Revista UNILUS Ensino e Pesquisa
v. 20, n. 60, jul./set. 2023
ISSN 2318-2083 (eletrônico)

FELIPE SANCHES EDAES
Universidade de São Paulo, USP, São Paulo, SP, Brasil.

CLEIDE BARBIERI DE SOUZA
Centro Universitário Lusíada, UNILUS, Santos, SP, Brasil.

Recebido em setembro de 2023.
Aprovado em dezembro de 2023.

PRP IN CICATRICIAL ALOPECIA: UNRAVELING MECHANISTIC INSIGHTS, ASSESSING CLINICAL EFFICACY, AND PAVING FUTURE DIRECTIONS

ABSTRACT

Cicatricial alopecia (CA) is a complex hair loss disorder with significant clinical and psychological implications. This review investigates the role of Platelet-Rich Plasma (PRP) in treating CA, employing a comprehensive literature search in databases such as PubMed, Scopus, Embase, and Web of Science. By synthesizing information from relevant articles, reviews, clinical trials, and case studies, the study assesses PRP's efficacy in enhancing hair density, highlighting the need for standardized methodologies. The results emphasize PRP's promising role in CA therapy, its regenerative potential, and the importance of further research and collaboration in the field. The review concludes by underscoring the multifaceted nature of CA and the transformative possibilities offered by PRP, paving the way for innovative and compassionate treatments.

Palavras-Chave: cicatricial alopecia. platelet-rich plasma therapy. hair loss treatment.

PRP EM ALOPECIA CICATRICIAL: DESVENDANDO PERSPECTIVAS MECÂNICAS, AVALIANDO EFICÁCIA CLÍNICA E TRAÇANDO DIREÇÕES FUTURAS

RESUMO

A alopecia cicatricial (AC) é um distúrbio complexo de perda de cabelo com implicações clínicas e psicológicas significativas. Esta revisão investiga o papel do Plasma Rico em Plaquetas (PRP) no tratamento da AC, empregando uma pesquisa bibliográfica abrangente em bancos de dados como PubMed, Scopus, Embase e Web of Science. Ao sintetizar informações de artigos, revisões, ensaios clínicos e estudos de caso relevantes, o estudo avalia a eficácia do PRP no aumento da densidade capilar, destacando a necessidade de metodologias padronizadas. Os resultados enfatizam o papel promissor do PRP na terapia da AC, seu potencial regenerativo e a importância de pesquisas e colaborações adicionais no campo. A revisão conclui destacando a natureza multifacetada da AC e as possibilidades transformadoras oferecidas pelo PRP, abrindo caminho para tratamentos inovadores e compassivos.

Keywords: alopecia cicatricial. terapia com plasma rico em plaquetas. tratamento da perda de cabelo.

Revista UNILUS Ensino e Pesquisa
Rua Dr. Armando de Salles Oliveira, 150
Boqueirão - Santos - São Paulo
11050-071
http://revista.lusiada.br/index.php/ruep
revista.unilus@lusiada.br
Fone: +55 (13) 3202-4100

INTRODUCTION

Hair, a multifaceted human tissue, comprises structures such as the cuticle and cortex, with the primary component being keratin, arranged in an α-helix structure (GUBITOSA et al., 2019). Often termed "miniorgans," hair follicles engage in a rigorously controlled cycle, essential for morphogenesis, with elements like Dermal Microcirculation (DM) and growth factors such as VEGF playing pivotal roles in hair health (LIN et al., 2015; BASSINO, GASPARRI; MUNARON, 2020).

Alopecia transcends mere aesthetic considerations to affect psychological well-being, presenting as a condition marked by hair loss (KIM et al., 2013). Cicatricial Alopecia (CA), a complex disorder culminating in permanent hair follicle loss, distinguishes itself through various factors, including environmental exposures and the use of skincare products (WANG et al., 2022; SINGH et al., 2023). The multifaceted nature of CA manifests further in its differentiation from non-cicatricial alopecia (non-CA), with each variant posing unique therapeutic obstacles and outcomes (VORONKOVA et al., 2012; TEJAPIRA et al., 2022).

Recently, Platelet-Rich Plasma (PRP) has risen as a promising treatment option, signifying a shift in the therapy of diverse alopecia forms. This review, entitled "Platelet-Rich Plasma in Cicatricial Alopecia: Unraveling Mechanistic Insights, Assessing Clinical Efficacy, and Paving Future Directions," provides an exhaustive analysis of PRP's role within alopecia, with a focus on cicatricial types. Integrating contemporary discoveries with innovative approaches, it assesses PRP's efficacy across conditions, laying the foundation for an inclusive examination and forward-thinking perspective.

The subsequent sections guide readers through PRP's inherent mechanisms, therapeutic tactics, challenges, and future possibilities concerning CA. The review investigates PRP's ability to augment hair density and its relevance in treating skin and hair maladies (XIAO et al., 2019; MERCURI et al., 2021), emphasizing the need for methodological standardization and pinpointing research imperatives. These insights strive to clarify the existing state of knowledge while encouraging a critical evaluation of future innovations and best practices in the multifaceted domain of dermatological science.

SEARCH STRATEGY

To investigate the role of PRP therapy in CA, we conducted an extensive literature search across key databases such as PubMed, Scopus, Embase, and Web of Science. We used relevant terms like "Cicatricial Alopecia," "Platelet-Rich Plasma," and "Hair Loss" to query these databases. Selected articles, reviews, clinical trials, and case studies were carefully analyzed for their relevance and scientific quality. Our review focuses on the mechanisms, effectiveness, and future prospects of PRP therapy in treating CA, aiming to provide a critical and comprehensive overview of the current state of the field.

UNDERSTANDING HAIR FOLLICLES AND THEIR ROLE IN SKIN HEALTH

Exploring the Structure and Function of Hair Follicles within the Integumentary System

Hair follicles, complex mini-organs in the integument system, play a central role in human skin health. Keratin's α-helix structure characterizes them, including amino acids like tyrosine, glycine, and cysteine. This composition—comprising cuticle layers and cortex—provides strength and flexibility, fulfilling protective and sensory functions (GUBITOSA et al., 2019).

The body tightly regulates the hair follicle cycle, crucial for morphogenesis and including accessory structures like sebaceous and sweat glands. This coordination sustains the growth, regression, and rest phases through intricate signaling pathways involving various cells and hormones (LIN et al., 2015).

DM controls hair health through growth factors such as Vascular Endothelial Growth Factor (VEGF), vital for nutrient, cytokine, and molecule transport. DM's role in immune response, wound healing, and skin homeostasis underscores the multifaceted nature of hair follicles within the integumentary system's broader context (BASSINO; GASPARRI; MUNARON, 2020).

Far from merely being sites of hair growth, hair follicles' specialized structures and functions contribute across various aesthetic subunits like the scalp, eyebrows, and other regions. These elements shape diverse human aspects such as facial expression, individual identity, and social and psychological well-being (EVIN; EVIN, 2023).

In CA, irreversible follicular damage causes visible follicular ostia to vanish and may lead to epidermal atrophy in scarred areas. The replacement of pilosebaceous structures with fibrous tracts results in permanent hair loss (SINGH; MUTHUVEL, 2021).

Classifying Alopecia: Forms, Classifications, and Connections to Cicatricial Alopecia

Beyond cosmetic concerns, alopecia is a complex disorder that causes hair loss, with genetic and environmental factors shaping its etiology. This disorder impacts self-esteem and quality of life and is classified into cicatricial (CA) and non-cicatricial (non-CA) types, adding complexity to diagnosis and treatment planning (KIM et al., 2013).

Specific alopecia forms such as alopecia areata (AA), alopecia totalis, and alopecia universalis exist. AA, a chronic inflammatory disorder, is marked by T cell infiltration into hair follicle bulbs and often correlates with other dermatological and autoimmune conditions (SENESCHAL; BONIFACE; JACQUEMIN, 2022).

CA results in irreversible follicle loss and scarring, seen in diseases like lupus erythematosus and sarcoidosis, whereas non-CA preserves follicle stem cells in the bulge area. This preservation distinguishes non-CA from CA, where stem cell destruction leads to permanent loss, underlining the necessity for accurate diagnosis and prompt intervention (VORONKOVA et al., 2012; SHIMIZU et al., 2022; TEJAPIRA et al., 2022).

The correct differentiation between alopecia types is vital for their distinct etiologies and treatments. CA accounts for roughly 5% of all cases, leading to scarring and follicle destruction, while various diseases cause non-CA, resulting in terminal loss and thinning. Recognizing these differences helps clinicians devise patient-specific strategies addressing both physical and psychosocial aspects (BARIKBIN et al., 2017; SHIMIZU et al., 2022).

Alopecia can be categorized broadly as cicatricial (scarring) or non-scarring, with the latter preserving the potential for regrowth. CA, where follicles are destroyed and replaced with scar tissue, contrasts with AGA, the main non-scarring form (EVIN; EVIN, 2023).

CA divides further into primary (PCA) and secondary types (SCA), categorized as stable or unstable. PCA involves targeted inflammation of follicle stem cells, while SCA results from destructive skin activities. Isolated incidents cause stable CAs, and unstable CAs experience intermittent progression and recurrence (SINGH; MUTHUVEL, 2021). The North American Hair Research Society (NAHRS) classifies PCA based on the predominant inflammatory cells in hair follicle biopsy samples, including lymphocyte-predominant, neutrophil-predominant, mixed, and non-specific subgroups (EVIN; EVIN, 2023).

INVESTIGATING CICATRICIAL ALOPECIA

Detailing Cicatricial Alopecia Etiology

CA encompasses a diverse range of disorders that permanently scar the hair follicles and replace them with fibrous tissue. These disorders fall into PCA, SCA, or hereditary/developmental categories, with PCA and SCA distinguished by inflammatory processes that destroy the hair follicles (EVIN; EVIN, 2023).

PCA specifically targets pluripotent stem cells in the "bulge" region of hair follicles through inflammation in a variety of conditions (SINGH; MUTHUVEL, 2021; EVIN; EVIN, 2023; SINGH et al., 2023).

In contrast, SCA often results from external insults like trauma, burns, or radiation therapy, culminating in scarring and permanent loss of follicles (EVIN; EVIN, 2023).

Disorders such as Central Centrifugal Cicatricial Alopecia (CCCA), Lichen Planopilaris (LPP), and Frontal Fibrosing Alopecia (FFA) display demographic patterns, with underlying multifactorial etiologies (HAMBLIN, 2019; GEORGE et al., 2022; LARRONDO; PETELA; LEEM et al., 2022; MCMICHAEL, 2022; WANG et al., 2022).

CA's complexity, further divided into stable (SCA) and unstable (UCA) types, mandates individualized treatment strategies. However, the irreversible nature of the hair loss often poses significant therapeutic challenges (EVIN; EVIN, 2023).

Examining Cicatricial Alopecia's Epidemiology

CA accounts for 3.2-7.3% of all hair loss cases and primarily manifests in females (EVIN; EVIN, 2023). Though more prevalent in adults, CA does occur in children, with SCA being notably common in pediatric instances, albeit constituting only a minor percentage of consultations (BUCH; CHOUHAN, 2023).

The epidemiology of PCA presents a puzzling variation across specialized centers, with prevalence rates ranging from 3.7% to 7.2%. This disparity emphasizes the urgent call for sweeping population-wide investigations to pinpoint the true extent of PCA (SINGH et al., 2023).

Particularly intriguing is the distribution of CCCA among middle-aged women of African descent. Factors such as specific skincare products and environmental conditions have been implicated in its occurrence. These findings not only forge new avenues for in-depth exploration but also demand a multifaceted approach, uniting various disciplines to decode the complex underlying causes (GEORGE et al., 2022; LARRONDO; PETELA; MCMICHAEL, 2022; WANG et al., 2022).

Identifying Clinical Presentations and Associated Skin Alterations

PCA manifests as permanent hair loss, marked by specific patterns and immune cell infiltration targeting follicles (WANG et al., 2022). This infiltration, particularly within the epithelial stem cell region, precipitates sebaceous gland destruction and ensuing fibrosis (WANG et al., 2022).

Fibrotic pathways that modify gene expression and cause sebaceous gland loss are evident across PCA subtypes, such as LPP, FFA, and CCCA, and may precede hair loss (WANG et al., 2022).

Clinical symptoms of CA, including the loss of follicular ostia and epidermal atrophy, can be deceptive, initially mimicking other forms of alopecia (SINGH; MUTHUVEL, 2021).

SCA, caused by underlying or external agents, requires meticulous diagnosis for associated conditions like chronic cutaneous lupus erythematosus (EVIN; EVIN, 2023).

Comprehensive diagnostic techniques involve tools like scalp dermoscopy (EVIN; EVIN, 2023).

Special cases and recent findings, such as hair loss following aesthetic procedures or pediatric follicular unit extraction (FUE), demand nuanced considerations and underline the multifaceted nature of CA (BARRERA-OCHOA et al., 2023; BUCH; CHOUHAN, 2023).

Delineating Pathological Changes Characteristic of Cicatricial Alopecia

CA encompasses a heterogeneous array of disorders that destroy hair follicles irreversibly, resulting in scarring and hair loss. Inflammatory disorders within this category, such as LPP, FFA, and CCCA, can be histologically characterized by the replacement of pilosebaceous structures with fibrous tracts. These changes define lymphocyte-mediated (LMPCA), neutrophil-mediated (NMPCA), or mixed CA classes (SINGH; MUTHUVEL, 2021; EVIN; EVIN, 2023).

Immune-mediated alopecia (IMA) specifically targets immune-protected areas in hair follicles, eliciting autoimmunity and inflammation (TEJAPIRA et al., 2022). PCA entails progressive inflammation in the follicular "bulge" area, leading to permanent stem cell damage and loss of follicle functionality. SCA follows generalized disruption, culminating in fibrotic scarring and hair loss (SINGH; MUTHUVEL, 2021; EVIN; EVIN, 2023).

Recent RNA-sequencing studies have revealed shared molecular pathways such as cholesterogenesis, fibrosis, and mast cell activity in CAs (WANG et al., 2022). The diagnostic challenges in CA emanate from inconsistent terminology and patient variability, but the combination of horizontal and vertical biopsies, along with scar analysis and treatment complexities, provides critical insights (UCHIYAMA, 2021; DOU et al., 2022; WANG et al., 2022; BARRERA-OCHOA et al., 2023; EVIN; EVIN, 2023).

Analyzing Molecular and Genetic Aspects of Cicatricial Alopecia

Cutting-edge research methodologies such as high-throughput RNA-sequencing and Genome-Wide Association Studies (GWAS) have elucidated gene similarities and potential therapeutic targets in LPP, FFA, and CCCA (WANG et al., 2022). These discoveries propose links between CA and environmental triggers like facial product allergens, enhancing our comprehension of PCA pathogenesis and unveiling novel intervention opportunities (GEORGE et al., 2022; WANG et al., 2022).

PCA's complexity is marked by the convergence of factors such as hair follicle stem cell destruction, self-maintenance impairment, and influences from environmental and genetic contributors. Collectively, these insights are expanding our understanding of PCA's pathobiology and opening new avenues for therapeutic innovations (GEORGE et al., 2022; TEJAPIRA et al., 2022; WANG et al., 2022).

Assessing Impact on Quality of Life and Exploring Treatment Modalities

CA, regarded as a trichological emergency, significantly impairs psychological well-being and self-esteem, particularly in younger patients (SINGH; MUTHUVEL, 2021; BUCH; CHOUHAN, 2023). The effects are amplified by pain, itching, and uncertainty over treatment outcomes (BANERJEE; SHARMA; NEMA, 2009; SHIMIZU et al., 2022; TEJAPIRA et al., 2022; SINGH et al., 2023).

The urgency for enhanced treatment is underlined by the substantial pursuit of medical interventions, with expenditure exceeding $3.5 billion annually in America (AVCI et al., 2013; KIM et al., 2013; HAMBLIN, 2019; YOUSSEF et al., 2022). Management success necessitates accurate diagnosis, early intervention, and versatile options

including topical minoxidil (MNX), oral pentoxifylline, intralesional steroids, and fractional CO2 laser treatments (SAEED; HOOTA; KHALLAF, 2021; BUCH; CHOUHAN, 2023).

The core of PCA treatment revolves around controlling inflammation and halting disease progression, with surgical interventions like FUE hair transplantation showing promise. The comprehensive impact of CA emphasizes the importance of holistic strategies such as PRP therapy (VORONKOVA et al., 2012; SINGH et al., 2023). A meticulous follow-up focusing on disease course, treatment efficacy, side effects, and psychosocial facets, coupled with a profound understanding of the condition, is pivotal for minimizing recurrence risks (EVIN; EVIN, 2023).

Discussing Recent Classifications in Cicatricial Alopecia

Recent advances in PCA classification enhance evaluations and diagnoses, despite persisting limitations in identifying specific subtypes (UCHIYAMA, 2021). Improved comprehension of common and unique features across multiple PCA subtypes aids not only in diagnostic accuracy but also in insights into disease progression and treatment response (MERCURI et al., 2021).

Newly developed tools enrich our ability for a more in-depth evaluation of hair growth and treatment response. Progress in PCA classification and nuanced understandings of features across subtypes heighten diagnostic precision (MERCURI et al., 2021; UCHIYAMA, 2021).

EXAMINING CURRENT TREATMENT APPROACHES TO CICATRICIAL ALOPECIA

Providing an Overview of Existing Treatments

Globally, Androgenetic Alopecia (AGA) affects nearly 70% of adults. Conventional treatments, such as MNX and finasteride, target male hormones but frequently lead to side effects (KIM et al., 2013; DAY; MCCARTHY; TALABER, 2021; RIANGJANAPATEE et al., 2022).

For CA, treatment strategies span from topical solutions to surgical interventions. Despite their FDA approval, limitations are evident in AGA treatments, including finasteride and MNX. In contrast, CA management usually incorporates anti-inflammatory agents and hormone modulators (VORONKOVA et al., 2012; CRUCIANI et al., 2021; DOU et al., 2022; WANG et al., 2022; ZHANG et al., 2023).

Innovations in the field comprise dietary interventions, photobiomodulation, Janus Kinase (JAK) inhibitors, nanofat grafting, and Kerascalp hair serum. The complexity of conditions such as Female Androgenetic Alopecia (FAGA) propels research into regenerative techniques, including stem cell and PRP therapies (LIN et al., 2015; GUPTA; CARVIEL, 2019; BASSINO et al., 2020; MERCURI et al., 2021; SHIMIZU et al., 2022; WANG et al., 2022; EVIN et al., 2023; KOHLI et al., 2023; PALMA et al., 2023).

The intricate nature of CA requires continuously evolving treatments. Early diagnosis and aggressive measures, such as immunosuppression, antimicrobials, or dapsone, are essential for specific PCA types. Despite controversy, pharmacological methods like topical MNX and oral finasteride might suppress progression, albeit with potential side effects (SINGH; MUTHUVEL, 2021; BUCH; CHOUHAN, 2023; EVIN; EVIN, 2023).

Professionals manage SCA using techniques such as hair transplantation, FUE, and scalp reduction. Recent advancements like the “no root touch technique” and minimally invasive follicular unit transplantation (FUT) methods present themselves, but with risks, including scarring and compromised outcomes in unstable CA (SAEED; HOOTA; KHALLAF, 2021; BUCH; CHOUHAN, 2023; EVIN; EVIN, 2023).

Various camouflage techniques encompass both medical and surgical procedures, such as prosthetic wigs and tattoo micro-pigmentation. Selection criteria consider

factors like age, sex, etiology, and scar characteristics in scarred CA (EVIN; EVIN, 2023).

While PRP-assisted post-burn CA treatment enhances scar maturity, reconstructive challenges persist with inherent limitations in each surgical approach (EVIN; EVIN, 2023).

Performing a Comparative Assessment with PRP Therapy

PRP is gaining recognition as an effective treatment for inflammatory alopecias, such as AA and PCAs, with studies highlighting its efficacy as equivalent or even superior to traditional methods (TEJAPIRA et al., 2022; SAHIN et al., 2023).

PRP shows promise in treating conditions like CCCA, LPP, and FFA, but its effectiveness has been inconsistent, with observed hair density increases possibly unsustainable in the long term (GEORGE et al., 2022; LARRONDO et al., 2022).

Despite early encouragement, formalizing PRP use in the U.S. and European Union awaits resolution, and evidence backing its application varies across studies (CRUCIANI et al., 2021).

An evaluation of FUE for SCA underscores this method's significance within hair transplantation. Although Otology hair transplantation remains potent, challenges with graft viability continue. Cutting-edge interventions like laser therapy, fat injections, and stem cell treatments may enhance scar tissue features. Within this scope, the inclusion of PRP in multimodal treatments heralds exciting prospects for future CA management (SAEED; HOOTA; KHALLAF, 2021; EVIN; EVIN, 2023).

ELUCIDATING PRP THERAPY: ITS PROMISE AND POTENTIAL

Detailing PRP's Composition and Preparation Techniques

PRP, an autologous serum comprising plasma, platelets, and growth factors, is obtained from an individual's venous blood and has experienced a surge in application for alopecia treatment due to its regenerative capability (EDAES; FERREIRA, 2020; TEJAPIRA et al., 2022). The preparation of PRP requires stringent sterility procedures, including blood drawing, anticoagulant treatment, and centrifugation, occasionally augmented with activators like calcium chloride (EDAES; FERREIRA, 2020; SHIMIZU et al., 2022).

Techniques within regenerative medicine are now able to achieve a high platelet density suitable for injection, and recent studies have uncovered disparities between activated and non-activated PRP (MERCURI et al., 2021; SHIMIZU et al., 2022; SAHIN et al., 2023). Activation of PRP employs an activator or accelerator to stimulate the platelets, eliciting the release of additional growth factors (MORKUZU et al., 2023).

PRP's physiological action sets off a healing cascade, positioning it as a non-surgical strategy for hair growth. Despite its promise, PRP faces challenges, including FDA classification issues and inconsistencies in clinical application, underlining the need for standardized research approaches (KRAMER; KEANEY, 2018; TEJAPIRA et al., 2022; PENSATO; AL-AMER; LA PADULA, 2023).

Charting PRP’s Historical Journey and Current Applications in Skin Repair

PRP has come to the forefront as a substance abundant in growth factors and chemokines, offering applications across various disciplines including dermatology, orthopedics, and sports medicine (EDAES; FERREIRA, 2020; CRUCIANI et al., 2021). Researchers have extended PRP's uses into areas such as tissue regeneration, scar modification, wound healing, severe ocular condition treatments, and contemporary dermatological practices. Systematic investigations into these applications have

unveiled improvements in hair density (EDAES; FERREIRA, 2020; SHIMIZU et al., 2022; TEJAPIRA et al., 2022). Nevertheless, the pursuit of PRP's full potential confronts obstacles, such as inconsistencies in standardization. This emphasizes the imperative need for comprehensive meta-analyses (CRUCIANI et al., 2021; PENSATO; AL-AMER; LA PADULA, 2023; SAHIN et al., 2023).

The historical evolution of hair transplantation, culminating in the advent of PRP therapy, is marked by significant milestones. The journey began with Japanese dermatologist Sasagawa in 1930, advanced by Dr. Okuda's improvements in 1939 for traumatic alopecia, and was further augmented by Dr. Orentreich's work on AGA in 1959. The unveiling of the FUE technique in 2002 by Rassman et al. provided a modern alternative to conventional methods, effectively eradicating linear scarring in the donor area. More recent applications of FUE to CA underscore the promising trajectory of PRP's potential within this realm (BUCH; CHOUHAN, 2023).

Unveiling PRP's Distinctive Biological Constituents

PRP, rich in therapeutic constituents like platelet-derived angiogenesis factor, EGF, NGF, IGF-I, and platelet factor IV, offers effective treatments in dermatology, orthopedics, and wound healing (EDAES; FERREIRA, 2020; CRUCIANI et al., 2021). Recent explorations of variations such as autologous activated (AA-PRP) and non-activated PRP emphasize their potential in AGA patients (GENTILE and GARCOVICH, 2020). PRP's biological action regenerates and repairs hair follicles by releasing key growth factors and cytokines, and by activating vital pathways such as the MAPK, Akt, and Wnt signaling pathways (XIAO et al., 2019; TEJAPIRA et al., 2022).

Assessing PRP’s Efficacy in Addressing Cicatricial Alopecia

Researchers have applied PRP therapy to various types of hair loss, including CA, and found mixed results. These variations are partially due to inconsistent protocols and a dearth of long-term studies extending beyond 12 months (CRUCIANI et al., 2021; LARRONDO; PETELA; MCMICHAEL, 2022). While some trials hint at its potential, substantial evidence supporting PRP's efficacy in AA remains elusive (SHAPIRO et al., 2020; MERCURI et al., 2021).

Investigations into the biological underpinnings have demonstrated that PRP augments hair growth by promoting growth factor receptor expression and activating pathways in dermal papilla cells (DPCs), including MAPK, Akt, and Wnt signaling (XIAO et al., 2019; CRUCIANI et al., 2021). The particular effectiveness of calcium gluconate-activated PRP originates from specific protein release; however, the contrasting responses between activated and non-activated PRP warrant continued mechanistic study (MERCURI et al., 2021).

Treating conditions such as FAGA with PRP raises concerns over standardization, safety, and minor side effects, underscoring the multifaceted nature of this therapeutic strategy (MERCURI et al., 2021; TEJAPIRA et al., 2022).

As PRP’s role in managing CA expands, the imperative for exhaustive research to guide clinical practice becomes increasingly apparent (SAEED; HOOTA; KHALLAF, 2021). PRP's applications extend into areas like wound healing, scar remodeling, and graft survival in PCA, frequently coupled with supplementary treatments such as steroids or immunosuppressants post-transplantation. This emphasizes its vital function within the complex landscape of this condition (BUCH; CHOUHAN, 2023).

NAVIGATING PRP'S EVOLVING ROLE IN CICATRICIAL ALOPECIA MANAGEMENT

Explaining PRP's Mechanism in Cicatricial Alopecia Mitigation

Researchers attribute the interest in PRP for CA treatment to its regenerative properties, specifically growth factors that promote tissue repair and cellular proliferation within hair follicles (SHIMIZU et al., 2022). In addition to ensuring dermal papilla cell survival through anti-apoptotic effects, these growth factors may enhance overall hair restoration when therapists combine them with other treatments (DAY; MCCARTHY; TALABER, 2021). PRP's multifaceted role in CA ranges from stimulating hair growth through up-regulated growth factors to enhancing the degradation of damaged extracellular matrix by increasing MMP-1 and MMP-3 expression. Anti-inflammatory effects of proangiogenic cytokines also contribute substantially (LARRONDO; PETELA; MCMICHAEL, 2022).

Reviewing Current Data on PRP in Cicatricial Alopecia: Insights from Preliminary Research

As a promising alternative to traditional therapies for treating various skin and hair disorders, PRP has established its effectiveness in managing AGA, and combined treatments have produced encouraging results (KIM et al., 2021; MERCURI et al., 2021; TEJAPIRA et al., 2022). Though promising for immune-mediated alopecias (IMAs), the field still demands high-quality studies and systematic evaluation (TEJAPIRA et al., 2022; SAHIN et al., 2023). A specialized review on FAGA treatment has underscored the limited documentation regarding PRP's efficacy in PCAs, reinforcing the need for expansive research (MERCURI et al., 2021; MORKUZU et al., 2023).

Addressing the Need for Rigorous Investigations of PRP in Cicatricial Alopecia

Novel avenues for alopecia treatment have emerged from recent gene expression analyses, accentuating the urgent need for detailed and meticulous research (WANG et al., 2022). Rigorous comparative studies must be conducted to evaluate PRP's long-term effects and to create standardized treatment protocols (MERCURI et al., 2021). The inconsistencies in study outcomes, combined with initial optimism surrounding PRP in CCCA, mandate an updated systematic review and comprehensive scrutiny (EDAES; FERREIRA, 2020; GEORGE et al., 2022). Given the significant emotional and psychological burden of alopecia, the development of therapies must be rooted in methodologically robust research (SUCHONWANIT; CHALERMROJ; KHUNKHET, 2018).

The diagnosis of CA necessitates a multifaceted approach, involving the integration of clinical, trichoscopic, and scalp biopsy findings. Specialists often recommend obtaining two biopsy specimens to thoroughly analyze the involvement of different hair follicle structures (SINGH; MUTHUVEL, 2021).

Exploring Future Avenues: PRP's Expanding Potential for Cicatricial Alopecia

The promising role of PRP in hair loss treatments demands further investigation to refine treatment protocols and clarify long-term implications (GUPTA; CARVIEL, 2019). The urgency for definitive evidence is underscored by unresolved questions about variations in PRP treatment methodologies (MERCURI et al., 2021). With suggestions for further optimization, such as shorter-than-6-month intervals for maintenance therapy in stabilized CCCA patients, the evidence of PRP's potential as an alternative therapy grows (LARRONDO; PETELA; MCMICHAEL, 2022). Its broader applicability in regenerative medicine, encompassing areas like orthopedic, maxillofacial, and periodontal surgeries, further highlights PRP's extensive therapeutic promise (EDAES; FERREIRA, 2020).

CLOSING REMARKS

This comprehensive review analyzes the hair's sophisticated structure, including essential elements like the cuticle, cortex, and the α-helix arrangement of keratin. It traces the intricate cycle of hair morphogenesis, underlining the vital functions of DM and growth factors such as VEGF in hair health. CA is highlighted as a multifaceted and complex hair loss disorder, extending beyond aesthetics to pose clinical challenges, permanent scarring, and significant emotional distress. The review explores CA's complex subtypes, underlying mechanisms, and unique inflammatory patterns.

PRP therapy stands out as an encouraging advancement, especially for CA. The review delves into PRP's regenerative potential, promoting cellular activities like proliferation, vascularization, and angiogenesis in hair follicles. While PRP's utilization needs further standardization and comprehension of its activated versus non-activated forms, its successes and extensive therapeutic applications mark a thrilling progress. Current innovations such as JAK inhibitors, photobiomodulation, and stem cell therapies add to a promising landscape for customized and transformative solutions.

Certain unresolved questions remain, notably about the subtleties of PRP treatments for CA and other IMAs. These necessitate rigorous research, enhancement, and standardized protocol creation. Collaborative and interdisciplinary efforts, including the incorporation of novel trichoscopic and histopathological techniques, are crucial for gaining deeper insights into CA and developing efficient therapies.

The intricate interplay of hair physiology, various alopecia types, and emerging treatments like PRP symbolizes a fast-evolving scientific frontier brimming with innovation and promise. The emphasis on CA's complexity, and the promising outcomes of PRP therapy, reassert our dedication to scientific excellence, cooperation, and inquiry. Together, these efforts lay the groundwork for empathetic, thorough, and effective therapies for those struggling with CA and other hair disorders. The way forward abounds with possibilities for exploration, healing, and advancement, painting a future radiant with potential for those affected by these complex conditions.

TAKE HOME MESSAGE

CA represents more than a cosmetic dilemma, creating a complex medical challenge that significantly influences patients' quality of life.

PRP, while promising as a novel therapeutic intervention for CA, requires meticulous standardization and comprehensive investigation to elucidate its full potential and underlying intricacies.

Advancing the treatment of CA calls for a synergistic, multidisciplinary approach that leverages the latest technological advancements, targeted research initiatives, and a commitment to patient-centered care, signifying a dynamic evolution in the field of dermatological science.

ACKNOWLEDGMENTS

Our deepest gratitude extends to researchers and healthcare professionals whose pioneering work in alopecia has shaped this review. Insightful evaluations from peer reviewers and colleagues have enriched this manuscript. The unwavering support from our affiliated institutions has been instrumental, providing necessary resources and an enriching research environment. This work is dedicated to individuals confronting hair loss, whose resilience continually inspires our research endeavors.

Initials List

AA	Alopecia Areata
AA-PRP	Autologous Activated Platelet-Rich Plasma
AGA	Androgenetic Alopecia
Akt	Akt - Protein Kinase B
CA	Cicatricial Alopecia
CCCA	Central Centrifugal Cicatricial Alopecia
DM	Dermal Microcirculation
DPCs	Dermal Papilla Cells
EGF	Epidermal Growth Factor
FAGA	Female Androgenetic Alopecia
FDA	Food and Drug Administration
FFA	Frontal Fibrosing Alopecia
FUE	Follicular Unit Extraction
FUT	Follicular Unit Transplantation
GWAS	Genome-Wide Association Studies
IGF-I	Insulin-like Growth Factor I
IMA	Immune-Mediated Alopecia
JAK	Janus Kinase
LMPCA	Lymphocyte-Mediated Primary Cicatricial Alopecia
LPP	Lichen Planopilaris
MAPK	Mitogen-Activated Protein Kinase
MMP-1	Matrix Metalloproteinase-1
MMP-3	Matrix Metalloproteinase-3
MNX	Minoxidil
NAHRS	North American Hair Research Society
NGF	Nerve Growth Factor
NMPCA	Neutrophil-Mediated Primary Cicatricial Alopecia
non-CA	Non-Cicatricial Alopecia
PCA	Primary Cicatricial Alopecias
PRP	Platelet-Rich Plasma
SCA	Secondary Cicatricial Alopecia
U.S.	United States
UCA	Unstable Cicatricial Alopecia
VEGF	Vascular Endothelial Growth Factor
Wnt	Wnt Signaling Transduction Pathway

REFERÊNCIAS

AVCI, Pinar et al. Low-level laser (light) therapy (LLLT) for treatment of hair loss. Lasers In Surgery And Medicine, [S.L.], v. 46, n. 2, p. 144-151, 23 ago. 2013. Wiley. http://dx.doi.org/10.1002/lsm.22170.

BANERJEE, Pooja S.; SHARMA, Megha; NEMA, Rajesh Kumar. Reparation, evaluation and hair growth stimulating activity of herbal hair oil. Journal Of Chemical And Pharmaceutical Research, [s. l], v. 1, n. 1, p. 261-267, 2009.

BARIKBIN, Behrooz et al. Comparison of the effects of 665 nm low level diode Laser Hat versus and a combination of 665 nm and 808nm low level diode Laser Scanner of hair growth in androgenic alopecia. Journal Of Cosmetic And Laser Therapy, [S.L.], p. 1, 17 maio 2017. Informa UK Limited. http://dx.doi.org/10.1080/14764172.2017.1326609.

BARRERA-OCHOA, Carlos A. et al. Secondary alopecia induced by aesthetic procedures: an unrecognized potential complication. Australasian Journal Of Dermatology, [S.L.], v. 64, n. 3, p. 322-329, 2 jun. 2023. Wiley. http://dx.doi.org/10.1111/ajd.14090.

BASSINO, Eleonora; GASPARRI, Franco; MUNARON, Luca. Protective Role of Nutritional Plants Containing Flavonoids in Hair Follicle Disruption: a review. International Journal Of Molecular Sciences, [S.L.], v. 21, n. 2, p. 523, 14 jan. 2020. MDPI AG. http://dx.doi.org/10.3390/ijms21020523.

BUCH, Jeta; CHOUHAN, Kavish. Hair transplantation by follicular unit extraction in cicatricial alopecia in children. Indian Journal Of Paediatric Dermatology, [S.L.], v. 24, n. 1, p. 1, 2023. Medknow. http://dx.doi.org/10.4103/ijpd.ijpd_68_22.

CRUCIANI, Mario et al. Platelet-rich plasma for the treatment of alopecia: a systematic review and meta-analysis. Blood Transfusion, [S.L.], v. 21, n. 1, p. 24-36, 15 nov. 2021. Edizioni SIMTI. http://dx.doi.org/10.2450/2021.0216-21.

DAY, Doris; MCCARTHY, Madison; TALABER, Iva. Non-ablative Er: yag laser is an effective tool in the treatment arsenal of androgenetic alopecia. Journal Of Cosmetic Dermatology, [S.L.], v. 21, n. 5, p. 2056-2063, 26 ago. 2021. Wiley. http://dx.doi.org/10.1111/jocd.14370.

DOU, Jinjin et al. Exploring the effects of Chinese herbal ingredients on the signaling pathway of alopecia and the screening of effective Chinese herbal compounds. Journal Of Ethnopharmacology, [S.L.], v. 294, p. 115320, ago. 2022. Elsevier BV. http://dx.doi.org/10.1016/j.jep.2022.115320.

EDAES, Felipe Sanches; FERREIRA, Eliana Cláudia Perroud Morato. O USO DO PLASMA RICO EM PLAQUETAS NO TRATAMENTO DA SÍNDROME DO OLHO SECO POR DISFUNÇÃO DAS GLÂNDULAS DE MEIBOMIUS. RUEP, Santos, v. 17, n. 48, p. 266-278, dez. 2020. Trimestral. Disponível em: http://revista.unilus.edu.br/index.php/ruep/article/view/1324. Acesso em: 30 dez. 2020.

EVIN, Nuh; EVIN, Seyda Guray. Camouflage of post-burn scarring alopecia using nanofat grafting and follicular unit hair transplantation. Plastic & Reconstructive Surgery, [S.L.], v. , p. 1-1, 26 maio 2023. Ovid Technologies (Wolters Kluwer Health). http://dx.doi.org/10.1097/prs.0000000000010759.

EVIN, Nuh; EVIN, Seyda Guray. Surgical Management of Scarring Alopecia. Alopecia Management - An Update, [S.L.], p. 1, 26 jul. 2023. IntechOpen. http://dx.doi.org/10.5772/intechopen.107323.

GENTILE, Pietro; GARCOVICH, Simone. Autologous activated platelet-rich plasma (AA-PRP) and non-activated (A-PRP) in hair growth: a retrospective, blinded, randomized evaluation in androgenetic alopecia. Expert Opinion On Biological Therapy, [S.L.], v. 20, n. 3, p. 327-337, 14 fev. 2020. Informa UK Limited. http://dx.doi.org/10.1080/14712598.2020.1724951.

GEORGE, Elisabeth A. et al. Beyond the Hot Comb: updates in epidemiology, pathogenesis, and treatment of central centrifugal cicatricial alopecia from 2011 to 2021. American Journal Of Clinical Dermatology, [S.L.], v. 24, n. 1, p. 81-88, 18 nov. 2022. Springer Science and Business Media LLC. http://dx.doi.org/10.1007/s40257-022-00740-w.

GUBITOSA, Jennifer et al. Hair Care Cosmetics: from traditional shampoo to solid clay and herbal shampoo, a review. Cosmetics, [S.L.], v. 6, n. 1, p. 13, 19 fev. 2019. MDPI AG. http://dx.doi.org/10.3390/cosmetics6010013.

GUPTA, A. K.; CARVIEL, J. L.. Meta-analysis of photobiomodulation for the treatment of androgenetic alopecia. Journal Of Dermatological Treatment, [S.L.], v. 32, n. 6, p. 643-647, 20 nov. 2019. Informa UK Limited. http://dx.doi.org/10.1080/09546634.2019.1688755.

HAMBLIN, Michael R. Photobiomodulation for the management of alopecia: mechanisms of action, patient selection and perspectives. Clinical, Cosmetic And Investigational Dermatology, [S.L.], v. 12, p. 669-678, set. 2019. Informa UK Limited. http://dx.doi.org/10.2147/ccid.s184979.

KIM, Min Jung et al. Visible-to-Near IR Quantum Dot-Based Hypermulticolor High-Content Screening of Herbal Medicines for the Efficacy Monitoring of Hair Growth Promotion and Hair Loss Inhibition. Slas Discovery, [S.L.], v. 18, n. 4, p. 462-473, abr. 2013. Elsevier BV. http://dx.doi.org/10.1177/1087057112464574.

KIM, Sun Jong et al. Innovative method of alopecia treatment by autologous adipose-derived SVF. Stem Cell Research & Therapy, [S.L.], v. 12, n. 1, p. 1-1, 28 ago. 2021. Springer Science and Business Media LLC. http://dx.doi.org/10.1186/s13287-021-02557-6.

KOHLI, Malavika et al. Prospective Efficacy and Safety Study of an Innovative Kerascalp Hair Growth Serum in Mild-to-Moderate Alopecia in India: regrowth study. Cureus, [S.L.], p. 1-1, 8 maio 2023. Springer Science and Business Media LLC. http://dx.doi.org/10.7759/cureus.38742.

KRAMER, Maryjo e; KEANEY, Terrence C. Systematic review of platelet-rich plasma (PRP) preparation and composition for the treatment of androgenetic alopecia. Journal Of Cosmetic Dermatology, [S.L.], v. 17, n. 5, p. 666-671, 22 maio 2018. Wiley. http://dx.doi.org/10.1111/jocd.12679.LEEM, Jungtae et al. A network pharmacology-based approach to explore mechanism of action of medicinal herbs for alopecia treatment. Scientific Reports, [S.L.], v. 12, n. 1, p. 1, 18 fev. 2022. Springer Science and Business Media LLC. http://dx.doi.org/10.1038/s41598-022-06811-6.

LARRONDO, Jorge; PETELA, John; MCMICHAEL, Amy J.. Transitory hair growth using platelet-rich plasma therapy in stabilized central centrifugal cicatricial alopecia. Dermatologic Therapy, [S.L.], v. 35, n. 11, p. 1, 13 set. 2022. Hindawi Limited. http://dx.doi.org/10.1111/dth.15798.

LEEM, Jungtae et al. A network pharmacology-based approach to explore mechanism of action of medicinal herbs for alopecia treatment. Scientific Reports, [S.L.], v. 12, n. 1, p. 1, 18 fev. 2022. Springer Science and Business Media LLC. http://dx.doi.org/10.1038/s41598-022-06811-6.

LIN, Wei-Hong et al. Fibroblast Growth Factors Stimulate Hair Growth through β-Catenin and Shh Expression in C57BL/6 Mice. Biomed Research International, [S.L.], v. 2015, p. 1-9, 2015. Hindawi Limited. http://dx.doi.org/10.1155/2015/730139.

MERCURI, Santo Raffaele et al. Investigating the Safety and Efficacy of Platelet-Rich Plasma (PRP) Treatment for Female Androgenetic Alopecia: review of the literature. Medicina, [S.L.], v. 57, n. 4, p. 311, 25 mar. 2021. MDPI AG. http://dx.doi.org/10.3390/medicina57040311.

MORKUZU, Suat et al. Use of Activated Platelet-Rich Plasma (A-PRP) on Alopecia: a systematic review and meta-analysis. Aesthetic Surgery Journal, [S.L.], v. 43, n. 8, p. 631-649, 21 mar. 2023. Oxford University Press (OUP). http://dx.doi.org/10.1093/asj/sjad073.

PALMA, Luiz Felipe et al. Photobiomodulation With a Continuous Wave Red Laser (660 nm) as Monotherapy for Adult Alopecia Areata: a case presentation. Journal Of Lasers In Medical Sciences, [S.L.], v. 14, p. 21, 15 jul. 2023. Maad Rayan Publishing Company. http://dx.doi.org/10.34172/jlms.2023.21.

PENSATO, Rosita; AL-AMER, Rasmieh; LAPADULA, Simone. Platelet-Rich Plasma for Treating Androgenic Alopecia: a systematic review. Aesthetic Plastic Surgery, [S.L.], p. 1-1, 13 jul. 2023. Springer Science and Business Media LLC. http://dx.doi.org/10.1007/s00266-023-03482-0.

RIANGJANAPATEE, Pornthida et al. Development of Tea Seed Oil Nanostructured Lipid Carriers and In Vitro Studies on Their Applications in Inducing Human Hair Growth. Pharmaceutics, [S.L.], v. 14, n. 5, p. 984, 4 maio 2022. MDPI AG. http://dx.doi.org/10.3390/pharmaceutics14050984.

SAEED, Mahmood; HOOTA, Abdel Monem; KHALLAF, Abdel Nasser. Follicular Unit Extraction in Management of Secondary Cicatricial Alopecia. Al-Azhar International Medical Journal, [S.L.], p. 0, 21 ago. 2021. Al-Azhar University. http://dx.doi.org/10.21608/aimj.2021.81847.1510.

SAHIN, Gokhan et al. Platelet-rich plasma in the treatment of alopecia areata: a retrospective evaluation of 17 patients. Dermatologica Sinica, [S.L.], v. 41, n. 2, p. 111, 2023. Medknow. http://dx.doi.org/10.4103/ds.ds-d-22-00205.

SENESCHAL, J.; BONIFACE, K.; JACQUEMIN, C.. Alopecia areata: recent advances and emerging therapies. Annales de Dermatologie Et de Vénéréologie, [S.L.], v. 149, n. 4, p. 222-227, dez. 2022. Elsevier BV. http://dx.doi.org/10.1016/j.annder.2022.03.006.

SHAPIRO, Jerry et al. Evaluation of platelet-rich plasma as a treatment for androgenetic alopecia: a randomized controlled trial. Journal Of The American Academy Of Dermatology, [S.L.], v. 83, n. 5, p. 1298-1303, nov. 2020. Elsevier BV. http://dx.doi.org/10.1016/j.jaad.2020.07.006.

SHIMIZU, Yusuke et al. Regenerative medicine strategies for hair growth and regeneration: a narrative review of literature. Regenerative Therapy, [S.L.], v. 21, p. 527-539, dez. 2022. Elsevier BV. http://dx.doi.org/10.1016/j.reth.2022.10.005.

SINGH, Rashmi et al. Health-related quality of life (hrQoL) among patients with primary cicatricial alopecia (PCA): a systematic review. Journal Of The European Academy Of Dermatology And Venereology, [S.L.], p. 1, ago. 2023. Wiley. http://dx.doi.org/10.1111/jdv.19381.

SINGH, Sukhbir; MUTHUVEL, Kumaresan. Role of Hair Transplantation in Scarring Alopecia—To Do or Not to Do. Indian Journal Of Plastic Surgery, [S.L.], v. 54, n. 04, p. 501-506, out. 2021. Georg Thieme Verlag KG. http://dx.doi.org/10.1055/s-0041-1739246.

SUCHONWANIT, Poonkiat; CHALERMROJ, Noppanun; KHUNKHET, Saranya. Low-level laser therapy for the treatment of androgenetic alopecia in Thai men and women: a 24-week, randomized, double-blind, sham device-controlled trial. Lasers In Medical Science, [S.L.], v. 34, n. 6, p. 1107-1114, 19 dez. 2018.

TEJAPIRA, Kasama et al. Platelet-rich plasma in alopecia areata and primary cicatricial alopecias: a systematic review. Frontiers In Medicine, [S.L.], v. 9, p. 1, 24 nov. 2022. Frontiers Media SA. http://dx.doi.org/10.3389/fmed.2022.1058431.

UCHIYAMA, Masaki. Primary cicatricial alopecia: recent advances in evaluation and diagnosis based on trichoscopic and histopathological observation, including overlapping and specific features. The Journal Of Dermatology, [S.L.], v. 49, n. 1, p. 37-54, 5 dez. 2021. Wiley. http://dx.doi.org/10.1111/1346-8138.16252.

VORONKOVA, M.V et al. Treatment of Cicatricial Alopecia. Russian Journal Of Skin And Venereal Diseases, [s. l], v. 2, n. 12, p. 58-60, 2012.

WANG, Eddy H C et al. Primary cicatricial alopecias are characterized by dysregulation of shared gene expression pathways. Pnas Nexus, [S.L.], v. 1, n. 3, p. 1, 1 jul. 2022. Oxford University Press (OUP). http://dx.doi.org/10.1093/pnasnexus/pgac111.

XIAO, Shune et al. The mechanism of activated platelet-rich plasma supernatant promotion of hair growth by cultured dermal papilla cells. Journal Of Cosmetic Dermatology, [S.L.], v. 18, n. 6, p. 1711-1716, 18 mar. 2019. Wiley. http://dx.doi.org/10.1111/jocd.12919.

YOUSSEF, Alaa et al. A Comprehensive Review of Natural Alternatives for Treatment of Alopecia with an Overview of Market Products. Journal Of Medicinal Food, [S.L.], v. 25, n. 9, p. 869-881, 1 set. 2022. Mary Ann Liebert Inc. http://dx.doi.org/10.1089/jmf.2021.0156.

ZHANG, Tikai et al. Combining rapid degrading microneedles with Slow-Released drug delivery system for the treatment of alopecia areata. Chemical Engineering Journal, [S.L.], v. 471, p. 144351-144351, set. 2023. Elsevier BV. http://dx.doi.org/10.1016/j.cej.2023.144351.