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Complex minoxidil and platelet-rich plasma therapy effectiveness and its impact on physical performance

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Abstract

Background

Minoxidil and platelet-rich plasma (PRP) are proven treatments for androgenetic alopecia, however their combined therapy is not as researched.

Research materials and methods

Materials used for our research consist of published papers that pertain to both minoxidil and platelet-rich plasma therapies. More comprehensive papers, such as those including other substances were also included although results about other substances were not included, we simply discarded them. Each of the found and chosen articles were added and processed by various formulas which aim were to calculate efficacy of combined therapy while minimizing the errors and biases that could prop up in the source papers. Overall goal was to consolidate knowledge of the efficacy of combined therapy of minoxidil and platelet-rich plasma with emphasis on effect that could affect the physical performance.

Results

All trials have shown statistically significant improvement when compared to minoxidil monotherapy. Compared to PRP monotherapy results had been superior although not always in statistically significant manner. No trials have shown additional, adverse interactions, side effects or impacts on physical performance beyond those expected from the monotherapies, proving combined is as safe as monotherapies.

Conclusion

Combined therapy is proven to yield better results, while remaining a safe and cost-effective method. It doesn't impact physical performance in any way if taken correctly. Still higher quantity of research is welcome to make those finding more stable and in order to better assess the positive effect of combining titular substances.

Keywords

minoxidil; platelet-rich plasma (PRP); androgenetic alopecia (AGA); monotherapy; combined therapy; review

Introduction

Androgenetic alopecia

Androgenetic alopecia (AGA) is one of the most common hereditary dermatological disorders affecting millions of people worldwide, more often occurring in men however it also has been observed in women. It usually begins by 20 years of age and affects nearly 50% of men by the age of 50 years while in 40% of women by the same age (Gan et al. 2005, Trink et al. 2013).

This condition is characterized by gradual and irreversible hair loss, primarily caused by the testosterone metabolite dihydrotestosterone (DHT) and the hair follicle-related androgen receptor (AR). There exist a few treatments, two of which are of our concern, namely platelet-rich plasma (PRP) (Cervelli et al. 2014, Gkini et al 2014) and minoxidil therapies (Olsen et al. 2007, Suchonwanit et al. 2018).

The condition itself doesn't impact physical capabilities of athletes can affect them mentally, especially if they perform in public settings. The onset of alopecia coincides with peak performance of most sportsmen and sportswomen, namely their twenties (Tanaka and Toussaint, 2023). Many athletes, therefore, are going to reach out for hair lost therapies.

Platelet-rich plasma

Platelet-rich plasma (PRP) is an autologous blood product with increased density of platelets compared to base blood's level (Mehta and Watson, 2008). Due to activation of granules, various growth factors are created including but not limited to: vascular endothelial growth factor (VEGF) (Anitua et al. 2004, Marx 2004, El-Sharkawy et al. 2007), platelet-derived growth factor (PDGF) (Mehta and Watson 2008, Steed et al. 1992, Anitua et al. 2004, Nikolidakis and Jansen, 2008), epithelial growth factor (EGF) (Steed et al. 1992, El-Sharkawy, et al. 2007, Nikolidakis and Jansen 2008) transforming growth factor beta (TGF- β) (Steed et al. 1992, Anitua et al. 2004, Marx 2004, Nikolidakis and Jansen 2008). Thus, it's also assumed it helps to treat alopecia because said growth factors stimulate stem cells in order to develop new follicles and promote neovascularization (Anitua et al. 2004, Khatu et al. 2014). Adverse effects are temporary and tolerable and include pain during treatment, mild headache, minimal itching, and transient erythema and edema at the treated area (Paichitrojana and Anand 2022). All of them are localized and rather mild. Thus, should have little to no impact on general sport performance. Furthermore, no antibiotics are required following the

injections, making it even more appealing for athletes. Since only professionals can conduct injections the risk of mistreatment or overdose is minimal. Furthermore, no case studies or even mentions of such unintentional mistakes were found.

Minoxidil

Minoxidil ($C_9H_{15}N_5O$) is a drug used to treat alopecia for both sexes. It can be administered orally (Goren and Naccarato, 2018, Ramos et al. 2019) and topically (Goren and Naccarato, 2018). Minoxidil is converted to minoxidil sulfate in hair follicles thanks to the sulfotransferase enzyme. This substance prolongs anagen while shortening the telogen/kenogen phase, thereby inducing production of new hairs as the next anagen phase begins (Goren and Naccarato, 2018). The oral route is being researched due to topical administration having tendency to cause no response or even cause irritation and destruction of hairs (Rossi et al. 2012).

Overdoses of topical minoxidil, although exceedingly rare (Dubrey et al. 2015) cannot be fully counted out, especially as it is an available, over the counter drug. Misuses such drinking of topical solution have been documented (Farrell and Epstein 1999, Garrard et al. 2011). Since Minoxidil administered orally is a potent vasodilator it can cause lower both systolic and diastolic blood pressure (Campese 1981, Chakar et al. 2023). Lowered pressure can be exacerbated by the postexercise hypotension (Halliwill, 2001, Chen and Bonham 2010) and lead hospitalization.

Motivation

Because alopecia is a highly prevalent condition affecting a considerable number of individuals globally. We wanted to consolidate knowledge about complex therapy of both minoxidil and PRP, as compared to monotherapies. Monotherapies are proven treatments, however the literature about combined effects is scarcer. It is especially important to check for the effectiveness of the complex therapy because it is the cost-effective one (Klifto et al. 2021). On top of assessing their combined effectiveness we aim to assess the risks of such therapy on the physical wellbeing of patients, even including their sport performance.

Material and Method

Literature search through various publication databases and engines has been done, focusing on most recent papers in both English and Polish language, as they are the only ones known by the authors. Google Scholar, Pubmed and OVID were scoured for publications that compare the effectiveness of only single therapy and complex PRP with minoxidil's treatments. The vast majority of trials were discarded because they mostly compared PRP to minoxidil and rarely used combined therapy. Not every trial measured result in the same way or to the same extent so we tried to use the highest common denominator which happens to be morphometric indicators of hair growth and subjective opinions of patients.

Matching publications had to, primarily, be the primary papers that directly compare the combined therapy of PRP and minoxidil to monotherapy. We were aware that randomized double-blind studies are the *de facto* gold standard and yield more truthful results. However, we did not put any restrictions regarding the types of accepted trials due to the small number of available materials.

Publications were accepted with approval of most or all members, the preliminary selection was based on the abstract. In case of uncertainties or diverging opinions in a team, full text became a deciding factor.

Results

Gathered and accepted publications are presented in the table below (Table 1).

Name and DOI	Publication date	Study type	Participants	Follow-up	Result
K Shah et al. (10.4103/ijt.ijt_75_16)	2017 Jan	Randomized controlled study	25 minoxidil, 25 minoxidil + PRP	6 months	Photographic assessment, self-assessment
R. Ray et al. (10.1016/j.mjafi.2020.11.010)	2017 May	Randomized controlled study	50 minoxidil, 50 minoxidil + PRP	12 months	Photographic and trichoscopic assessment
R. Alves et al. (10.1097/DSS.00000000000001198)	2018 Jan	Double-blinded randomized controlled study	12 minoxidil, 12 minoxidil + PRP, (24 finasteride)	6 months	Trichoscopic assessment
A. Jha et al. (10.1111/jocd.12864)	2018 Jul	Controlled study	31 minoxidil, 31 minoxidil + PRP, (31 minoxidil + PRP + microneedling)	3 months	Trichoscopic assessment, patient self-assessment, hair pull test
S. Singh et al. (10.4103/ijdvl.IJDVL_589_18)	2020 Mar	Double-blinded randomized controlled study	19 saline placebo 17 minoxidil, 19 PRP, 20 minoxidil + PRP	5 months	Trichoscopic assessment, self-assessment
W. Ramadan et al. (10.1111/jocd.13935)	2020 Oct	Single-blinded randomized controlled study	42 minoxidil + finasteride/spironolactone, 84 minoxidil + finasteride/spironolactone + PRP (two administration)	3 months	Photographic and trichoscopic assessment, self-assessment, hair pull test
S. Pachar et al. (10.4103/JCAS.JCAS_232_20)	2022 Jan	Randomized controlled study	50 total Left scalp minoxidil, Right scalp minoxidil + PRP	4 months	Photographic and trichoscopic assessment, self-assessment, hair pull test
E. Elena et al. (10.4103/ijt.ijt_50_19)	2022 Jan	Single-blinded randomized controlled study	22 minoxidil, 22 PRP, 25 minoxidil + PRP	6 months	Trichoscopic assessment

References, for clarity, in order as they appear in Table 1: (Shah et al. 2017), (Ray and Sharma, 2021), (Alves and Grimalt 2018), (Jha et al. 2019), (Singh et al. 2020), (Ramadan et al. 2021), (Pachar et al. 2022), (Elena and Irina 2022)

Data Description

Participants

As pointed out, only eight publications have met the criteria and have been chosen for further examination. In summary 556 people have been involved and relevant in the trials, while all participants count was 611 including those under therapies that were not of interest for us.

Gender ratio of trials is heavily skewed towards the men of the relevant people only, in most (n=6) only male patients were chosen, in trials (Alves and Grimalt 2018, Ramadan et al. 2021) there were 45.8% and 36.5% of males respectively. However, the trial (Alves and Grimalt 2018) did not mention the genders of the control group.

The race or ethnicity of participants was usually not disclosed or noted, only (Alves and Grimalt 2018) mentioned that participants were of Caucasian origin. However, based on the university/hospital location and the photographic documentation, we can infer hypothesis about the ethnicity representation. Most studies (n=5) were done in India and all their photos contained patients of Indian descent, trial (Elena and Irina 2022) was conducted in Russia and again photos suggest participants of matching descent, i.e. Caucasian. Only the trial (Ramadan et al. 2021) done in Egypt proved to be difficult to hypothesize about. What is highly probable is the general lack of substantial data about people of African, American and East Asian descent, while mostly the Caucasian and Indian descendants seem to be covered.

Most common inclusion criterion was score in Norwood-Hamilton scale (Norwood 1975). Usually, II to V were chosen but some (Jha et al. 2019, Pachar et al. 2022) included I, while (Ramadan et al. 2021, Ray and Sharma 2021) even included VI. None included people with a score of VII.

Bias

The design of a study plays a crucial role in determining the risk of bias, which can lead to incorrect conclusions, understated or overstated results, or even accidental falsification of data. Out of all the trials conducted, only two (Alves and Grimalt 2018, Singh et al. 2020) followed the gold standard of the double-blind design, while two others (Ramadan et al. 2021, Elena and Irina 2022) were single-blinded, with investigators measuring efficacy being blinded. The rest of the trials (Shah et al 2017, Jha et al. 2019, Ray and Sharma 2021, Pachar et al. 2022) were open.

All trials, except one (n=7), specified that participants were randomly assigned to groups, while only one trial (Jha et al. 2019) did not have clear randomization.

Most (n=7) trials used different people serving in control and experimental groups. Only (Pachar et al. 2022) split the scalp of a single person into halves: control - minoxidil only, and experimental - PRP + minoxidil. Thus, making it harder to determine bias or interaction. Efficacy measurements in one trial (Shah et al. 2017) were based purely on the subjective tests increasing risk of bias. In other trials (n=6), a combination of more objective methods, such as hair density or hair count, and subjective methods like hair pull were used. Only (Elena and Irina 2022) focused solely on the objective measurements. Additionally, some trials (n=5) also included the various self-assessments by participants, which, although extremely subjective and prone to biases, are particularly important in the case of alopecia, as it significantly impacts mental health.

In all cases the vast majority completed their therapies, only 5 out of 80 patients in (Singh et al. 2020) thus having low impact on results.

Results

Follow-up times varied immensely between trials therefore it is difficult to pairwise compare their results. However, trends can be observed.

The most common measurements were self-satisfaction and hair density (n=5) assessment however details of the latter differed between the trials.

Hair density varied, mainly due to short follow-up periods and seemed to steadily improve over time even till the 6th month, which is the latest data point available. The average percentage increase was $37.17\% \pm 18.20\%$, for 95% confidence level. That high margin of error is a consequence of varied follow-up times and inclusion of women against or additional use of finasteride/spironolactone in combined treatment in (Ramadan et al. 2021).

Second most common (n=3) was the mean diameter of the hairs which increased by $19.2365 \pm 5.26\%$ for 95% confidence level. It's also worth noting that only (Elena and Irina 2022) and (Ramadan et al. 2021) using microneedling found statistically significant differences with p-value at 0.00004 and <0.001 respectively.

Other measured results included percentage of vellus, terminal, telogen and anagen hairs. Ratio of anagen to telogen and terminal to vellus.

Findings

Our findings highlight that complex therapy outperformed both monotherapies in all measurable and subjective parameters, although not every in a statistically significant way. After two months complex therapy starts to show a significant difference when compared to minoxidil alone and improvements when compared to PRP monotherapy, though not significantly different from it in every aspect. Still, it makes combined therapy a more promising option.

Moreover, patients expressed higher levels of satisfaction with the results obtained from the complex therapy, which even though are very subjective, are a vital factor as alopecia has mild physical symptoms but can cause more severe mental trauma.

One of the key advantages of complex therapy is the faster improvement observed in the number of trials especially when compared to minoxidil alone, platelet-rich plasma on its own had similar improvement time skewing towards slower side.

Additionally, the combination therapy demonstrated a favorable safety profile, with little to no reported severe or unexpected side effects. Reported side effects were expected by authors due to the nature of the monotherapies itself. Thus, we can conclude the viability of combining PRP and minoxidil.

Based on the lack of reported adverse effects, negative interactions or any other unexpected side-effects we concluded that there is no negative impact of combined therapy on the sport performance. Problems reported were on the mild side and would not affect performance if they occurred for athletes during their carrier.

Drawbacks

On the other hand, there are a couple of flaws regarding the substantial amount of available literature. Due to the scarcity of publications on the topic and the lack of high-quality randomized, double-blind studies are even more apparent. A couple of studies included in the review were open trials, thus were not randomized nor blind suggesting that there might be a higher risk of bias.

Another more concrete problem with the majority of found trials was too short follow-up time, it was even pointed out by authors of said publications. It is particularly unfortunate when compared to minoxidil monotherapy as its the typical peak hair growth is about a year in. Short follow-up obviously unable to draw definitive conclusions regarding long-term efficacy.

Various trials reported their findings in diverse ways, often using only subjective or unrepeatable assessments, such as hair-pulling tests or self-assessments. This inconsistency in data reporting makes it challenging to make comprehensive comparisons and evaluate the treatments' objective effectiveness.

There is no drawback for undergoing combined therapy when it comes to physical performance.

Athletic performance impact

As expected from the Platelet-Rich Plasma (PRP) therapy had no examples of case studies describing the side-effects of overdose or misapplication, therefore only the expected side-effects occurred. Which, for the for the scalp injection, are localized on top of the head. There are no mainstream sports that heavily rely on that part of the head. Even if some existed the effects are localized and very brief, usually lasting from couple of hours up to a day. Therefore, it can be concluded that PRP therapy has no negative effect on the performance of any athletes and can be safely used during their carriers. Minoxidil, when taken as prescribed without any accidents or misuse, caused absolutely no side-effects. Neither adverse effects nor impaired performance or physical wellbeing was reported by the patients.

As mentioned, combined therapy has no additional or significant side-effects on the patients on its own. The same sport performance impact, if any, is expected from the combined therapy as from either the mono-minoxidil therapy or Platelet-Rich Plasma therapy alone.

Conclusion

In conclusion, the findings from the reviewed trials suggest that complex therapy of PRP and minoxidil is a very promising, effective, and well-tolerated treatment option for androgenetic alopecia. Without introducing any adverse effects. Still, further research based on even more robust study designs and longer follow-up periods is needed to fully validate and cement combined therapy's superiority over individual monotherapies. Especially when comparing the effectiveness of PRP with combined therapy.

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Data Availability

Articles used by this review are available via links to their digital object identifiers attached to every reference. Other data used in are to be accessed via contact with the corresponding author.

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Conflict of interests

Authors declare no conflict of interests nor any funding.

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