ISSN No:-2456-2165

Platelet-Rich Plasma in Orthodontics- A Review

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Abstract:- The last few decades have seen a growth in the use of Protein-rich plasma in dentistry, predominantly related to dental implants, oral surgery and periodontology. There is emerging literature on the use of these derivatives in orthodontics. With increasing awareness of orthodontic treatment in all age groups of society, emphasis on enhancing the intensity of tooth movement has increased. This article discusses the use and application of platelet rich plasma in orthodontic treatment modalities.

Keywords:- *Platelet Rich Plasma (PRP); Tooth Movement; Orthodontics.*

I. INTRODUCTION

Form the beginning of the practice of Orthodontics, tooth movement and associated biological reaction has been one of the domain in research. Many researchers have studied all possible approaches to achieve tooth movement with maximum pace in most physiological manner. As the demand for orthodontic treatment in the adult patients has increased, it has given impetus to discover the methods to achieve accelerated orthodontic tooth movement which has led to research in different modalities including chemical, surgical and mechano-surgical methods.

In 1983, Frost gave the concept of Regional acceleratory phenomenon(RAP), denoting the principle that when bone is surgically irritated, a cascade of inflammatory process is started which results in increased osteoclastogenesis causing faster tooth movement.[1] Majority of the procedures involve a direct insult to the bony tissue which alternatively promoted the need for non-invasive to less invasive procedures, leading to increased research in field of acceleration of orthodontic tooth.

The invasive techniques such as conventional corticotomy have been significantly more effective than the non-surgical procedures or the less invasive procedure like micro-osteoperforations or peizopuncture.[2] The reason for this is that the mechanical stimulation of higher osteoclastic activity leads to the alveolar bone resorption causing decrease thickness and weight of the alveolar bone, and loss of alveolar bone of the target teeth. This phenomenon is absent in non-invasive procedures and thus, are not long lasting. So, in order to achieve effective biological response from minimally invasive procedures, biochemical adjuncts may be used which involves cytokines like prostaglandin and hormones like relaxin. But these supplementary hormones may cause unwanted systematic effects.

The process of healing wound initiates through formation of clot, further of proliferative stage which comprises of new epithelial formation, blood vessel formation, granulation tissue formation, deposition of collagen and finally maturation and contraction of collagen.[3] This involves aggregation and adherence of platelets which favours the formation of thrombin and fibrin. Platelet-rich plasma (PRP) which is considered to be a rich source of autologous growth factors, is defined as an autologous concentration of platelets in a small volume of plasma. GFs are natural biologic mediators which are responsible for the regulation of key cellular events which are part of the tissue repair and regeneration process.[4] Platelets contain biologically active proteins. Binding of these proteins within a developing fibrin mesh or to the extracellular matrix creates chemotactic gradients leading to aggregation of stem cells resulting in cell migration, differentiation, and promoting repair. Thus, use of autologous platelet concentrates is a promising application in clinical situations requiring rapid healing.

II. PRP: DEFINITION AND BIOLOGICAL COMPOSITION

Platelet-rich plasma (PRP) is an autologous concentration of human platelets in a small volume of plasma. Basically, it comprises of the concentrated platelets and the seven-fundamental growth factor which are actively secreted by platelets for commencement of wound healing.[5] In 1998, Robert Marx introduced PRP in dental literature as an adjunct in mandibular reconstructive procedure, enhancing the radiographic maturation rate of the graft alone.

❖ *Growth Factors Include:*

- 3 isomers of platelet-derived GF (PDGFaa, PDGFbb, and PDGFab),
- 2 of the numerous transforming GFs-b (TGFb1 and TGFb2),
- Vascular endothelial GF (VEGF), and
- Epidermal GF (EGF)

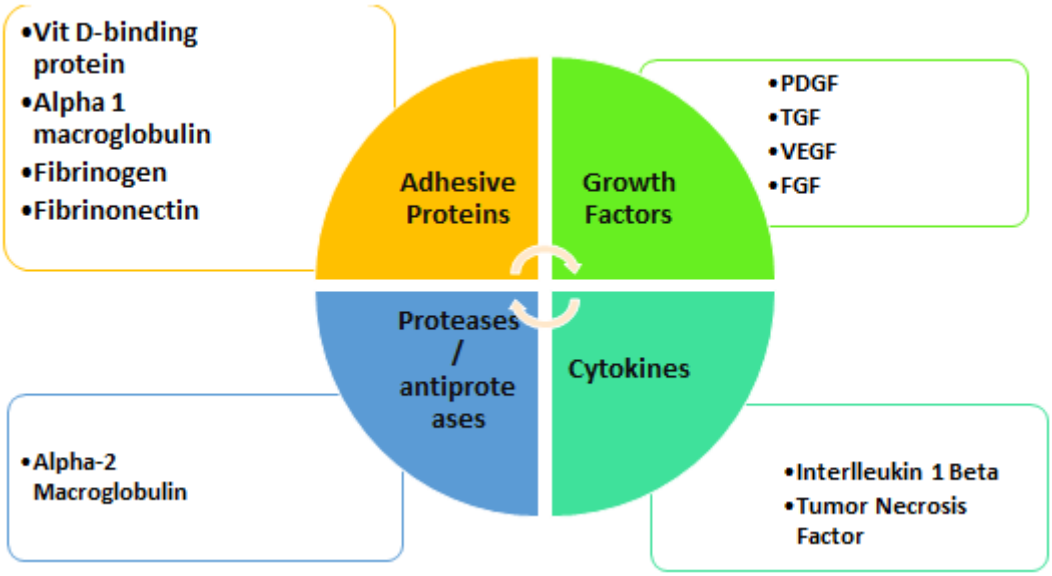

Fig 1

The small volume of plasma encompassing the platelet concentration contains three cell adhesion proteins viz. fibrin, fibronectin, and vitronectin, which are essential for osteoconduction and osteoid formation, connective tissue linkage, and epithelial migration., all of which are critical in the process of healing.[6]

III. MECHANISM OF ACTION

The action of PRP is initiated with the degranulation of cellular alfa-granules which consists of growth factors and cytokines which are generated during the clotting process while the coagulation occurs. Its initiation starts with the secretion of growth factors within the 1st 4 hours of clotting process with majority messengers derived in 1-2 hours. For next 5-7 days, the synthesis of additional GFs by the platelets continue after the initial burst of PRP-GFs following the stimulation of healing process by secretion of similar growth factors through inflammatory macrophages. Thus, the wound healing rate is dependent on the quantity of platelets present in the blood clot. PRP being a rich source of platelets provides an increased concentration of GF thus promoting the cellular activity and enhancement of healing procedure.[5]

The process of release of cytokines and their interaction with the cells can be appreciated in the figure.

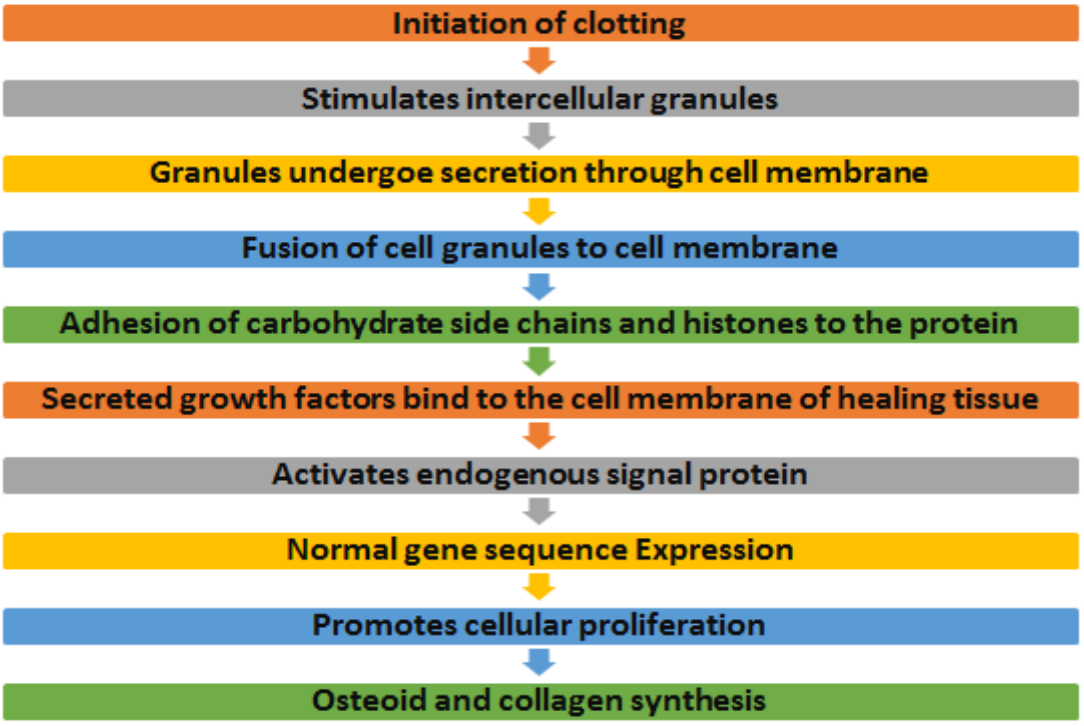

Fig 2

ISSN No:-2456-2165

The anti-inflammatory effect of the PRP attributes the healing potential on bone tissue.

Due to the multiple and overlapping effects of the constituents of the PRP, the effect on the bone tissue is considered multifactorial.

Therefore, the PRP's effectiveness is influenced by-

- Concentration of the platelets
- Cellular composition of PRP
- Balance between anabolic and catabolic activities (Pro and anti-inflammatory cellular activity).[7]

According to Hesham et al, the action of PRP can be considered as an anti-inflammatory, by directly influencing the monocytic secretory activity.

- Promotes manufacturing of RANTES (*regulated on activation, normal t-cell expressed and secreted*),
- Blocks MCP-1 (*monocyte chemotactic protein*) release from monocytes,
- Increases the concentration of LXA4, suggesting that PRP facilitates healing by controlling the local inflammatory response.[8]

Orthodontic tooth movement microscopically is an inflammatory process, and therefore the presence of ILs and TNFs contributes in the tooth movement acceleration. For orthodontics, an injectable form has been considered more suitable without the use of calcium chloride and thrombin so it can be maintained in liquid form and has a longer lasting effect.[9]

Applications of PRP in orthodontics consists its potential use to accelerate tooth movement, reducing post-surgical pain in patients treated with periodontally accelerated osteogenic orthodontics as well as to potentially promote the bone formation in alveolar cleft repair patients.[10,11.]

A. PRP and Tooth Movement

Orthodontic tooth movement is because of gradual remodeling supporting alveolar bone which involves the process of osteoclastic resorption of established bone and osteoblastic formation of new bone. The quality and quantity of orthodontic tooth movement is dependent on the turnover rate of alveolar bone. To shorten orthodontic treatment and to move the teeth faster, alteration of the balance between resorption and deposition is required.[12]

For accelerating tooth movement, several non-invasive as well as invasive techniques have been proposed both clinically and experimentally which includes direct electric current stimulation[13], low dose laser therapy[14] and vibrational stimulation[15], injection of prostaglandin[16,17] and relaxin[18] and corticotomy[19]-facilitated tooth movement.

Use of PRP has shown to improve orthodontic tooth movement as it is based on Rapid Accelerated Phenomenon. Mangal et al.[20] found that localized acceleration of tooth movement the effect of PRP is dependent on the concentration used and advised the method of synthesis for the success of accelerating tooth movement. Rashid.A et al.[21] investigated the effect of PRP on the orthodontic tooth movement rate in 6 skeletally mature males. The maxillary first premolar in each was bilaterally extracted. PRP was prepared and injected around the canine in one maxillary quadrant while the other served as the control. Closed Coil springs (150 g) were used to distalise the canine for 68 days using temporary anchorage devices. The results showed total maxillary tooth movement on the experimental side was significantly faster compared to the control side (mean movement of 15.60mm versus 9.46mm). Thus, with no obvious clinical or microscopic side effects, local injection of PRP in this study resulted in accelerated orthodontic tooth movement.

Güleç A et al.[22] have studied the effects of PRP with different concentrations on orthodontic tooth movement and alveolar bone density. Seventeen individuals were grouped into two: A PRP injection with moderate concentration group and a PRP injection with high concentration group. In each group, 5-time points were studied: Third, Seventh, Fourteenth, Twenty-first, and Sixtieth day. Before orthodontic mesialization of the maxillary 1st molar, on the right sides of the molar buccal sulcus moderate and high concentrations of PRP were infused with injection, and the left sides served as the controls. 3-dimensional digital models were used for tooth movements measurement. Histomorphometric analysis was done for the evaluation of osteoclastic activity and alveolar bone volume density in the 1st molar intraradicular region. The results suggested reduction in the density of alveolar bone in the experimental groups compared with the control groups at Third, Seventh, Fourteenth, Twenty-first, and Sixtieth day. On third day, osteoclastic activity was higher with the experimental groups as compared to controls. On twenty-first day, the tooth movement rate with the high-concentration experimental group was 1.7 times greater than in the high-concentration control group and 1.4 times greater than in the moderate-concentration experimental group. On sixtieth day, in all groups alveolar bone density increased to original levels. The study found accelerated orthodontic tooth movement by reduction in density of alveolar bone on para-dental tissues by osteoclastic activity enhancement in a unique way by injecting both moderate and high concentrations of PRP.[22] Faster tooth movement is often not without risk, primarily related to increased caution for root resorption. The rate of root resorption with and without the use of PRP is likely to need investigation with well-conducted clinical trials. Marx mentioned that the growth factors in PRP include platelet-derived growth factor (PDGF), insulin-like growth factor (IGF), vascular endothelial growth factor (VEGF), and transforming growth factor-β (TGF- β).

Further studies are required for the investigation of the use of PRP for tooth movement.[23-26.]

B. PRP in Cleft Patients: Alveolar Bone Grafting

Cleft lip and/or palate are one of the most common congenital anomalies which affects the orofacial region. The use of PRP in the management of these conditions is based on the tremendous quantities of growth factors released by the platelets aid in bone graft maturation. In a preliminary study, to evaluate the PRP's efficacy for secondary alveolar bone graft procedures, 20 patients with unilateral or bilateral CLCP were studied.[27] Twenty patients between the ages of 8 and 30 were randomly allocated to receive cancellous bone grafts from the anterior iliac crest mixed with PRP whilst the same without PRP was received by control group. Bone grafts with the use of PRP showed significantly more bone density up to 6-months post-surgery (1028.00 +/- 11.30 HU versus 859.50 +/- 27.73 HU).

Giudice G et al.[28] studied bone regeneration and soft tissue healing in sixteen patients aging between 9 and 11 years of age with alveolar clefts unilaterally. The patients were equally split between those treated with autologous bone grafts alone and autologous bone grafts with PRP and then followed up for 36 months. The authors found that the autologous bone graft group with PRP, underwent earlier and shorter duration of orthodontic treatment with mean time to orthodontics 155.0 days compared to 298.4 days and mean duration of orthodontics 294.5 days compared to 356.0 day.

The preceding study evaluated bone changes using plain film radiography, however, Sakio R et al.[29] used computed tomography. The authors acknowledge the low numbers in their study, with 23 patients receiving autologous iliac bone and marrow grafts with PRP and 6 patients the same intervention without PRP. All patients were aged between 7 and 8 and were not randomly allocated. Results of the analysis of the graft sites showed the remaining bone was not significantly different between those treated with PRP and those without at 1year post-surgery. This is consistent with earlier work that suggested bone changing through remodeling in the early phase may be enhanced by PRP[30].

C. PRF and Periodontally Accelerated Osteogenic Orthodontics

Periodontally Accelerated Osteogenic Orthodontics (PAOO) is procedure that is thought to accelerate movement of teeth by orthodontic forces combined with corticotomies and alveolar bone grafting. Such corticotomy/osteotomy procedures are not new and were described over half a century ago[31]. Muñoz F et al have studied pain post-operatively, infection, inflammation and stability post-orthodonticly by using Leukocyte and Platelet-Rich Fibrin (L-PRF) in PAOO. Eleven patients in need of orthodontic treatment whom were considered periodontally suitable were monitored immediately post-operatively and then 2 years post-treatment.[32] Accelerated wounding healing with absence of any infection or toxic reactions was observed with mild or moderate post-surgical pain. Complete resolution was achieved in all patients by day 8 and active orthodontic treatment time was reported to be 9.3 months. All cases were seemed stable for 2 years. While these results are promising, the few number of patients enrolled in the study and the absence of a control group will warrant further studies in this area. A case report has also been presented in the literature of a patient with a high buccal canine and bimaxillary protrusion where PRF was used alongside other treatment modalities. This was thought to enhance the healing of a segmental osteotomy and a localized single tooth corticotomy around the canine, all of which were performed under local anesthesia. The authors conclude that this resulted in a decrease in canine retraction time[33].

D. PRF and Alveolar Ridge Preservation in Orthodontics

Che Y et al. have proposed the use of PRF to minimize resorption of hard tissues immediately post-extraction. The authors put forward that by preserving the alveolar ridge at this time in orthodontic cases, the problems of orthodontic tooth movement, root resorption, alveolar bone cleft and gingival invagination could be minimized. This would be achieved by ensuring there is sufficient alveolar bone during space closure. Similarly, where extractions are followed by pre-prosthetic orthodontics, PRF use may contribute to preservation of hard tissue morphology improving the condition of implant sites and making for more aesthetic restorations.[34]

E. Safety of PRP and Possibility of Infection

- The safety of PRP largely depends on the source of the blood used to synthesize the concentrate. With autologous source, the chances of adverse reaction and are negligible. In a sterile protocol, the chance of transmissibility of the blood-borne infections is also avoided.
- As the PRP concentrate of the platelets is essentially like the natural clotting, the concentrate does not promote bacterial proliferation.
- Also, the PRP derived GF are only trans-membranous, they are not mutagenic and hence only stimulate natural healing process and have no role in tumor formation.[20]

IV. CONCLUSION

The application of PRP and PRF is becoming well established in many fields of both medicine and dentistry. While use in areas such as implant dentistry and oral surgery may seem obvious, in orthodontics, we are only just starting to see the publication of a handful of studies. The PRP's effect with localized acceleration of tooth movement is dependent on the concentration used. However, the method of synthesis is critical to the success of PRP based acceleration of tooth movement. The use of injectable PRP at a different stage of orthodontic treatment can improve the quality of the treatment outcome by influencing the bone quality and

enhancing the rate of tooth movement. It is anticipated the use of PRP and PRF is likely to extend beyond just tooth movement however, the clinical efficacy of this rapidly evolving area will need to be carefully watched as laboratory based studies are undertaken in clinical practice. Further studies should involve well-planned randomized controlled trials investigating not only the potential benefits of PRP and PRF but also any potential risks or complications.

REFERENCES

[1]. Frost H. The regional acceleratory phenomenon: a review. Henry Ford Hosp Med J. 1983;31(1):3-9.
[2]. Kalemaj Z, DebernardI CL, Buti J. Efficacy of surgical and non-surgical interventions on accelerating orthodontic tooth movement: a systematic review. Eur J Oral Implantol. 8(1):9-24 (2015).
[3]. Agrawal M, Agrawal V. Platelet rich fibrin and its applications in dentistry - A review article. Natl J Med Dent Res 2014;2:51-8.
[4]. Marx RE. Platelet-rich plasma (PRP): what is PRP and what is not PRP? Implant Dent 2001;10:225-8.
[5]. MANGAL, Influence of Platelet Rich Plasma on Orthodontic Tooth Movement: A Review Biomed. & Pharmacol. J., Vol. 10(3), 1463-1468.
[6]. Marx RE, Carlson ER, Eichstaedt RM, Schimmele SR, Strauss JE, Georgeff KR. Platelet-rich plasma: Growth factor enhancement for bone grafts. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 85(6):638-646 (1998).
[7]. Marx RE. Platelet-Rich Plasma: Evidence to Support Its Use. J Oral Maxillofac Surg.; 62(4):489-496 (2004).
[8]. El-Sharkawy H, Kantarci A, Deady J, et al. Platelet-Rich Plasma: Growth Factors and Pro- and Anti-Inflammatory Properties. J Periodontol.; 78(4):661-669.
[9]. S. Henneman, J.W. Von den Hoff, J.C. Maltha, “Mechanobiology of tooth movement,” European Journal of Orthodontics, vol. 30, pp. 299–306, June 2008.
[10]. C. Verna, M. Dalstra, B. Melsen, “The rate and the type of orthodontic tooth movement is influenced by bone turnover in a rat model,” European Journal of Orthodontic, vol. 22, pp. 343- 352, 2000.
[11]. Erliera Erliera Sufarnap et al. The Effect of Platelet-Rich Plasma to Orthodontic Tooth Movement. Advances in Health Science Research, vol 8, 80-83,2018.
[12]. Davidovitch Z. Tooth movement. Crit Rev Oral Biol Med. 1991; 2: 411-450.
[13]. Spadari GS, Zaniboni E, Vedovello SA, Santamaria MP, do Amaral ME, Dos Santos GM, Esquisatto MA, Mendonca FA, Santamaria M Jr. Electrical stimulation enhances tissue reorganization during orthodontic tooth movement in rates. Clin Oral Investig. 2017; 21: 111-120.
[14]. Qamruddin I, Alam MK, Mahroof V, Fida M, Khamis MF, Husein A. Effects of low-level laser irradiation on the rate of orthodontic tooth movement and associated pain with self-ligating brackets. Am J Orthod Dentofacial Orthop. 2017; 152: 622-630.
[15]. Leethanakul C, Suamphan S, Jitpukdeebodintra S, Thongudomporn U, Charoemratrote C. Vibratory stimulation increases interleukin-1 beta secretion during orthodontic tooth movement. Angle Orthod. 2016; 86: 74-80.
[16]. Yamasaki K, Miura F, Suda T. Prostaglandin as a mediator of bone resorption induced by experimental tooth movement in rates. J Dent Res. 1980; 59: 1635-1642.
[17]. Yamasaki K, Shibata Y, Fukuhara T. The effect of prostaglandins on experimental tooth movement in monkeys. J Dent Res. 1982; 61: 1444-1446.
[18]. Liu ZJ, King GJ, Gu GM, Shin JY, Stewart DR. Does human relax in accelerate orthodontic tooth movement in rates? Ann N Y Acad Sci 2005; 1041: 388-394.
[19]. Mostafa YA, Mohamed Saleh Fayed M, Mehanni S, ElBokle NN, Heider AM. Comparison of corticotomy-facilitated vs standard tooth-movement techniques in dogs with mini screws as anchor units. Am J Orthod Dentofacial Orthop 2009; 136: 570-577.
[20]. Mangal U. Influence of platelet rich plasma on orthodontic tooth movement: A review. Biomed & Pharmacol J. 2017; 10: 1463-1468.
[21]. Rashid A, ElSharaby FA, Nassef EM, Mehanni S, Mostafa YA. Effect of platelet-rich plasma on orthodontic tooth movement in dogs. Orthod Craniofac Res. 2017; 20: 102-110.
[22]. Güleç A, Bakkalbasi BC, Cumbul A, Uslu U, Alec B, Yarat A. Effects of local platelet-rich plasma injection on the rate of orthodontic tooth movement in a rat model: A histomorphometric study. Am J Orthod Dentofacial Orthop. 2017; 151: 92-104.
[23]. Seifi M, Badiee MR, Abdolazimi Z, Amdjadi P. Effect of basic fibroblast growth factor on orthodontic tooth movement in rats. Cell J 2013;15:230-7.
[24]. Verna C, Zaffe D, Siciliani G. Histomorphometric study of bone reactions during orthodontic tooth movement in rats. Bone 1999; 24:371-9.
[25]. A. Gulec, C.B. Banu, A. Cumbuk, U. Uslu, B. Alev, A. Yarat, “Effects of local platelet-rich plasma injection on the rate of orthodontic tooth movement in a rat model: A histomorphometric study,” Am. J. Orthod. Dentofacial Orthop., vol. 151, pp. 92-104, May 2017.
[26]. V.S. Raja, E.M. Naidu, Platelet-rich fibrin: Evolution of a second-generation platelet concentrate,” Indian Journal of Dental Reaserch, vol. 19(1), pp. 42-6, August 2008.
[27]. Gupta C, Mehrotra D, Mohammad S, Khanna V, Singh GK, Singh G, et al. Alveolar bone graft with platelet rich plasma in cleft alveolus. J Oral Biol Craniofac Res. 2013; 3: 3-8.
[28]. Giudice G, Cutrignelli DA, Leuzzi S, Robusto F, Sportelli P, Nacchiero E. Autologous bone grafting

with platelet-rich plasma for alveolar cleft repair in patient with cleft and palate. Ann Ital Chir. 2016; 87: 5-12.
[29]. Sakio R, Sakamoto Y, Ogata H, Sakamoto T, Ishii T, Kishi K. Effect of platelet-rich plasma on bone grafting of alveolar clefts. J Craniofac Surg. 2017; 28: 486-488.
[30]. Lee C, Nishihara K, Okawachi T, Iwashita Y, Majima HJ, Nakamura N. A quantitative radiological assessment of outcomes of autogenous bone graft combined with platelet-rich plasma in the alveolar cleft. Int J Oral Maxillofac Surg. 2009; 38: 117-125.
[31]. Köle H. Surgical operation on the alveolar ridge to correct occlusal abnormalities. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1959; 12: 515-529.
[32]. Muñoz F, Jiménez C, Espinoza D, Vervelle A, Beugnet J, Haidar Z. Use of leukocyte and platelet-rich fibrin (L-PRF) in periodontally accelerated osteogenic orthodontics (PAOO): clinical effects on edema and pain. J Clin Exp Dent. 2016; 8: 119-124.
[33]. Iskenderoglu NS, Choi BJ, Seo KW, Lee Y. Single-tooth osteotomy combined wide linear corticotomy under local anesthesia for correcting anterior protrusion with ectopically erupted canine. J Craniofac Surg. 2017; 28: e30-33.
[34]. Che Y, Li P, Tian L, Wang M, Xiong R, Lei X, et al. The research progress of platelet-rich fibrin applications in orthodontic treatment. Adv Comp Sci Res. 2016; 59: 524-529.