JPPT | Case Report

Teriparatide Therapy in a 4-Month-Old With Severe Hypoparathyroidism

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Teriparatide is a human parathyroid hormone analog approved for the treatment of osteoporosis in adult patients. Its use for hypocalcemia and hypoparathyroidism in the pediatric population is described through case reports and small case series; however, larger studies that demonstrate long-term efficacy and safety are limited. At our institution, a 4-month-old premature (gestational age: 32 weeks) infant with multiple congenital anomalies, functional athymia, and severe hypoparathyroidism and receiving calcitriol, vitamin D, and calcium carbonate supplementation was initiated on subcutaneous injection of teriparatide. During the course of treatment, her calcium carbonate, vitamin D, and calcitriol supplementation requirements substantially decreased. Teriparatide effectively increased serum ionized calcium concentrations and decreased serum phosphorus concentrations in the present case-study over a 6-month period. Teriparatide was well tolerated, and no evidence of hypercalcemia was observed throughout treatment.

ABBREVIATIONS FDA, US Food and Drug Administration; IV, intravenous; PTH, parathyroid hormone

KEYWORDS dilution; hypocalcemia; hypoparathyroidism; pediatrics; teriparatide

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Introduction

Primary hypoparathyroidism is a rare pediatric endocrine disease characterized by low serum concentration of parathyroid hormone (PTH). Parathyroid hormone is responsible for regulating the body's calcium, phosphorus, and vitamin D concentrations. Hypoparathyroidism results in hypocalcemia, hyperphosphatemia, and elevated urine calcium excretion. Symptoms of hypoparathyroidism in children include dry skin, muscle spasms, seizures, and numbness in toes, fingers, and lips. The goals of therapy are to prevent the symptoms of hypocalcemia, to maintain a serum calcium concentration at the lower end of normal, a phosphorus concentration at the upper end of normal, and a calcium-phosphate product below 55 mg^2/dL^2. Close laboratory and dietary monitoring are needed to prevent hypocalcemia or hypercalciuria, which could lead to renal insufficiency or nephrocalcinosis.[1] Acute management of hypocalcemia involves IV administration of calcium gluconate, which may need to be given frequently if hypocalcemia continues. Chronic management of hypoparathyroidism typically includes oral calcium, oral vitamin D, and oral active vitamin D analog supplementation as well as phosphate binders.[1] Dietary changes may include incorporating foods that have a high calcium content and avoiding foods that are rich in phosphorus. Parathyroid hormone replacement therapy is often not considered in the pediatric population owing to a deficiency of long-term safety and efficacy data, no recommended pediatric dose, and the lack of an available agent for administration in pediatric patients.[1]

Teriparatide (Forteo, Eli Lilly and Company, Indianapolis, IN) is a recombinant, 34-amino-acid-sequence, human PTH analog that is FDA approved to treat osteoporosis in adult patients who are at high risk for fracture.[2] Its use in pediatrics for hypocalcemia and hypoparathyroidism is limited. Teriparatide has a US FDA box warning for potential risk of osteosarcoma observed in rats given supraphysiologic doses (3–60 times the normal 20-mcg adult dose).[2] Long-term osteosarcoma has not been reported in primates.[3] The Osteosarcoma Surveillance Study evaluated the association of osteosarcoma and teriparatide use in adult patients over 7 years and concluded there was not an association between osteosarcoma and teriparatide in humans.[4] However, this warning has caused caution in the medical community regarding its use, especially in the pediatric population, where there is a dearth of long-term studies. The aim of this case report is to discuss our 6-month experience with teriparatide therapy for a 4-month-old patient with severe hypoparathyroidism.

Case

Our patient was a 4-month-old preterm (current weight: 5.5 kg, gestational age: 32 weeks) Caucasian female infant with multiple congenital anomalies. Her newborn screen was significant for an abnormal T-cell receptor excision circle, which was concerning for severe combined immunodeficiency disease. After an extensive workup, she was found to have atypical

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Table. Teriparatide Dilution Preparation

Steps
1. Attach a new NovoTwist needle to the teriparatide prefilled pen cartridge.
2. Add drug (1 actuation) from the pen device into an empty 2-mL vial.
3. Using a 1-mL syringe draw up 0.42 mL of sterile water for injection and transfer it to the same 2-mL vial as above. This is now the 40 mcg/mL (40 mg/L) stock dilution vial. Total volume of dilution is 0.5 mL.

The stock dilution has a 24-hour expiration date. Refrigerate.

complete DiGeorge syndrome (functional athymia without identifiable genetic mutation) and was in need of a thymus transplant. She was followed up by pediatric nephrology for solitary right kidney in the setting of unilateral renal agenesis, hypocalcemia, hyperphosphatemia, and hypoparathyroidism. For her hypoparathyroidism, she was managed with calcium carbonate 840 mg by G-tube 5 times daily (~760 mg/kg/day elemental calcium), cholecalciferol 1000 units by G-tube daily, and calcitriol 1 mcg by G-tube daily. Despite receiving these medications, serum ionized calcium concentrations continued to be less than 1 mmol/L, necessitating IV calcium gluconate 200-mg/kg replacements 3 to 4 times per week. In addition, PTH continued to be undetectable at less than 4 ng/mL, and serum phosphorus concentrations were elevated at 12 mg/dL despite enteral nutrition being decanted with sevelamer, a phosphate binder.

Upon recommendation by her pediatric nephrologist, teriparatide therapy was considered. Teriparatide (600 mcg/2.4 mL) is formulated as a multidose prefilled pen-injector containing 28 doses. Each actuation delivers the adult dose of 20 mcg (equivalent to 0.08 mL). The doses published in the literature for pediatric patients started at smaller initial doses (range, 0.3–0.8 mcg/kg/day)[5–10]; therefore, a dilution was required to adequately measure and administer the dose. Fox and Gilbert[5] published a case report in which teriparatide was used to treat a 4-year-old patient with autosomal dominant hypocalcemia. They prepared a 40-mg/L dilution, using sterile water, and initiated therapy at a dose of 0.4 mcg/kg subcutaneous twice daily. From this concentration and the literature, we determined that 2 mcg = 0.05 mL twice daily (0.7 mcg/kg/day) was a reasonable and measurable starting dose. Currently, there are no published data on the stability of the dilution. Linglart et al[6] published a study on the use of continuous subcutaneous parathyroid hormone infusion in children with refractory hypoparathyroidism. To prepare the infusion, teriparatide was diluted with sterile water, in which the reservoir and infusion sets were changed every 3 days. From this information, we prepared a 40-mcg/mL dilution each morning that was used to dispense the morning and evening doses. We used an empty 2-mL vial to add 1 actuation of teriparatide (0.08 mL) and 0.42 mL of sterile water. This vial was labeled as teriparatide 40-mg/L dilution. The dose was drawn up with a subcutaneous syringe and labeled with a patient-specific label. The evening dose was stored in the refrigerator until the due time. Each pen was stable for 28 days in the refrigerator; therefore, preparing a daily dilution versus a twice daily dilution allowed 1 pen to be used for 28 days, rather than 14 days. This method proved to be more cost-effective because the average wholesale price for 1 teriparatide pen is $3350.[2] Clear communication was sent to the pharmacy department regarding dilution preparation instructions (Table). The order was entered as a customized, non-formulary medication.

Upon initiation of teriparatide, serum calcium was monitored 3 times per day and ionized calcium continued to be monitored daily. These laboratory test results were eventually spaced out as time progressed. Teriparatide, calcium carbonate, and calcitriol doses were adjusted to maintain a goal serum ionized calcium concentration greater than 1 mmol/L. The Figure demonstrates the trend of serum ionized calcium concentrations over 6 months with the associated dose changes of teriparatide and calcitriol. The teriparatide dose was increased to 2.4 mcg (0.4 mcg/kg) twice daily on day 14 of therapy, increased to 3.2 mcg (0.6 mcg/kg) twice daily on day 18 of therapy, and then increased to 3.9 mcg (0.7 mcg/kg) twice daily on day 28 of therapy as serum ionized calcium concentrations decreased. The patient remained on this dose for 2 months, but the dose was increased to 4.8 mcg twice daily and then 5.6 mcg twice daily a week later, owing to continued decreasing serum ionized calcium concentrations. The final dose change occurred during month 5 when the dose was decreased back to 4.8 mcg twice daily because the serum ionized calcium concentration was above 1.3 mmol/L. Given the dilution concentration of 40 mg/L, teriparatide dose changes were made by using the next measurable increment to ensure accuracy. All teriparatide doses were administered via subcutaneous route, and the injection sites were rotated throughout therapy.

Calcitriol is a vitamin D analog that plays a role in enhancing the absorption of calcium and phosphate from the gastrointestinal tract as well as helping the body regulate the production of PTH. Mechanistically, calcitriol works in concert with PTH to regulate calcium concentrations. Adjustments to the calcitriol and teriparatide doses throughout therapy were based on clinical discretion of the medical team after analysis of the serum ionized calcium trend, with the goal to maintain serum ionized calcium concentrations above 1 mmol/L without exceeding the upper limit of normal for total serum calcium concentrations.

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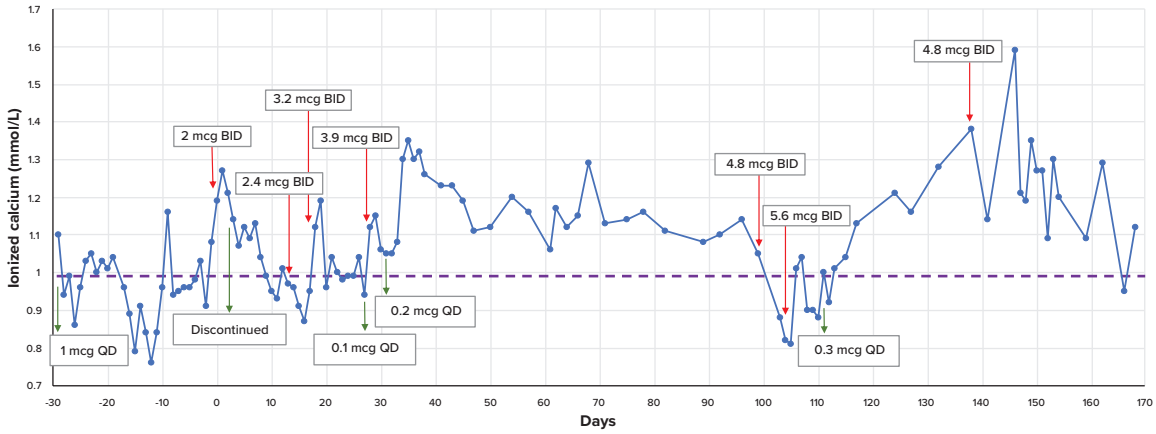
Figure. Ionized calcium trend.



BID, twice daily; QD, daily.

Trend of serum ionized calcium concentrations after the start of teriparatide therapy; purple dashed line represents the goal serum ionized calcium concentration; teriparatide dose changes listed in boxes with red arrows; calcitriol dose changes listed in boxes with green arrows.

The calcitriol dose was discontinued on day 3 of teriparatide because serum ionized calcium concentrations increased remarkably. Calcitriol was restarted at 0.1 mcg daily on day 28 of teriparatide therapy and increased to 0.2 mcg daily on day 34 because serum ionized calcium concentrations slightly decreased despite the increased teriparatide dose. The calcitriol dose was increased to 0.3 mcg daily during the fourth month of therapy, and this dose was maintained throughout treatment duration. In addition, after starting teriparatide, the calcium carbonate dose of 840-mg elemental calcium 5 times a day was decreased over the course of 5 weeks, and the dose was maintained at 320 mg 3 times a day (150 mg/kg/day).

During the fourth month of therapy, the calcium carbonate dose was increased to 380 mg 3 times a day, and this dose was maintained throughout treatment duration. Only 7 IV calcium gluconate doses were required during the 6 months of therapy, which was a substantial decrease compared with her requirements prior to starting therapy. Moreover, prior to starting teriparatide, our patient was receiving Elecare (Abbott, Lake County, IL) 100 mL every 3 hours over 1 hour, which had to be decanted with sevelamer owing to hyperphosphatemia. Each feed had to be separated from her calcium carbonate doses, therefore there was not much flexibility with her feed schedule and calcium supplement administration times when she required 5 times per day dosing. Phosphorus concentrations were monitored daily, therefore the decanting of her enteral nutrition with sevelamer was discontinued the day after teriparatide was initiated because the serum phosphorous concentrations decreased rapidly. Before teriparatide therapy, serum phosphorus concentrations ranged between 5 and 12 mg/dL.

Immediately after starting therapy, serum phosphorus concentrations decreased and were maintained between 4 and 8 mg/dL throughout treatment. Prior to teriparatide initiation, our patient was treated with cholecalciferol 1000 units daily. Two weeks after starting teriparatide, this dose was decreased to 600 units daily because her vitamin D concentration increased from 32.3 ng/mL to 47.6 ng/mL. During the fourth month of therapy, her vitamin D concentration decreased to 32.7 ng/mL, therefore her dose was increased back to 1000 units daily. She remained on this dose throughout treatment duration. Over the 6 months of therapy, her serum PTH remained undetectable at less than 4 pg/mL.

Adverse effects of teriparatide include hypercalcemia, nausea, and joint pain with reported long-term effects of bone lesions and renal insufficiency. Since teriparatide therapy was initiated, our patient did not experience hypercalcemia and her creatinine level remained at her baseline of 0.2 mg/dL.

Discussion

Teriparatide was FDA approved in November 2002 for the treatment of osteoporosis in adult patients who are at high risk for fracture. In recent years, teriparatide has shown efficacy in the treatment of hypoparathyroidism in adults. Currently, there is no recommended pediatric dose or large, randomized studies published demonstrating efficacy and safety of teriparatide use in children. Winer et al[7] published a 3-year randomized trial comparing twice daily calcitriol, calcium, and cholecalciferol versus teriparatide in 12 children (ages 5–14 years) with chronic hypoparathyroidism, starting at a mean teriparatide dose of 0.4 mcg/kg twice daily. The authors[8] subsequently published a 10-year study of 14 children (ages 7–12 years) receiving a mean dose of 0.75 ± 0.15 mcg/kg/day. Tuli et al[9] published a 9-year study of 6 pediatric patients with congenital hypoparathyroid-

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ism. These patients had a maximum teriparatide dose of 25 mcg twice daily and were eventually maintained on lower doses of calcitriol, calcium, and vitamin D after teriparatide therapy. It was also effective in the reduction of urinary calcium excretion. Over 9 years, therapy did not cause bone lesions or renal failure.[9] Fox and Gilbert[5] published a case report on teriparatide use in a 4-year-old male with autosomal dominant hypocalcemia, in which they used an average dose 0.4 mcg/kg twice daily and observed no adverse reaction of hypercalcemia after 9 months of therapy.

We report a case describing 6 months of teriparatide therapy for a 4-month-old patient. Teriparatide was shown to be safe and effective at maintaining serum ionized calcium concentrations above 1 mmol/L and decreasing calcium carbonate supplement requirements by 80%. Though she still required calcium carbonate supplementation, the frequency was decreased from 5 to 3 times daily. In addition, calcium gluconate doses decreased considerably. The Figure depicts the teriparatide and calcitriol dose changes and subsequent serum ionized calcium concentrations, which demonstrates that teriparatide was effective in maintaining a goal serum ionized calcium concentration above 1 mmol/L. Though calcitriol was discontinued early in therapy, it was restarted and maintained at a much lower dose.

A notable impact of teriparatide therapy was the ability to optimize our patient's nutrition. After starting teriparatide, feeds no longer needed to be decanted with sevelamer, and calcium carbonate dosing decreased in frequency from 5 to 3 times daily, allowing flexibility in the feeding schedule to avoid decreasing the absorption of the calcium supplement. During therapy, sevelamer did not need to be restarted because serum phosphorus concentrations were within normal limits.

Our patient tolerated teriparatide with no adverse effects. Winer et al[8] published a 10-year long-term study of 14 pediatric patients with hypoparathyroidism and reported normal bone accrual, mean serum and 24-hour urine calcium levels, and mean calcium-phosphate product. They reported no significant change in creatinine clearance despite the progression of nephrocalcinosis in 5 patients who had nephrocalcinosis at baseline. One patient developed bone pain and 4 patients experienced headaches while on teriparatide therapy. The limitations in our case include the age of the patient because we were unable to appropriately assess for joint pain as well as our short-term experience. A longer assessment is required to monitor the effects of teriparatide on renal function and the development of bone lesions in our patient.

Our patient was ultimately discharged from the hospital on teriparatide therapy. The pharmacist provided education to the parent on how to prepare the dilution and measure the dose, and a modified version of the instructions from the Table was provided to the family. Our outpatient pharmacy dispensed the prefilled teriparatide (Forteo) pen-injector, sterile water vials, empty vials, and subcutaneous syringes. It may be difficult for retail chain pharmacies to dispense this medication, and the supplies needed to dilute and administer the medication, because its use is not well published in pediatric patients. Our patient was followed up in the outpatient setting by her immunologist and nephrologist 2 to 3 times per week. Currently, there is no planned stop date to teriparatide therapy.

To our knowledge, our patient was the youngest to have received a 6-month course of teriparatide for the management of hypoparathyroidism. One of the limiting steps to teriparatide therapy in the pediatric population is the ability to safely measure and administer a smaller dose than what is commercially available, so it was important for us to outline our dilution and preparation process. We also wanted to report how we monitored serum calcium concentrations when teriparatide was initiated in order to evaluate the efficacy and prevent hypercalcemia. Dose changes and the discontinuation and re-initiation of medications were based on the careful laboratory monitoring and analysis by the medical team.

Conclusion

We conclude that teriparatide has proved to be a safe and effective therapy for our patient during this period. Over 6 months, teriparatide allowed our patient to maintain serum ionized calcium concentrations, ultimately resulting in less calcium gluconate replacement doses, decreased calcium carbonate, calcitriol, and vitamin D supplementation requirements, and no adverse effects were observed. Therefore, teriparatide therapy can be a potential option for patients with hypoparathyroidism refractory to conventional management; however, larger studies are needed to demonstrate long-term safety and efficacy of teriparatide use in pediatrics.

Article Information

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Ethical Approval and Informed Consent. Given the nature of this study, institution review board/ethics committee review and informed consent were not required.

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References

1. Di Maio S, Soliman AT, De Sanctis V, et al. Current treatment of hypoparathyroidism: theory versus reality waiting guidelines for children and adolescents. *Acta Biomed*. 2018;89(1):122–131.
2. Teriparatide [package insert]. Indianapolis, IN: Eli Lilly and Company; 2002.
3. Vahle JL, Zuehlke U, Schmidt A, et al. Lack of bone neoplasms and persistence of bone efficacy in cynomolgus macaques after long-term treatment with teriparatide [rhPTH(1-34)]. *J Bone Miner Res*. 2008;23(12):2033–2039.
4. Andrews EB, Gilsenan AW, Midkiff K, et al. The US postmarketing surveillance study of adult osteosarcoma and teriparatide: study design and findings from the first 7 years. *J Bone Miner Res*. 2012;27(12):2429–2437.
5. Fox A, Gilbert R. Use of teriparatide in a four year old patient with autosomal dominant hypocalcaemia. *Arch Dis Child*. 2016;101(9):e2.
6. Linglart A, Saraff V, Rothenbuhler A, et al. Continuous subcutaneous recombinant parathyroid hormone (1-34) infusion in the management of childhood hypoparathyroidism associated with malabsorption. *Horm Res Paediatr*. 2018;89(4):271–277.
7. Winer K, Sinaii N, Reynolds J, et al. Long-term treatment of 12 children with chronic hypoparathyroidism: a randomized trial comparing synthetic human parathyroid hormone 1-34 versus calcitriol and calcium. *J Clin Endocrinol Metab*. 2010;95(6):2680–2688.
8. Winer K, Kelly A, Johns A, et al. Long-term parathyroid hormone 1-34 replacement therapy in children with hypoparathyroidism. *J Pediatr*. 2018;203:391–399.e1.
9. Tuli G, Buganza R, Tessaris D, et al. Teriparatide (rhPTH 1–34) treatment in the pediatric age: long-term efficacy and safety data in a cohort with genetic hypoparathyroidism. *Endocrine*. 2020;67(2):457–465.
10. Cho Y, Tchan M, Roy B, et al. Recombinant parathyroid hormone therapy for severe neonatal hypoparathyroidism. *J Pediatr*. 2011;160(2):345–348.

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