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PRP: Is There a Valid Role in Hair Loss Treatment?

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Editorial

PRP has been used mostly for androgenetic alopecia and alopecia areata since these are the most common types of hair loss. Especially androgenetic alopecia is an extremely prevalent disorder resulting in gradual conversion of terminal hairs into vellus hairs. This is more obvious in men affecting more than 50%, with its well-known hair loss pattern, although there are studies suggesting an almost equal prevalence for women too. A self-renewal of the hair follicle by the keratinocyte stem cells of the bulge have been indicated in androgenetic alopecia, making growth factors signalling a promising future therapy.

In alopecia areata an autoimmune destruction of the hair in part or parts of the body, usually in the scalp, is taking place resulting in spot balding. Quite often balding is asymmetrical causing serious aesthetic issues. Alopecia areata can be reversible in the type where the hair shafts are gone but the hair follicles are preserved. However there is also a type where inflammation results in fibrosis and irreversible hair loss. Histopathological findings show an accumulation of T-lymphocytes around hair follicles in areas of alopecia areata suggesting an autoimmune aetiology. That there is trichoscopy shows regularly distributed "yellow dots" (hyperkeratotic plugs), small exclamation-mark hairs, and "black dots" (destroyed hairs in the hair follicle opening).

PRP Use for Hair Loss-Basic Science

Various studies trying to delineate the physiology and the various molecular mechanisms behind hair growth have implicated several growth factors such as PDGF, TGF, VEGF and IGF. For example, endothelial cells and keratinocytes and possibly other types of cells located in the area of a hair follicle produce Platelet Derived Growth Factors (PDGF) which is fundamental for cell growth and proliferation. Thus, PDGF signals are involved in both epidermis-follicle interaction and the dermal mesenchyme interaction required for hair canal formation and the growth of dermal mesenchyme [1]. In experimental animal models, PDGF expression, which is either positively or negatively modified by various cytokines, has been shown to induce and maintain anagen phase [2]. In addition, IGF-I extends the overall anagen phase whereas both IGF-I and IGF-II prevent the HF from developing catagen like status [3].

Vascular Endothelial Growth Factor (VDGF) also plays an important role in hair follicle growth and cyclin by improving follicle revascularization, since anagen-associated angiogenesis has been suggested as one of the important factors in active hair growth [4]. Conversely TGF-b1, which is induced by androgens, seems to act as an inhibitory paracrine mediator in androgenetic alopecia.

As reported previously, platelets concentrate contain an increased concentration of growth factors, such as VEGF, PDGF and IGF. Thus the utilization of PRP for the treatment of baldness is a rational consequence of the knowledge we have so far on the physiology of hair growth. Although there are several studies for the treatment of androgenic alopecia and alopecia areata, the exact mechanisms of action as well as the molecular signalling pathways remain largely unknown.

In general, PRP increases proliferation of epidermal and hair follicle bulge cells, as indicated by the Ki-67 marker of cell proliferation in both androgenic alopecia and alopecia areata [5,6]. Several molecular pathways have been implicated in this action, such as ERK signalling, WNT b-catenin pathway and Akt signalling activity.

In more details, phosphorylation of extracellular signal-regulated kinases (ERK) and Akt by PRP that has been shown recently [7] are important steps in well-established molecular cascades that result in mutagenesis, cell growth or apoptosis. Growth factors, such as PDGF, trigger complex downstream signalling cascades upon their interaction with their specific receptors, e.g. tyrosine kinase receptor, and the phosphorylation and activation of molecules such as phosphoinositide 3-kinases (PI3Ks), and PIP2. Phosphorylation of PIP2 to PIP3 causes its activation and further

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phosphorylation and activation of AKT that is an anti-apoptotic signalling molecule implicated also in cellular growth, metabolism and angiogenesis [8].

In addition, modulation of WNT signalling activity affects the fate of hair follicle cells significantly. In an animal study, WNT10a mRNA and protein as well as WNT5a mRNA and protein, were higher among skin samples treated with PRP. WNTs 10a and 10b act as the first epidermal signals of the canonical WNT/β-catenin signaling pathway that regulates stemness and hair regeneration [9].

Nevertheless the increased transcriptional activity of b-catenin, which plays an important role in the differentiation of stems cells to hair follicle cells and the prolongation of survival of derma papilla cells [10] may not be the indirect result of the activation of signalling pathways within the hair follicle. As it has been shown in an in vitro model the activated PRP approximately doubled transcriptional activity of b-catenin Autologous platelet-rich plasma: a potential therapeutic tool for promoting hair growth [11]. Indicating that activated PRP may have additional direct actions through exogenously expressed molecules, such as b-catenin.

Other molecules that have been shown to be upregulated by PRP are the FGF-7, which is known to stimulate hair growth [10], and the FGF-9 that enhances follicular neogenesis [9]. In addition, the expression of cyclin D1and Cdk4 is also significantly affected by PRP [7] as well as the synthesis of anti-apoptotic protein Bcl-2 [11]. The study of these proteins was not random since similar results have been shown with Minoxidil. Minoxidil, which is one of the very few FDA approved medications for androgenetic alopecia along with Finasteride, promotes the survival of dermal papilla cells by increasing Bcl-2/Bax ratio and by activating ERK and Akt [12]. It seems that this mechanism succeeds through the stimulation of potassium channels and prostaglandin endoperoxide synthase-1, which has been shown to increase anagen phase [5]. Finasteride also induces the prolongation of anagen hairs and activates anagen hair growth, as shown by the gradual thickening and elongation of the hairs in clinical studies, by affecting the expression of caspases and apoptosis inhibitors [5].

Briefly, activation of wingless (Wnt)/β-catenin, extracellular signalling regulated kinase (ERK), and protein kinase B (Akt) signalling pathways leads to the necessary cellular proliferation and differentiation that encourages hair follicles to enter and extend the duration of the anagen phase of the growth cycle [13]. Another possible mechanism that is activated through growth factors and affects hair growth is the promotion of vascularization and angiogenesis. It is well known since many years that PRP improves cutaneous ischemic conditions and increases vascular structures around hair follicles. This is a very important process in hair transplantation (FUT) since in the early phases of folliculoneo genesis, that is initiated before angiogenesis, grafted cells can obtain only limited nutrition and growth factors from surrounding tissue fluid [14]. Thus loss or reduction of nutrients and signalling factors does not allow full development of hair follicles and explains at least partially the up to 30% HF loss that have been reported in FUT. VEGFs and platelet-derived growth factors contribute in increasing peri-follicular vasculature thus, improving the blood supply and nourishment to the transplanted grafts [10].

It is obvious that the exact pathophysiologic mechanisms that are being initiated by PRP are still unknown. For example the importance of slower and steadier increase of growth factors in PRF by endogenous activation or the role of increased numbers of leucocytes have not been studied yet. A steady unlock of the expression of normal gene sequences that are related to the anagen phase may be beneficial in the long term or on the contrary the release of proinflammatory cytokines of leucocytes could have negative effects on hair growth. Nevertheless, PRP and PRF action on hair restoration remains an active and interesting field of study.

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