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THE ROLE OF PLATELET-RICH PLASMA (PRP) IN PEDIATRIC SURGERY AND REGENERATIVE MEDICINE

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Abstract

Background. Platelet-rich plasma (PRP) is an autologous plasma concentrate containing platelets, growth factors, and cytokines. It promotes tissue regeneration by accelerating healing, reducing inflammation, and enhancing recovery. The use of an autologous source minimizes the risks of immune rejection. PRP is particularly valuable in pediatric surgery, particularly for enhancing tissue regeneration after trauma, correcting congenital anomalies, and improving postoperative healing, offering advantages where traditional methods are less effective.

The aim. To analyze and summarize data on the effectiveness of platelet-rich plasma (PRP) in tissue regeneration in pediatric surgery patients. The study focuses on the role of PRP in accelerating wound healing, stimulating bone regeneration, and reducing the risk of postoperative complications. The key objective is to evaluate the potential of PRP as an

adjunct to standard surgical techniques, particularly bone grafts or reconstructions, for its integration into routine pediatric practice.

Materials and methods. The research methodology consisted of a systematic review of scientific publications from the PubMed and ELSEVIER databases from 2000 to 2024. The selection criteria were English-language articles (clinical studies and reviews) that focused on the clinical application of PRP for tissue regeneration in pediatric surgery (patients under 18 years of age). The analysis focused on evaluating the efficacy and safety of PRP in the pediatric population.

Results. PRP acts as a controlled delivery system for bioactive molecules, modulating inflammation, stimulating cell proliferation, angiogenesis, and extracellular matrix synthesis. Growth factors released from α-granules, such as PDGF, TGF-β, VEGF, and EGF, are the basis for regeneration. In a randomized study of infants with meningomyelocele, PRP gel applied to the defect site significantly reduced cerebrospinal fluid leakage (5% vs. 45%), meningitis (0% vs. 35%), partial skin necrosis (15% vs. 65%), and wound dehiscence (15% vs. 35%; all $p < 0.05$). In treating pilonidal sinus in adolescents, PRP gel reduced healing time, pain, and antibiotic use ($p < 0.001$). In Snodgrass urethroplasty (hypospadias), PRP reduced the incidence of urethrocutaneous fistulas (10% vs. 25%). In pediatric maxillofacial surgery (children aged 8-15 years), the combination of PRP with autogenous bone grafting after cyst enucleation showed significantly higher regeneration (94% defect filling after 6 months compared to 47% in the control group; $p < 0.05$).

Conclusions. PRP is a safe, biocompatible adjuvant in pediatric surgery. It improves wound healing and bone regeneration outcomes and reduces complications in procedures such as treating hypospadias, pilonidal sinus, and meningomyelocele. The autologous nature of PRP eliminates the risks of immune rejection and infection. Adding PRP to bone grafts significantly enhances bone regeneration in children. Further research is needed to standardize preparation and dosage protocols, as variability affects outcomes.

Keywords: platelet-rich plasma; PRP; pediatric surgery; tissue regeneration; bone regeneration; wound healing; children

Introduction

Platelet-rich plasma (PRP) is a plasma concentrate enriched with platelets, growth factors, and cytokines that promote tissue regeneration by accelerating healing, reducing inflammation, and enhancing recovery. This technology is based on an autologous source, which minimizes the risks of immune rejection, making it cost-effective and versatile in

surgery, especially in pediatrics, where healing can be complicated due to the delicacy of procedures such as the reconstruction of congenital defects. The history of autologous PRP dates back to the mid-20th century, when in 1954 the term ‘platelet-rich plasma’ was first used for standard platelet concentrates in transfusion medicine. In the 1970s, PRP began to be used in reconstructive surgery to reduce blood loss, and in the 1980s, for the regeneration of damaged tissues, such as skin ulcers, through the release of growth factors, including platelet-derived growth factor (PDGF), epidermal growth factor (EGF), and vascular endothelial growth factor (VEGF) [1]. In pediatric surgery, PRP is particularly valuable for stimulating tissue regeneration in cases of congenital anomalies, trauma, and post-operative healing, where traditional methods may not be sufficiently effective. Platelets are rich in growth factors and cytokines that induce wound healing and tissue regeneration mechanisms, including an osteogenic effect to improve implantation in maxillofacial surgery. PRP is a natural source of growth factors and is successfully used in dentistry, plastic surgery, traumatology, and orthopedics for the regeneration of various tissues, although a standardized protocol for preparation and application has not yet been established [2, 3].

The aim of the study

This article aims to review the use of platelet-rich plasma (PRP) in pediatric surgery for tissue regeneration, emphasizing its effectiveness in pediatric procedures such as wound healing, bone regeneration, and reduction of postoperative complications. The review is based on an analysis of clinical studies and systematic reviews demonstrating the role of PRP as an autologous biostimulant that enhances cell proliferation, migration, and differentiation in the healing process, focusing on pediatric patients to minimize risks and optimize recovery. The study aims to evaluate PRP as an adjunct to standard methods, such as bone grafts or surgical reconstructions, to establish its potential in routine clinical practice for children.

Materials and methods

This review article is based on a systematic analysis of scientific literature on the use of platelet-rich plasma (PRP) in pediatric surgery for tissue regeneration. Data from clinical studies, systematic reviews, and preclinical studies published in peer-reviewed journals were used to ensure objectivity and reliability. The literature search was conducted in PubMed, ELSEVIER, and other medical archives using keywords such as: ‘platelet-rich plasma’, “PRP”, ‘pediatric surgery’, ‘tissue regeneration’, ‘bone regeneration’, ‘wound healing’, ‘children’, and their combinations. The inclusion criteria covered articles in English published between 2000 and 2024, focusing on pediatric patients (aged under 18), clinical applications

of PRP for tissue regeneration, and the availability of quantitative or qualitative data on efficacy.

Results and discussion

Platelet-rich plasma (PRP) is an autologous product obtained from the patient's blood by Centrifugation, containing a platelet concentration 3-5 times higher than the baseline level in peripheral blood. PRP acts as a controlled delivery system for bioactive molecules that promote tissue regeneration by modulating inflammation, stimulating cell proliferation, angiogenesis, and extracellular matrix (ECM) synthesis [4, 5]. Its mechanisms of action are based on the release of platelet contents upon activation, which mimics the physiological processes of wound healing and tissue repair, emphasizing the synergy of growth factors, cytokines, and structural elements such as the fibrin scaffold [6, 20].

PRP is prepared from the patient's venous blood (volume 10-60 ml), anticoagulated with sodium citrate (better than heparin, as it preserves platelet function and reduces microvesicular secretion). In pediatric surgery, PRP preparation is adapted to age characteristics: for children older than 12 months, autologous venous blood (volume 10-20 ml) is used, while for infants, umbilical cord blood or donor PRP from parents is often used [7, 21]. Centrifugation (1500-3000 rpm for 3-15 minutes) separates the blood into layers: erythrocytes (discarded to avoid inflammation from hemolysis), a buffer layer (leukocytes, often excluded in leukocyte-poor PRP to reduce pro-inflammatory effects), and platelet-enriched plasma (concentration 2-3 times higher than baseline, 150,000-400,000 platelets/μl). The optimal platelet concentration avoids inhibition of cell proliferation at excessive doses [8]. Activation initiates the release of platelet contents and the formation of a fibrin mesh for controlled delivery of molecules. Exogenous activation occurs by physical methods (freezing-thawing) or additives, such as calcium chloride (preferably to avoid hypocalcemia from anticoagulants) or thrombin, forming an injectable solution or fibrin clot/membrane for surgical use. Endogenous activation occurs naturally after administration. Activation leads to platelet degranulation, release of α-granule contents (growth factors, inflammatory mediators), δ-granules (coagulation factors, vasoactive amines), and lysosomes, followed by polymerization of fibrinogen into a fibrin mesh that traps molecules for gradual release [9].

PRP contains plasma biomolecules and platelet contents, forming a synergistic cocktail of thousands of molecules that regulate hemostasis, repair, inflammation, and protection. Platelets (disc-shaped, non-nucleated, 2-3 μm in diameter, with a lifespan of 7-10 days) store materials in granules: α-granules (growth factors, inflammatory mediators), δ-granules (coagulation factors, vasoactive amines), and lysosomes. The released elements

include adhesive proteins (fibrin, fibronectin, vitronectin), fibrinolysis/coagulation factors, antimicrobial agents, cytokines, growth factors, microparticles (anti-inflammatory), and exosomes (for cell communication). Plasma adds circulating molecules, and variations (platelet count, presence of leukocytes, erythrocytes — avoided to prevent stress/inflammation) affect efficacy; leukocyte-poor PRP is optimal for joints. The concentration of growth factors in PRP is significantly higher: TGF-β — 7 times, PDGF — 30 times, EGF — 10 times compared to whole blood, according to ELISA data [10, 11].

Growth factors released from α-granules upon activation are the basis of regeneration:

• PDGF (platelet-derived growth factor): Chemotactic for cells (fibroblasts, bone marrow stem cells, preosteoblasts); stimulates mitogenesis (cell proliferation), angiogenesis (formation of new blood vessels), macrophage activation; promotes cartilage and meniscus repair; activates cell membrane receptors, generating high-energy phosphate bonds for signaling proteins.

• TGF-β (transforming growth factor-beta): Antiproliferative for epithelial cells; acts paracrinally and autocrinally on fibroblasts, stem cells, preosteoblasts; inhibits osteoclast formation, promotes bone regeneration and remodeling; influences early repair, stem cell differentiation, cartilage/subchondral bone maintenance; stimulates tendocyte proliferation, collagen I/III synthesis

• VEGF (vascular endothelial growth factor): Stimulates vasculogenesis and angiogenesis; increases vascular density, supports tendon healing; originally identified as a vascular permeability factor.

• EGF (epidermal growth factor): Binds to the EGFR receptor; stimulates cell growth, proliferation, and differentiation; promotes cell migration

• IGF-1 (insulin-like growth factor-1) and HGF (hepatocyte growth factor): Stimulate tendocyte proliferation and collagen synthesis; anti-inflammatory, inhibit the NF-κB pathway, reduce pro-inflammatory cytokines (IL-1β, TNF-α, IL-6, IL-10, PGE2).

• bFGF (basic fibroblast growth factor): Key for migration, proliferation, differentiation, and angiogenesis [4, 5, 7, 12].

PRP affects inflammation, pain, lubrication, and cellular response:

Control of local inflammation is a key mechanism; platelets recruit immune cells (neutrophils, monocytes, macrophages) via chemokines and interleukins, clearing debris and pathogens but preventing excessive reaction; macrophage transition from M1 (pro-inflammatory) to M2 (reparative) via microparticles and IL-1Ra; inhibition of pro-inflammatory molecules (IL-1β, TNF-α, PGE2) in chondrocytes, fibroblasts, osteoblasts,

macrophages [4]. Pain reduction through inflammation reduction (PGE2 via NF-κB inhibition) and stimulation of the endocannabinoid system (anandamide, 2-arachidonoylglycerol as CB1/CB2 receptor agonists), reducing the nociceptive response. Increased growth, migration, proliferation of chondrocytes; reduced apoptosis; enhanced synthesis of glycosaminoglycans (GAG), proteoglycans, collagen; for mesenchymal stem cells (MSC) — increased proliferation, chondrogenic potential [13]. Angiogenesis and epithelialization: VEGF, PDGF, FGF, and EGF promote neovascularisation and re-epithelialization; in full-thickness wounds, there is accelerated closure [14].

In pediatric general surgery, PRP reduces postoperative complications and accelerates healing. In a randomized study by Arabacı Ö., Akyol ME. et al. (2023), 40 infants with meningomyelocele (mean age 1.5 days) after primary reconstruction of the sac, PRP gel applied to the defect site significantly reduced cerebrospinal fluid leakage (5% vs. 45% in the control group), meningitis (0% vs. 35%), partial skin necrosis (15% vs. 65%) and wound dehiscence (15% vs. 35%; all $p < 0.05$), with no significant differences in complete skin necrosis (0% vs. 5%; $p > 0.05$). This is associated with enhanced angiogenesis, fibroblast proliferation, and collagen synthesis, which improves tissue integration in vulnerable infants [15].

In the treatment of pilonidal sinus (a disease common in adolescents) in a randomised study by Di Mitri M., D'Antonio S. et al. (2024) 49 patients (mean age 25 years, but with paediatric implications) PRP gel after excision reduced healing time ($p < 0.001$), pain on the VAS scale ($p < 0.001$), antibiotic use ($p < 0.001$) and angiogenesis ($p < 0.001$), with a correlation between cavity volume and recovery time ($p < 0.001$), reduction in analgesics ($p < 0.001$) and faster return to activity ($p \leq 0.003$), demonstrating potential for adolescent surgery [1, 16].

For hypospadias, PRP as a barrier layer in Snodgrass urethroplasty (33 patients) reduced the incidence of urethrocutaneous fistulas (10% vs. 25%), stenosis (5% vs. 20%) and infections ($p < 0.05$) at 1-5 months; in 180 patients, PRP over urethroplasty reduced overall complications (fistulas, infections, dehiscence, stenosis; $p < 0.05$) [23].

In enterocutaneous fistulas, PRP gel from umbilical cord blood closed an oesophagocutaneous fistula in an infant after oesophagoplasty, with complete healing after three applications, improved scar quality, and no recurrence. In musculoskeletal surgery, PRP is used for juvenile idiopathic arthritis (intra-articular injections reduce inflammation) and ligament injuries (accelerates tendon repair), with potential for congenital anomalies such as spina bifida, where PRP as an adjuvant improves neuronal regeneration [17].

PRP is a powerful osteoinducer enriched with growth factors to enhance bone and soft tissue regeneration in pediatric maxillofacial surgery and dentistry. In a clinical study by Nagaveni NB., Praveen RB. et al. (2010), 20 children (aged 8-15 years) after enucleation of a jaw cyst, the combination of PRP with autogenous bone graft demonstrated significantly higher regeneration: 58% defect filling after 1 month, 72% after 2 months, 84% after 4 months, and 94% after 6 months, compared to 31%, 36%, 41%, and 47% in the control group without PRP ($p < 0.05$ at all intervals), without complications, indicating potential for routine use in paediatric bone defects [18, 19, 22].

Conclusions

PRP is a safe, biocompatible adjuvant in pediatric surgery that improves outcomes in a variety of applications, such as wound healing, bone regeneration, and reduction of complications in procedures such as hypospadias repair, pilonidal sinus, and meningomyelocele. Its autologous nature eliminates the risks of immune rejection and infection. Adding PRP to bone grafts significantly enhances bone regeneration in children, with potential for routine clinical use in the regeneration of bone defects after cyst enucleation. The combination of PRP with stem cells improves osteogenesis and cartilage regeneration, although results are controversial for periodontal regeneration. PRP may become an invaluable tool for tissue regeneration for pediatric dentists worldwide. Further research is needed to standardize protocols and dosages and to confirm efficacy in larger samples, as variability in preparation affects results.

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Conflict of interest.

The authors declare that the study was conducted with no conflicts of interest, financial, authorship, or other nature that could have influenced the course and results of the research in this article.

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