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Homologous and Autologous Injectable Platelet-Rich Fibrin with Hydroxyapatite for Periapical Healing in Uncontrolled Diabetes: A Systematic Review

Dr Surbhi Patel (PHD scholar)
Associate professor
Conservative dentistry and endodontics
MGVKBH dental College and hospital Nashik
Dr Aditya Patel (Supervisor)
HOD professor, Conservative dentistry and endodontics, SPDC Wardha (Sawangi)
Dr Pawan Patel
HOD professor, Conservative dentistry and endodontics, SMBT IDSR Dhamangaon Nashik
Dr Shrunkhal Bhupal
Sr lecturer, Conservative dentistry and endodontics, MGVKBH dental College and hospital Nashik
Dr Swati Pustake
Professor, Prosthodontics MGVKBH dental College and hospital Nashik

***Corresponding Author:**
Dr Surbhi Patel (PHD scholar)
Associate Professor, Conservative dentistry and endodontics,
MGVKBH dental College and hospital Nashik

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Abstract

Uncontrolled diabetes mellitus compromises periapical healing by impairing angiogenesis and bone remodeling. Injectable platelet-rich fibrin, especially when combined with hydroxyapatite, enhances regeneration, while homologous platelet concentrates may offer advantages over autologous preparations in diabetic patients.

Aim:

To systematically evaluate available evidence on the role of autologous and homologous injectable platelet-rich fibrin, alone or polymerized with hydroxyapatite, in enhancing periapical healing in uncontrolled diabetic patients.

Materials and Methods:

A systematic review was conducted according to PRISMA guidelines. Electronic searches were performed using PubMed, MEDLINE (Ovid), Cochrane Library, and Google Scholar for studies published in indexed journals within the last 15 years.

Results:

Out of 20 identified articles, 11 met the inclusion criteria and were included for qualitative synthesis. The included studies demonstrated favorable regenerative outcomes with i-PRF and hydroxyapatite individually; however, no clinical study directly compared homologous and autologous i-PRF for periapical healing in uncontrolled diabetic patients.

Conclusion:

Injectable platelet-rich fibrin polymerized with hydroxyapatite appears to be a promising regenerative adjunct in compromised healing conditions. The lack of comparative clinical evidence between homologous and autologous i-PRF in uncontrolled diabetic patients represents a significant gap in current literature.

Keywords: Injectable platelet-rich fibrin, hydroxyapatite, uncontrolled diabetes mellitus, homologous PRF, autologous PRF, periapical healing

Introduction

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by persistent hyperglycemia and associated microvascular and immunological disturbances. Poor glycemic control adversely affects collagen synthesis, angiogenesis, and bone metabolism, thereby impairing wound healing. In endodontics, uncontrolled diabetes has been consistently associated with an increased prevalence of apical periodontitis and delayed periapical repair following root canal treatment[1–3].

Epidemiological studies have reported a significantly higher incidence of apical periodontitis among diabetic patients compared with non-diabetic individuals, indicating that diabetes acts as a disease modifier rather than a coincidental finding[4]. Periapical healing requires effective microbial elimination, resolution of inflammation, vascular ingrowth, and new bone formation—processes that are markedly compromised in uncontrolled diabetic patients.

Conventional endodontic materials such as calcium hydroxide, mineral trioxide aggregate, and bioceramic sealers demonstrate predictable outcomes in systemically healthy individuals; however, their regenerative effectiveness may be limited in medically compromised patients. Consequently, biologically active regenerative approaches have gained increasing attention.

Injectable platelet-rich fibrin (i-PRF) has emerged as a promising regenerative biomaterial due to its sustained release of growth factors and ability to enhance tissue repair. When polymerized with hydroxyapatite, i-PRF combines biological stimulation with mechanical scaffold support, offering potential advantages for periapical regeneration in compromised systemic conditions.

Materials and Methods

Protocol and Reporting

This systematic review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Search Strategy

Electronic literature searches were performed using PubMed, MEDLINE (Ovid), Cochrane Library, and Google Scholar. The search strategy included combinations of Medical Subject Headings (MeSH) terms and keywords such as injectable platelet-rich fibrin, platelet concentrates, autologous PRF, homologous PRF, allogeneic platelets, hydroxyapatite bone graft, diabetes mellitus, periapical healing, and endodontic treatment.

Inclusion Criteria

1. Studies published in indexed journals
2. Human studies evaluating platelet concentrates in bone, periodontal, or periapical regeneration
3. Studies involving diabetic or systemically compromised healing conditions
4. Original research articles, systematic reviews, and narrative reviews

Exclusion Criteria

1. Non-indexed journals
2. Incomplete abstracts
3. Studies unrelated to regenerative outcomes
4. Animal studies with limited clinical relevance

Study Selection

A total of 20 articles were initially identified. After title and abstract screening, 9 articles were excluded due to irrelevance or weak methodology. Eleven studies were included for qualitative synthesis (PRISMA flow diagram: Figure 1).

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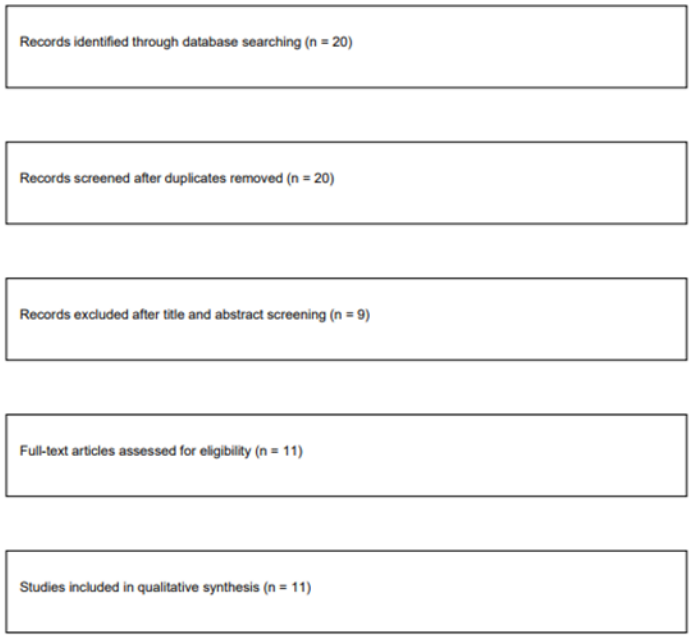
PRISMA flow diagram: Figure 1



Results

Characteristics of Included Studies

Among the 11 included studies:

1. Seven were original research articles
2. One was a systematic review
3. One was a narrative review
4. Two were clinical or translational studies

The majority of studies focused on periodontal regeneration, orthopedic bone healing, or diabetic wound management. Direct clinical evidence addressing periapical healing in uncontrolled diabetic patients was limited.

Injectable Platelet-Rich Fibrin and Periapical Healing

Platelet-rich fibrin is a second-generation platelet concentrate composed of a fibrin matrix enriched with platelets, leukocytes, and growth factors. Injectable PRF is obtained using low-speed centrifugation and remains in liquid form before gradually polymerizing, allowing superior adaptation to osseous defects[7,8].

Clinical reports have demonstrated enhanced bone formation and accelerated healing when PRF is used as an adjunct in periapical surgery[9]. However, most available evidence is derived from studies involving systemically healthy individuals.

Autologous Injectable Platelet-Rich Fibrin

Autologous i-PRF is derived from the patient's own blood and is widely used due to its excellent biocompatibility and minimal immunological risk. Nevertheless, uncontrolled diabetes is associated with altered platelet function, abnormal platelet indices, and reduced growth factor release, which may compromise the regenerative potential of autologous platelet concentrates[10].

Although autologous PRF has demonstrated favorable outcomes in periodontal and periapical regeneration, its effectiveness in uncontrolled diabetic patients remains uncertain.

Homologous Injectable Platelet-Rich Fibrin

Homologous platelet concentrates obtained from healthy, screened donors provide standardized platelet content and preserved biological activity. Experimental and clinical studies have demonstrated enhanced osteoblast proliferation and bone regeneration with homologous platelet preparations[11,12].

Clinical investigations in orthopedic and wound-healing applications have reported acceptable safety profiles for homologous PRP[13]. In diabetic wound management, allogeneic platelet concentrates have been proposed as an effective alternative to autologous

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preparations due to impaired platelet function in diabetic patients[14]. Recent literature highlights the expanding role of allogeneic platelets in regenerative medicine[15].

Role of Hydroxyapatite in Platelet-Based Regeneration

Hydroxyapatite is an osteoconductive biomaterial widely used in regenerative dentistry due to its chemical similarity to natural bone mineral. It provides a stable scaffold that supports cellular adhesion and new bone formation. When combined with i-PRF, hydroxyapatite enhances fibrin stability and prolongs growth factor release[16].

Clinical trials have demonstrated improved outcomes when i-PRF is polymerized with hydroxyapatite compared to hydroxyapatite alone in intrabony defects[17]. However, evidence supporting its use in periapical healing among uncontrolled diabetic patients is limited.

Discussion

This systematic review highlights the biological plausibility and clinical potential of injectable platelet-rich fibrin polymerized with hydroxyapatite for enhancing periapical healing, particularly in patients with uncontrolled diabetes mellitus.

Diabetes-related impairment of angiogenesis, immune response, and bone remodeling significantly delays periapical repair and reduces the success of conventional endodontic treatment. Platelet-based regenerative strategies offer a biological means to deliver growth factors directly to the site of tissue injury, potentially compensating for impaired host healing capacity.

Autologous i-PRF, although widely accepted, may exhibit reduced regenerative efficacy in uncontrolled diabetic patients due to intrinsic platelet dysfunction and diminished growth factor bioavailability. In contrast, homologous i-PRF derived from healthy donors provides standardized platelet quality and preserved biological activity, which may translate into improved regenerative outcomes in such patients.

The incorporation of hydroxyapatite provides mechanical stability, space maintenance, and osteoconductive support, further enhancing the regenerative environment. The synergistic interaction between biological stimulation from i-PRF and scaffold support from hydroxyapatite may be particularly beneficial for large or chronic periapical defects.

Despite encouraging indirect evidence from periodontal, orthopedic, and diabetic wound-healing studies, direct comparative clinical data evaluating homologous versus autologous i-PRF in periapical healing among uncontrolled diabetic patients are lacking. This represents a clear knowledge gap and methodological gap in existing literature.

Conclusion

Based on available evidence, injectable platelet-rich fibrin polymerized with hydroxyapatite appears to be a promising regenerative adjunct for enhancing periapical healing in compromised systemic conditions. Homologous platelet concentrates may offer potential advantages over autologous preparations in uncontrolled diabetic patients. Well-designed randomized controlled clinical trials are required to establish definitive evidence and guide clinical practice.

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