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Peer Review

Review of: "Bisphosphonate-Related Osteonecrosis of the Jaws Treated with Platelet-Rich Plasma: Preliminary Results from a Case Series"

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Review Report

Assessment of Background Information and Literature Review

- While the anti-osteoclastic and antiangiogenic effects of bisphosphonates are mentioned, the unique susceptibility of the jaw (vs. other bones) is not thoroughly explained. Add a paragraph on jaw-specific vascular anatomy or microbial flora contributing to BRONJ (e.g., *Favia et al., 2009*).
- The manuscript briefly lists other BRONJ therapies (e.g., hyperbaric oxygen, ozone) but does not compare their efficacy to PRP. Include a table summarizing outcomes of different treatments (e.g., success rates, recurrence) from meta-analyses like *El-Rabbany et al., 2017*.
- Some sections (e.g., BP mechanisms) are well-referenced, while others (e.g., PRP growth factors) lack citations. Add references for specific growth factors (e.g., VEGF, PDGF) and their roles in bone healing (*Marx & Garg, 2005*).
- No mention of staging systems (e.g., AAOMS 2009 guidelines) to contextualize patient severity. Describe how patients were staged and whether PRP is more effective for early vs. advanced BRONJ.
- Absence of control groups (e.g., PRP vs. conventional debridement) limits claims of superiority. Cite randomized controlled trials (RCTs) like *Curi et al., 2007* to support PRP's advantages.
- The 12-month follow-up is adequate but lacks discussion of recurrence rates beyond this period. Reference studies with longer follow-ups (e.g., *Mozzati et al., 2012*).

Methodology

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- Detailed description of PRP preparation (centrifugation, fractionation) and surgical steps.
- Regular post-op assessments (7 days to 12 months) enhance reliability.

- Small sample (n=35) with no control group or randomization. Acknowledge limitations and propose future RCTs.
- No p-values, confidence intervals, or comparative statistics (e.g., maxilla vs. mandible healing rates). Include basic statistics or reference similar studies with statistical rigor.
- "Clinical success" is defined vaguely (e.g., "intact mucosa"). No quantitative measures (e.g., radiographic bone density). Use standardized scales (e.g., *O'Ryan & Lo, 2012*).

Discussion

- Fails to address potential confounders (e.g., concurrent antibiotic use). Discuss how adjunct therapies may skew results.
- A 100% success rate is atypical; compare to literature (e.g., *Adornato et al.* reported 83%). Attribute success to stringent patient selection or protocol uniqueness.

Conclusion

- No proposal for multi-center trials or mechanistic studies. Outline next steps (e.g., "Validate results in a Phase III RCT").

Final Recommendations

- Add jaw-specific pathophysiology and comparative treatment data.
- Enhance Methodology, include statistical analysis and control group comparisons.
- Balance Discussion by addressing limitations (e.g., bias, confounders) and temper success claims.
- Update References and incorporate recent meta-analyses (e.g., *El-Rabbany et al., 2017*) and RCTs.

Declarations

Potential competing interests: No potential competing interests to declare.