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Review Article

Platelet rich plasma in androgenetic alopecia: A critical analysis of current treatment modalities

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Abstract

We aimed to review the clinical research using PRP for the treatment of Androgenic alopecia. Furthermore, our other objective was to compare the PRP therapy with the traditional finasteride treatment to assess the better treatment in terms of efficacy. This systematic review was conducted by following the protocol defined by Khan *et al.*[8] containing 5 step procedure to access high-quality relevant literature. Best Evidence Topic (BET) reports protocol was used for accessing the protocol, patient characteristics, intervention or defining question and relevant outcomes. All articles from Google scholar, PubMed, Conference Proceedings, Medline, and Cochrane Central Register for Controlled Trials were used in the first screening for gathering relevant information. Two independent authors were assigned to evaluate the study design. Only 5 studies of platelet-rich plasma and 5 studies of finasteride treatment were included. All the evidence was fulfilling the level 2 CEMB criteria. A total of 3538 patients were suffering from baldness. None of the study achieved 10 points. Only two platelet rich plasma studies while single study of finasteride treatment, were given 9 score. Results concluded that PRP is far way better than finasteride in terms of high hair growth in less duration, with minimum to no side effects.

Key words
Hair loss; Platelet rich plasma; Hair regeneration.

Introduction

Hair loss, alopecia, is a dermatology problem that leads to thinning hair and eventually person losing hair from his scalp. This could be due to many factors including genetics, an autoimmune process, side effect of any treatment, clinical conditions including cancer chemotherapy and local influences.[1] Many types of hair loss were observed including pattern baldness or androgenetic alopecia, alopecia areata, cicatricial alopecia, etc. This clinical depressing condition affects at least 30% of the male population under 30's years of lifespan. This condition gets worsens with time.[1,2] Massive hair treatments have flooded the market promising miraculous results in a short period.[1] However, due to limited efficacy and adverse side effects of treatments, researchers still finding better therapies or treatments.[3,4] Vitamin deficiency is highly linked with hair loss problems and many physicians recommended biotin supplements for alopecia.[5] Besides this, anti-androgen therapy is widely used as a treatment and shows improvement in hair retention and regeneration by improving the conditions of female pattern baldness.[6]

Recently, platelet-rich plasma caught the attention of researchers by giving positive outcomes in hair regeneration.[7] This technique has the potential to restore the tissues to their

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working capacity with minimal side effects and might have the potential to become a successful hair regeneration therapy.[8] Hair loss sooner or later becomes psychological or sociological problem for people.[8] This study was designed to critically analyze the hair loss interventions and measure the efficacy of platelet-rich plasma techniques eliciting hair follicle growth in patients suffering from pattern baldness or Androgenic alopecia. We aimed to review the clinical research using PRP for the treatment of Androgenic alopecia. Furthermore, our other objective was to compare the PRP therapy with the traditional finasteride treatment to assess the better treatment in terms of efficacy.

Methods

This systematic review was conducted by following the protocol defined by Khan *et al*.[9] This protocol contains 5 step procedure to access high-quality and relevant literature. These five steps consisting of framing the question, identifying the relevant work, assessing the quality of studies, summarizing the evidence and interpreting the findings. Meanwhile Best Evidence Topic (BET) reports protocol[10] was also used to find the quality of research questions designed specifically for randomized clinical trials. According to BET protocol, patient characteristics, intervention or defining question and relevant outcomes were measured.

All articles from Google scholar, PubMed, Conference Proceedings, Medline, and Cochrane Central Register for Controlled Trials were used in the first screening for gathering relevant information. The secondary screening was based on abstract screening which leads to full-text screening. During the secondary screening of titles and abstracts, the relevance and appropriateness of data were accessed. Two independent authors were assigned to evaluate the study design, study protocol, and targeted population/ sample intervention method. Keywords like "hair loss treatment", "pattern baldness", "Platelet Rich Plasma" "Androgenic" or "Androgenetic alopecia", and "Finasteride" or "steroid" were used for the data collection procedure. All the review papers, duplicated research and critical reviews were excluded.

Those researches which contain male and female patients diagnosed with pattern baldness or androgenic alopecia treated with platelet-rich plasma or finasteride were included. The research uses immunohistochemistry, hair pull test, histological evaluation, global photographs, and trichograms were included for final analysis. Studies containing other types of hair disorders, taking minoxidil, nicorandil, pinacidil and herbal supplements were excluded.[11]

Important details like author name, sample population and trial data were extracted during the second screening and structured in tables. Quality assessment was performed using a predefined list for the relevance and significance of selected data. Under the BET methodology, two quality appraisals were conducted based on the intervention method and evidence presentation. Only level 1 and level 2 articles were selected based on the intervention method and evidence grading system. Other than this, the critical appraisal was also used for determining the efficacy analysis of the selected studies. In the final step, 0-10 ratings were given to the selected studies based on quality and risk of bias.

Results

The research was conducted on different databases to find the relevant information on platelet-rich plasma efficacy in hair regeneration finasteride. We found a total of 434 records, only 25 clinical trials were extracted from them. During the full-text screening, studies with unclear interventions were excluded. Based on the inclusion and exclusion criteria of our review

only 5 studies of platelet-rich plasma and 5 studies of finasteride treatment were included. All the evidences were fulfilling the level 2 CEMB criteria. A total of 3538 patients were suffering from baldness. Different outcomes were measured in selected studies including Trichogram, global photographs, hair density, hair count, histological examination and Immunohistochemistry. All the studies were typically focused on hair density, hair count and the regeneration process. Among these studies, only 4 were randomized controlled clinical trials while four were based on long-term efficacy studies. PRP therapy studies have a relatively small sample size than the finasteride treatment. Detailed demographic information was mentioned in **Table 1**. Meanwhile, **Tables 2-4** represent the study efficacy in terms of study design, methodology, statistical analysis, discussion, interpretation and implementation. Sample size was not measuring while some studies did not obtain any ethical considerations. None of the study achieved 10 points. Only two platelet rich plasma studies while single study of finasteride treatment were graded 9 score.

Discussion

In this critical review, we observed that articles based on platelet-rich plasma intervention were of high quality than others. Studies by Alves *et al.*[12] and Cervelli *et al.*[13] conducted in 2016 and 2014 had equivalent ratings. Both studies observed similar parameters in their respective years. We observed that studies based on PRP had a small sample size while finasteride studies were conducted significantly on larger sample size. Although the study of Alves *et al.*[12] had a very small sample of 25 patients and the study duration was of 6 months still their results were considered highly significant due to measurement of different outcomes and statistical performance. Moreover, in their study, a unique association between the growth of anagen hairs and the age of the patient suffering from AGA was observed. A study by Cervelli *et al.*[13] observed a wide range of parameters including Immunohistochemistry, histological evaluation, hair density and photo trichograms hence achieving wide scope of efficacy assessment. Meanwhile, the lowest efficacy was inappropriate in a study by Borhan *et al.*[15] in which inappropriate involvement of the control group was observed. Furthermore, their study lacks a clear indication of the assessment procedure (either blinded or non-blinded). Moreover, they only had two parameters of observation measuring Trichogramma and cosmetic assessment. However, the inclusion of self-assessment was only the major measurement of the study which gave a complete insight into the improvement in patient's quality of life after treatment. Only one study used non-activated PRP[15] while the rest of them injected activated PRP into their patients. Studies observed a large number of growth factors by activating blood plasma using different agents. These growth factors assisted in regeneration through angiogenesis. Burhan's[15] study argued that there is inappropriate need for pre-activation as dermal fibroblasts would help in platelet activation which leads to the release of growth factors.[22]

We further considered the finasteride efficacy studies on pattern baldness since it was the established treatment procedure for ages and can be used with newly developed PRP-based treatment. We included five studies for this systematic review and all five received high ratings of efficacy. Their efficacy assessment was based on the large population size and prolonged treatment duration. We found a unique correlation between large sample sizes and outcome-type measurements. Usually, these studies made global photographs which could enhance the risk of biases. In clinical trials, the risk of bias is far more in subjective assessment-based outcomes than the measurable outcomes including hair density hair count, etc.[23]

Table 1 Detailed demographic information.

Study Name	*Study Design*	*Study population*	*Mean age*	*Trial duration*	*Control*	*Intervention*	*Outcomes*
Alves R *et al.*[12] [20016]	Double blind Randomized controlled trial	25	39 years	6 months	Injected with placebo	Injected with PRP	Average hair count, density and terminal hair density
Cervelli V *et al.*[13] [2014]	Inappropriate randomized clinical trial (without blinding)	10	-	12 months	Inappropriate t mentioned	Activated PRP injection	Hair count, density, thickness, dermoscopy itching sensation
Gentile *et al.*[14] [2012]	Randomized controlled trial (blinded placebo)	23	-	2 years	Placebo injection	PRP Injection	Measuring follicles count, hair count, density, microscopic evaluation of thickness and Ki67+ keratinocytes
Borhan R *et al.*[15] [2015]	Inappropriate n randomized study (without control group)	14	-	4 months	Inappropriate t mentioned	PRP injection	Measuring hair count and density, cosmetic and quality of life assessment tool and trichogram
Gkini MA *et al.*[16] [2014]	Inappropriate n randomized (Inappropriate n-controlled)	20 patients (2 females)	34 years	6th months	Single group controlled Inappropriate t mentioned	Activated PRP injection	Using hair pull test, Dermoscopic photomirographs, Macroscopic Photographs and using questionnaire for rating patient satisfaction
Finasteride Treatment							
Oliveira-Soares R *et al.*[17] [2013]	Inappropriate n-randomized single center Inappropriate n control study	40	-	18 months	Inappropriate t taking	5mg finasteride tablet	Assessment of patient satisfaction and global photographs
Price VH *et al.*[18] [2006]	Double blinded single center randomized controlled trial	66	-	4 years	Placebo	1% finasteride tablet	Adverse events, hair count and weight
Sato A *et al.*[19] [2012]	Inappropriate n-randomized single center Inappropriate n control study	3177	37.5	3.5 years	Inappropriate t taking	1% finasteride tablet	Global photographs
Hajheydari Z *et al.*[20] [2009]	Double blinded randomized trial	45	22.8	6 months	Placebo tablet and gel	1% finasteride gel	
Rossi A *et al.*[21] [2011]	Inappropriate n-randomized Inappropriate n control study	118	-	10 years	Inappropriate t taking	1% finasteride tablet	Global photographs

Table 2 Efficacy assessment of study design.

Author	*Rating*	*Clear hypothesis and objectives*	*Suitable study design and sample size*	*Clearly identified and identical comparison group*	*Exposure proceeds the outcome*	*Study large Inappropriate enough to achieve the objectives/ sample size estimation performed*	*Appropriate outcomes considered*	*Obtaining ethical approval*
Alves R *et al.*[12] [2016]	9	Appropriate	Appropriate	Appropriate	Appropriate	Inappropriate, Inappropriate sample size estimation	Lack of histological test, Immunohistochemistry test	Appropriate
Cervelli V *et al.*[13] [2014]	8	Appropriate	Appropriate	Inappropriate	Appropriate	Inappropriate and Inappropriate t sample size estimation considered	Appropriate	Appropriate
Gentile *et al.*[14] [2012]	9	Appropriate	Appropriate	Appropriate	Appropriate	Appropriate , but Inappropriate sample size estimation	Appropriate	Inappropriate t reported
Borhan R *et al.*[15] [2015]	6	Appropriate	Appropriate	Inappropriate	Appropriate	Inappropriate and Inappropriate t sample size estimation considered	Histological test, hair pulling test, Immunohistochemistry tests were missing	Appropriate
Gkini MA *et al.*[16] [2014]	7	Appropriate	Appropriate	Inappropriate	Appropriate	Inappropriate and Inappropriate t sample size estimation considered	Histological evaluation and Immunohistochemistry were missing	Appropriate
Hajheydari Z *et al.*[20] [2020]	8	Appropriate	Appropriate	Appropriate	Appropriate	Inappropriate	Lack of hair pull test, self-assessment test, Microphotography, histological evaluation and Immunohistochemistry	Appropriate
Price VH *et al.*[18] [2006]	9	Appropriate	Appropriate	Appropriate	Appropriate	Inappropriate	Lack of hair pull test, self-assessment test, Trichogram, histological evaluation and Immunohistochemistry	Appropriate
Rossi A *et al.*[21] [2011]	8	Appropriate	Appropriate	Appropriate	Appropriate	Appropriate	Lack of hair pull test, self-assessment test, Trichogram, histological evaluation and Immunohistochemistry, hair count are also missing	Appropriate
Sato A *et al.*[19] [2012]	8	Appropriate	Appropriate	Appropriate	Appropriate	Appropriate	Lack of hair pull test, self-assessment test, Trichogram, histological evaluation and Immunohistochemistry, hair count and weight are also missing	Appropriate
Oliveira-Soares R *et al.*[17] [2013]	7	Appropriate	Appropriate	Appropriate	Appropriate	Appropriate	Lack of hair pull test, self-assessment test, Trichogram, histological evaluation and Immunohistochemistry, hair count and weight are also missing	Appropriate

Table 3 Efficacy assessment of measurement, observation and data representation.

Author	*Clarification of study parameters and outcomes*	*Outcomes measured in the same way in all comparative group*	*assessments of exposure blinded to outcome*	*Sufficient follow up duration*	*Valid reliable and reproducible measurements*	*Basic parameters of data described*	*Data presented clearly, objectively and results consistent*	*Data described in tables*	*Dose of response effect described?*
Alves R *et al.*[12] [2016]	Appropriate	Appropriate	Appropriate	Inappropriate	Appropriate	Appropriate	Appropriate	Appropriate	Inappropriate
Cervelli V *et al.*[13] [2014]	Appropriate	Appropriate	Appropriate	Inappropriate	Appropriate	Appropriate	Appropriate	Appropriate	Inappropriate
Gentile *et al.*[14] [2012]	Appropriate	Appropriate	Appropriate	Inappropriate	Appropriate	Appropriate	Appropriate	Appropriate	Inappropriate
Gkini MA *et al.*[16] [2014]	Appropriate	Inappropriate	Inappropriate	Inappropriate	Appropriate	Appropriate	Appropriate	Appropriate	Inappropriate
Borhan R *et al.*[15] [2015]	Appropriate	Inappropriate	Inappropriate t reported	Inappropriate	Inappropriate, Appropriate	Appropriate	Appropriate	Appropriate	Inappropriate
Hajheydari Z *et al.*[20] [2009]	Appropriate	Appropriate	Appropriate	Inappropriate	Appropriate	Appropriate	Appropriate	Appropriate	Appropriate
Price VH *et al.*[18] [2006]	Appropriate	Appropriate	Appropriate	Appropriate	Appropriate	Appropriate	Appropriate	Appropriate	Inappropriate
Rossi A *et al.*[21] [2011]	Appropriate	Appropriate	Inappropriate	Appropriate	Appropriate	Appropriate	Appropriate	Appropriate	Appropriate
Sato A *et al.*[19] [2012]	Appropriate	Appropriate	Appropriate	Inappropriate	Appropriate	Appropriate	Appropriate	Appropriate	Appropriate
Oliveira-Soares R *et al.*[17] [2013]	Appropriate	Appropriate	Inappropriate	Inappropriate	Appropriate	Appropriate	Appropriate	Appropriate	Appropriate

Table 4 Efficacy assessment of statistical analysis, discussion, conclusion and implementation.

Author	*Data suitable for analysis or method suitable for analysis*	*Statistical analysis performed*	*Relative risks and odd ratios presentation*	*Results compared with the existing literature in discussion portion*	*Justified casual relationship build in discussion*	*Biased discussion*	*appropriate conclusion*	*Level of evidence*	*any necessary change be implemented in practice*
Alves R *et al.*[12] [2016]	Appropriate	Appropriate	Inappropriate	Appropriate	Appropriate	Inappropriate	Appropriate	2	Appropriate
Cervelli V *et al.*[13] [2014]	Appropriate	Appropriate	Inappropriate	Appropriate	Appropriate	Inappropriate	Appropriate	2	Inappropriate
Gentile *et al.*[14] [2012]	Appropriate	Appropriate	Inappropriate	Appropriate	Appropriate	Inappropriate	Appropriate	2	Appropriate
Gkini MA *et al.*[16] [2014]	Appropriate	Appropriate	Inappropriate	Appropriate	Appropriate	Inappropriate	Appropriate	2	Appropriate
Borhan R *et al.*[15] [2015]	Inappropriate,	Appropriate	Inappropriate	Appropriate	Appropriate	Appropriate	Appropriate	2	Appropriate
Hajheydari Z *et al.*[20] [2009]	Appropriate	Appropriate	Inappropriate	Appropriate	Appropriate	Inappropriate	Appropriate	2	Appropriate
Price VH *et al.*[19] [2006]	Appropriate	Appropriate	Appropriate	Appropriate	Appropriate	Inappropriate	Appropriate	2	Appropriate
Rossi A *et al.*[21] [2011]	Appropriate	Appropriate	Inappropriate	Appropriate	Appropriate	Inappropriate	Appropriate	2	Appropriate
Sato A *et al.*[19] [2012]	Appropriate	Appropriate	Appropriate	Appropriate	Appropriate	Inappropriate	Appropriate	2	Appropriate
Oliveira-Soares R *et al.*[17] [2013]	Appropriate	Appropriate	Appropriate	Appropriate	Appropriate	Inappropriate	Appropriate	2	Appropriate

In finasteride trials commercially available 1% gel or 1mg oral tablets were highly used. Meanwhile study by Soares *et al.*[17] tested a 5mg tablet for treating androgenetic alopecia in postmenopausal women on behalf of previous study.[24] All the studies found changes in hair growth while very less highlight the changes in follicle level. Out of 10 studies, only 5 were using the self-assessment tool as a measurable outcome. This indicated that the efficacy of treatment options is the major concern of the researchers than the personal satisfaction of patients. Lack of sample size estimation, a dose of response effect, relative risks, and application of a range of outcome measurement tools were the major flaws of all studies. The high cost of PRP treatment and lack of significant data applicable for commercial treatment is the major obstacle to considering it as an effective form of treatment.

Conclusion

Results concluded that PRP is far way better than finasteride in terms of high hair growth in less duration, with minimum to no side effects. Further studies need to be conducted in order to validate the efficacy of PRP treatment and for commercial recognition.

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Conflict of interest Authors declared no conflict of interest.

Author's contribution

KAS, LH, SW: Substantial contributions to the conception, analysis, interpretation of data, drafting of the work, reviewing it critically, has given final approval of the wok.

SKB, SM: Substantial contributions to the conception, design of the work, drafting of the work, has given final approval of the wok.

SK: Substantial contributions to acquisition, interpretation of data, drafting of the work, has given final approval of the wok.

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