Impact of Autologous Platelet Concentrates on Replanted Teeth

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Autologous platelet concentrates (APCs) are produced by centrifuging the patient's own blood and injecting or topically injecting the isolated plasma, which is rich in grown factors, regenerative cells and leukocytes, into the wound or defect. Although majority of the studies indicate that autologous platelet concentrates (APCs) may improve outcomes of tooth replantation, majority of the studies contained numerous sources of bias. Additionally, the sample size of the included subjects is inadequate to predict the clinical efficacy of APCs in management of replanted teeth. Large-scale, multi-center and long-term studies are required to ascertain the efficacy of APCs in improve the outcomes of tooth replantation.

Keywords: tooth replantation ; autologous platelet ; platelet-rich fibrin ; platelet-rich plasma ; tooth avulsion

1. Introduction

Avulsion of a tooth occurs when it is completely dislodged from its socket as a result of trauma [1]. Replanting teeth that have been left out extra-orally for more than 60 min is very unlikely to survive, hence immediate replantation is the best therapy for tooth avulsion. Delaying replantation for more than fifteen minutes reduces the success probability of tooth replantation [2]. Additionally, in many cases, immediate replantation of the avulsed tooth is not possible, and tooth may be either kept in inappropriate storage media or left out to dry, leading to necrosis of the pulp and damage to the attached periodontal tissue on the root [1]. If quick replantation is not possible, the avulsed tooth should be stored in a suitable medium, such as saliva, milk, or Hank's Balanced Salt Solution (HBSS) [3][4]. However, due to the lack of awareness or unavailability of such media, many patients or their guardians bring the avulsed tooth in clinical improperly handled. Therefore, delayed replantation of teeth can lead to many complications such as resorption of the root and periapical periodontal tissues, ankylosis of the tooth and necrosis of the pulp [2]. According to studies, the rate of inflammatory root resorption following tooth replantation is as high as 23%, while the rate of replacement root resorption is around 51% [2]. To improve the outcomes of delayed tooth replantation, several treatments may be carried out. Pulpectomy involves the removal of the potentially necrotic pulp that may cause internal resorption [5]. Additionally, after pulpectomy calcium hydroxide (CH) paste or mineral trioxide aggregate may be placed in the canal for several days to prevent resorption and promote the formation of a calcific barrier in immature teeth with an open apex [6]. Furthermore, surface treatment with anti-resorptive agents such as sodium fluoride may decrease the likelihood of root or bone resorption post replantation [7]. Other drugs, such as bisphosphonates [8] and growth factors, such as fibroblast growth factor-2 (FGF-2) and enamel matrix derivative [9], have recently been studied for their potential anti-resorptive and regenerative effects, but no large-scale studies documenting their clinical efficacy have been published to date.

In dentistry, two generations of APCs have been studied. Platelet-rich plasma (PRP) are first generation APCs that are produce by double-spin centrifuging of the blood [10]. PRPs contain a high concentration of plarelets and growth factors that have been used to promote wound healing and periodontal regeneration. On the other hand, the second-generation platelet-rich fibrin (PRF) is produced by single-spin centrifuging and has the fibrin matrix network intact [10]. Efficacy of platelet concentrates in promoting wound healing and tissue regeneration is at the center of a recent academic debate [11]. Systematic reviews indicate that APCs promote root development and apical closure in immature or young permanent teeth [12][13][14]. Similarly, recently published case reports and animal studies indicate that APCs may improve the outcomes of tooth replantation [15][16]. However, no systematic review summarizing the outcomes and appraising quality of the literature focusing on the effect of ACs on the outcomes of tooth replantation has been published.

2. Current Insights

APCs have been utilized to treat pattern baldness [17] and enhance wound healing because to their regenerative capacity [18]. Their regenerative potential has been mainly attributed to the high concentration of platelets. Platelets emit many

regenerative growth factors, including platelet-derived growth factor (PDGF), transforming growth factor (TGF), and insulin-like growth factor-1 and -2 (IGF-1 and -2), which have been shown to enhance periodontal tissue regeneration [19][20][21]. Hence, it is not surprising that APCs have been studied for their potential in improving the outcomes of periodontal regeneration [22]. Similarly, three systematic reviews have been published that have focused on appraising and summarizing the literature on using APCs in regenerative endodontics [12][13][14]. Studies included in these reviews suggest that APCs may promote root formation and apical closure in immature teeth that have been treated endodontically [12][13][14]. However, in each of these reviews, only one study (by Priya et al. [23]) describing replantation of a tooth had been included.

Replantation of teeth may be carried out as a first line treatment of traumatically avulsed teeth [24] or to improve the prognosis of periodontally compromised or hopeless teeth [25]. In this entry, autologous platelet concentrates have been used to improve the outcomes of replantation in both the scenarios [15][23][26][27][28][29][30][31][32]. Using APCs to improve the outcomes of replantation is not new. A 1986 study by Nasjleti et al. observed effect of PRP on the cellular proliferation on and around teeth replanted 5 min after extraction in monkeys [33]. It is noteworthy to mention that the proliferative effects of autologous platelet have been documented in literature published more than three decades ago. In vitro studies have attempted the research the effect of APCs on avulsed teeth. Hiremath et al. studied the effects of PRF on the PDL cells attached on extracted teeth that been tried for an hour. They observed that a combined use of PPP and PRF stimulated the proliferation of PDL cells [34]. In vitro experiments by Zhou et al. have attempted to use autologous platelet in combination with stem cells to regenerate the attached periodontal tissue on avulsed teeth [35]. In the same research the researchers observed that PRF induced a higher expression of ALP, OCN, BSP and coll-1—all of which are biomarkers of bone and PDL regeneration [35]. However, the in vivo or clinical potential of using both APCs and stem cells are yet to be seen. Nevertheless, in all the case reports reviewed in this entry, autologous platelet usage resulted in favourable outcomes and no adverse effects were reported [15][23][26][27][28][29][30][31][32][36].

Perhaps, the most significant observation in the case reports is the amount of bone regeneration post-replantation after APC application. Tözüm et al. (2005) reported a decrease of a Class III mobility to Class I [26] and an improvement in bone levels of as much as 6 mm was reported by Demit et al. [27] after applying PRF in the socket. This bone regenerative potential of PRF has a significant clinical potential in improving the outcomes of teeth replanted because of severe periodontal bone loss or mobility. This is most likely because PRF has been observed to stimulate pro-osteoblastic factor RUNX and a reduction in the mineralization inhibitor MGT in vitro [37]. Furthermore, clinical studies suggest that a combined use of PRF and xenografts may improve outcomes of bone augmentation [38]. Similarly, one case report in this entry described the use of PRP in combination of a xenograft and a collagen membrane [30]. Therefore, PRP, in combination with other regenerative materials, holds potential in regenerating bone around periodontally compromised teeth that have been intentionally replanted. PRF is a second-generation APC and it is produced by a single spin during centrifugation [34] which is in contrast to the double-spin centrifugation needed to produce PRP [39]. The advantage of PRF is that the fibrin network is still intact and can release growth factor for a period of 7 to 14 days which is significantly better than the growth factor release duration of 14 h from PRP [11]. Due to its superior space-maintenance and mechanical integrity compared to PRP, PRF has an added advantage of functioning as a guided tissue regeneration (GTR) membrane. Nevertheless, one study has found no significant difference between the efficacy of PRP and PRF in periodontal regeneration [40]. Therefore, more studies are required before the superiority of PRF over PRP can be ascertained.

Replantation of teeth that have been left out extra-orally for extended periods of time present a particular challenge due to several factors. Firstly, dehydration of the periodontal tissues attached to the root leads to the necrosis of regenerative cells that play a vital role in periodontal healing [41]. Furthermore, necrosis of the pulp tissue adversely affects the outcomes of tooth [1]. Also, bacterial contamination of the pulp and/or the root also leads to failure of the replantation process [42]. Therefore, root resorption and ankylosis are common complications following delayed replantation [43]. Loss of periodontal support caused by periapical bone loss following root replantation can also lead to failure of tooth replantation [44]. Although a number of pre-replantation intracanal and root surface treatments have been advocated to improve the outcomes, prevalence of root resorption and ankylosis following delayed replantation remains high [43]. Three case reports analyzed APCs for their regenerative properties when used as an intracanal medicament after delayed replantation [23][28][36]. In another case report, although PRP was placed in the canal, the pulp vitality was not evaluated or reported [23]. Therefore, in that research, it is unknown what effect if any, did APC have on pulp tissues. The authors of another case report a positive pulp test at 24-month follow up which indicates that PRF may stimulate regeneration of the radicular pulp tissue to an extent [28]. Torabinejad and Turman (2011) report that using PRP not only results in healing of periapical tissues but also results in regeneration of vital tissues in a root canal that had previously contained necrosed pulp [15]. However, in this case the follow up period was only 5.5 month and it is unknown if subsequent follow up was carried out to reaffirm this return of pulp vitality. None of the three animal studies included in this research attempted to

assess the pulp-related outcomes of APC [16][45][46]. Therefore, to date, there is insufficient evidence from clinical and pre-clinical studies to ascertain the efficacy of APCs in regenerating pulp tissues.

There have been no large-scale or long-term clinical investigations evaluating the efficacy of APCs on the results of replanted teeth to yet. Quality assessment of the case reports revealed numerous additional limitations. Firstly, in each case report, there was only one patient treated [15][23][26][27][28][29][30][31][32][36]. Hence, only 10 replanted teeth, after being treated with APC, have been documented in the literature to date. This small sample is insufficient to conclude the effectiveness of APCs in improving the outcomes of tooth replantation. Furthermore, majority of the case reports [23][27][29][30][31][32][36] did not report if any of the patients treated had any other comorbidities or congenital disorders. Therefore, it is unknown if similar successful results would be observed if the teeth were replanted (after being treated with APCs) in patients who are otherwise systemically unhealthy. Only four studies declared any or no conflicts of interests or their sources of funding behind the studies [15][28][29][31] which could mean that the remaining six studies may have a high likelihood of funding or experimenters' bias. Similarly, only one animal study out of the three included in this research employed any blinding to reduce any sources of observer's bias [16]. Additionally, none of the animal studies included in this research stated whether there were any animals or teeth lost during the experiments. Although animal models are widely used to study the effect of interventions in periodontology and endodontics, due to the difference in the microflora and dietary patterns between animals and humans, it is difficult to predict to certainty that the results from in vivo studies will translate to clinical practice [47].

As with all pre-replantation regimens, the main factor governing the success of replantation is the extra-oral drying time the tooth may undergo following avulsion [5]. An attractive aspect of APCs as a regenerative material that, because it is dervided from the host's own blood, it has an extremely low probability of rejection. To date, no reports have documented any adverse reactions caused by APCs themselves. Nevertheless, one case report has recorded an allergic reaction following PRP therapy which was most likely due to calcium citrate, an anticoagulant that is added to APCs [48]. The data regarding the safety of APC when used periodontally or intracanal is scarce. Moreover, in other fields or surgery and medicine, studies have found inconclusive evidence regarding the safety of APCs. Another clinical aspect that the future studies should focus on long-term safety of the APC procedures in endodontics and tooth replantation. Clinically, APCs may be applied either on the root, the socket or both but no study has compared the efficacy of these routes. In majority of the case reports included in this research, APCs were applied in the socket (extraradicular) and only two studies documented the intracanal use of APCs in open apices before replantation which warrants further research focusing on the usage of APCs in the apexogenesis of immature teeth [15][23]. Therefore, it is evident that there is a lack of standardization of APCs application on replanted teeth. Furthermore, the relatively short follow-up time of the studies makes the long term efficacy of APCs debatable [15][16][23][26][27][28][29][30][31][32][34][35][36][45][46]. Therefore, further studies should evaluate the intracanal efficacy of APC in improving the outcomes of tooth replantation. In particular, long-term randomized controlled trials are essential to ascertain the clinical efficacy of APCs as pre-replantation treatment.

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