

Teriparatide therapy for Medication Related Osteonecrosis of the Jaw: Case report and literature review.

Mohamed MM¹Gunasekera WMA¹, Glew D, Bell C, Bhalla AK.

¹Peterborough City Hospital. Northwest Anglia NHS Foundation Trust. Bretton Gate. Peterborough. PE12 OSP

Introduction: Medication-related osteonecrosis of the jaw (MRONJ) is a recognised complication of antiresorptive therapy¹. Emerging evidence suggests impaired epithelialisation post dental surgery, local pro-inflammatory response and inhibition of angiogenesis in its pathogenesis². Risk factors include old age, prolonged medication exposure, IV bisphosphonates (BP), smoking, glucocorticoid therapy, anaemia, obesity, diabetes and cancer³.

For 14 months she underwent conventional therapy with limited debridement of the exposed bone, long-term antibiotics and Chlorhexidine wash out of the exposed areas, but her condition deteriorated. On referral to rheumatology, her vitamin D deficiency was corrected, P1NP and CTX were within normal limits. She was commenced on subcutaneous Teriparatide 20mcg daily for 2 years.

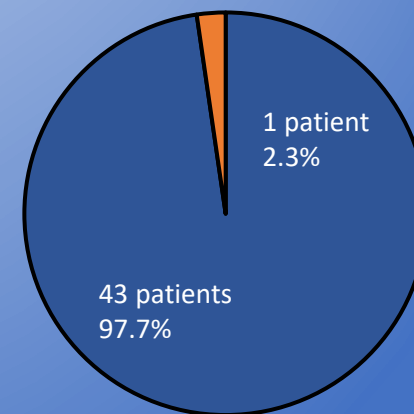
Teriparatide induces an “anabolic window” where there is early response of the bone formation markers with delayed catch-up of resorption marker in MRONJ patient within the first 9 months of treatment leading to a positive bone balance and indicating a role for these in monitoring treatment response.⁸

The incidence of MRONJ in the UK is 620 per year. At the time of treatment we reviewed 11 case reports, two case series and one retrospective study using Teriparatide to treat MRONJ that was resistant to conventional treatment in a total of 44 patients, where all but one patient found a favourable outcome.^{4,5}

Within 2 months there was full soft tissue coverage of the intramural lesion, the fistula was lined with healthy oral mucosa and she did not require further debridement. Within 5 months her P1NP doubled and CTX remained the same. She then underwent surgical closure of the orocutaneous fistula. This healed successfully leading to improved appetite and gradual weight gain. She was then provided with upper and lower dentures.

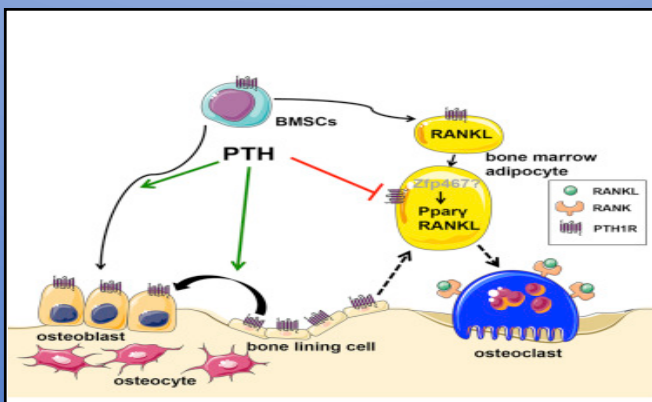
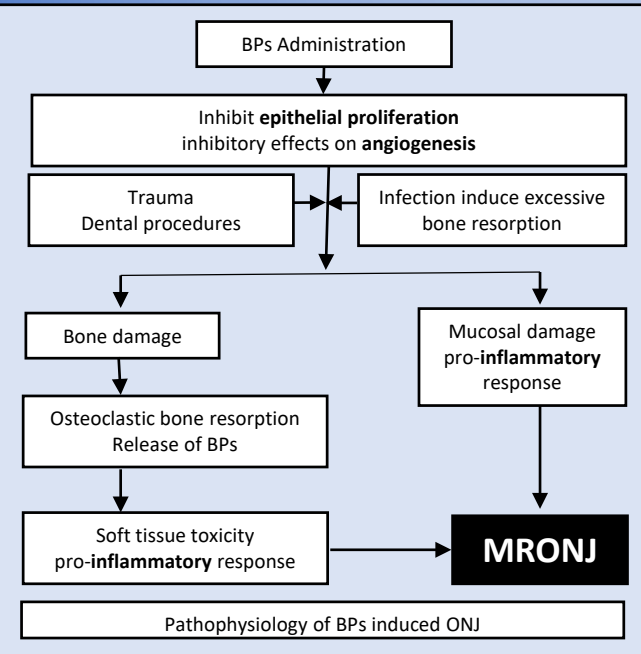
Discussion: The biological rationale for the benefit of Teriparatide which is a recombinant Parathyroid hormone (rPTH) could lay in the fact that rPTH increases the proliferation of T-cells thereby increasing Wnt-10b production and enhancing osteoblast differentiation.⁶ Teriparatide enhances osteoblast RANKL production to drive osteogenesis and augments osteoclast recruitment.⁷ These cells are pivotal to bone healing and a prerequisite for the anabolic effect of Teriparatide on osteoblasts.

Outcome of reviewing 11 case reports, 2 cases series and 1 retrospective study using Teriparatide to treat MRONJ



■ Significant improvement ■ No significant improvement

Over the past 2 years a systematic review and an RCT has finally established the beneficial effect of Teriparatide in the treatment of MRONJ, which provides welcome relief to the rare patients afflicted with this condition.^{9,10}



YiFan, (2017). Parathyroid Hormone Directs Bone Marrow Mesenchymal Cell Fate. Cell Metabolism, 25(3) page 661-672 Elsevier/Science Direct
[Parathyroid Hormone Directs Bone Marrow Mesenchymal Cell Fate - ScienceDirect](https://doi.org/10.1016/j.cmet.2017.05.004)

We present the case of an 81-year-old lady with severe osteoporosis and ischaemic heart disease, who had been on Alendronate 70mg weekly for 3 years when she had a tooth extraction. 3 months later she presented to Maxillofacial Surgery with non-healing extraction sites, facial pain and erythema and a malodorous discharging sub-mantle sinus. She received a diagnosis of stage 3 MRONJ confirmed on Orthodontogram and CT scan. She had Proteus mirabilis on tissue culture. She had no history of osteosarcoma or local radiotherapy.