Autologous Platelet Concentrates for Pulp and Dentin Regeneration: A Literature Review of Animal Studies

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Abstract

Introduction: The purpose of this study was to evaluate the effectiveness of autologous platelet concentrates (APCs) in promoting pulp and dentin regeneration in animal models. **Methods:** An electronic search was performed on MEDLINE, Embase, Scopus, SciELO, LILACS, and CENTRAL. Animal studies using APC as a root filling material after pulpectomy in mature or immature teeth were included. Articles underwent risk of bias assessment. Histologic evaluation of intracanal neoformed tissue was the primary outcome; root development, root wall thickening, apical closure, and periapical healing in apical periodontitis were the secondary outcomes. **Results:** Seven articles were included. Platelet-rich plasma (PRP) was used as root filling material during regenerative procedures in the experimental group in either mature or immature teeth. After revascularization with PRP alone or in conjunction with stem cells of a different source, the histologic analyses revealed that, in addition to an odontoblastic cell layer or dentinlike structure, the neoformed intracanal tissues were mainly cementumlike, bonelike, and connective tissues. **Conclusions:** True regeneration of necrotic pulp may not be achieved with current techniques using PRP, all of which stimulated tissue repair. Benefits of PRP adjunct for pulp tissue regeneration in preclinical studies remain unclear. Further studies with standardized protocols are necessary to assess the actual contribution of PRP in endodontic regenerative therapies. *(J Endod 2016;42:250–257)*

Key Words

Endodontic regeneration, immature teeth, platelet-rich plasma, pulpectomy

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The goal of tissue regeneration is to form a new tissue with the same anatomy and function as the original one (1). Regenerative endodontic procedures rely on tissue engineering and are defined by the American Association of Endodontists as "biologically-based procedures designed to physiologically replace damaged tooth structures including dentin and root structures as well as cells of the pulp-dentin complex" (2). Although several approaches have been used to date, there is still no protocol able to achieve predictable endodontic tissue regeneration (3, 4).

In cases of immature teeth, the necrotic process involving pulp tissue halts further root development and condemns it to a lack of apical closure and reduced thickness of dentinal walls, which compromises the prognosis of the tooth. In the same manner, the pulp necrosis of mature teeth may produce tooth discoloration and infection of the periapical tissues, among other complications. Root canal therapy has been the traditional approach for mature necrotic teeth as well as for immature teeth after an apexification procedure. However, a vital pulp is critical for the maintenance of tooth homeostasis and longevity (4). In cases of absence of a functional pulp tissue and vascular perfusion, the root canal is not able to support the new tissue formation on its own (5–7). Consequently, current revascularization procedures using blood clot or hemocomponents represent an aid for the management of necrotic teeth.

Regeneration of pulp tissue may be enhanced by the combination of the patient's own growth factors and bioscaffold. Autologous platelet concentrates (APCs) have recently emerged as a possible tool for enhancing regeneration procedures in the medical field; APCs gained popularity among oral and maxillofacial surgeons as well as in other fields such as orthopedics, plastic surgery, and sports medicine, assuming an important role for increasing the predictability of hard and soft tissue regeneration procedures (8–13). APCs are hemocomponents obtained through the centrifugation of a blood sample of the patient. The basic concept of this technology is to collect the most active components of the blood sample (eg, platelets, fibrin, and in certain cases leukocytes). This process produces a very high-concentration gradient of platelets whose granules are rich with many substances fundamental to promote the healing process including adhesive proteins; procoagulant factors; cytokines and chemokines; antimicrobial proteins; and a number of mitogenic growth factors such as platelet-derived growth factors, transforming growth factor-beta, epidermal growth factors, and vascular endothelial growth factors (14–17), which may trigger angiogenesis and improve tissue vascularization. The APCs can be classified based on the fibrin architecture and cellular content as follows: platelet-rich plasma (PRP) with or without leukocytes (L-PRP and P-PRP, respectively) and platelet-rich fibrin (PRF) with or without leukocytes (L-PRF and P-PRF) (18). L-PRP is characterized by the presence of leukocytes and a high platelet concentration (up to 5–8 times the baseline value). It is prepared from anticoagulated blood undergoing a double centrifugation step and requires an activator before use. P-PRP is characterized by the absence of leukocytes and a modest increase in platelet concentration (2–3 times the baseline value). It is prepared from anticoagulated blood undergoing a single centrifugation step and requires an activator before use (14). L-PRF is characterized by the presence of most platelets and leukocytes in a dense fibrin matrix that does not require an activator before use (19). It is prepared from nonanticoagulated blood undergoing a single centrifugation step. The rational basis for the use of APCs for the treatment of depulped teeth rests on the assumption that the high concentration of growth factors represents a potent stimulation for tissue healing obtained through the patient's own

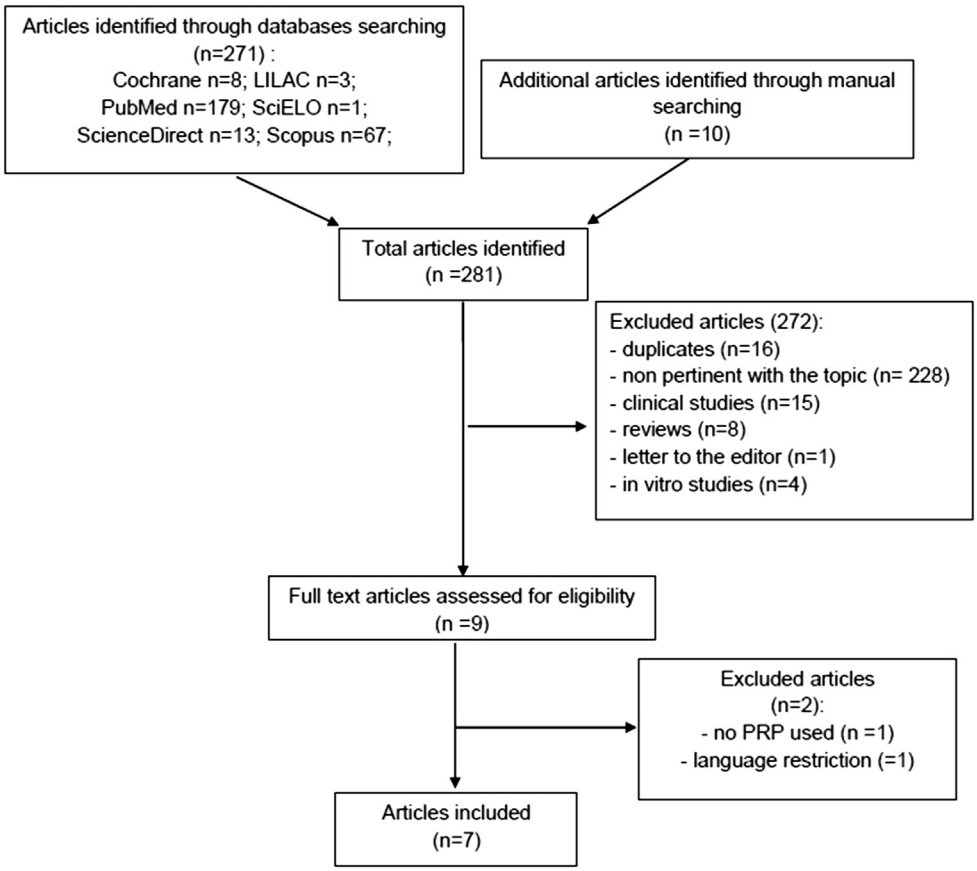

Figure 1. Flowchart of the article selection procedure.

molecules, mimicking the physiological process. In addition to granule content release, the polymerization of fibrinogen into a fibrin mesh forms a platelet gel or clot that is delivered to the surgical site (14).

Current protocols developed in the context of regenerative endodontic therapy aim at meeting the 3 main ingredients of tissue engineering: scaffold, growth factors, and stem cells. Specifically, fibrin within the blood clot or autologous platelet concentrates may act as a natural scaffold through which stem cells from the apical tissues may embed and repopulate the canal space. Growth factors released from an intracanal blood clot or APCs may modulate such cellular recruitment as well as stem cell proliferation and differentiation (20).

Early animal studies in beagle dogs treated using blood clot observed new tissue formation inside the root canal after revascularization (5, 21–24). In particular, Wang et al (21) in 2010 reported that neoformed intracanal tissues, after blood clot induction, in immature teeth consisted of cementoid and osteoid tissues (that were hypothesized to be responsible for root lengthening and thickening) and periodontal ligament–like tissue. Similar results have been shown in revitalization procedures in mature teeth (25). This suggested that the neoformed intracanal tissues may have little similarity to the healthy pulp tissue and raised the question whether the revascularization procedures with blood components might lead to pulp regeneration or just tissue repair.

The growth factors released by platelet concentrates proved to be effective in inducing angiogenesis and regeneration of different tissues and might therefore represent a useful tool for necrotic pulp treatment (26–28).

The aim of the present systematic review of the literature was to evaluate current preclinical evidence about the effectiveness of APCs in restoring the pulp-dentin complex of a necrotic tooth by promoting pulp and dentin tissue regeneration when they are used after pulpectomy.

Materials and Methods

Search Strategy

A systematic literature search was performed on the following electronic databases (PubMed, SCieLO, LILACS, ScienceDirect, Scopus, and Cochrane Central Register of Controlled Trials) using (platelet OR fibrin) AND (endodont* AND regenerat* OR apex*) as the search string. Once the studies were identified, the search was then restricted to only animal studies in which histologic outcomes were reported. An additional hand search of issues from 2000 up to the last issue available on December 15, 2014, including the "early view" (or equivalent) section was undertaken on the following journals: *Australian Endodontic Journal*; *Dental Traumatology*; *International Endodontic Journal*; *Journal of Endodontics*; and *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology and Endodontology*. The reference lists of the retrieved reviews and the included studies were also searched for possible additional eligible studies not identified by the electronic search. The last electronic search was performed on January 15, 2015. Only articles published in English were considered, and no restrictions regarding publication date were placed.

Inclusion Criteria

Animal studies assessing the effectiveness of APCs for stimulating the regeneration of pulp tissue and/or inducing radicular development