Letter to Editor

Preserving Vital Pulp Versus Complex Regeneration: Ethical and Clinical Considerations in Exosome-Based Endodontic Therapy

Dear Editor

I read with interest the recent case report by Jafari and colleagues describing the use of exosomes derived from human umbilical cord mesenchymal stromal/stem cells (hUCMSCs) in a mandibular premolar diagnosed with irreversible pulpitis and treated with pulpectomy.[1] The authors are to be commended for applying an innovative tissue engineering strategy and for detailed exosome characterization and follow-up assessments. Preliminary clinical signs of healing and integration without adverse events are intriguing and align with basic research demonstrating that stem cell exosomes may enhance dental pulp cell migration, proliferation, and dentin-pulp regeneration pathways *in vitro* and in preclinical models.[2]

However, I am concerned about how this case report might be interpreted in the context of current clinical evidence and evolving standards of care. In the treatment of teeth diagnosed clinically (or histologically) with irreversible pulpitis, a substantial body of evidence now shows that vital pulp therapy (VPT), including seven techniques using hydraulic calcium silicate cements, can achieve high long-term success rates, often comparable to nonsurgical root canal therapy (NSRCT).[3] A systematic review reported radiographic and clinical success rates between approximately 78 and 90% for VPT in mature teeth with symptomatic irreversible pulpitis, and in some studies, outcomes of VPT and NSRCT were comparable at 1 and 5 years.[4] Larger cohort data also showed survival and success rates exceeding 90% for various VPT techniques over long observation periods.[5]

Many contemporary position statements now reflect this paradigm shift: the American Association of Endodontists and European endodontic organizations acknowledge that conservative therapies might be indicated even in teeth previously considered to require pulp extirpation. Importantly, VPT achieves this while preserving vital tissue, maintaining natural proprioception and immune function, and avoiding the invasiveness, extended chair time, and cost associated with pulpectomy followed by a complex regenerative procedure. In contrast, exosome application, while biologically promising, was conducted here only after complete pulpectomy, effectively removing residual vital tissue that might have been preserved with simpler therapy.

Framing exosome-assisted regeneration primarily as a treatment for irreversible pulpitis risks a conceptual inversion: rather than addressing the fundamental question of whether residual pulp can be preserved and allowed to heal, it suggests removal followed by artificial regeneration. This “technological imperative” fallacy, the assumption that because a complex procedure can be performed, it should therefore be performed, may inadvertently lead clinicians to favor overtreatment over evidence-based, minimally invasive care. Given the emerging data supporting VPT’s efficacy and the ethical mandate to choose the simplest, least invasive, and safest effective intervention, it would be more appropriate to contextualize experimental regenerative methods such as exosome application as exploratory, adjunctive strategies to be investigated in well-controlled clinical trials, specifically after maximal conservative therapy has been exhausted or is contraindicated.

In conclusion, while Jafari and colleagues contribute valuable preliminary data to the regenerative endodontics literature, the published article would benefit from clearer framing that aligns clinical recommendations with current evidence favoring vital pulp preservation when feasible. Exosome-based therapies hold scientific promise but require larger studies with rigorous comparators before they can be recommended as standard alternatives to VPT or NSRCT.

Declaration of AI

During the preparation of this work, the author used DeepSeek solely for language refinement and editing assistance, and the author takes full responsibility for the content.

Conflict of Interest: None declared.

Keywords ● Vital pulp therapy ● Exosome therapy ● Irreversible pulpitis ● Regenerative endodontics ● Ethical considerations

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Authors' Reply

Dear Editor

We thank the author of this Letter to the Editor for their careful review of our published case report entitled "The Effect of Exosomes Derived from Human Umbilical Cord Mesenchymal Stromal/Stem Cells on the Regeneration of Human Pulpectomized Tooth: A Case Report".[1] We appreciate the opportunity to clarify the scope, interpretation, and intended clinical positioning of our work.

We fully agree that vital pulp therapy (VPT) is a crucial, minimally invasive treatment strategy for appropriately selected permanent teeth, and that the preservation of vital pulp should remain a primary clinical goal whenever it is biologically and clinically feasible. Contemporary endodontic position statements emphasize case-specific assessment and support vital pulp preservation in selected situations, including some teeth that previously would have been managed by complete pulp extirpation.[2, 3] We wish to clarify that our case report was designed as an initial proof-of-concept and feasibility observation. It was not intended to recommend pulpectomy over VPT or nonsurgical root canal treatment (NSRCT), nor should it be interpreted as evidence that human umbilical cord mesenchymal stromal/stem cell (hUCMSC)-derived exosomes can replace established endodontic treatment modalities. The clinical decision to perform a pulpectomy in the reported patient was based on case-specific clinical judgment at the time of treatment.

We also agree that the suitability of VPT cannot be assumed retrospectively from the diagnostic label alone. It depends on multiple clinical factors, including pulp exposure status, bleeding control and hemostasis, the extent and distribution of inflammation, restorability, radiographic findings, operator assessment, and the overall clinical diagnosis. Therefore, our report should not be used to infer whether VPT was or was not definitively indicated in this specific tooth, nor should it imply that a more complex regenerative approach is preferred when vital pulp preservation remains achievable.

The aim of this report was more specific: to explore whether a cell-free, exosome-based regenerative strategy could be delivered within a controlled intracanal environment after pulpectomy and subsequently monitored clinically and radiographically in a human subject. From this perspective, this observation might be considered an exploratory translational step, particularly for future contexts in which vital pulp has already been removed, or in which necrotic, immature, traumatized, or previously pulpectomized teeth require regenerative strategies.

We acknowledge the important limitations of our report, including the single-patient design, absence of a control group, relatively short follow-up, lack of histological confirmation, and the need for more rigorous product standardization and extracellular vesicle characterization. Accordingly, the findings should be regarded as exploratory and hypothesis-generating only, not as evidence of clinical superiority or as justification for replacing simpler evidence-based therapies.

Future studies should include well-designed controlled clinical trials with appropriate comparators, including VPT and NSRCT when clinically relevant. These trials should incorporate standardized clinical and radiographic outcomes, long-term follow-up, systematic safety monitoring, and transparent extracellular vesicle characterization and reporting in accordance with current international recommendations, such as MISEV2023.[4] Such studies should also clearly distinguish whether exosome-based therapy is being evaluated as an adjunctive strategy or as a regenerative intervention for cases in which conventional pulp preservation is no longer feasible.

In conclusion, we appreciate the valuable perspective provided in the Letter to the Editor. We agree that preservation of vital pulp should remain the preferred goal whenever feasible, and that exosome-based pulp regeneration should currently be framed as an experimental and carefully monitored approach. Our case report contributes preliminary translational information to the field of regenerative endodontics. However, it should not be interpreted as a routine alternative to established, less invasive,

evidence-supported treatments.

Declaration of AI

Generative AI was used only to assist with English language polishing, wording refinement, and document formatting of this response. All scientific content, interpretation, references, and final wording were reviewed, revised, and approved by the authors, who take full responsibility for the accuracy and integrity of the submitted response.

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