Section: Dentistry

Original Research Article

HISTOPATHOLOGICAL EVALUATION OF INFLAMMATORY RESPONSE TO BIOACTIVE RESTORATIVE MATERIALS IN SURGICALLY TREATED TEETH INCLUDING ROOT CANAL TREATMENT

Muhammad Arsalan Raffat[1], Naveed Khawaja[2], Mohammad Abdullah[3], Kauser Parveen[4], Sana Ikram[5], Ayman Ashraf[6]

[1]*Associate Professor, Department of Oral & Maxillofacial Pathology, Shahida Islam Medical Complex, Lodhran, Pakistan*
[2]*Associate Professor, Department of Oral & Maxillofacial Pathology, CIMS Dental College, Multan, Pakistan*
[3]*Demonstrator, Department of Oral Surgery, HBS Dental College, Islamabad, Pakistan*
[4]*Assistant Professor & Head, Department of Paediatric Dentistry, CIMS Dental College, Multan, Pakistan*
[5]*Associate Professor, Department of Oral Biology, Shahida Islam Medical Complex, Lodhran, Pakistan*
[6]*Demonstrator, Department of Oral Pathology, CIMS Dental College, Multan, Pakistan*

Received *: 12/07/2026*
Received in revised form *: 18/08/2026*
Accepted *: 22/08/2026*

Corresponding Author:
Dr. Naveed Khawaja,
Associate Professor, Department of Oral & Maxillofacial Pathology, CIMS Dental College, Multan, Pakistan.
Email: nakhawajadr@gmail.com

DOI: 10.70034/ijmedph.2026.3.733

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2026; 16 (3); 4742-4748

ABSTRACT

Background: Bioactive restorative materials are increasingly used in restorative and endodontic procedures because of their ability to interact with surrounding tissues, release biologically active ions, promote mineralization, and support tissue repair. Their histopathological response is particularly important in root canal-treated teeth requiring subsequent surgical management, where restorative materials may directly influence periapical healing. The objective is to evaluate and compare the histopathological inflammatory response, tissue-healing characteristics, radiographic healing, and clinical outcomes associated with bioactive and conventional restorative materials in surgically treated teeth following root canal treatment.

Materials and Methods: This comparative clinical study included 72 patients contributing 72 teeth, with one eligible tooth analyzed per participant, from January 2025 to June 2025 at CIMS Dental College, Multan, Pakistan. Root canal treatment was performed according to the standardized institutional endodontic protocol before clinically indicated surgical management. Thirty-six teeth were restored with a bioactive restorative material and 36 with a conventional restorative material. Histopathological assessment included inflammatory severity, inflammatory-cell infiltration, fibroblast proliferation, collagen deposition, vascular proliferation, granulation tissue, necrosis, foreign-body reaction, and mineralized-tissue formation. Radiographic healing and clinical outcomes were also assessed. Statistical significance was set at $p < 0.05$.

Results: No or mild inflammation was observed in 80.6% of teeth in the bioactive group compared with 55.6% in the conventional group, whereas moderate-to-severe inflammation occurred in 19.4% versus 44.4%, respectively ($p = 0.023$). The mean inflammatory-response score was significantly lower with bioactive material (0.97 ± 0.77 vs. 1.47 ± 0.94; $p = 0.016$). Moderate-to-marked fibroblast proliferation (83.3% vs. 61.1%), organized collagen deposition (77.8% vs. 55.6%), and mineralized-tissue formation (72.2% vs. 44.4%) were more frequent in the bioactive group. Favorable radiographic healing occurred in 88.9% versus 69.4%, while overall treatment success was 86.1% versus 66.7% ($p = 0.049$).

Conclusion: Bioactive restorative material was associated with reduced inflammatory response, enhanced tissue repair and mineralization, improved radiographic healing, and greater overall treatment success than conventional

restorative material in root canal-treated teeth requiring surgical management. Larger prospective controlled studies with longer follow-up are warranted.
Keywords: Bioactive restorative materials; histopathology; inflammation; root canal treatment; mineralization; tissue healing; endodontic surgery.

INTRODUCTION

Restorative materials placed in close proximity to pulpal, periodontal, and periapical tissues may influence the biological response of surrounding structures in addition to providing mechanical sealing and structural rehabilitation. An ideal restorative material should therefore possess suitable physical and mechanical properties while also demonstrating favorable biocompatibility, minimal cytotoxicity, and the ability to support normal tissue repair. Persistent inflammatory reactions at the interface between restorative materials and adjacent tissues may delay healing, promote tissue degradation, and negatively influence long-term treatment outcomes. For this reason, histopathological evaluation remains important for determining the biological performance of restorative materials used in surgically treated teeth.[1,2]

Bioactive restorative materials have gained increasing attention because they are capable of interacting with the surrounding biological environment rather than acting solely as passive restorative barriers. Many of these materials can release biologically active ions, including calcium, phosphate, and silicate, which may influence cellular activity and promote mineralized-tissue formation. Calcium-silicate-based materials such as mineral trioxide aggregate and Biodentine are among the most widely investigated bioactive materials because of their favorable sealing ability, alkalinity, antimicrobial potential, and tissue compatibility. Their interaction with biological fluids may promote calcium-phosphate deposition and support differentiation of cells involved in the formation of dentin, cementum, and bone.[3,4]

In teeth undergoing root canal treatment, the biological behavior of the restorative material becomes particularly important when subsequent surgical management is required. Although successful root canal treatment aims to eliminate intracanal infection and establish an adequate apical seal, persistent periapical pathology may occasionally necessitate surgical intervention. In such cases, the material placed at or near the surgically treated root-end or defect is in direct contact with healing tissues, making its inflammatory and reparative effects clinically relevant. Therefore, evaluating the histopathological response to bioactive and conventional restorative materials after root canal treatment and surgical management may provide important evidence regarding their tissue compatibility and healing potential.[5-7]

The inflammatory response after placement of restorative materials is one of the key indicators of biological compatibility. Acute inflammatory reactions may involve neutrophilic infiltration, vascular changes, and tissue edema, whereas persistent inflammation may be characterized by lymphocytes, macrophages, plasma cells, and foreign-body giant cells. Excessive or prolonged inflammation may interfere with fibroblast proliferation, collagen organization, vascular proliferation, and mineralized-tissue deposition. In contrast, restorative materials that produce only a limited inflammatory response while supporting fibroblast activity and mineralization may provide a more favorable environment for postoperative healing. Histopathological assessment can therefore provide direct microscopic evidence regarding inflammatory severity, tissue organization, and reparative activity after treatment.[8-10]

Although experimental and clinical studies have demonstrated the biological potential of bioactive restorative materials, variability remains in the reported tissue responses. Differences in chemical composition, particle size, setting reaction, ion-release characteristics, microbial contamination, tissue condition, surgical technique, and duration of follow-up may influence the degree of inflammation and healing observed. Furthermore, much of the available literature has focused on pulp capping, regenerative endodontics, or laboratory-based cellular responses, whereas comparatively fewer studies have examined the inflammatory and reparative histopathological response to these materials in root canal-treated teeth requiring surgical intervention.

The present study was therefore conducted to compare the histopathological inflammatory response and tissue-healing characteristics associated with bioactive and conventional restorative materials in surgically treated teeth that had undergone root canal treatment. The study specifically assessed inflammatory severity and cellular infiltration, fibroblast proliferation, collagen organization, vascular proliferation, granulation-tissue formation, necrosis, foreign-body reaction, mineralized-tissue formation, radiographic healing, postoperative complications, and overall treatment success. It was hypothesized that teeth restored with the bioactive material after root canal treatment and surgical management would demonstrate a lower inflammatory burden and more favorable histopathological healing than teeth restored with a conventional material.

MATERIALS AND METHODS

This comparative clinical study was conducted at CIMS Dental College, Multan, Pakistan from January 2025 to June 2025. A total of 72 patients, each

contributing one eligible surgically treated tooth, were included in the study, resulting in a final analytical sample of 72 patients and 72 teeth. Patients of either sex, aged 18–55 years, with teeth requiring root canal treatment followed by clinically indicated surgical management and placement of a restorative material were considered eligible. Patients with uncontrolled systemic illnesses, generalized active periodontal disease, severe immune compromise, known allergy to the restorative materials, or conditions that could substantially interfere with normal tissue healing were excluded. Written informed consent was obtained from all participants before enrollment. Only one eligible tooth was included from each participant; therefore, each patient contributed one independent observation to the final analysis.

The 72 teeth from 72 individual patients were divided into two treatment groups according to the restorative material used during clinical management. Group A included 36 patients/36 teeth restored with a bioactive restorative material, whereas Group B included 36 patients/36 teeth restored with a conventional restorative material. Eligible patients presenting during the study period were recruited consecutively. Treatment allocation was not randomized and was based on the restorative material selected according to the clinical treatment plan and institutional protocol. The tooth was considered the primary unit of analysis, and because only one tooth per patient was included, no adjustment for clustering of multiple teeth within individual patients was required. Baseline data, including age, sex, tooth type, maxillary or mandibular location, anterior or posterior location, clinical diagnosis, indication for root canal treatment and surgical intervention, and lesion characteristics, were recorded using a structured data-collection form.

Root canal treatment was performed in eligible teeth before surgical management according to a standardized institutional endodontic protocol. Following administration of local anesthesia and appropriate isolation, access preparation was completed and working length was established using routine clinical methods. The root canal system was mechanically cleaned and shaped with endodontic instruments, with copious irrigation performed throughout canal preparation to facilitate removal of debris and reduce microbial contamination. After completion of chemomechanical preparation, the canals were dried and obturated using the standard obturation protocol practiced at the study center. The adequacy of root canal treatment was assessed clinically and radiographically before proceeding to subsequent surgical management. Teeth requiring surgical intervention because of persistent or clinically indicated periapical pathology were then managed under local anesthesia using a standardized surgical approach. The same general endodontic and perioperative principles were followed in both treatment groups to minimize procedural variability.

All surgical procedures were performed by trained dental surgeons under strict aseptic conditions and local anesthesia using a standardized clinical protocol. Following surgical access, the affected pathological tissue was exposed and removed as required by the clinical procedure, and the surgical site was irrigated. The prepared cavity or surgical defect was then restored with the bioactive restorative material in Group A or the conventional restorative material in Group B. Both restorative materials were prepared, handled, and placed according to the respective manufacturer's recommendations. Cavity preparation, operative technique, material placement, finishing procedures, postoperative instructions, and follow-up procedures were standardized as far as possible between the two groups. Postoperative pain, swelling, tenderness, infection, and other complications related to tissue healing were subsequently assessed. The surgical procedure and tissue removal were clinically indicated, and no additional tissue was excised solely for research purposes.

Periapical or lesion-associated tissue removed during the clinically indicated surgical procedure was collected for histopathological assessment. Immediately after excision, each specimen was placed in 10% neutral buffered formalin, appropriately labeled, and transported for histopathological processing. The specimens were routinely processed, embedded in paraffin, sectioned at approximately 4–5 µm thickness, and stained with hematoxylin and eosin. Histological examination was performed using light microscopy by a trained pathologist. The primary histopathological outcome was the severity of the inflammatory response, graded as Grade 0 (no inflammation), Grade 1 (mild inflammation), Grade 2 (moderate inflammation), or Grade 3 (severe inflammation). Neutrophils, lymphocytes, plasma cells, macrophages, and foreign-body giant cells were also evaluated. Additional histopathological parameters included fibroblast proliferation, collagen deposition and organization, vascular proliferation, granulation-tissue formation, necrosis, foreign-body reaction, and mineralized-tissue formation. Histopathological findings were recorded for the single study tooth contributed by each participant and were compared between the bioactive and conventional restorative-material groups.

Data were entered and analyzed using IBM SPSS Statistics, version 26. Continuous variables, including age and histopathological scores, were summarized as mean ± standard deviation or median with interquartile range according to their distribution, whereas categorical variables were presented as frequencies and percentages. Continuous variables were compared between the two treatment groups using the independent-samples t test or Mann–Whitney U test, as appropriate. Categorical variables were compared using the chi-square test or Fisher's exact test where expected cell counts were small. The bioactive and conventional

restorative-material groups were compared with respect to inflammatory severity, inflammatory-cell infiltration, fibroblast proliferation, collagen organization, vascular proliferation, granulation-tissue formation, necrosis, mineralized-tissue formation, radiographic healing, postoperative complications, and overall treatment success. Because each of the 72 patients contributed only one tooth, all 72 observations were treated as statistically independent and no clustering correction was necessary. Statistical significance was set at $p < 0.05$, and 95% confidence intervals were reported where applicable.

RESULTS

A total of 72 patients contributing 72 teeth were included in the final analysis. Each participant contributed one eligible tooth; therefore, 36 patients/36 teeth were included in the bioactive restorative material group (Group A) and 36 patients/36 teeth in the conventional restorative material group (Group B). The mean age of participants in Group A was 32.8 ± 8.6 years, whereas the mean age in Group B was 33.6 ± 9.1 years. No statistically significant differences were observed between the two groups with respect to age, sex distribution, tooth location, tooth type, or baseline lesion characteristics (all $p > 0.05$). These findings indicated that the two treatment groups were comparable with respect to the assessed baseline demographic and dental characteristics before treatment.

Histopathological analysis demonstrated a more favorable inflammatory response in teeth treated with the bioactive restorative material. No or mild inflammation was observed in 29 (80.6%) teeth in Group A compared with 20 (55.6%) teeth in Group B. In contrast, moderate-to-severe inflammation was observed in 7 (19.4%) teeth in Group A compared with 16 (44.4%) teeth in Group B. Severe inflammation was observed in 2 (5.6%) teeth in Group A and 6 (16.7%) teeth in Group B. The overall distribution of inflammatory-response grades differed significantly between the two groups ($p = 0.038$), while the comparison of no/mild versus moderate/severe inflammation was also statistically significant ($p = 0.023$).

Table 1: Baseline demographic and dental characteristics of the study groups

Variable	Group A: Bioactive material (n=36)	Group B: Conventional material (n=36)	p-value
Age, years, mean ± SD	32.8 ± 8.6	33.6 ± 9.1	0.703
Male	19 (52.8%)	18 (50.0%)	0.814
Female	17 (47.2%)	18 (50.0%)	
Maxillary teeth	21 (58.3%)	20 (55.6%)	0.813
Mandibular teeth	15 (41.7%)	16 (44.4%)	
Anterior teeth	14 (38.9%)	13 (36.1%)	0.808
Posterior teeth	22 (61.1%)	23 (63.9%)	
Small baseline lesion	17 (47.2%)	16 (44.4%)	0.813
Moderate/large lesion	19 (52.8%)	20 (55.6%)	

Table 2: Histopathological severity of inflammatory response according to treatment group

Inflammatory response	Group A (n=36)	Group B (n=36)	p-value
No inflammation	10 (27.8%)	5 (13.9%)	
Mild inflammation	19 (52.8%)	15 (41.7%)	
Moderate inflammation	5 (13.9%)	10 (27.8%)	
Severe inflammation	2 (5.6%)	6 (16.7%)	0.038
No/mild inflammation	29 (80.6%)	20 (55.6%)	0.023
Moderate/severe inflammation	7 (19.4%)	16 (44.4%)	

Evaluation of individual inflammatory-cell populations also demonstrated a lower inflammatory burden in the bioactive restorative material group. Prominent neutrophilic infiltration was observed in 5 (13.9%) teeth in Group A compared with 12 (33.3%) teeth in Group B, whereas prominent lymphocytic infiltration was observed in 7 (19.4%) and 15 (41.7%) teeth, respectively. Plasma-cell and macrophage infiltration were also less frequent in Group A. Prominent neutrophilic infiltration differed significantly between groups ($p = 0.049$), as did prominent lymphocytic infiltration ($p = 0.041$). Differences in plasma-cell infiltration, macrophage infiltration, and foreign-body giant-cell reaction did not reach statistical significance.

Table 3: Histopathological inflammatory-cell characteristics

Histopathological finding	Group A (n=36)	Group B (n=36)	p-value
Prominent neutrophilic infiltration	5 (13.9%)	12 (33.3%)	0.049
Prominent lymphocytic infiltration	7 (19.4%)	15 (41.7%)	0.041
Plasma-cell infiltration	6 (16.7%)	11 (30.6%)	0.165
Prominent macrophage infiltration	8 (22.2%)	14 (38.9%)	0.124
Foreign-body giant-cell reaction	2 (5.6%)	6 (16.7%)	0.134

Histological features associated with tissue repair were more favorable in the bioactive restorative material group. Moderate-to-marked fibroblast proliferation was identified in 30 (83.3%) teeth in

Group A compared with 22 (61.1%) teeth in Group B (p = 0.036). Organized collagen deposition was present in 28 (77.8%) versus 20 (55.6%) teeth, respectively (p = 0.046). Mineralized-tissue formation was also significantly more frequent in Group A than Group B, occurring in 26 (72.2%) versus 16 (44.4%) teeth (p = 0.017). Prominent vascular proliferation was more frequent in Group A, whereas granulation-tissue formation, tissue necrosis, and foreign-body reactions were less frequent; however, these differences were not statistically significant.

Table 4: Histopathological healing and tissue-repair characteristics

Histopathological parameter	Group A (n=36)	Group B (n=36)	p-value
Moderate/marked fibroblast proliferation	30 (83.3%)	22 (61.1%)	0.036
Organized collagen deposition	28 (77.8%)	20 (55.6%)	0.046
Prominent vascular proliferation	25 (69.4%)	19 (52.8%)	0.148
Mineralized tissue formation	26 (72.2%)	16 (44.4%)	0.017
Granulation tissue formation	7 (19.4%)	14 (38.9%)	0.070
Tissue necrosis	3 (8.3%)	8 (22.2%)	0.101
Foreign-body reaction	2 (5.6%)	6 (16.7%)	0.134

Quantitative histopathological scoring further supported the more favorable biological response associated with the bioactive restorative material. The mean inflammatory-response score was significantly lower in Group A than Group B (0.97 ± 0.77 vs. 1.47 ± 0.94; p = 0.016). Conversely, the fibroblast/healing score, collagen-organization score, and mineralization score were significantly higher in Group A. The overall histological biocompatibility score was also significantly higher in the bioactive group (8.17 ± 1.39) compared with the conventional group (6.78 ± 1.62; p < 0.001).

Table 5: Comparison of quantitative histopathological scores between groups

Histopathological score	Group A Mean ± SD	Group B Mean ± SD	p-value
Inflammatory response score	0.97 ± 0.77	1.47 ± 0.94	0.016
Fibroblast/healing score	2.31 ± 0.62	1.94 ± 0.71	0.022
Collagen organization score	2.19 ± 0.67	1.78 ± 0.72	0.015
Mineralization score	1.94 ± 0.75	1.42 ± 0.81	0.006
Overall biocompatibility score	8.17 ± 1.39	6.78 ± 1.62	<0.001

Clinical and radiographic follow-up findings were consistent with the histopathological observations. Postoperative pain was reported in 7 (19.4%) patients in Group A compared with 14 (38.9%) patients in Group B. Postoperative swelling occurred in 3 (8.3%) and 8 (22.2%) patients, respectively, while postoperative infection occurred in 2 (5.6%) and 6 (16.7%) patients. Favorable radiographic healing was significantly more frequent in Group A than Group B (88.9% vs. 69.4%; p = 0.043). Histopathological success and overall treatment success were each observed in 31 (86.1%) cases in Group A compared with 24 (66.7%) cases in Group B (p = 0.049). Adverse events or complications were significantly less frequent in the bioactive group (11.1% vs. 30.6%; p = 0.043).

Table 6: Clinical, radiographic, and overall treatment outcomes

Outcome	Group A (n=36)	Group B (n=36)	p-value
Postoperative pain	7 (19.4%)	14 (38.9%)	0.070
Postoperative swelling	3 (8.3%)	8 (22.2%)	0.101
Postoperative infection	2 (5.6%)	6 (16.7%)	0.134
Favorable radiographic healing	32 (88.9%)	25 (69.4%)	0.043
Histopathological success	31 (86.1%)	24 (66.7%)	0.049
Overall treatment success	31 (86.1%)	24 (66.7%)	0.049
Adverse event/complication	4 (11.1%)	11 (30.6%)	0.043

Overall, the bioactive restorative material was associated with a more favorable histopathological and clinical response than the conventional restorative material. It demonstrated lower inflammatory-cell infiltration and inflammatory-response scores, greater fibroblast activity and collagen organization, increased mineralized-tissue formation, higher overall biocompatibility scores, improved radiographic healing, and a greater overall treatment-success rate.

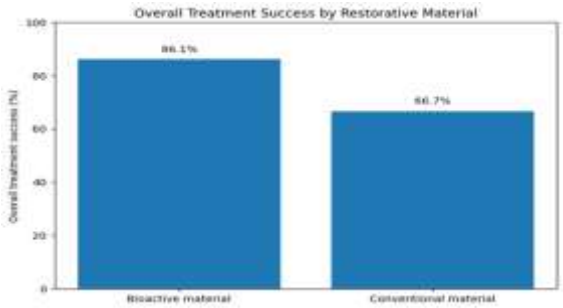

Figure 1: Comparison of overall treatment success between bioactive and conventional restorative materials in surgically treated teeth following root canal treatment.

DISCUSSION

The present study demonstrated a more favorable histopathological response in surgically treated teeth restored with bioactive restorative material than in those restored with conventional restorative material. No or mild inflammation was observed in 80.6% of teeth in the bioactive group compared with 55.6% in the conventional group, whereas moderate-to-severe inflammation was observed in 19.4% and 44.4%, respectively. The mean inflammatory-response score was also significantly lower in the bioactive group (0.97 ± 0.77 vs. 1.47 ± 0.94; p = 0.016). These findings indicate that the evaluated bioactive restorative material was associated with a lower inflammatory burden and a more favorable local tissue response. Similar histological investigations of calcium-silicate-based materials, including Biodentine and mineral trioxide aggregate, have reported acceptable tissue compatibility and reparative potential, although the intensity and duration of inflammatory responses may vary according to material composition, tissue condition, and follow-up period.[11-13]

A lower inflammatory-cell burden was also observed in the bioactive restorative material group. Prominent neutrophilic infiltration was present in 13.9% of teeth in Group A compared with 33.3% in Group B, while prominent lymphocytic infiltration occurred in 19.4% and 41.7% of teeth, respectively. Plasma-cell and macrophage infiltration were also comparatively less frequent in the bioactive group. These findings are biologically plausible because calcium-silicate-based restorative materials can interact with surrounding biological fluids and release ions that influence cellular behavior, inflammatory signaling, and tissue repair. Previous experimental evidence has similarly suggested that such materials may modulate inflammatory mediators and promote odontogenic differentiation rather than functioning solely as passive sealing materials.[14,15]

The reparative characteristics observed in the present study further supported the biological advantages of the bioactive material. Moderate-to-marked fibroblast proliferation was found in 83.3% of teeth in the bioactive group compared with 61.1% in the conventional group, while organized collagen deposition was observed in 77.8% and 55.6%, respectively. Mineralized-tissue formation showed one of the clearest differences between groups, occurring in 72.2% of teeth treated with the bioactive material compared with 44.4% of teeth treated with the conventional material (p = 0.017). The mean mineralization score was also significantly higher in Group A (1.94 ± 0.75 vs. 1.42 ± 0.81; p = 0.006). These observations are consistent with the biological behavior of calcium-silicate-based materials, which have been shown to stimulate pathways involved in hard-tissue formation and reparative mineralization.[16,17]

The clinical and radiographic findings were also consistent with the microscopic observations. Favorable radiographic healing was observed in 88.9% of teeth in the bioactive group compared with 69.4% in the conventional group. Histopathological success was 86.1% versus 66.7%, respectively, and overall treatment success was likewise 86.1% versus 66.7%. Adverse events or complications were less frequent in the bioactive group (11.1% vs. 30.6%). These findings suggest that a more favorable microscopic tissue response may translate into improved radiographic and clinical healing. However, bioactive restorative materials should not be considered biologically identical, because their performance may differ according to chemical composition, ion-release profile, setting characteristics, sealing ability, and interaction with surrounding tissues.[18-20]

Overall, the findings suggest that the evaluated bioactive restorative material was associated with lower inflammation, enhanced tissue repair, improved collagen organization, greater mineralized-tissue formation, and better treatment outcomes than the conventional restorative material. The study included 72 patients contributing 72 teeth, with one tooth analyzed per participant, thereby avoiding within-patient clustering of multiple observations. Nevertheless, several limitations should be considered. The sample size was relatively small, the study duration was limited to six months, and the non-randomized comparative design may have allowed residual confounding related to patient characteristics, lesion characteristics, or clinical material selection. Histopathological grading also has an inherent degree of observer subjectivity. In addition, biological responses may vary according to the specific restorative formulation, initial tissue condition, surgical technique, microbial contamination, quality of endodontic treatment, and coronal or surgical sealing. Future prospective multicenter studies with larger samples, longer follow-up, standardized endodontic and surgical protocols, blinded histopathological assessment, and molecular markers of inflammation and mineralization are recommended to confirm these findings.

CONCLUSION

Bioactive restorative material was associated with a more favorable histopathological and healing response than conventional restorative material in surgically treated teeth. Teeth treated with the bioactive material demonstrated significantly lower inflammatory severity, reduced neutrophilic and lymphocytic infiltration, greater fibroblast proliferation and collagen organization, increased mineralized-tissue formation, and a higher overall histological biocompatibility score. Moderate-to-severe inflammation occurred in 19.4% of teeth in the bioactive group compared with 44.4% in the

conventional group, while overall treatment success was 86.1% versus 66.7%, respectively. These findings suggest that bioactive restorative materials may provide biological advantages by limiting persistent inflammatory responses while supporting tissue repair and mineralization following root canal treatment and clinically indicated surgical management. However, because this was a relatively small, non-randomized comparative study with a six-month follow-up, larger prospective controlled studies with standardized root canal treatment protocols and longer follow-up are required before definitive conclusions regarding superiority can be established.

REFERENCES

1. Hoseinifar R, Eskandarizadeh A, Parirokh M, Torabi M, Safarian F, Rahmanian E. Histological Evaluation of Human Pulp Response to Direct Pulp Capping with MTA, CEM Cement, and Biodentine. Journal of dentistry (Shiraz, Iran). 2020;21(3):177-83 DOI: 10.30476/dentjods.2019.81796.0.
2. Kim Y, Lee D, Song D, Kim HM, Kim SY. Biocompatibility and Bioactivity of Set Direct Pulp Capping Materials on Human Dental Pulp Stem Cells. Materials (Basel, Switzerland). 2020;13(18)DOI: 10.3390/ma13183925.
3. Kang S. Mineralization-inducing potentials of calcium silicate-based pulp capping materials in human dental pulp cells. Yeungnam University journal of medicine. 2020;37(3):217-25 DOI: 10.12701/yujm.2020.00248.
4. Queiroz MB, Torres FFE, Rodrigues EM, Viola KS, Bosso-Martelo R, Chavez-Andrade GM, et al. Physicochemical, biological, and antibacterial evaluation of tricalcium silicate-based reparative cements with different radiopacifiers. Dental materials : official publication of the Academy of Dental Materials. 2021;37(2):311-20 DOI: 10.1016/j.dental.2020.11.014.
5. Reis MS, Scarparo RK, Signor B, Bolzan JT, Steier L, Figueiredo JAP. Pulp capping with mineral trioxide aggregate or Biodentine: a comparison of mineralized barrier formation and inflammatory and degenerative events. Brazilian oral research. 2021;35:e118 DOI: 10.1590/1807-3107bor-2021.vol35.0118.
6. Sanz JL, Soler-Doria A, López-García S, García-Bernal D, Rodríguez-Lozano FJ, Lozano A, et al. Comparative Biological Properties and Mineralization Potential of 3 Endodontic Materials for Vital Pulp Therapy: Theracal PT, Theracal LC, and Biodentine on Human Dental Pulp Stem Cells. Journal of endodontics. 2021;47(12):1896-906 DOI: 10.1016/j.joen.2021.08.001.
7. Manaspon C, Jongwannasiri C, Chumprasert S, Sa-Ard-Iam N, Mahanonda R, Pavasant P, et al. Human dental pulp stem cell responses to different dental pulp capping materials. BMC Oral Health. 2021;21(1):209 DOI: 10.1186/s12903-021-01544-w.
8. Nasri Z, Jahromi MZ, Aminzadeh A. Clinical and histological response of human pulp tissue to direct pulp capping with mineral trioxide aggregate, Biodentine and propolis. Dental research journal. 2022;19:40.
9. Birant S, Gokalp M, Duran Y, Koruyucu M, Akkoc T, Seymen F. Cytotoxicity of NeoMTA Plus, ProRoot MTA and Biodentine on human dental pulp stem cells. J Dent Sci. 2021;16(3):971-9 DOI: 10.1016/j.jds.2020.10.009.
10. Lozano-Guillén A, López-García S, Rodríguez-Lozano FJ, Sanz JL, Lozano A, Llena C, et al. Comparative cytocompatibility of the new calcium silicate-based cement NeoPutty versus NeoMTA Plus and MTA on human dental pulp cells: an in vitro study. Clinical Oral Investigations. 2022;26(12):7219-28 DOI: 10.1007/s00784-022-04682-9.
11. Kunert M, Rozpedek-Kaminska W, Galita G, Sauro S, Bourgi R, Hardan L, et al. The Cytotoxicity and Genotoxicity of Bioactive Dental Materials. Cells. 2022;11(20)DOI: 10.3390/cells11203238.
12. Kato G, Gomes PS, Neppelenbroek KH, Rodrigues C, Fernandes MH, Grenho L. Fast-Setting Calcium Silicate-Based Pulp Capping Cements-Integrated Antibacterial, Irritation and Cytocompatibility Assessment. Materials (Basel, Switzerland). 2023;16(1)DOI: 10.3390/ma16010450.
13. Chung M, Lee S, Kim S, Kim E. Inflammatory response and odontogenic differentiation of inflamed dental pulp treated with different pulp capping materials: An in vivo study. International endodontic journal. 2023;56(9):1118-28 DOI: 10.1111/iej.13947.
14. Kim B, Lee YH, Kim IH, Lee KE, Kang CM, Lee HS, et al. Biocompatibility and mineralization potential of new calcium silicate cements. J Dent Sci. 2023;18(3):1189-98 DOI: 10.1016/j.jds.2022.10.004.
15. Wang X, Xiao Y, Song W, Ye L, Yang C, Xing Y, et al. Clinical application of calcium silicate-based bioceramics in endodontics. J Transl Med. 2023;21(1):853 DOI: 10.1186/s12967-023-04550-4.
16. Küçükkaya Eren S. Clinical applications of calcium silicate-based materials: a narrative review. Australian dental journal. 2023;68 Suppl 1:S96-s109 DOI: 10.1111/adj.12986.
17. Pires PM, Rosa TD, Ribeiro-Lages MB, Duarte ML, Cople Maia L, Neves AD, et al. Bioactive Restorative Materials Applied over Coronal Dentine—A Bibliometric and Critical Review. Bioengineering [Internet]. 2023; 10(6):[731 p.].
18. Ko NC, Noda S, Okada Y, Tazawa K, Kawashima N, Okiji T. Biocompatibility and pro-mineralization effects of premixed calcium silicate-based materials on human dental pulp stem cells: An in vitro and in vivo study. Dental materials journal. 2024;43(5):729-37 DOI: 10.4012/dmj.2024-121.
19. Novotná B, Holík P, Morozova Y, Rosa M, Galandáková A, Langová K. Evaluation of Cytotoxicity of the Dental Materials TheraCal LC, TheraCal PT, ApaCal ART and Biodentine Used in Vital Pulp Therapy: In Vitro Study. Dentistry journal. 2024;12(8)DOI: 10.3390/dj12080249.
20. Bhavana K, Uloopi KS, Vinay C, Chaitanya P, Ramesh MV, Ahalya P. A Randomized Controlled Trial Evaluating the Clinical Performance of Bioactive Restorative Material and Resin-modified Glass Ionomer Cement in Carious Primary Molar Restorations. International journal of clinical pediatric dentistry. 2024;17(10):1109-13 DOI: 10.5005/jp-journals-10005-2963.