Plus with Full Text and Academic Search Premier collectively, PubMed.gov, EBSCO MegaFILE, and Google Scholar. The evidence collected was organized
and selected around the ACE Star Model of Knowledge Transformation (Figure 3), using each point on the model as a guide.

Figure 3. Ace Star Model of Knowledge Transformation.

\[\text{ACE Star Model}\]

Figure 3. From Stevens, 2004.

The ACE Star Model of Knowledge Transformation consists of five stages. The first stage is discovery. This is the stage in which knowledge is generated through traditional research methodologies and scientific inquiry. Original research is used to make one solid research study using evidence-based practice (Stevens, 2004).

The discovery stage proved to be the most difficult as the amount of knowledge on this subject was minimal. In my search for hyperphosphatemia, the knowledge available was specifically for the use of renal failure. Note how the search for hyperphosphatemia resulted in 53 in Table 2. Table 2 lists my keywords and results used for each search.
Table 2

*Keywords and Results*

<table>
<thead>
<tr>
<th>Keyword(s)</th>
<th>Results</th>
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<td>Academic Search Premier and CINAHL Plus with Full Text (2000-2010)</td>
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<td>Hypoparathyroidism</td>
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<tr>
<td>Hypoparathyroidism and hyperphosphatemia</td>
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<tr>
<td>Hypoparathyroidism and treatment</td>
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<td>Hypoparathyroidism and diet</td>
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<td>Hypoparathyroidism and diuretics</td>
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<td>Hyperphosphatemia and diuretics</td>
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<td>Hyperphosphatemia and diet</td>
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<td>EBSCO MegaFILE (2000-2010)</td>
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<td>Hypoparathyroidism and diuretics</td>
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<td>PubMed.gov (Full Free Text) (No time limit)</td>
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<tr>
<td>Hypoparathyroidism</td>
<td>837</td>
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</table>

Evidence summary is the second stage, in which the task is to synthesize all research into a single, meaningful statement. This is the knowledge generating stage. In my search, the Evidence Summary is that there is little knowledge about hyperphosphatemia in hypoparathyroidism.

I did use the research provided on hyperphosphatemia, even though it was specifically for renal failure applications. The fact that hyperphosphatemia treatments focus on reducing phosphate levels renders this research usable for my application. The limit on its utilization for hypoparathyroidism is that in renal failure parathyroid hormone is secreted in response to increased phosphate levels. In hypoparathyroidism, there is not this response, therefore I used the application of this information with more scrutiny. Also, dialysis is a treatment for
hyperphosphatemia for renal failure. I did not include this information in this research report, even though renal failure is a common consequence of hyperphosphatemia in hypoparathyroidism.

The third stage is translation, in which the summary of the scientific evidence is considered in context of clinical expertise and the other information to result in a practice recommendation (Stevens, 2004). My translation is that there is a gap in knowledge about treating hyperphosphatemia in hypoparathyroidism, and nurses have the opportunity to support, educate, assist, and collect data for our hypoparathyroid patients.

The fourth stage is integration, which involves implementation of innovations. Implementation requires a change in professional practice at the individual clinician and organization levels (Stevens, 2004).

The final stage of the ACE Star Model is transformation. In this stage, evaluation is made of the impact of evidence-based practice on patient health outcomes, provider and patient satisfaction, efficacy, efficiency, economic analysis, and health status impact. This final outcome is evidence based quality improvement of health care (Stevens, 2004). My translation is that nurses need to utilize the knowledge available to support hypoparathyroid patients in a humanistic, open approach. Nurses need to respond to our hypoparathyroid patients “call.”

**Findings**

The type of evidence as a whole is a Level II. A Level II consists of at least one well-designed experimental study. There was no meta-analysis, but five well-designed experimental studies. The findings were generally consistent. The overall rating for the evidence is most consistent with a 2. There is evidence of types II, IV, V, and type VI. The types of evidence are based on the following guidelines obtained from the Oncology Nursing Society:
- **Level I**: Evidence from a systematic review or meta-analysis of all relevant randomized control trials (RCTs) or evidence-based clinical practice guidelines based on systematic reviews of RCTs or three of more RCTs of good quality that have similar results.
- **Level II**: Evidence obtained from at least one well-designed RCT
- **Level III**: Evidence obtained from well-designed controlled trials without randomization
- **Level IV**: Evidence from well-designed case-control or cohort studies
- **Level V**: Evidence from systematic reviews of descriptive and qualitative studies
- **Level VI**: Evidence from a single descriptive or qualitative study
- **Level VII**: Evidence from the opinion of authorities and/or reports of expert committees

The Winer, Ko, Reynolds, Dowdy, Keil, Peterson, et al.; Wine, Sinai, Peterson, Sainz, and Cutler; Winer, Sinaii, Reynolds, Peterson, Dowdy, and Cutler; and Husebye, Perheentupa, Rautemaa, and Kampe articles were my best resources. Although I found clinical studies regarding hypoparathyroidism, only the Winer et al. studies on PTH 1-34 used phosphate levels as an end-point. The Rubin and Bilezikian study using PTH 1-84 did measure phosphorus levels, but did not use this as an endpoint. The Husebye et al. article reviewing APS-I was the best article concerning treatment of hypoparathyroidism, and regarded the treatment of hyperphosphatemia in its discussion. Mori et al. was a case study on only one hypoparathyroid patient, and did not address phosphorus levels once. These were the articles that addressed hypoparathyroidism, but only a few addressed hyperphosphatemia.

The Robb; Tonelli, Pannu, and Manns; and Eddington and Heaf articles addressed hyperphosphatemia and its treatment in *ESRD or renal failure*. These were not specific to hypoparathyroidism, therefore limited their use in my findings. Renal failure and hypoparathyroidism both deal with elevated phosphate levels, and the means by which these levels are lowered in renal failure do apply to hypoparathyroidism. Plus, there was no literature available on hyperphosphatemia and diuretics or phosphate binders for the hypoparathyroid patient. Table 2 summarizes my research findings.
Table 3. Research Findings and Results

<table>
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<tr>
<th>Article/Source/ Year</th>
<th>Purpose</th>
<th>Sample</th>
<th>Design/ *level of evidence</th>
<th>Variables/ Measurement</th>
<th>Results/ Findings</th>
<th>Implications</th>
<th>Framework</th>
<th>Database</th>
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<tr>
<td>Eddington &amp; Heaf. CANNT Journal. (2009)</td>
<td>Clinical management of disturbances of calcium and phosphate metabolism in dialysis patients</td>
<td>Integrative review of experimental studies</td>
<td>A large number of treatment options are now available for dialysis patients to control hyperphosphatemia. More research needs to be done.</td>
<td>Applicable to HPTH in the context of hyperphosphatemia treatment.</td>
<td>EBSCO MegaFILE</td>
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<td>Friedman. Kidney International. (2005)</td>
<td>An introduction to phosphate binders for the treatment of hyperphosphatemia in patients with CKD</td>
<td>Integrative review of experimental studies</td>
<td>Sevelamer hydrochloride and calcium acetate are the two most common clinical treatments for minimizing phosphate intake.</td>
<td>Studies for renal failure, but also controlling serum phosphate.</td>
<td>EBSCO MegaFILE</td>
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<td>Husebye et al. Journal of Internal Medicine. (2009).</td>
<td>Clinical manifestations and management of patients with autoimmune polyendocrine syndrome type I</td>
<td>Qualitative study - Includes personal experience and published studies overview</td>
<td>Treatment and follow-up of patients is demanding and requires collaboration of specialists in several fields. Literature is sparse. Future treatment should include immunomodulatory therapy.</td>
<td>Applicable is the HPTH overview for treatment.</td>
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<td>Horwitz &amp; Stewart. (2008).</td>
<td>Editorial for hormone replacement in HPTH</td>
<td>Integrative review of experimental studies</td>
<td>The studies of Winer et al. provide an important and novel advance in treatment of HPTH, but more research is needed.</td>
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<td>Robb. RN. (2008).</td>
<td>Nursing care of hyperphosphatemia in renal failure</td>
<td>Qualitative study</td>
<td>Nurses have an important role in in the ESRD patient population in preventing hyperphosphatemia.</td>
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<td>Rubin &amp; Bilezikian. Arquivcios Brasileiros de Endocrinologia &amp; Metabologia. (2010).</td>
<td>PTH 1-84 treatment for HPTH and its effect on the skeletal microstructure</td>
<td>Experimental study</td>
<td>With PTH 1-84, bone turnover and bone mineral density increased in lumber spine. Requirements for calcium and vitamin D fell while serum and urinary calcium did not change.</td>
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<td>Slatopolsky et al., <em>Kidney International.</em> (2010).</td>
<td>The use of Renagel to lower serum phosphorus and PTH</td>
<td>Experimental study</td>
<td>Mean serum phosphorus decreased with use of RenaGel. Studied in hemodialysis patients with intact PTH. Applicable to hyperphosphatemia in HPTH.</td>
<td>Multicenter, open-label, dose-titration study</td>
<td>Cochrane Central Register of Controlled Trials</td>
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<td>Tonelli, Pannu &amp; Manns, <em>NEJM.</em> (2010).</td>
<td>Oral phosphate binders in patients with kidney failure</td>
<td>Integrative review of experimental studies</td>
<td>Normophosphatemia will be unattainable for most patients. Sevelamer and Lanthanum are promising, but not proven superior to calcium-based agents. Select binder for individual patient. Intended for renal failure patients. Treatments applicable to hyperphosphatemia in HPTH.</td>
<td></td>
<td>Google Scholar</td>
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<td>Winer et al. <em>JCEM.</em> (2008). Study to compare the response of once-daily vs. twice daily PTH 1-34 treatment in children with HPTH</td>
<td>14 children</td>
<td>Experimental</td>
<td>Serum calcium, phosphorus, vitamin D, magnesium levels, 24-h urine calcium, phosphorus, and magnesium excretion</td>
<td>Treatment with twice-daily PTH provides a more effective treatment of HPTH than once daily.</td>
<td>Randomized cross-over trial, lasting 28 weeks, comparing two dose regimens</td>
<td>Cochrane Central Register of Controlled Trials</td>
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<td>Winer et al. <em>JCEM.</em> (2003). To establish the long-term efficacy of PTH vs. calcitriol and calcium in HPTH</td>
<td>27</td>
<td>Experimental</td>
<td>Calcium levels in serum and urine</td>
<td>PTH 1-34 may be a superior treatment for HPTH.</td>
<td>Randomized, parallel, open-label trial comparing conventional treatment with PTH 1-34</td>
<td>PubMed.gov</td>
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<td>Winer et al. <em>JCEM.</em> (2010). Assess the efficacy and safety of long-term PTH 1-34 vs. calcitriol treatment in children with HPTH</td>
<td>12 children</td>
<td>Experimental</td>
<td>Serum calcium and urine calcium levels. (Secondary end points included phosphorus)</td>
<td>PTH 1-34 is safe and effective at maintaining stable calcium homeostasis in children with HPTH. No differences in bone mineral accrual, linear growth, or weight gain between the two treatment arms.</td>
<td>Randomized, parallel, open-label, 3 year study comparing calcitriol (plus calcium) vs. PTH 1-34 therapy</td>
<td>Cochrane Central Register of Controlled Trials</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Note. JCEM = Journal of Clinical Endocrinology & Metabolism; HPTH = hypoparathyroidism; NJEM = New England Journal of Medicine.*
Discussion

In an article reviewing the management of patients with autoimmune polyendocrine syndrome type I (APS-I), Husebye et al. presented clinical characteristics, treatment and follow-up on personal experience and published studies (2009). APS-I is an autoimmune disorder presenting itself with one of its components as hypoparathyroidism. Husebye et al. stated that twice-daily administration of PTH has shown to give reasonably stable calcium levels, but since it is not yet routine, vitamin D is the mainstay of therapy (2009). A daily calcium supplement (2-3 daily doses of 100-500 mg elementary calcium), preferably Ca-citrate, is also given plus a diet with adequate Magnesium intake (Husebye et al., 2009). Vitamin D plus the calcium supplementation normalizes hyperphosphatemia in most patients (Husebye et al., 2009). In those patients where it does not, a low-phosphorus diet should be initiated (Husebye et al., 2009). Husebye et al. does not mention the use of diuretics or phosphate binders as adjunct therapy to control hyperphosphatemia. This was my best article concerning treatments for hypoparathyroidism.

Tonelli, Pannu, and Manns stated that the low-phosphorus diet effectively reduces phosphate levels (2010). They also consider adherence to the diet a real problem. This article discusses oral phosphate binders in patients with chronic renal failure. For these patients, Tonelli, Pannu, and Manns stated that the calcium-based binders are the best option as they are less expensive and best tolerated. They stated that sevelamer and lanthanum are promising, but their superiority to calcium-based binders has not been established. They would use the magnesium-based binders for short-term purposes and suggested careful watch on magnesium levels. The problem, they state, is that the ideal level of phosphorus is unknown.
Eddington and Heaf performed an in-depth clinical review of clinical management of calcium and phosphate metabolism in dialysis patients. They stated that for phosphate control the first-line therapy for managing increasing serum phosphate levels is a phosphate-restricted diet (2009). Phosphorus binders are then introduced, choosing from a list of different binders depending on budget, availability, benefits and problems of each one (Eddington and Heaf, 2009). They do not inquire into the effectiveness of each binder as to how phosphate levels are lowered, but more into the side effects. Again, this article is applicable in dialysis patients, but I included the treatments for hyperphosphatemia for reasons already mentioned.

Another article about hyperphosphatemia in renal failure included a low-phosphorus diet as treatment. Robb explained why adherence to the diet is a difficult task for patients, and discussed the nurse’s role in educating about phosphorus in the diet and the importance of controlling phosphate levels. Robb continued to discuss medications and hemodialysis as treatment to remove phosphorus. She stated that “phosphorus binders used in conjunction with dietary compliance have been proven to effectively control hyperphosphatemia” (2008). Robb’s inquiry into treatment for hyperphosphatemia targeted the ESRD patient. The different pathophysiologies, again hinder the utilization of this information into the hypoparathyroid’s hyperphosphatemia, but it does address hyperphosphatemia and it’s treatments. This article was my only article addressing the nurse’s role in controlling hyperphosphatemia.

According to Schucker and Ward, a phosphate binder’s efficacy is highly dependent on the dosage used (2005). They discussed how phosphate binders provide an effective means for managing serum phosphate in patients with ESRD as dialysis, and dietary restrictions are unable to control hyperphosphatemia. Selection of phosphate binder should be based on patient
characteristics, including serum phosphate, serum calcium, parathyroid concentration, and patient tolerability (Schucker & Ward, 2005).

In a study performed by Slatopolsky, Burke, Dillon, and the Renagel Study Group, the use of Renagel was administered to hemodialysis patients for eight weeks to determine its effects on lowering serum phosphorus. The mean serum phosphorus at beginning was 9.1 ± 2.4 mg/dl and declined to 6.6 ± 1.9 mg/dl by the end of the treatment period (Slatopolsky, Burke, Dillon, & the Renagel Study Group, 1998). Although, the effectiveness for lowering phosphate has been proven for renal failure patients, there are no studies on the effectiveness on hypoparathyroid patients. The fact that it would lower phosphate is clear, but in non-hypoparathyroid patients, there is a response of the parathyroids to increase secretion. This factors into the negative feedback system in these patients, whereas there is not that parathyroid response in hypoparathyroid patients.

There was one case study and one article containing the use of thiazide diuretics as an adjunct therapy for hypoparathyroidism. The article regarded possible hormone replacement therapy for hypoparathyroidism, and did mention diuretic use in a paragraph. Horowitz and Stewart stated, “they (thiazide diuretics) simply shift the tightrope to a new location” (2008). With the possible new side effects and the delicate electrolyte disturbances already in play with hypoparathyroidism, Horowitz and Stewart cautioned their use.

In a case study of a hypoparathyroid infant, Mori, Mei, Watanabe, Yasuda, Brown, and Shiohara showed hydrochlorothiazide lowered urinary calcium excretion when used in conjunction with calcium and vitamin D supplementation (2004). The authors stressed that the usage of thiazide diuretics puts the patient at risk of hypokalemia and alkalosis, and further renal
damage (Mori, Mei, Watanabe, Yasuda, Brown, & Shiohara, 2004). The limit of this article is that it studied only one patient, but the patient was hypoparathyroid.

The clinical study comparing PTH 1-34 and calcium versus calcitriol treatment showed both treatments as effective at maintaining serum calcium levels. However, the PTH group showed urinary calcium excretion was lower (and normalized) than the calcitriol group. There were no clear results indicating a superiority concerning phosphorus levels. Phosphorus levels remained slightly above normal levels throughout the three-year study for both treatment groups (Winer, Ko, Reynolds, Dowdy, Keil, & Peterson, 2003). The study concluded that PTH 1-34 is a safe and effective alternative to treating hypoparathyroidism.

There is one study by Winer et al. (2010) that assessed the efficacy and safety of long-term PTH 1-34 vs. calcitriol treatment in children with hypoparathyroidism. Winer et al. found that mean predose serum calcium levels were maintained at or just below the normal range, and urine calcium levels remained in the normal range with no significant differences between the two treatment groups. They did find that PTH 1-34 to be a safe and effective treatment to maintain stable calcium, just as the Winer study in adults. One of the study’s secondary end points was the phosphorus level. In the PTH 1-34 group, there was a significant downward trend over time, with levels only slightly above normal at the end of the study (Winer, Sinaii, Reynolds, Peterson, Dowdy, & Cutler, 2010).

In a subsequent study by Winer et al., the effects of once versus twice-daily PTH 1-34 injections were studied in children with hypoparathyroidism (2008). Serum phosphorus levels remained above normal during both dose schedules of PTH 1-34. Nighttime phosphorus levels were also measured and found to be similar during both dosing regimens (Winer, Sinaii,
Peterson, Sainz, & Cutler, 2008). However, fluctuations of calcium levels were improved in the twice-daily regimen.

In the Rubin and Bilezikian study on skeletal microstructure and PTH 1-84 replacement, phosphorus levels were mentioned only briefly stating, “serum phosphate levels fell from 1.44+/-0.2 to 1.29 +/- 0.2 mmol/L” through the 2-year clinical trial (2010). The number of subjects on hydrochlorothiazide for hypercalciuria decreased at the end of the study from 10 to 3. This brings the questions as to whether this may factor into the results of the study and to whether calcium and phosphorus levels may have been different if there were no use of diuretics. There were only 10 subjects at the baseline on hydrochlorothiazide, and only three at the end of the study. This may also prove that PTH 1-84 is effective at normalizing hypercalciuria, which is the main indication for use of diuretics.

The dosage of PTH 1-84 was every other day, so it is hard to compare to the studies on PTH 1-34, which scheduled daily injections. This study did conclude that “requirements for supplemental calcium and 1,25-dihydroxyvitamin D were significantly reduced while maintaining, normal, stable serum calcium concentrations” (Rubin & Bilzekian, 2010).

One unexpected benefit of the PTH injections was reported by the subjects of a 2003 study comparing PTH 1-34 versus calcitriol and calcium as treatment. Subjects welcomed the change from the multiple pill regimen required for calcitriol and calcium. Subjects also reported an improved quality of life and greater physical endurance with PTH therapy (Winer et al., 2003).

In my research, the only literature intended for nursing practice in hypoparathyroidism was Brunner & Sudderth’s Textbook of Medical-Surgical Nursing (2008). Smeltzer et al.
provided one paragraph for nursing management of the patient with acute hypoparathyroidism (2008). The other paragraph was applicable to chronic hypoparathyroidism.

Smeltzer et al. listed nursing management strategies of the patient with hypoparathyroidism:

An important aspect of nursing care is teaching about medications and diet therapy. The patient needs to know the reason for high calcium and low phosphate intake and the symptoms of hypocalcemia and hypercalcemia; he or she should know to contact the physician immediately if these symptoms occur (2008).

Robb’s article focused on nursing care intended for hyperphosphatemia in the renal failure patient, but was adaptable for hyperphosphatemia in the hypoparathyroid patient (2008). For the patient with hyperphosphatemia, the nurse promotes health, provides care, offers support, and educates patients on the prevention of illness (Robb, 2008). Nursing interventions include communicating with physicians, monitoring a patient’s diet, following medication guidelines, and providing patient teaching (Robb, 2008). Through these strategies, hyperphosphatemia can be prevented. Patient teaching includes topics about the disease (hypoparathyroidism), signs and symptoms of hypocalcemia and hyperphosphatemia, medications, and adherence to lab draws and understanding their results (Robb, 2008).

Table 4 lists treatments for hyperphosphatemia and their effects on calcium and phosphate levels. The articles used in this research paper are categorized by treatment. Overall, there is a clear lack of research on treatments for hypoparathyroidism.
### Table 4

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Effects on Calcium</th>
<th>Effects on Phosphate</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Phosphate Binders</strong> <em>(Tonelli, Pannu &amp; Manns, 2010)</em></td>
<td></td>
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<tr>
<td>Calcium carbonate (Tums, Os-Cal, Caltrate)</td>
<td>Increases by 0.5 mg/dl on average</td>
<td>Declines by 0.9 mg/dl on average</td>
<td>Effective, may contribute to hypercalcemia, reduction in serum phosphate and calcium are dose-dependent</td>
</tr>
<tr>
<td>Calcium acetate (Phoslo, Eliphos)</td>
<td>Similar to calcium carbonate</td>
<td>Reduction is slightly greater than with calcium carbonate</td>
<td>Effective, phosphate control appears to be superior, may contribute to hypercalcemia</td>
</tr>
<tr>
<td>Magnesium Hydroxide (Milk of Magnesia)</td>
<td></td>
<td></td>
<td>Effective, often used as add-on therapy with calcium-based agents</td>
</tr>
<tr>
<td>Magnesium carbonate (Gaviscon)</td>
<td></td>
<td></td>
<td>Effective, often used as add-on therapy with calcium-based agents</td>
</tr>
<tr>
<td>Sevelamer hydrochloride (Renagel)</td>
<td>Lower with sevelamer, Increases 0.3 mg/dl</td>
<td>Lower with calcium-based binders, Decrease by 2.5 mg/dl</td>
<td>Effective, does not contain calcium, studies conducted were on patients with advanced renal failure</td>
</tr>
<tr>
<td>Sevelamer carbonate (Renvela)</td>
<td>Similar to sevelamer hydrochloride</td>
<td>Similar to sevelamer hydrochloride</td>
<td>Effective, does not contain calcium</td>
</tr>
<tr>
<td>Lanthanum (Fosrenol)</td>
<td>Similar to calcium-based binders</td>
<td>Similar to calcium-based binders</td>
<td>Effective, does not contain calcium</td>
</tr>
<tr>
<td><strong>Calcium Supplementation &amp; Vitamin D</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ca-citrate and vitamin D supplementation (Husebye et al., 2009)</td>
<td></td>
<td></td>
<td>In some patients high-phosphate foods should be restricted if substitution therapy does not normalize phosphate levels</td>
</tr>
<tr>
<td><strong>Thiazide Diuretics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydrochlorothiazide (Mori et al, 2003)</td>
<td>Increased</td>
<td>Not addressed</td>
<td>Lowered urinary calcium excretion, risk hypokalemia and alkalosis, and renal damage</td>
</tr>
<tr>
<td><strong>Parathyroid Hormone</strong></td>
<td></td>
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<tr>
<td>Teriparatide (PTH 1-34) (Forteo)</td>
<td>Maintains levels in the normal range</td>
<td>Reduces levels 2.23 to 2.08 mmol/L, mean 24-h serum levels still above normal</td>
<td>Reduces urinary calcium excretion in hypoparathyroid patients, reduces use of calcitriol</td>
</tr>
<tr>
<td>Winer et al. study comparing PTH 1-34 vs. calcitriol and calcium (2003)</td>
<td>Mean level 1.92 ± 0.02 mmol/L</td>
<td>Mean level 4.6 ± 0.08 mg/dl, no significant difference in treatment groups</td>
<td>Normalized mean 24-h urine calcium excretion</td>
</tr>
<tr>
<td>Winer et al. study comparing once versus twice-daily PTH 1-34 in children with hypoparathyroidism (2008)</td>
<td>Twice-daily increased levels more effectively than once daily</td>
<td>Levels remained elevated during both dose schedules, no significant difference</td>
<td>Both schedules normalized mean 24-h urine calcium excretion</td>
</tr>
<tr>
<td>Winer et al. study of 12 children comparing PTH 1-34 vs. calcitriol and calcium (2010)</td>
<td>Mean levels maintained at or just below normal, no difference between PTH (1-34) and calcium and calcitriol</td>
<td>Significant decrease trend over time on PTH 1-34, mean level slightly above normal; lower than baseline calcitriol</td>
<td>Growth did not differ between treatment groups</td>
</tr>
<tr>
<td>Rubin &amp; Bilezikian study on skeletal microstructure and PTH 1-84 (2010)</td>
<td>Maintains a stable level in the normal range</td>
<td>Reduces levels 1.44 to 1.29 mmol/L</td>
<td>Decreases need for supplemental calcium, vitamin D, and hydrochlorothiazide for HPTH patients</td>
</tr>
<tr>
<td><strong>Low-Phosphorus Diet</strong></td>
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<td></td>
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<tr>
<td>Robb, 2008</td>
<td></td>
<td></td>
<td>Is effective at controlling hyperphosphatemia when used in conjunction with phosphorus binders</td>
</tr>
<tr>
<td>Eddington &amp; Heaf, 2009</td>
<td>First line therapy at control hyperphosphatemia</td>
<td></td>
<td>If not effective, phosphate binders should be introduced</td>
</tr>
</tbody>
</table>
Recommendations for Nursing Practice

Based on the findings from the literature, more research is needed concerning hyperphosphatemia in hypoparathyroidism overall, and specifically, more researching is needed on the treatments and effectiveness. There is a definite lack of knowledge regarding treatment of hyperphosphatemia in hypoparathyroid patients.

The treatments showing considerable promise for the hypoparathyroid patient are the parathyroid hormone replacement therapies. One problem with the research on these is that the small amount of existing research is split between PTH 1-34 and PTH 1-84. I recommend that the PTH 1-84 as the mainstay of hormone replacement therapy as it has already been granted FDA orphan drug status. Continuing to divide the research between the two will only slow the progress on this already minimal dataset.

More research is needed on the effectiveness of the low-phosphorus diet and phosphate binders and their effectiveness on lowering phosphate levels in hypoparathyroidism. Nurses need to beware that the existing research is on renal disease patients and not hypoparathyroid patients. This research needs to be scrutinized accordingly, but still can be applied to hypoparathyroidism.

I recommend further research on calcium and vitamin D supplementation as a comparative and adjunct treatment only. I would not recommend diuretics for further research, as it is not the most promising treatment at this time.

Nurses have the opportunity to support hypoparathyroid patients by educating, assisting, and providing more evidence-based practice. Nursing interventions include communicating with the physicians, monitoring a patient’s diet, following medication guidelines, and providing patient teaching. Patient teaching include topics about hypoparathyroidism, signs and symptoms
of hypocalcemia and hypercalcemia, adherence to lab draws and understanding their results, diet therapy, the importance of controlling phosphate levels, medications, the importance of adherence to a restricted diet and medications, and when to contact the physician. Nurses need to utilize the knowledge available to support the hypoparathyroid patient’s in a humanistic, open approach. Nurses need to respond to our hypoparathyroid patient’s “call.”

**Conclusion**

Hypoparathyroidism is a rare disorder caused most commonly by surgical removal or autoimmune destruction of the parathyroids. Although hypocalcemia may be the most significant problem, hyperphosphatemia can precipitate hypocalcemia and lead to greater cardiovascular mortality. In patients with hypoparathyroidism, hyperphosphatemia is not always a problem, therefore making a rare problem even rarer. Treatments for hyperphosphatemia in hypoparathyroidism include a low-phosphorus diet, phosphate binders, thiazide diuretics, PTH 1-34, and PTH 1-84. Nurses have the opportunity to support hypoparathyroid patients by educating, assisting, and providing more evidence-based practice. There is a clear lack of research. It would enhance patient care and outcomes to conduct more studies in regard to treatment of hyperphosphatemia in hypoparathyroidism.
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