

Teriparatide in cervical fracture consolidation

Cláudio Cordeiro Albino¹
 Carmine Porcelli Savarani²
 Carolina Aguiar Moreira^{3,4}

¹ Instituto de Diabetes e Endocrinologia de Maringá (IDEM) & Núcleo Diagnóstico, Maringá-Paraná, Brasil

² Hospital Santa Casa, Maringá-Paraná, Brasil

³ Serviço de Endocrinologia e Metabologia da Universidade Federal do Paraná (SEMPR) Curitiba-Paraná, Brasil

⁴ Laboratório PRO, setor de histomorfometria óssea, Fundação Pró Renal, Curitiba-Paraná, Brazil

Address for correspondence:

Carolina Moreira

Serviço de Endocrinologia e Metabologia da Universidade Federal do Paraná (SEMPR) Curitiba-Paraná, Brasil

Laboratório PRO, setor de histomorfometria óssea,

Fundação Pró Renal, Curitiba-Paraná, Brazil

E-mail: carolina.aguiar.moreira@gmail.com

Summary

The occurrence of high cervical (C1-C2) fractures in the elderly has high rates of morbidity and mortality. Proposed treatments include both surgical fixation and conservative treatment. The first has a high mortality rate (up to 45%) and the second is ineffective in up to 78% of cases in fracture consolidation. In non-consolidated fractures, there is an indication of surgical fixation or prolonged rigid external immobilization, which, regardless of the choice of treatment, brings risk, discomfort and low quality of life to the patient. Our report shows the case of a woman of 80 years, treated with osteoanabolic medication (teriparatide) for 12 weeks, obtaining full consolidation and symptom resolution. There are several experimental and clinical studies suggesting a potential role of Teriparatide in the consolidation of fractures. Our report suggests that this medication may play an important role in the conservative consolidation of high cervical fractures in the elderly.

KEY WORDS: teriparatide; fracture consolidation; cervical fractures; osteoanabolic agents.

Introduction

Cervical spine fractures in the elderly has high rates of morbidity and mortality (1). Osteoporosis is the main cause,

even if cervical vertebrae not being the most frequent location of osteoporotic vertebral fractures. In addition, in this age group, other factors, such as a higher incidence of falls and motor vehicle accidents, also contribute to the presence of cervical fractures (1, 2). It is expected that there will be an increase in the incidence of this type of fracture in the coming years, due to a significant increase in the percentage of elderly individuals, both in developed and developing countries (3). Stabilization of the fracture of the high cervical spine is the main objective of the treatment, however there is no consensus in the literature, which would be the management of choice (4). Although surgical fixation achieves better levels of fracture consolidation (5), it is associated to a higher rate of complications and mortality (5). The external fixations, by halo or outer vests, are not effective for consolidation of the fracture and in addition, they are associated with a greater risk of instability and neurological injuries (5, 6). Teriparatide (PTH 1-34) is the active metabolic component of human parathyroid hormone. Its use is indicated in the treatment of severe osteoporosis, especially in the presence of multiple vertebral fractures (1, 7-9). It is an anabolic medication that induces an increase in bone formation. For this reason, it has been used to accelerate fracture healing period, both osteoporotic, and stress fractures of athletes and military personnel. In this report, we describe our experience with the use of rhPTH 1-34 in the consolidation of vertebral fractures in an elderly patient.

Case report

An 80-year-old female patient suffered a car accident in September 2014. There was a loss of consciousness at the time, but when she arrived at the emergency room she was awake, without any neurological deficit. Computed tomography (CT) showed a fracture of C1). Conservative treatment was chosen, with the cervical spine immobilized with an external Philadelphia collar. After 12 weeks of follow-up, the patient remained with pain in the cervical region and presented functional limitation by cervical fixation. The control CT showed that the fracture remained the same as in the beginning, with no signs of consolidation (the space between the fragments remained the same: 5 mm) and with a high risk of instability. As the surgical treatment was not accepted by the patient and family members, the use of teriparatide 20 mcg daily was suggested aiming to accelerate fracture consolidation. It was started in January 2015, after evaluation of the bone metabolism throughout exams such as calcium dosage, PTH, 25OH vitamin D, phosphorus, and creatinine. After 8 weeks of treatment, an improvement in the fracture consolidation was observed through a significant reduction of the space between the fragments. At the end of 12 weeks of treatment, complete cervical fracture consolidation was evidenced without any sign of cervical instability. In addition, in this 12 week period of

treatment, patient tolerated well the use of teriparatide and did not report any adverse event.

Discussion

Cervical spine fractures are relatively frequent in the elderly and its treatment is controversial, since surgical fixation, despite a higher rate of fracture consolidation, demands a higher surgical risk, higher cost and subsequent functional limitation (5). Prolonged external immobilization is associated with low levels of fracture consolidation (20-45%), and is related to cardiac and respiratory problems due to the functional limitation (5). The development of a fibrosis between the fracture ends (*não entendi*) is a common finding in the elderly and even accepted by some Authors as a reasonable evolution in this age group. However, there are described cases of late myelopathy with this type of evolution (10). Human Parathyroid Hormone (PTH) has important modulatory action on the metabolism of calcium, phosphorus and active metabolites of vitamin D. Analogs of the amino-terminal portion of PTH stimulate bone formation and lead to an increase in bone mass and have been used as treatment of severe osteoporosis with a significant reduction in the risk of osteoporotic fractures (11-13).

In animal models, teriparatide has demonstrated effective action in accelerating fracture healing (14, 15). It is also worth mentioning that the anabolic action continues after its suspension (15). Andreassen et al. (16) compared the effect of the use of teriparatide on fracture healing in old rats (21 months) and young rats (2 to 3 months), since it was observed that in old rats there was a reduction of osteoprogenitor cells and pre-osteoblasts in osteoblasts (16), so it was hypothesized that these findings could interfere with the action of PTH in old rats. The results showed an acceleration of bone healing in both groups and there was an increase in the final load on the fracture of 270% (56 days) in both groups, in relation to the control (16). Clinical studies have shown controversial results (17, 18). The first meta-analysis published by Lou et al. (17) included 258 patients in 5 randomized controlled trials. Patients treated with teriparatide had an earlier resolution of the fracture. The second meta-analysis did not confirm these findings (18). A new meta-analysis has recently been published, including 11 studies, 6 clinical trials, and 5 retrospective studies. In 70% of the studies, there was a benefit of using teriparatide, both in radiological recovery, as well as in pain symptoms. The conclusion of the meta-analysis was that teriparatide may be beneficial in osteoporotic fractures, however, the findings did not occur in all the studies included in the meta-analysis and there was great heterogeneity between the fracture sites and final objectives (19). More specifically, in the consolidation of cervical fractures, there are only 4 cases described in the literature. In these cases, 4 elderly patients with high cervical spine fractures and delayed healing were treated with teriparatide 20 μ g daily for 12 weeks. In all the cases described, there was fracture consolidation and functional resolution and pain (20, 21). Similarly to these cases, our patient presented an adequate response to teriparatide in the cervical fracture repair and improvement of the associated symptoms.

These positive results encourage the treatment with teriparatide for unconsolidated cervical spine fractures in elderly since the risk of surgery is high in this population. We

believe that teriparatide due to its anabolic effect presents a great potential for the acceleration of fracture healing and that its indication in elderly patients with contraindication to surgical treatments should be considered. Randomized clinical trial of the use of teriparatide in frail elderly individuals who suffered cervical fractures would be of great importance.

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