Editorial

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Plasma Rich Plasma for Traumatic Non-Union Fractures: A Novel but Controversial Bone Regeneration Strategy

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The bone skeleton is the main part of musculoskeletal system which serves as the basis of the loco-motor system. Although stubborn and stiff, the bony skeleton is the most vulnerable part of the loco-motor system to the trauma and high energy shuts. The ultimate result of the trauma to bones is the fracture or deformity. The bones have the potential of healing without scar formation; however the regenerative capacity of the bones is limited. The regeneration of large bone defects without intervention is a rare phenomenon, although some scientists have reported spontaneous healing of extensive bone defects [1]. Currently several strategies are available for treatment of large bone defects. The most recommended method for filling the small bone defects in those with appropriate soft tissue coverage is using bone substitutes or conventional cancellous autologous bone grafting [2-4]. For large bone defects exceeding 5 cm of diameter, the conventional methods are associated with high rate of failure and thus more advanced and specialized methods are required [5].

Large bone defects after traumatic fractures may lead to non-union fractures which is devastating entity in orthopedic surgery. The prevalence of non-union fractures is readily low being reported to be 2-6%, 2-8% and 3-6.4% in humerus, femur and tibia respectively [6,7]. Although they have low prevalence rate, however they are of matter of interest and research because of tremendous social and economical burden. It was reported that mean expense for treatment of non-union of humerus, femur and tibia is 31132, 34400 and 32660 USD respectively [8]. The risk factors of non-union fractures are primary injury, surrounding soft tissue injuries, inappropriate primary reduction technique, inappropriate surgical technique, infection and osteomyelitis, concomitant vascular injuries, nicotine abuse, old age and presence of co-morbidities (peripheral vascular disease, cardiovascular disease, collagen-vascular disease, etc.) [6]. Thus prevention of non-unions via appropriate aligning the fracture site using internal or external fixators is the main strategy for management of this entity [9,10]. Debridement of necrotic tissue along with intramedullary nailing has also been successfully used for preventions and treatment of non-union of the femoral bone [11]. Several other strategies have also been introduced and used with controversial results. Among these are electromagnetic fields [12], biodegradable implants [13], recombinant bone morphogenetic protein 7 (rhBMP-7) [14] and plasma rich platelet (PRP) [15].

PRP is an autologous blood product with high activated platelet concentrations (approximately 1 million per each micro-liters) containing considerable amounts of platelet derived growth factor (PDGF), vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), fibroblast growth factor (FGF) and transforming growth factor (TGF-β1, TGF-β2)

which are responsible for repair and granulation tissue formation in human body [15]. PRP has been successfully used in treatment of musculoskeletal injuries [16]. Several studies have investigated the role of local PRP application in treatment of non-union fractures with conflicting results [17-24]. Although some studies have shown that this therapy increases the healing rate of the non-union fractures in animal models [17-20] and human subjects [21,22], some others found that PRP poses no advantage over placebo or rhBMP-7 [23,24]. A recent meta-analysis indicated that there is lack of standard randomized clinical trials to shed light on effectiveness of PRP application on healing rate of non-union of long bones [25].

This application has been the subject of interest in several animal studies. Hakimi and co-workers [12] demonstrated that PRP combined with autologous cancellous bone leads to a significantly better bone regeneration compared to isolated application of autologous cancellous bone in an in vivo critical size defect on load-bearing long bones of mini-pigs during a time period of 6 weeks. Gerard and colleagues [18] also studied the effects of PRP on healing rate of maxillary non-unions in animal model of dog. They demonstrated that PRP enhances the early healing rate of autologous bone grafts in maxillary bone. However the PRP healing rate enhancement was not found significant after 2 months. This could be explained due to the fact that PRP enhances the removal of non-viable grafted autologous bones, but does not affect the regeneration and formation of new bone. Thus PRP has been concluded to affect the early healing rate. They also demonstrate that PRP administration does not increase the trabecular density in the bone grafts [18]. Kanthan and co-workers [19] found that application of PRP in combination with bone rafting improved the bone healing rate of rabbit tibial fractures when compared to bone graft alone. They also demonstrated that use of PRP alone (without bone grafting) does not affect the outcome and healing rate and provides limited advantage over placebo [19]. The result of these experimental studies was further supported by a clinical study that reported the results of successful treatment of 17 patients with persistent non-union of long bones using combination of PRP and autologous bone grafting [12]. Galasso and colleagues [21] also used a combination of self locking intramedullary nailing and PRP for treatment of atrophic diaphyseal long bone non-unions. They reported a healing rate of 91% which is comparable with previous reports. In contrast these studies, Aghaloo and co-workers [26] did not observe any additive effects of PRP and autologous bone grafting for treatment of bone defects of rabbit animal model. This could be explained due to the methodology of this single experimental study. The platelet concentration used in this study was 7.3 times higher than the native blood which is higher compared to other studies and ours [17-24]. It is postulated that therapeutic effects of PRP occurs in a narrow platelet concentration, probably 3-5 times higher than the native blood. Higher concentrations leads to platelet aggregation and the effects are limited; in the same way, low concentrations do not provide appropriate amounts of platelet derived growth factors needed for enhancing the healing environment [27].

Taking all these together it should be indicated that there is lack of appropriate clinical trials and evidence for using the PRP in treatment of non-union fractures. But the results of several experimental studies indicate that PRP increases the early healing rate and alleviates the final outcome especially when used in combination with autologous bone graft. Currently several clinical trials are being performed addressing this issue (based on a search in Clinical Trial Registries). Thus the future of this method of treating non-union fractures is shinny and might change the current management.

Conflict of Interest: None declared.

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