INTRODUCTION

BRONJ has emerged as a significant health problem in recent years, affecting around 7% of patients receiving long-term Bisphosphonates, 67% of whom report history of dental procedures. Unlike other anti-resorption medication, bisphosphonates become absorbed on hydroxyapatite crystals in the bone matrix and localized to sites of osteoclast activity by forming a 3D structure capable of binding to calcium, in addition to their direct anti-osteoclast action, rendering the matrix itself toxic for osteoclasts for years after the treatment has been stopped.

HYPOTHESES AND SPECIFIC AIMS

1) To prove the hypothesis that the local deposition of bisphosphonates in the bone matrix is important for the induction of BRONJ.
2) To prove the hypothesis that local chelation of Zoledronate at the time of trauma will rescue the healing and prevent Bisphosphonates Related osteonecrosis of the jaw.

METHODS

1st Experimental Design

10 Sprague Dewley Rats
FRFP [0.16 mmol/g] IV
One dose (the day before procedure)

Procedure
Bilateral mandibular first molar extraction and a defect is drilled/applying EDTA/H2O for 10 min.

Scarcification

Histology Analysis

To detect the degree of Fluorescent density and the depth of decalcification

RESULTS

Histology Analysis

EDTA caused a significant decrease in the integrated density of the fluorescence (p=0.031) when compared to the internal controls.

EDTA significantly increased the depth of the post-extraction decalcification along the socket walls compared on the control side.

Micro-CT Analysis

EDTA-applied side showed normal socket healing, with uniform new bone extending from the base and sides to fill the socket cavity, and extruding any remaining root tips towards the surface. In contrast, all PBS-applied side showed lack of bone formation within the socket, in addition to substantial fragmentation of the alveolar bone, extending from the extraction site. Large blocks of sequestered bone were consistently evident in multiple planes, with fissures and fracture lines scattered throughout the remaining alveolar bone.

CONCLUSION

Apart from that We proved that the local deposition of bisphosphonates is an important factor for the induction of BRONJ, we also demonstrated that Targeted chelation of localized ZA from the bone matrix will rescue the healing and prevent osteonecrosis. In addition, EDTA treatment at the time of extraction will augment the effect of local chelation, accelerating the healing process.

FUTURE DIRECTION

We begin to design the experiment with a larger Controlled sample to investigate the dynamic of Zoledronate chelation induced by different chelating agents.

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