REPLACEMENT THERAPY WITH RECOMBINANT PARATHYROID HORMONE (1-84) IN HYPOPARATHYROIDISM

S. Galoiu*

"C. I. Parhon" Institute of Endocrinology - Neuroendocrinology, Bucharest, Romania

Abstract

Hypoparathyroidism is a disease characterized by low serum calcium and inappropriate low parathyroid hormone (PTH) levels. Common therapy for chronic hypoparathyroidism usually includes oral calcium and activated vitamin D supplementation (calcitriol), hypoparathyroidism being the one of few endocrine disorders not replaced by the missing hormone. In January 2015, FDA approved PTH (1-84) for the treatment of hypoparathyroidism in patients who cannot be well-controlled on calcium and active forms of vitamin D alone and for whom the potential benefits are considered to outweigh this potential risk. Until now, there are 4 phase 3 clinical trials investigating the role of human recombinant PTH (1-84) for the treatment of hypoparathyroidism: Replace, Race, Relay, and Repeat. These studies demonstrated a more than 50% reduction in calcium and active vitamin D requirements. Future strategies for the treatment of hypoparathyroidism could be stem cell therapy recombinant with PTH and viral or nonviral factors or parathyroid gland transplantation.

Key words: PTH, hypoparathyroidism.

INTRODUCTION

Hypoparathyroidism is a disease characterized by low serum calcium and inappropriate low parathyroid hormone (PTH) levels. Its major cause is accidental surgical removal or damage of the parathyroid glands during surgical neck surgery and in about 25% of cases, hereditary or acquired hypoparathyroidism in the absence of parathyroid surgery. Long term complications of hypoparathyroidism include nephrocalcinosis leading to renal failure; soft-tissue brain calcifications and low quality of life (1).

Common therapy for chronic hypoparathyroidism usually includes oral calcium and activated vitamin D supplementation (calcitriol), hypoparathyroidism being the one of few endocrine disorders not replaced by the missing hormone. The disadvantages of vitamin D supplementation are large, unphysiological fluctuations of serum calcium levels, leading to hypercalcemia or hypercalciuria, with increased risk of chronic renal disease (2). Moreover, PTH has other physiologic functions not accomplished by vitamin D supplementation: low PTH is also complicated by hyperphosphatemia, hypercalciuria, and low bone turnover. Also, PTH receptors were found in other tissue not participating in bone metabolism, such as central nervous system receptors (3), which could be responsible for low quality of life and psychiatric comorbidities in patients with hypoparathyroidism.

In January 2015, FDA approved PTH (1-84) for the treatment of hypoparathyroidism in patients who cannot be well-controlled on calcium and active forms of vitamin D alone and for whom the potential benefits are considered to outweigh this potential risk. Until now, there are 4 phase 3 clinical trials investigating the role of human recombinant PTH (1-84) for the treatment of hypoparathyroidism: Replace (4), Race (5), Relay, and Repeat (6). These studies demonstrated a more than 50% reduction in calcium and active vitamin D requirements. Also, Cusano et al. showed an increase in bone turnover: lumbar spine BMD was reduced by 5.5 ± 9% at 4 years (P < .0001) and bone turnover markers increased by 3-fold at 6-12 months (P < .05 for all), steady-state levels at 30 months (7).

Regarding the safety of rhPTH(1-84), 3 years follow-up in 38 patients from RACE study, the open-label extension of REPLACE and RELAY, was recently presented at the 17th European Congress of Endocrinology at Dublin and confirmed its efficacy and safety (5). However, keeping in mind the potential risk of osteosarcoma found in rats, FDA issued a REMS program (Risk Evaluation and Mitigation Strategy) for the information of physicians, pharmacists and patients. Future strategies for the treatment of hypoparathyroidism could be stem cell therapy recombinant with PTH and viral or nonviral factors (8) or parathyroid gland transplantation.

*Correspondence to: Simona Galoiu MD, “Carol Davila” University of Medicine and Pharmacy, “C.I.Parhon” National Institute of Endocrinology, 34-36 Blvd Aviatorilor, Bucharest, 011863, Romania, E-mail: simona.galoiu@gmail.com

Acta Endocrinologica (Buc), vol. XI, no. 3, p. 413-414, 2015
Conflict of interest

The author declares that there is no conflict of interest concerning this article.

References