Retrospective Study

# The Effect of Local Skin Precooling on Alleviating Injection Site Pain in Patients With Androgenetic Alopecia Receiving a Scalp Nerve Block

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**Background:** Scalp platelet-rich plasma (PRP) mesotherapy is commonly used to increase hair density and improve scalp health in patients with androgenetic alopecia. While PRP therapy is favored for its lower risk of adverse effects and reduced treatment frequency compared to other methods, the potential for injection site pain remains a significant challenge, potentially reducing patient compliance and treatment continuation.

**Objective:** To evaluate the effectiveness of local skin precooling in reducing injection site pain during scalp PRP mesotherapy in patients with androgenetic alopecia.

**Study Design:** A single-center retrospective study.

**Setting:** This study was conducted at the Precision Health Management Center of the Shanghai East Hospital, Tongji University School of Medicine, People's Republic of China.

**Methods:** Data were collected from 100 patients (82 men, 18 women) aged 18-50 years who underwent scalp PRP mesotherapy from August 2020 through July 2024. Patients were divided into 2 groups: Group A (n = 50) received local skin precooling administered using sterile gloves by way of soft ice packs for 2 minutes pre scalp nerve block; Group B (n = 50) did not receive local skin precooling pre scalp nerve block. All patients received scalp PRP mesotherapy. Pain perception was measured using a 100-mm Visual Analog Scale (VAS) at multiple time points: 30 seconds post scalp nerve block at 2 nerve points, at immediate posttreatment, and at one- and 24-hours posttreatment. Demographic data and Positive and Negative Affect Schedule scores were also collected. Safety outcomes included the incidence of adverse events.

**Results:** VAS scores were significantly lower in Group A compared to Group B at all measured time points. At 30 seconds post scalp nerve block, Group A showed a 34.08% pain reduction at the supraorbital nerve and the supratrochlear nerve and an 18.86% pain reduction at the greater occipital nerve compared to Group B. VAS scores for Group A at immediate posttreatment, and one and 24 hours posttreatment were significantly lower than those for Group B ($P < 0.05$). The primary adverse reactions reported were mild. They included headache, injection site pain, and scalp sensitivity, all of which resolved quickly.

**Limitations:** The retrospective nature of the study, limited data collection, small sample size, and short follow-up period are notable limitations. Larger-scale prospective studies with extended follow-up periods are recommended for future research.

**Conclusion:** local skin precooling is a simple and effective technique for reducing injection site pain during a scalp nerve block. PRP mesotherapy, thereby enhancing patient comfort and compliance. Our study is the first to analyze the analgesic effects of local skin precooling on scalp nerve block injection site pain in patients undergoing scalp mesotherapy.

**Key words:** Mesotherapy, androgenetic alopecia, local skin precooling, injection site pain, scalp nerve block, visual analog scale, pain management

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Epidemiological studies indicate that 80% of White men and 40%–50% of White women will be diagnosed with androgenetic alopecia in their lifetime (1). Androgenetic alopecia is a multifactorial, polygenic inherited chronic disease characterized by the gradual miniaturization of hair follicles, leading to decreased hair density in androgen-sensitive areas of the scalp (2).

Hair loss significantly affects quality of life, leading to a loss of confidence and self-esteem (3). Thousands seek treatment to alleviate the associated psychological stress. Medications approved by the US Food and Drug Administration for androgenetic alopecia include topical minoxidil for women and both topical minoxidil and oral finasteride for men. The local application of platelet-rich plasma (PRP) is a recently developed treatment for hair loss. It involves injecting autologous platelet components rich in growth factors into the scalp dermis (4).

A key issue in hair loss treatment is low patient compliance, as most treatments require long-term adherence. Approximately 10% of patients experience excessive fear of injections; needle phobia affects about 2% of the general population (5). Injection site pain (ISP) is a significant concern, particularly for patients undergoing scalp mesotherapy. Effective pain management is crucial for improving patient compliance with treatment (6-8). Therefore, managing ISP is essential, especially for those requiring long-term mesotherapy or other scalp injection treatments (9).

Scalp nerve block (SNB) is a technique that causes localized sensory loss in the scalp, reducing pain for an extended period. This technique, used for more than a century, is important in various neurosurgical procedures and pain treatments (10). A major advantage of an SNB is its ability to provide effective anesthesia with fewer injections over a large skin area.

However, the most challenging aspect for many patients is the pain associated with SNB-ISP and local anesthetic infiltration. Minimizing patient pain is crucial for hair specialists to provide better treatment experiences and outcomes (11).

Recent evidence supports cooling analgesia as an effective physical pain relief technique. This simple and easy-to-perform strategy has been considered to have analgesic effects for some time (12,13). However, the effect of local skin precooling (LSPC) on relieving SNB-ISP during scalp mesotherapy remains to be studied.

Our study aimed to evaluate the effectiveness of LSPC for reducing pain associated with a ropivacaine injection at the SNB injection site. The effectiveness of LSPC was primarily assessed by comparing Visual Analog Scale (VAS) scores between patients receiving an SNB at 2 minutes post-LSPC and a control group that did not receive LSPC. SNB-ISP severity was measured using the VAS at immediate postinjection of ropivacaine (0.75%) at 2 SNB points on the scalp. The VAS is the gold standard for quantifying pain intensity (14,15). In our study, a VAS score below 10 mm was considered mild pain, below 20 mm acceptable, and above 20 mm unacceptable. The minimal clinically significant difference (greater than 10 mm on the VAS) was used to identify clinically significant differences in SNB-ISP (16,17).

## Methods

### Study Design

This was a single-center retrospective study conducted at the Precision Health Management Center of Tongji University's Shanghai East Hospital, People's Republic of China. Data from the medical records of 187 patients who received scalp PRP mesotherapy at the center from August 2020 through July 2024 were collected. The project leader included 100 patients aged 18-50 who received scalp PRP mesotherapy at the hospital, based on the treatment process they underwent.

The enrolled patients were divided into 2 groups based on their actual treatment records, with 50 patients in each group. The experimental group (Group A) used sterile gloves to self-administer soft ice packs to cool the injection site for 2 minutes before receiving an SNB (Fig. 1b). The control group (Group B) received an SNB without prior local skin cooling.

All procedures were performed by the same medical team at Tongji University's Shanghai East Hospital. All patients received scalp PRP mesotherapy. Pain assessments were performed by the same nurse for all patients. Additionally, since this project was a retrospective medical record review and quality improvement study, patient informed consent was not required. The primary objective of the study was to evaluate whether LSPC could reduce SNB-ISP based on VAS scores. Secondary objectives included identifying potential side effects of LSPC. Patients who may have received multiple scalp PRP mesotherapy treatments were included in the analysis using only data from their first treatment.

An academic ethics committee reviewed and approved all study-related documents, including the study protocol and amendments, in accordance with the requirements of Good Clinical Practice. These trials were conducted according to consensus ethical principles

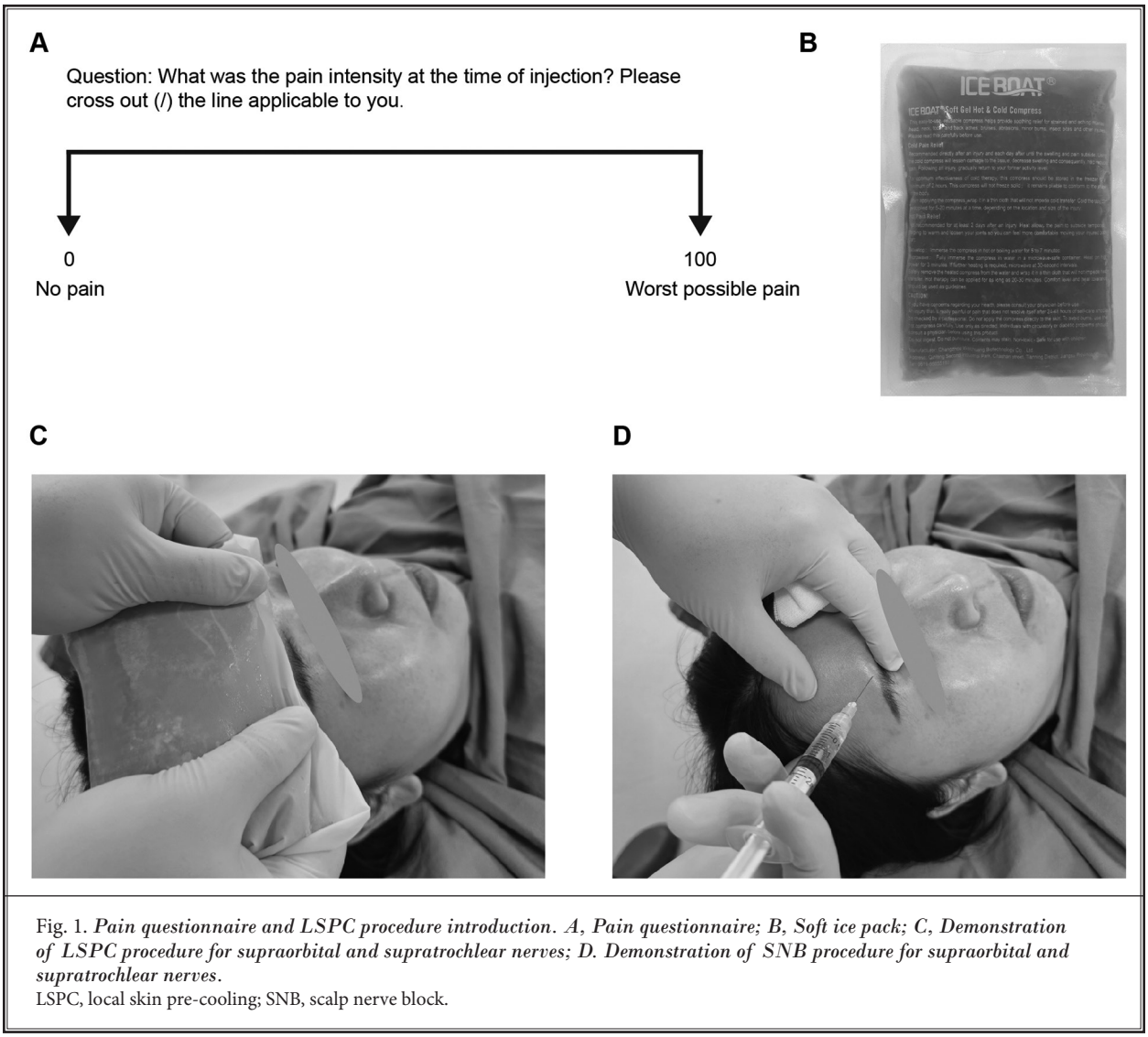


Fig. 1. *Pain questionnaire and LSPC procedure introduction. A, Pain questionnaire; B, Soft ice pack; C, Demonstration of LSPC procedure for supraorbital and supratrochlear nerves; D. Demonstration of SNB procedure for supraorbital and supratrochlear nerves.*
LSPC, local skin pre-cooling; SNB, scalp nerve block.

derived from international ethical guidelines, including the International Ethical Guidelines for Health-related Research Involving Humans, the Good Clinical Practice principles of the International Ethical E6 guidelines, and all applicable laws and regulations. Our study was conducted with the appropriate permissions from the hospital and was approved by the Medical Ethics Committee of Shanghai East Hospital, with the ethics approval number 2024YS-138, and the protocol version number 1.0. Additionally, the trial was registered and filed at medicalresearch.org.cn after completion (registration number: MR-31-24-029333).

## Patient Population

The inclusion criteria were: individuals diagnosed with androgenetic alopecia aged between 18–50 years.

The exclusion criteria were: 1) known or suspected allergy to the investigational product or related products; 2) alcohol consumption within the previous 24 hours (self-reported) or a positive alcohol breath test; 3) consumption of illegal drugs within the previous 48 hours (self-reported) or a positive urine drug screen; 4) use of any painkillers or analgesics in the previous 7 days; 5) receipt of any investigational medical products that might affect pain perception in the previous 14 days; 6) anticoagulant therapy within the previous month (low-dose aspirin for cardiovascular prevention was allowed but not on the day of injection); 7) smokers or recent quitters using nicotine withdrawal products within the previous 6 months;

8) known skin diseases at the injection area or any condition that might affect pain perception; 9) any localized or characteristic pain unrelated to the study; 10) any localized tissue damage at the intervention site; 11) a moderate to severe lipodystrophy syndrome as assessed by the investigator; 12) severe neuropathy; 13) any chronic or serious illness deemed by the investigator to potentially endanger patient safety or affect compliance with the protocol; 14) patients under 18 years of age or unable to complete the pain scale or other test forms; 15) patients who did not complete any part of the trial content were excluded from the analysis.

## Treatment Procedures

Before the first injection, patients filled out a Positive and Negative Affect Schedule (PANAS) questionnaire, providing information related to their mood, emotions, and well-being. The 20 questions in the PANAS questionnaire were scored on a 5-point scale (from "very slightly or not at all" to "extremely").

Before mesotherapy, the scalp was disinfected. Group A patients (n = 50) used sterile gloves to self-administer soft ice packs for 2 minutes in order to cool the injection site. Two minutes was chosen since prolonged cooling could cause an unacceptable cold sensation (Fig. 1c).

After skin cooling, a supraorbital nerve block was performed with the patient's head facing forward and eyes closed. The supraorbital nerve was blocked as it passed through the orbit. The supraorbital notch was palpated, and a needle was inserted vertically one cm medial to the notch. Approximately one mL of 0.75% ropivacaine was injected on the periosteum. The supratrochlear nerve block location was similar to that of the supraorbital nerve block (Fig. 1d). The supratrochlear nerve runs parallel to the supraorbital nerve, about one finger's width above the medial aspect of the eyebrow. After blocking the supraorbital nerve, the needle was directed medially from the same insertion point, and one mL of 0.75% ropivacaine was injected to block the supratrochlear nerve.

The greater occipital nerve block can be performed by turning the patient's head to one side or having the patient sit up. The greater occipital nerve was blocked by subcutaneous infiltration of local anesthetic at the midpoint between the external occipital protuberance and the mastoid process, 2.5 cm lateral to the midline. The best landmark is palpating the occipital artery (about 3 to 4 cm lateral to the external occipital protuberance along the superior nuchal line). After careful aspiration, the injection was administered medial to the artery to avoid potential intra-arterial injection. The needle was inserted at a 90° angle toward the occiput until bone contact was made, then retracted slightly for a subcutaneous injection of 3 mL of 0.75% ropivacaine. Gentle massage with gauze after each injection helped to spread the local anesthetic. Group B (n = 50) received an SNB at 2 sites, with the same ropivacaine injection method and volume as Group A, but without the LSPC step.

## Outcome Assessment

Data collected using a demographic questionnaire included the patients' age, weight, height, Body Mass Index (BMI), PANAS questionnaire scores, and medical history data, such as chronic diseases and past surgical history. Pain perception was assessed using a 100-mm VAS (0 mm = no pain, 100 mm = extreme pain). As the primary endpoint variable, each patient was asked to score the relevant SNB-ISP by marking a vertical line on the VAS at 30 seconds postinjection at each nerve block anesthesia point (Fig. 1a).

Posttreatment, patients were transferred to an observation room and pain scores were measured using the VAS at immediate, one, and 24 hours posttreatment. The number and percentage of patients in each pain severity category were summarized by treatment group. The overall acceptability of the treatment was also assessed at the fifth visit (7 days posttreatment). Acceptability responses were recorded on a 5-point Likert scale: Strongly Agree, Agree, Neutral, Disagree, and Strongly Disagree (18). Telephone follow-ups were conducted on posttreatment days 2 and 7 to further assess injection site reactions and the occurrence of adverse events. If an injection site reaction or adverse event occurred, patients returned to the center for further evaluation (19). Safety outcomes included the incidence of all adverse events that occurred during treatment. Adverse events were coded using the Medical Dictionary for Regulatory Activities (MedDRA) version 20.0; adverse event severity was graded using the Common Terminology Criteria for Adverse Events (CTCAE) version 4.0.

## Statistical Analysis

Statistical analysis of the data obtained from the study was performed using IBM SPSS Statistics 20.0 (IBM Corporation). Descriptive statistics or frequency tables, or both, were provided for all baseline variables, VAS, acceptability surveys, satisfaction surveys, and safety surveys. Descriptive statistics were presented using numbers (n), percentages (%), mean ± SEM values, and median and interquartile range (IQR) values.

For the purposes of our study, the minimal clinically

significant difference between VAS scores was defined as 10 mm (17,20). The Shapiro-Wilk test was used to assess the conformity of the data to a normal distribution. Continuous variables with nonnormal distributions were presented as medians and interquartile ranges and analyzed using the Mann-Whitney U test. When the quantitative data followed a normal distribution, independent t tests were used to compare continuous quantitative data between the 2 groups, such as age, weight, height, BMI, and PANAS questionnaire scores, with the mean ± SEM values provided. A $P$ value < 0.05 was considered statistically significant; all tests were 2-tailed. For ordinal variables, such as VAS grade comparisons and acceptability survey results, the Mann-Whitney U test was used to compare differences between the 2 groups, with a significance level of $P < 0.05$). Categorical data were presented as absolute numbers and proportions. The association of categorical data (e.g., gender) was determined using the $\chi^2$ test, with a significance level $P < 0.05$; all tests were 2-tailed.

## Results

Our study's primary objective was to evaluate the effect of adding local skin precooling treatment to the pain control regimen for reducing pain associated with scalp PRP mesotherapy, as assessed by VAS scores. The study was designed and implemented simply, with no losses or exclusions in the analysis.

Out of 187 patients who received scalp PRP mesotherapy from 2020 through 2024, data from 100 patients were obtained from hospital records: 82 men (82%) and 18 women (18%).

The mean (SD) age of the patients was 39.19 ± 0.80 years, mean weight was 70.85 ± 1.09 kg, mean height was 171.44 ± 0.67 cm, and mean BMI was 23.98 ± 0.18. The mean positive PANAS score for psychological health was 33.54 ± 0.83, and the mean negative PANAS score was 11.84 ± 0.23.

The 2 groups were well-matched in basic characteristics such as age (39.14 ± 1.08 years old [Group A] vs 39.24 ± 1.19 years old [Group B]; $P = 0.9507$), weight (71.59 ± 1.64 kg [Group A] vs 70.11 ± 1.46 kg [Group B]; $P = 0.4998$), height (171.50 ± 1.08 cm [Group A] vs 171.37 ± 0.81 cm [Group B]; $P = 0.9247$), and BMI (24.15 ± 0.25 [Group A] vs 23.80 ± 0.26 [Group B]; $P = 0.3390$). The psychological health mean (SD) positive PANAS score (32.32 ± 1.19 [Group A] vs 34.76 ± 1.15 [Group B]) and mean negative PANAS score (11.88 ± 0.30 [Group A] vs 11.80 ± 0.34 [Group B]) indicates that both groups were within the normal psychological health range, with no significant differences between the groups. Despite not matching any variables at the time of treatment, the demographic characteristics of the 2 groups were similar (Figs. 2a-g, Table 1).

Statistical analysis comparing the 2 groups during SNB revealed that at 30 seconds post SNB injection at the supraorbital nerve and supratrochlear nerve points,

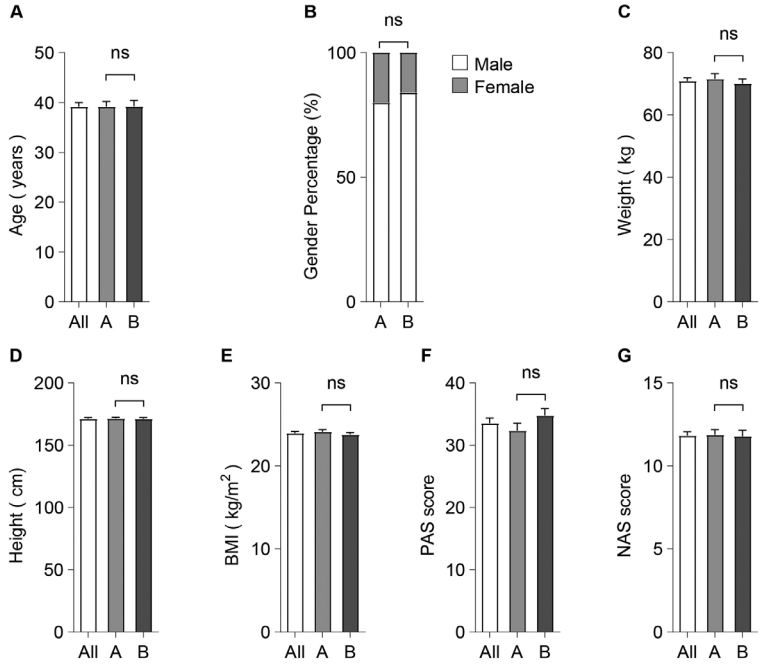


Fig. 2. *Demographic characteristics and clinical features of patients at baseline. A, Age of patients at baseline; B, Gender percentage of patients; C, Weight of patients at baseline; D, Height of patients at baseline; E, BMI of patients at baseline; F, Positive Affect Schedule of patients at baseline; G, Negative Affect Schedule of patients at baseline. Ns: No significance. BMI: body mass index, PAS: positive PANAS, NAS: negative PANAS, PANAS: Positive and Negative Affect Schedule.*

Table 1. *Demographic characteristics and clinical features of patients at baseline.*

| Variables | Total n (%) or mean ± SEM (range) | Group A n (%) or mean ± SEM (range) | Group B n (%) or mean ± SEM (range) | $\chi^2$ | *P* Value |
|---|---|---|---|---|---|
| Age (years) | 39.19 ± 0.80 (22-61) | 39.14 ± 1.08 (22-54) | 39.24 ± 1.19(24-61) | | 0.9507 |
| Weight (kg) | 70.85 ± 1.09 (38.59-99.99) | 71.59 ± 1.64 (52.80-99.99) | 70.11 ± 1.46 (38.59-91.9) | | 0.4998 |
| Height(cm) | 171.44 ± 0.67 (155.57-189.86) | 171.50 ± 1.08 (155.57-189.86) | 171.37± 0.81 (157.90-182.93) | | 0.9247 |
| BMI (kg/m$^2$) | 23.98 ± 0.18 (19.13-28.37) | 24.15 ± 0.25 (21.22-28.37) | 23.80± 0.26 (19.13-27.46) | | 0.3390 |
| Gender | 100 (100%) | 50 (100%) | 50 (100%) | 0.7953 | |
| Men | 82 (82 %) | 40 (80 %) | 42 (84 %) | | |
| Women | 18 (18 %) | 10 (20 %) | 8 (16 %) | | |
| PANAS score | | | | | |
| PAS score | 33.54 ± 0.83 (7-50) | 32.32 ± 1.19 (11-47) | 34.76 ± 1.15 (7-50) | | 0.1438 |
| NAS score | 11.84 ± 0.23 (6-18) | 11.88 ± 0.30 (6-16) | 11.80 ± 0.34 (7-18) | | 0.8611 |

Abbreviations: n: number, SEM: Standard Error of Mean; BMI: Body Mass Index, $\chi^2$: Chi-Square Value, PANAS: Positive and Negative Affect Schedule, PAS: Positive PANAS, NAS: Negative PANAS.

Group A had significantly reduced pain compared to Group B ($P < 0.0001$) (Fig. 3a, Figs. 4a-b, Table 2). Group A's average pain reduction was 34.08% compared to Group B, and the median VAS score was below the preset minimal clinically significant difference. There was a significant difference in the distribution of pain severity VAS score groups between Group A and Group B ($P = 0.0016$) (Fig. 5a). The combined proportion of the "mild pain" and "acceptable mild pain" groups was significantly higher in Group A than in Group B (46% vs 22%) (Table 3).

At the greater occipital nerve point, at 30 seconds post SNB injection, Group A had significantly reduced pain compared to Group B ($P = 0.0003$) (Fig 3b, Fig. 4c, Table 2). Group A's average pain reduction was 18.86% compared to Group B. There was a significant difference in the distribution of pain severity VAS score groups between Group A and Group B ($P = 0.0006$) (Fig. 5b). The combined proportion of the "mild pain" and "acceptable mild pain" groups was significantly higher in Group A than in Group B (48% vs 22%) (Table 3).

According to the results (Figs. 3c-e; Figs. 4d-f; Table 2), Group A's VAS scores were significantly lower than Group B's at immediate, one, and 24 hours posttreatment ($P = 0.0021$, $P < 0.0001$, $P = 0.0092$, respectively).

At the immediate posttreatment time point, there was a significant difference in the distribution of pain severity VAS score groups between Group A and Group B ($P = 0.003$) (Fig. 5c). The combined proportion of the "mild pain" and "acceptable mild pain" groups was significantly higher in Group A than in Group B (82% vs 32%) (Table 3). At one hour posttreatment, there was a significant difference in the distribution of pain severity VAS score groups between Group A and Group B ($P = 0.003$) (Fig. 5d). The combined proportion of the "mild pain" and "acceptable mild pain" groups was significantly higher in Group A than in Group B (70% vs 64%) (Table 3). At 24 hours posttreatment, there was a significant difference in the distribution of pain severity VAS score groups between Group A and Group B ($P = 0.0042$) (Fig. 5e). The combined proportion of the "mild pain" and "acceptable mild pain" groups was significantly higher in Group A than in Group B (98% vs 88%) (Table 3).

At the fifth visit (7 days posttreatment), the agreement rates (including "Agree" and "Strongly Agree" Likert scale responses) for the 5 questions about overall treatment acceptability were 92%, 98%, 88%, 96%, 88% for Group A and 66%, 74%, 80%, 72%, 74% for Group B (Table 4). $\chi^2$ tests revealed statistically significant differences between the groups for Q1, Q2, Q4, Q5, and Q6 ($P < 0.0001$, $P < 0.0001$, $P < 0.0001$, $P = 0.0116$, $P = 0.0011$, respectively).

The main reported adverse reactions were pain during the procedure and posttreatment sensitive scalp or head. Specific adverse reactions reported included headaches in 3% (3/100) of patients, burning sensations in 2% (2/100), and pruritis in 4% (4/100). There were no differences in adverse reactions between the groups. Additionally, no cases of injection site infections were found. Few patients reported sensitivity over the entire scalp, with most indicating sensitivity in the injection areas of the forehead/temples or sides of the scalp. No other serious adverse events were reported.

## Discussion

Scalp PRP mesotherapy is typically aimed at increasing hair density and improving scalp health.

Due to its lower risk of adverse effects and reduced treatment frequency compared to current treatments, PRP therapy for androgenetic alopecia has garnered significant interest. However, a notable challenge in mesotherapy is the potential for ISP, which can lead to decreased compliance or even discontinuation of treatment. Pain and anxiety are known to deter some patients from undergoing any treatment, including SNB (21). Effective pain management throughout the process can significantly enhance patient satisfaction, boost confidence in the treatment, increase compliance, and ultimately improve treatment outcomes for hair loss (22)

Mahshidfar, et al (23) demonstrated in their study on patients with superficial lacerations that cooling the injection site before administering local anesthesia can significantly reduce the pain and discomfort associated with the injection. Other studies have also found that soft tissue cooling helps reduce pain during the injection of local anesthetics in pediatric dental procedures (24). A previous study indicated that ice pack analgesia effectively reduces pain during local anesthetic infiltra-

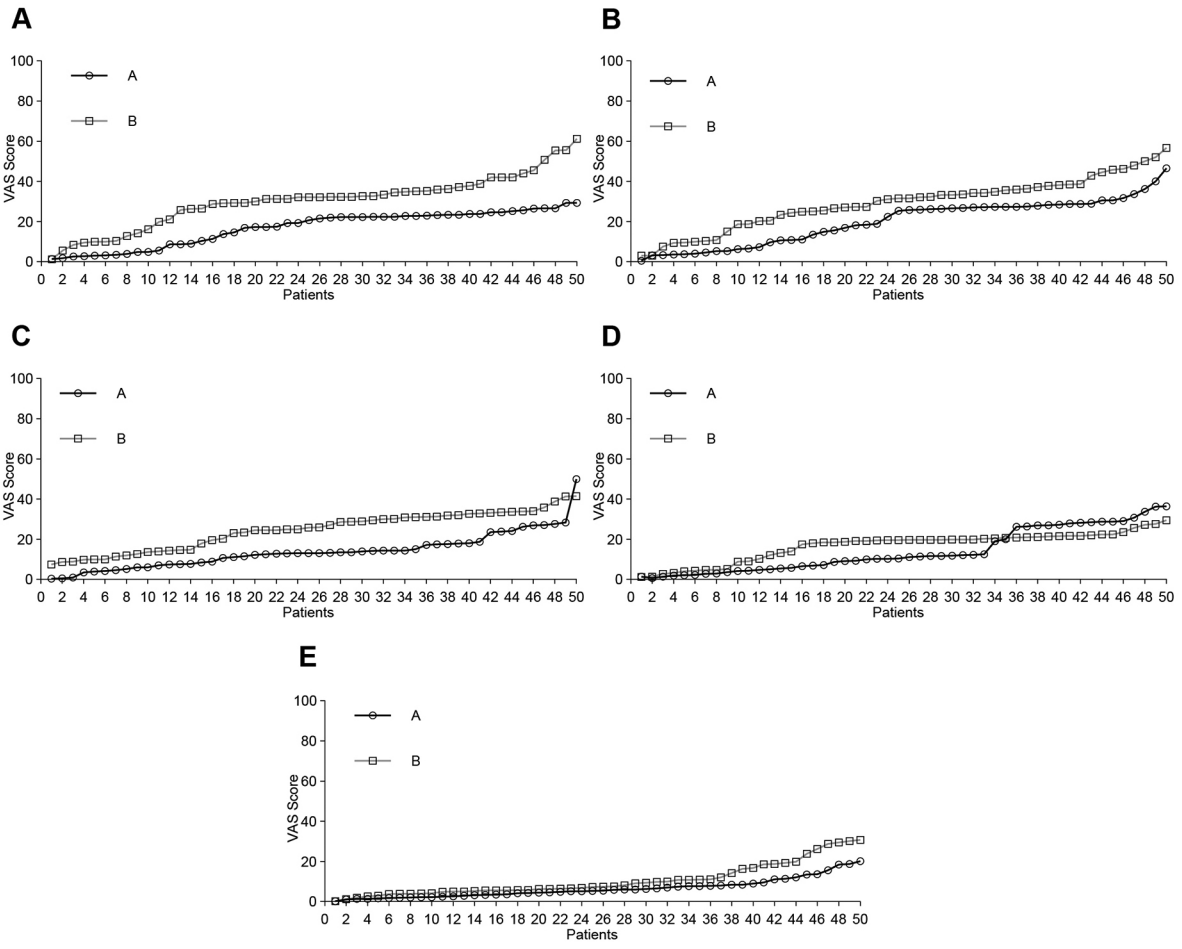


Fig. 3. *Raw data of every patient's VAS scores.*
*A, Raw data from injection points for SNB between the A and B groups 30 seconds post-SNB at SON and STN; B, Raw data from injection points for SNB between the A and B groups 30 seconds post-SNB at GON; C, Raw data from injection points for SNB between the A and B groups at immediate posttreatment; D, Raw data from injection points for SNB between the A and B group at one hour posttreatment; E. Raw data from injection points for SNB between the A and B groups at 24 hours posttreatment. VAS: Visual Analog Scale; SNB: scalp nerve block; SON: supraorbital nerve; STN: supratrochlear nerve; GON: greater occipital nerve.*

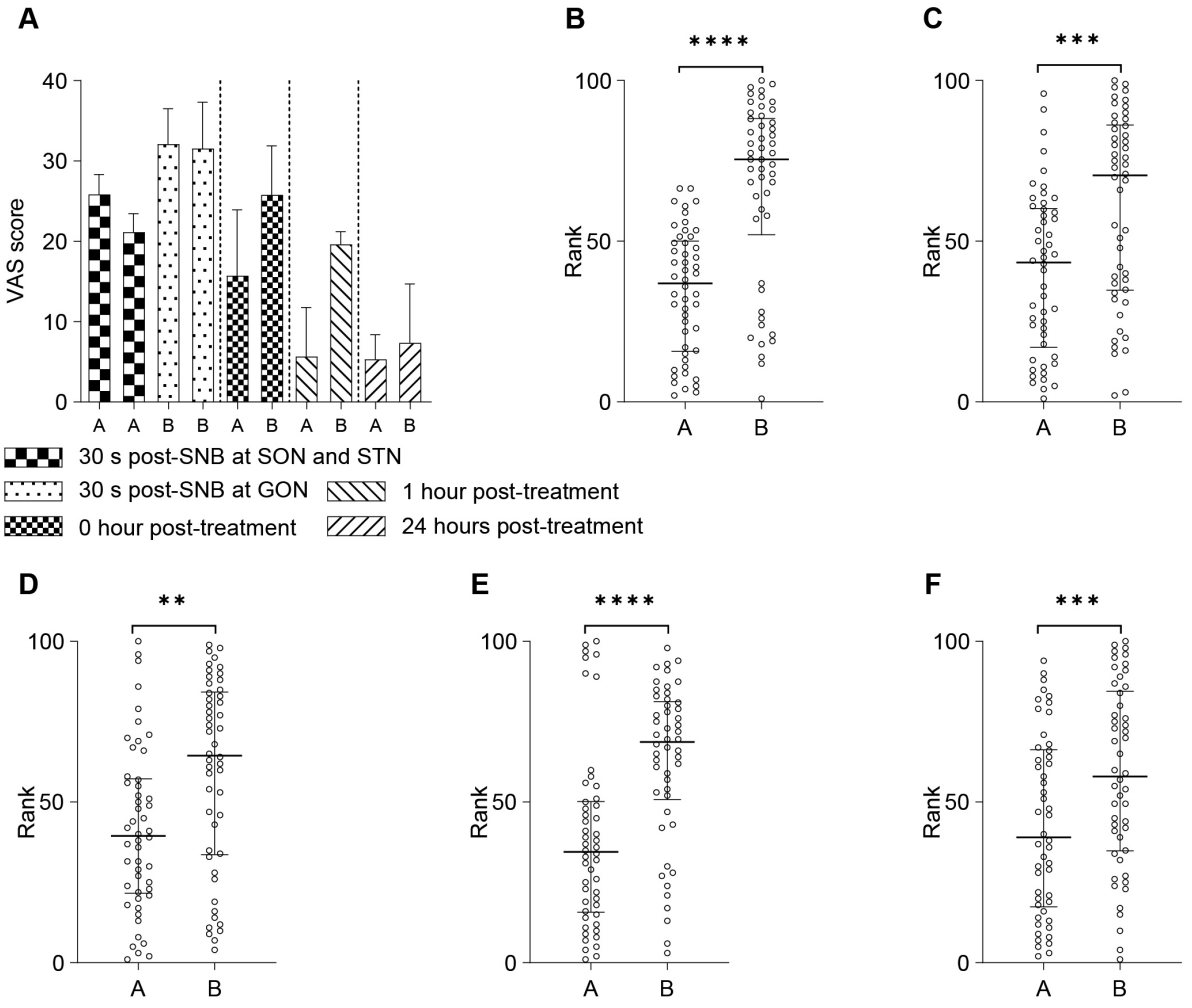


Fig. 4. *VAS scores comparison at the different time points between Groups A and B.*
*A, VAS score at different time points; B, 30 seconds post-SNB at SON and STN; C, 30 seconds post-SNB at GON; D, at immediate posttreatment; E, one hour posttreatment; F, 24 hours posttreatment. **: P < 0.01, **: P < 0.001, ****: P < 0.0001.*

Table 2. *VAS pain score (0–100 mm) summary collected during injection and posttreatment among both groups.*

| Variables | Group A Median (IQR) | Group B Median (IQR) | *P* Value |
|---|---|---|---|
| VAS Score at 30 s post-SNB in SON and STN | 21.18 (14.58) | 32.13 (10.25) | <0.0001 |
| VAS Score at 30 s post-SNB in GON | 25.59 (17.85) | 31.54 (15.76) | 0.0003 |
| VAS Score at immediate posttreatment | 13.091 (9.91) | 25.79 (17.14) | 0.0021 |
| VAS Score at one hour posttreatment | 10.07 (15.42) | 19.62 (8.72) | <0.0001 |
| VAS Score at 24 hours posttreatment | 5.34 (5.31) | 7.37 (8.58) | 0.0092 |

Abbreviations: IQR: Interquartile Range, VAS: Visual Analog Scale, SON: Supraorbital nerve, STN: Supratrochlear nerve, GON: Greater occipital nerve.

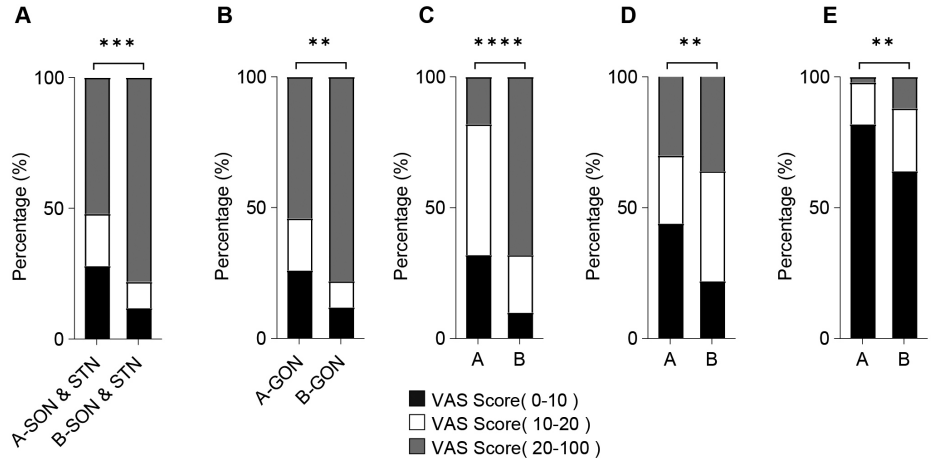


Fig. 5. *The distribution of patients between the groups ranked by Visual Analog Scale score at different time points. A, 30 seconds post-SNB at SON and STN; B, 30 seconds post-SNB at GON; C, at immediate posttreatment; D, one hour posttreatment; E, 24 hours posttreatment.*

Table 3. *The distribution of VAS score classifications between the 2 groups.*

| Variables | | 0 < VAS score ≤ 10 | 10 < VAS score ≤ 20 | 20 < VAS |
|---|---|---|---|---|
| VAS Score at 30 s post-SNB in SON and STN | Group A | 28 | 20 | 52 |
| | Group B | 12 | 10 | 78 |
| VAS Score at 30 s post-SNB in GON | Group A | 26 | 20 | 54 |
| | Group B | 12 | 10 | 78 |
| VAS Score at immediate posttreatment | Group A | 32 | 50 | 18 |
| | Group B | 10 | 22 | 68 |
| VAS Score at one hour post treatment | Group A | 44 | 26 | 30 |
| | Group B | 22 | 42 | 36 |
| VAS Score at 24 hours posttreatment | Group A | 82 | 16 | 2 |
| | Group B | 64 | 24 | 12 |

Abbreviations: VAS: Visual Analog Scale, SON: Supraorbital nerve, STN: Supratrochlear nerve, GON: Greater occipital nerve.

tion for eyelid surgery (25). However, there have been no reports on the use of local skin precooling analgesia for managing SNB-ISP pain in patients undergoing scalp PRP mesotherapy.

The patients in our study were within the normal range of psychological health before receiving their injections, making it unlikely that their psychological state affected their perception of injection pain (26). Pain is a subjective experience that can only be measured by the patient. In this study, we used a content-valid and purpose-appropriate VAS to assess SNB-ISP.

We observed the positive effects of LSPC on comprehensive pain management for patients undergoing scalp PRP mesotherapy. The results showed statistically significant differences in VAS scores between the 2 groups. During SNB, VAS scores at the 2 peripheral injection points on the scalp in Group A were significantly lower than in the group that did not receive skin precooling. Additionally, at immediate, one, and 24 hours posttreatment, Group A's VAS scores were significantly lower than those in Group B.

The most common side effects of mesotherapy are mild and usually resolve within a few days (27). The most frequently reported issues are headaches, injection site pain, and scalp tightness or pruritis, with some studies also mentioning redness and swelling. Of the 19 studies that observed hair regrowth, 9 did not report any adverse effects (28). No serious adverse events occurred in our study either. The primary adverse reactions were pain during the

injection and postprocedure scalp sensitivity, which resolved quickly.

### Limitations

Although VAS pain measurement is highly reliable and correlates well with other pain scoring methods (17), pain is a multidimensional subjective experience that involves both sensory and emotional characteristics, which may vary between individuals (29,30). Other research findings emphasize numerous factors that can influence VAS scores (19).

Many studies have attempted to establish the minimal clinically important difference or minimal clinically important change for VAS pain scores. However, estimates vary significantly depending on the source of pain, chronicity, and disease. We designated the minimal clinically significant difference as 10 mm, consistent with published practices, but there is no absolute consensus on the minimal clinically significant difference threshold.

Table 4. *Acceptability questionnaire agreeable (agree and strongly agree Likert scale) responses at 7 days posttreatment.*

| Questions | Responses at 7 days post-treatment | |
|---|---|---|
| | Group A | Group B |
| Q1: I felt comfortable during the treatment. | 92% | 66% |
| Q2: The treatment process did not cause discomfort or pain. | 98% | 74% |
| Q3: I would recommend this treatment to other patients. | 88% | 80% |
| Q4: I am willing to undergo this treatment again. | 96% | 72% |
| Q5: I did not experience any side effects after the treatment. | 88% | 74% |
| Q6: The side effects after the treatment were within an acceptable range. | 94% | 78% |

Note: Responses were per 5-point Likert scale (strongly disagree, disagree, neutral, agree, and strongly agree).

## Conclusion

Patients with androgenetic alopecia undergoing scalp PRP mesotherapy require SNB. We have demonstrated that LSPC is highly effective in reducing SNB-ISP. It can lower the pain levels for patients receiving scalp mesotherapy. The simplicity and effectiveness of local skin precooling make it a suitable technique for alleviating SNB-ISP and enhancing overall patient comfort. To our knowledge, this is the first study to analyze the analgesic effects of LSPC on SNB-ISP in patients undergoing scalp mesotherapy.

### Data Availability

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

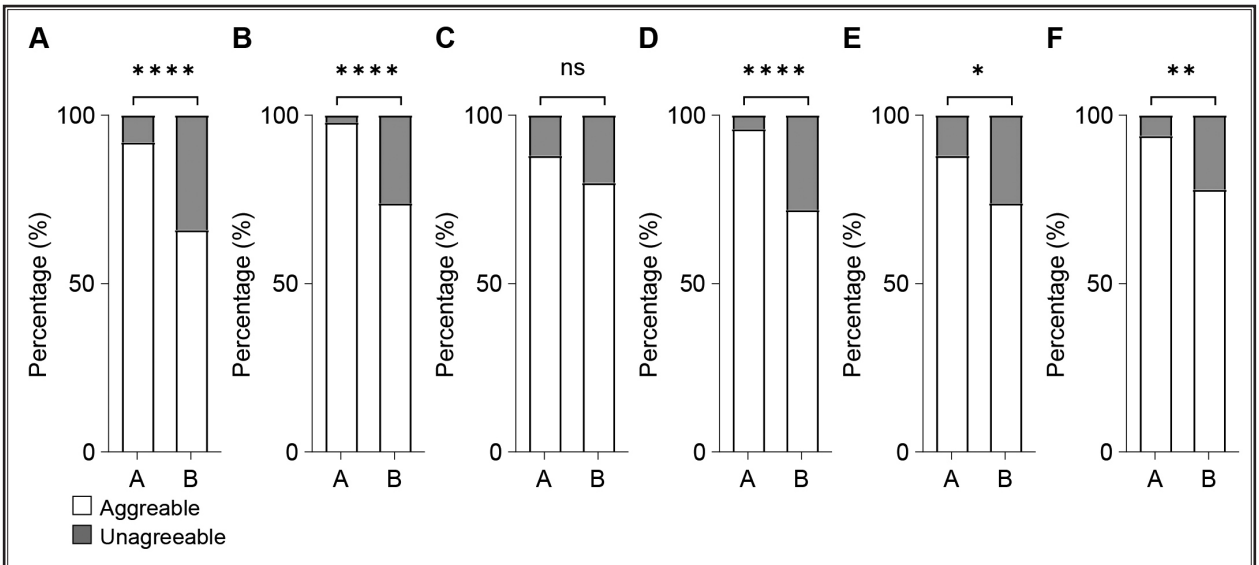


Fig. 6. *Comparison of responses to acceptability survey questions between Groups A and B.*
*A, Likert Scale score of Q1; B, Likert Scale score of Q2; C, Likert Scale score of Q3; D, Likert Scale score of Q4; E, Likert Scale score of Q5; F, Likert Scale score of Q6. *: $P < 0.05$.*

## Author Contributions

Zhongmin Liu designed the study and made the final corrections. Bangda Chai and Ling Gao wrote most of the manuscript. Weiting Liu and Wenjun Le corrected and supervised the information. Yanling Song and Yue Wang contributed to the data collection and analysis. Xiaowen Pan assisted with data interpretation and provided critical revisions. All authors discussed the results and contributed to the final manuscript.

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