INPLASY PROTOCOL

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Corresponding author:
Guoqiang ZHANG

zlx090702@163.com

Author Affiliation:
The First hospital of Hebei Medical University.

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None declared.

Efficacy and safety of combined with microneedling therapy for androgenic alopecia: A systematic review and meta-analysis of randomized clinical trials

Pei, DN[1]; Zeng, LX[2]; Huang, X[3]; Wang B[4]; Liu, L[5]; Zhang, GQ[6].

Review question / Objective: **The aim of this study was to systematically evaluate the efficacy and safety of MN combined with other hair growth promoting therapies in the treatment of AGA, and to provide a reliable basis for its clinical application.**
Condition being studied: **Androgenetic alopecia (AGA) is the most common type of hair loss characterized by progressive microminiaturization of hair follicles. Hair loss has a tremendous impact on the patient's appearance, mental health and quality of life. Microneedling (MN) can stimulate the release of various growth factors, the formation of collagen and the neovascularization by puncturing the stratum corneum. MN as a minimally invasive technique has been widely used in various skin diseases. Recently, combined MN with other hair growth promoting therapies for AGA has been reported more frequently. However, there is a lack of systematic review of its efficacy and safety.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 11 November 2022 and was last updated on 11 November 2022 (registration number INPLASY2022110051).

INTRODUCTION

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METHODS

Search strategy: Two independent researchers individually carried out a full systematic literature search of PubMed, Embase, the Cochrane Library for any study on MN for the treatment of AGA. The time frame for the search was from the creation of the database to September 2022. No language restrictions were applied. The mesh and entry Terms employed in the search were as follows: "Hair Loss"、"Androgenetic Alopecia"、"Androgenic Alopecia"、"Pattern Baldness"、"Male Pattern Alopecia"、"Male Pattern Baldness"、"Female Pattern Alopecia"、"Female Pattern Baldness" combined with "microneedle"、"microneedling"、"needling"、"needling dermabrasion"、"collagen induction therapy". Two independent researchers' search results were merged to remove duplicate studies. Disagreements were adjudicated by a third researchers.

Participant or population: AGA subjects, regardless of race, age, gender, severity and duration of disease.

Intervention: Combined MN with other hair growth promoting therapies (such as minoxidil, Platelet-Rich Plasma (PRP), Solution of growth factors, Dutasteride, Finasteride, Spironolactone,etc.).

Comparator: Only use the above medications or treatment methods except MN; single MN or MN plus normal saline.

Study designs to be included: RCT.

Eligibility criteria: Inclusion Criteria were as follows: (a) AGA subjects, regardless of race, age, gender, severity and duration of disease; (b) Experimental group: Combined MN with other hair growth promoting therapies (such as minoxidil, Platelet-Rich Plasma (PRP), Solution of growth factors, Dutasteride, Finasteride, Spironolactone, etc.); (c) Control group: only use the above medications or treatment methods except MN; single MN or MN plus normal saline; (d) Outcomes: The primary outcomes are the changes in hair density and thickness. Secondary Outcomes are investigator and/or subjects assessment of hair growth. Other outcomes include ratio of vellus hair/terminal hair (RVHTH), changes in scalp tissue structure and amount of hair follicles, pain assessment, pull test and adverse events; (e) Type of study: all published RCTs on combined with MN in the treatment of AGA.Exclusion Criteria were as follows: (a) non-AGA forms of alopecia; (b) studies without MN therapy; (c) duplicate publications; (d) study type: reviews, meta-analysis, clinical conference, comments, letter to editor, case reports/series, animals experiment; (e) unable to get full-text or available data literature.

Information sources: We conducted a comprehensive search of RCTs on combined MN therapy for AGA in PubMed, Embase, the Cochrane Library. The search time range is from the establishment of each database to September 2022.

Main outcome(s): A total of 13 RCTs with 696 AGA subjects were included. Meta-analysis demonstrated that hair density were significant better in the combined MN group than single MN group and single medication group [MD (95%CI): 13.36 (8.55, 18.16), $P < 0.00001$; MD (95%CI): 18.11 (13.70, 22.52), $P < 0.00001$]. Similarly, combined MN group showed a significant increased in hair thickness comparing the single MN group and single medication group [MD (95%CI): 13.36 (8.55, 18.16), $P < 0.00001$; MD (95%CI): 2.50 (0.99, 4.02), $P = 0.001$]. Investigators satisfaction with hair growth in the combined MN group were significantly better than Monotherapy

group, with pooled RR were 2.03 [95%CI = (1.62, 2.53), P < 0.00001]. There was no statistically significant difference in subject's satisfaction between the two groups [RR (95%CI): 3.44 (0.67, 17.59), P = 0.14]. For safety, the most common adverse event of MN is scalp tingling. Other rare adverse events include enlargement of cervical or posterior auricular lymph nodes, increased scurf, scalp pruritus and erythema, etc. However, these adverse events were mild and transient. And there was no statistical difference in the risk of adverse events between the combined with MN group and the Monotherapy group, with a pooled RR of 0.83 [95%CI = (0.62, 1.12), P = 0.22].

Quality assessment / Risk of bias analysis: Two researchers independently used the Cochrane Risk of Bias tool to evaluate the quality of the included studies, and then negotiated and summarized after completion. In case of disputes, through mutual discussion or decision-making by a third researcher. Revman 5.3 is used to make a summary graph of risk and bias.

Strategy of data synthesis: Revman 5.3 and Stata 15.1 were used for statistical software. The effect index of binary variables and continuous variables were selected for statistical analysis by risk ratio (RR) and mean difference (MD) , respectively. Each effect index was expressed by a 95% confidence interval. The heterogeneity of each RCT was judged by the Q test and the I2 test. If there was no significant heterogeneity among the studies results (I2≤50% and Q test P>0.1), the fixed-effect model was used. Otherwise, the random-effect model was used. When there is strong heterogeneity among the studies results (I2>50% and Q test P<0.1), sensitivity analysis and subgroup analysis are used to find the causes of heterogeneity as much as possible. The major outcome were examined by funnel plot and Egger's test for publication bias to assess the stability of study's results.

Subgroup analysis: When there is strong heterogeneity among the studies results (I2>50% and Q test P<0.1), sensitivity analysis and subgroup analysis are used to find the causes of heterogeneity as much as possible. The major outcome were examined by funnel plot and Egger's test for publication bias to assess the stability of study's results.

Sensitivity analysis: When there is strong heterogeneity among the studies results (I2>50% and Q test P<0.1), sensitivity analysis and subgroup analysis are used to find the causes of heterogeneity as much as possible. The major outcome were examined by funnel plot and Egger's test for publication bias to assess the stability of study's results.

Language restriction: No.

Country(ies) involved: China.

Keywords: Androgenic Alopecia, Microneedling, Efficacy, Safety, Systematic review, Meta-analysis.

Contributions of each author:

Author 1 - Danning PEI - acquisition, analysis, interpretation of data, drafting of the manuscript and statistical analysis.
Email: 374160957@qq.com
Author 2 - Linxi Zeng - acquisition, analysis, or interpretation of data.
Email: 895162267@qq.com
Author 3 - Xin Huang - acquisition, analysis, or interpretation of data.
EMail: hx970131@163.com
Author 4 - Bin Wang - statistical analysis.
Email: wangbin19951214@163.com
Author 5 - Lu Liu - statistical analysis.
Email: liulu9972@163.com
Author 6 - Guoqiang Zhang - GZ: supervision, concept, and design.
Email: zlx090702@163.com