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REVIEW ARTICLE OPEN ACCESS

Therapeutic potential of adult platelets and cord blood platelets in future clinical directions

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Abstract

Platelet rich plasma (PRP) is currently obtaining a natural concentration of autologous growth factors, and is used in different medical conditions. This review is aimed to establish several treatment options using adult PRP and scope of the therapeutic benefits of cord blood platelet rich plasma (CB-PRP) for future clinical directions. A literature search was done based on the clinical applications of PRP in the fields of dermatology, orthopaedic, dental, ophthalmology and gynaecology. The field keywords were searched in major indexing services for collecting the relevant articles from January 2010 to June 2023. PRP therapies are potential and efficient treatment options and established protocols for certain diseases but there is a need to establish CB-PRP opportunities of improving efficacy for promoting clinical application. Further research can focus on CB-PRP and it may be considered as immunologically compatible to use as allogenic.

Keywords: platelet rich plasma; therapy; cord blood PRP; hair loss; poor ovarian reserve; osteoarthritis

Introduction

Platelet rich plasma (PRP) is concentrated up to 4–5 times from an individual's own blood that is rich in growth factors (GFs) like PDGF, TGFβ, VEGF, and EGF etc. PRP can be produced from both adult peripheral and cord blood. The adult PRP is injected into an injured or diseased part of a human body to treat different clinical conditions i.e., dermatology, orthopaedic, dental, ophthalmology and gynaecology [1].

Cord blood platelet rich plasma (CB-PRP) therapies are need to be established to treat clinical conditions as it is immunologically compatible and it may be used as allogenic. CB-PRP contains GFs similar to that of adult PRP, and also albumin, minerals, vitamin A & E, several fatty acids, transferrin, fibronectin, fibrinogen and adiponectin [2], which are helpful in treating diabetic wounds and other clinical conditions. Cord blood plasma may be used to treat immune-mediated diseases, such as autoimmune, allergic, and inflammatory diseases [3].

A number of investigations have been conducted to show the potentiality of PRP but the CB-PRP has more potentiality to use in the same conditions for improving the quality of life. This review is aimed to establish the several treatment options using adult PRP and scope of the therapeutic benefits of CB-PRP for future clinical applications in different research fields i.e., dermatology, orthopaedic, dental, ophthalmology, and gynaecology.

Different types of articles are accessed from major indexing services such as PubMed, Science Direct and Google Scholar from January 2010 to June 2023. Presently established PRP therapies in major fields of dermatology, orthopaedic, dental, ophthalmology and gynaecology were considered for the review and applicability of CB-PRP in future therapies.

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Dermatology

Wound healing, scar revision, skin rejuvenation, striae distensae, vitiligo, and hair loss or alopecia are treated with PRP, which is ethically appropriate autologous treatment from the past decade. Adult PRP has been investigated and showed beneficial effects in the dermatological conditions for several years. The researchers may work with CB-PRP to show beneficial effects and try to use immunologically compatible platelets as allogenic in the field of dermatology for future therapies.

Wound healing: Chronic wounds take years to heal or never heal due to long stay of inflammatory phase, in such conditions autologous PRP is used to treat these non-healing wounds for better quality of life. This treatment is based on the GFs that supports healing and repair cascade [4]. Patients with venous ulcer complaints reported reduced pain that usually were treated with painkillers. All patients with complex multifactorial wounds, diabetic foot ulcers, or minor venous ulcers showed complete remission when treated with leukocytes PRP. Leukocyte-PRP treatment accelerated the healing process for patients with diabetic ulcers that were persistent. PRP may aid in the regeneration of peripheral nerves and the healing of ulcers caused by neuropathy. Patients with leprosy lesions displayed full re-epithelialization [5]. CB-PRP treatment is possible in treating wounds without any scar and also help in larger wounds and diabetic wounds.

Scar revision: Burn scars, postsurgical scars, and acne scars are treated with PRP alone or with other combination can improve collagen and elastic fibers for quality of the skin [6]. PRP appears to be a safe and an effective treatment for various types of atrophic scars [7]. The research can be focussed on scarless treatment, which is possible with CB-PRP due to quality of GFs.

Skin rejuvenation: PRP is safe and well tolerated treatment for skin rejuvenation. It is used in facial rejuvenation, wrinkles, skin texture, nasolabial folds and facial appearance all showing beneficial improvements [8, 9].

The blood samples are combined with acid citrate dextrose A, and anticoagulant and then the PRP is injected into the cheeks and results showed an improvement in patients. Studies suggest that PRP for facial rejuvenation may at least temporarily improve the visual appearance of photo aged skin [9]. Concentrated biologically active molecules, including anti-aging proteins that can delay skin aging, can be obtained in significant quantities using PRP. A variety of GFs and cytokines are released by PRP after injected into the tissues and combine with their corresponding receptors to stimulate human adipose stem cells and skin fibroblasts, angiogenesis, and cell migration. Additionally, PRP is known to up regulate the expression of MMP-1, MMP-2, and MMP-3, stimulate extracellular matrix remodelling, synthesis of new collagen, all of which can lengthen dermal epidermal junctions, improve skin elasticity, and decrease tissue edema, ultimately accomplish the goal of anti-aging tissue regeneration [10].

Striae distensae: Stretch marks, or striae distensae, are benign cutaneous lesions that are characterized by linear bands and are usually linked to females, pregnancy, obesity, and/or hormonal changes. Stretch marks are not harmful to health, but they can cause severe psychological discomfort to people. With so many different therapeutic techniques available, some literature sources say that PRP is a promising strategy for treating striae distensae [11]. PRP treatment for acne scars resulted in less erythema and edema. Treating scars also benefited enhanced collagen and fibroblasts as well as improved skin elasticity [12].

Vitiligo: Amelanotic skin lesions are the clinical characteristic of vitiligo, an acquired idiopathic condition that significantly lowers a patient's quality of life. There has been a growing interest in the use of PRP and when combined with fractional carbon dioxide laser showed potentially useful therapeutic method for vitiligo and other dermatological conditions [13]. PRP stimulates melanocyte regeneration, anti-inflammatory pathways, and the increase of intracellular adhesions [14]. It regulates a number of important functions in the local microenvironment, including the migration, proliferation, and differentiation of stem cells such as dermal fibroblasts, epithelial cells, and endothelial cells, the formation of new collagen, the modulation of immune and inflammatory responses, angiogenesis, and antimicrobial effects [15] in vitiligo.

Hair loss or alopecia: The most common cause of hair loss is androgenetic alopecia, also known as male pattern and female pattern hair loss. The primary action of PRP in treating androgenic alopecia arises from its significant release of GFs, which is crucial in lowering follicular apoptosis and stimulating follicular cell proliferation. Dihydrotestosterone (DHT) decreases local IGF-1 production and is a major factor in the reduction of hair follicles, because PRP has a high IGF-1 content, it can counteract DHT's inhibitory effect on hair follicles [16, 17]. PRP can be activated with calcium chloride to promote the release of GFs, which is believed to promote gene up regulation linked to angiogenesis, cell survival, and proliferation in hair growth [18].

The CB platelet gel has shown favourable *in vivo* outcomes in the treatment of epidermolysis bullosa, diabetic foot ulcer healing, and chemotherapy-induced

mucositis. It is commonly known that cord blood has a high concentration of growth agents. When autologous PRP is not suitable due to patient discomfort or refusal, unsuitability of venous access, or coexistence of autoimmune, hematological, or inflammatory conditions, cord blood platelet lysate may be an effective replacement [19]. A study showed the use of umbilical cord platelet gel dressing has the potential to improve patients' overall quality of life by increasing the epithelialization and healing of wounds, reducing discomfort, and shortening the recovery period following surgery [20].

Orthopaedics

Over the past few decades, the PRP injections in the treatment of orthopaedic conditions involving osteoarthritis, musculoskeletal, bone, ligament, articular cartilage lesions, enthesopathy, peripheral nerve due to its abundant GFs and cytokines present in the PRP, which are key in initiating and accelerating to repair soft and hard tissues.

Osteoarthritis (OA) is the most common form of arthritis and the global prevalence of knee OA alone is 3.8%, affecting over 250 million individuals worldwide [21]. The concentration of GFs and the quantity of platelets determines the clinical effectiveness of PRP. PRP is frequently used to transfer mesenchymal stem cells into defects in the bone. It is currently used for tendon, cartilage, and bone repair in regenerative medicine due to its widespread acceptance. PRP helps promote bone healing and has proven to be clinically useful in the management of fractures. Therefore, the ability of PRP to treat non-union fractures is now being investigated. PRP and stem cells together will promote vasculogenesis in the newly formed bone tissue, accelerating the healing process. PRP can also be used to treat acute traumatic bone fractures in canines when used with external skeletal fixation strategies [22].

Studies have shown that when PRP was used in combination with adipose tissue derived mesenchymal stem cells helped in the process of bone healing. PRP can improve the capacity for mineralization and proliferation, improves revascularization and reinnervation, it also helps the graft mature after anterior cruciate ligament reconstruction [21].

PRP is used for managing several musculoskeletal disorders, such as bursitis, tendinitis, tendon/ligament rupture, osteoarthritis, osteochondral dissecans, joint laxity, lumbosacral stenosis, and patellar luxation [23]. PRP therapy can restore both structure and function; intra-articular injections of PRP can simultaneously reduce synovial inflammation, protect cartilage, and reduce pain [24].

In recent years, the treatment of knee osteoarthritis is done with intra-articular injections of hyaluronic acid (HA) combined with PRP. Macrophages and GFs are increased in multifolds after activation of platelets. Studies showed beneficial effects in removing necrotic tissue and reducing the inflammatory response for articular cartilage repair and regeneration. HA is a high molecular weight polysaccharide that is found in synovial fluid and articular cartilage. Through physiologically nourishing articular cartilage and encouraging the manufacture of endogenous HA and injecting into the knee joint cavity can physically lubricate the articular surface, lessen wear, and delay the progression of joint disease [25, 26]. Raeissadat et al compared the efficacy of intra articular injections of HA, platelet poor plasma, plasma rich in GFs for treating knee osteoarthritis, and they observed plasma rich in GFs and PRP groups had more effect [27]. High-quality evidence is available to support the use of leukocyte rich-PRP injection for osteoarthritis of the knee and leukocyte poor-PRP injection for lateral epicondylitis bends [28]. Studies proved that it is an easy, secure, and efficient way to treat a range of ailments and diseases in canines [22].

According to the study, allogenic cryopreserved cord blood platelet concentrates can be produced consistently and used to prepare clinical-grade cord blood platelet gel at a later time. The CB-PRP units were previously processed, cryopreserved, and it showed good therapeutic effects in the treatment of osteoarthritis in the knee [29]. CB-PRP has therapeutic advantages over adult PRP as the latter contains more pro-inflammatory molecules which can aggravate certain conditions, while CB-PRP contains higher levels of anti-inflammatory molecules [30]. There is an opportunity to develop new therapies with CB-PRP and applying it clinically in treatment of orthopaedic conditions.

Dental

PRP is becoming more and more common in the medical field, particularly in the field of regenerative dentistry, which includes oral and maxillofacial surgery, periodontics, and regenerative endodontics (pulpotomy, apical surgery, and apexification), as well as periodontics (treatment of infrabony periodontal defects and periodontal plastic surgery). Promising outcomes were observed with the use of PRP in numerous dental regeneration procedures [31]. PRP can significantly aid in tissue restoration since it is rich in GFs and cytokines that affect dental wound healing and also promotes bone regeneration and soft tissue healing.

Miron et al revealed that, in comparison to open flap debridement (OFD) alone, the use of platelet rich fibrin (PRF) greatly improved clinical outcomes in

intrabony defects, with comparable levels being seen between OFD/PRF and OFD/bone graft [32]. Future studies focused on understanding possible strategies to improve PRF regeneration qualities with different tiny biomolecules could be beneficial for later therapeutic uses. It is also necessary to conduct further study on PRF at the histology level. PRF/ PRP are used in different surgical techniques, when placed in sockets may reduce the incidence of dry socket [33].

PRP therapy in the alveolar socket following tooth extractions might certainly enhance soft tissue healing and have a beneficial effect on bone regeneration. However, the latter benefit appears to diminish a few days following the extraction. When combined with other materials, PRP has been shown to yield improved results in periodontal therapy compared to when used alone. When PRP was employed alone as a covering material, promising outcomes were also seen in implant surgery. For the treatment of refractory BRONJ (Bisphosphonate Related Osteonecrosis of the Jaw), the combination of necrotic bone curettage and PRP application is promising because it has demonstrated positive results with little invasiveness. PRP can be used as a viable adjuvant in many oral and dental surgical procedures because it has no threat to patients and is easy to obtain and administer [34]. CB-PRP treatment options are need to be established in the dental field.

Ophthalmology

High concentrations of GFs in PRP enhance the healing of damaged tissues of eye and play an essential role in tissue repair and regeneration processes. Ophthalmologic use of PRP has shown assurance in treating a variety of conditions, including dry eye, post-laser *in situ* keratomileusis ocular surface syndrome, dormant ulcers, and surgical reconstruction of the ocular surface following corneal perforation brought on by amniotic membrane transplantation, bovine pericardium membrane transplantation, or autologous fibrin membrane combined with solid PRP clot [35].

The treatment of ocular surface diseases with PRP, is a safe and efficient therapeutic option that promotes epithelial wound repair. PRP offers a significant concentration of vital platelets in a small quantity of plasma to concentrate GFs and chemicals involved in cell adhesion. Through eye drops or clots, these GFs and cell adhesion molecules stimulate the functioning of cells at the site of the injury/surgery and play an essential role in wound healing [36].

There are different clinical applications of PRP in treatment of dormant corneal ulcers. The PRP is used in the form of eye drops and is given in a particular dose. Satisfactory outcomes were observed like the reduction in size of corneal ulcer, improvement in vision, reduction in pain or discomfort, decrease in conjunctival or ciliary hyperemia, or conjunctival edema. Also in treatment of moderate to severe dry eye syndrome, E-PRP is used in the form of eye drops. Studies have shown that subjective symptoms disappeared after treatment, increase in visual acuity, tear meniscus height and tear breakup time, decrease in inflammation and fluroscein staining and improvement of impression cytology. The use of autologous platelets concentrates has also been described to enhance the healing of the idiopathic macular hole [36].

CB-PRP can be utilized to create regenerative medicine methods that can be applied topically to treat a variety of ocular surface disorders, including severe dry eye disease, corneal ulcers, and burns. It can also be used as a source of plasma and platelets [36]. Eye drops prepared by cord blood platelet lysate were a novel therapeutic blood component with unique GFs and anti-inflammatory compounds that could be an effective and safe treatment option in managing persistent corneal ulcers of different causes [37]. The future research options showed great potentiality of CB-PRP and its products in ophthalmological clinical conditions.

Gynaecology

PRP is an effective therapy for gynaecological conditions due to initiation of inflammatory reactions in wound healing process. Among certain infertility causes, autologous PRP is a distinct adjuvant treatment and management strategy, particularly for women who are not responding to conventional treatments. It provides an affordable, accessible treatment option for these individuals. As per the Busnelli et al and Sharara et al studies, PRP may be a promising treatment for reproductive disorders because it can demonstrate endometrial regeneration, menstrual cycle restoration, repeated embryo implantation failure, folliculogenesis improvement, endometrial receptivity enhancement, and an increase in clinical pregnancy and live birth rate [38, 39].

Women with poor ovarian reserve, intra ovarian PRP therapy are an innovative option. Following the active PRP collection, the ovarian cortex is injected with the help of ultrasound guidance. FSH, AMH, and AFC levels were usually repeated after intra ovarian PRP injection on days two or three of the next menstrual cycle in order to assess the effects of PRP. In women with thin endometrium, the literature shows an increase in endometrial thickness and increase in chemical and

clinical pregnancy rates following autologous PRP therapy [39].

Erectile dysfunction (ED) and Peyronie disease (PD) are two issues associated with penile health. In order to solve these problems, restorative treatments such as PRP injections are suggested. PRP is considered the potential restorative therapies for a host of urological issues ranging from erectile dysfunction to hypogonadism [40]. PRP plays a crucial role in regenerating nerve cells, myelination of axons, homing and migration of progenitor cells, and anti-fibrosis and anti-apoptosis of damaged cavernous nerve in corporal tissues.

The table 1 shows summary of different available treatment options for diseases. It is mainly focussed on the emerging treatment plans, which are PRP and CB-PRP. Beneficial results were observed while using these methods in different conditions like dermatology, orthopaedic, dental, ophthalmology and gynaecology.

Table 1: Summary of different treatment options.

Condition	*Type of condition*	*Treatment plan/ method*	*Observations*
Dermatology	Wound healing [5]	PRP injections	Complete remission
	Epidermolysis bullosa, diabetic foot ulcer healing, and chemotherapy-induced mucositis [19]	CB-PRP gel	Healing of wounds, reducing discomfort, and shortening the recovery period.
	Scar revision [6]	PRP injection	Improvement in the quality of the skin and leading to an increase in collagen and elastic fibers.
	Skin rejuvenation [8]	PRP is injected	Temporary improvement in the visual appearance of photoaged skin.
	Striaedistensae [11]	PRP injection	Acne scars resulted in less erythema and edema. Enhanced collagen and fibroblasts, improved skin elasticity.
	Vitiligo [13]	PRPinjection	Stimulates melanocyte regeneration, anti-inflammatory pathways, increase of intracellular adhesions.
	Alopecia [18]	PRP+CaCl2 injection	Promoting gene upregulation linked to angiogenesis, cell survival, and proliferation.
Orthopaedics	Osteoarthiritis, knee osteoarthritis, tendinopathies, cartilage pathologies, and acute traumatic bone fractures [22]	PRP injections	Bone repair and healing, mineralization and proliferation, reduce synovial inflammation, protect cartilage, and reduce pain.
	Knee osteoarthritis [29]	CB-PRP injections	Improved results, reduced pain and inflammation.
Dental	Oral and maxillofacial surgery, periodontics, and regenerative endodontics [33]	PRP gels, injections	Promising outcomes, beneficial effect on bone regeneration.
Ophthalmology	Dry eye, post-laser in situ keratomileusis ocular surface syndrome, dormant ulcers, and surgical reconstruction of the ocular surface, corneal perforation [36]	PRP eye drops/ gels	Reduced symptoms, increase in visual acuity, tear meniscus height and tear breakup time, decrease in inflammation and improvement of impression cytology. Enhanced healing of the idiopathic macular hole.
	Corneal ulcers [36]	CB-PRP eye drops	CB-PRP in treating corneal ulcers.
Gynaecology	Repeated embryo implantation failure [38]	PRP injection	Significantly increased chance of clinical pregnancy.
	Poor ovarian reserve, thin endometrial lining [39]	PRP injection	Increased anti-Mullerian hormone levels, decreased follicle-stimulating hormone. Increase in endometrial thickness and increase in chance of pregnancy.
	Poor ovarian reserve with premature ovarian failure or menopause [41]	PRP injection during the early follicular phase	Significant benefits for increasing FSH, LH, and estradiol levels, MII oocytes and good-quality embryos.
	Erectile dysfunction [40]	PRP injection	Regeneration of nerve cells, myelination of axons, homing and migration of progenitorcells, and anti-fibrosis and anti-apoptosis of damaged cavernous nerve in corporal tissues.

Future aspects

Therapeutic advances in PRP preparation shows beneficial results, and full potential of CB-PRP indications and applications has yet to be determined. Last decade, PRP has been commercially marketed as an autologous blood product, which is offering physicians the ability to use in specific disease or disorders. The development of allogenic therapies with potential CB-PRP in applicable disease conditions will be futuristic therapies for clinical practitioners. The development of PRP and CB-PRP therapies are of importance to ensure natural therapy, long-term success, and patient satisfaction. The relevance and accomplishment of platelet rich plasma in the fields of dermatology, orthopaedic, dental, ophthalmology and gynaecology will hopefully receive more attention in research and daily clinical practice in the future.

Conclusion

PRP therapy is an important treatment option in last decades with many clinical applications in dermatology, orthopaedic, dental, ophthalmology and gynaecology. CB-PRP has the potential to improve patients' overall quality of life due to presence of higher levels of anti-inflammatory molecules, GFs and cytokines. It is evident that the importance of more studies should be conducted in this platelet product to prove the efficiency and compatibility. CB-PRP is an effective treatment and also it showed beneficial effects in few clinical conditions and the research can be extended where PRP is being used. Future research can focus on CB-PRP and it may be considered as immunologically compatible to use as allogenic.

Conflicts of interest

Authors declare no conflicts of interests.

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