Comparative Efficacy of Topical Chitosan and Minoxidil in Hair Loss: A Controlled Study With Microneedling

Jovian Wan, MBChB, Olena Sydorchuk, BS,† Irwan Junawanto, MD,‡ Wonseok Choi, MD,§ Nil Namthongton, MD,‖ Putri Hendira, MD, PhD,¶ Ardhiah Iswanda Putri, MD,# Pattra Chansataporn, MD,** Ruri Pamela, MD,†† and Kyu-Ho Yi, MD, PhD‡‡*

Background: Chitosan, a natural polysaccharide with immunomodulatory and regenerative properties, has shown promise in enhancing tissue repair. While 5% minoxidil remains the standard treatment for androgenetic alopecia, interest in non-hormonal or adjunctive therapies such as chitosan is growing.

Objective: To evaluate the clinical efficacy and safety of topical 2% chitosan applied after microneedling in comparison with 5% topical minoxidil and a no-treatment control group in patients with androgenetic alopecia or diffuse hair loss.

Methods: A prospective, controlled study enrolled 30 patients (aged 22–58 y), randomized equally into 3 groups (n = 10 each): (1) microneedling followed by 4 mL of 2% chitosan (Chitosan group), (2) twice-daily application of 5% topical minoxidil (Minoxidil group), and (3) untreated control (Control group). Treatments continued for 6 months. Primary outcomes included trichoscopic hair density and hair shaft diameter; secondary outcomes included patient satisfaction scores and adverse events. A representative scalp biopsy from the chitosan group was evaluated histologically.

Results: After 6 months, both the chitosan and minoxidil groups demonstrated significant increases in mean hair density compared with the control group (+30.5% and +22.3%, respectively; $P = 0.032$ and $P = 0.048$). Although the chitosan group showed a numerically greater improvement than the minoxidil group, this difference was not statistically significant ($P = 0.62$). Hair shaft diameter and patient satisfaction scores improved in both treatment groups. No meaningful changes were observed in the control group. Mild, transient erythema occurred in 3 patients (1 in the chitosan group and 2 in the minoxidil group). Histologic analysis in a chitosan-treated subject showed increased follicular density and improved dermal matrix organization.

Conclusions: In this small controlled study, microneedling followed by topical 2% chitosan resulted in significant improvements in hair growth parameters compared with no treatment, and outcomes were generally comparable to those observed with 5% minoxidil. While these results are promising, the small sample size limits definitive conclusions regarding comparative efficacy. Larger, adequately powered trials are warranted to confirm these preliminary findings and to better delineate the role of chitosan as a standalone or adjunctive therapy.

Evidence-based level: Level II.

Key Words: Chitosan, microneedling, minoxidil

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Androgenetic alopecia affects ~50% of men and women over the age of 40, representing the most prevalent form of hair loss globally.[1] Traditional therapeutic approaches, while moderately effective, often present limitations including systemic side effects and variable patient response rates.[2] The integration of microneedling therapy with bioactive compounds has emerged as a promising adjunctive treatment modality.[3,4]

Chitosan, a linear polysaccharide obtained through the deacetylation of chitin, possesses unique biological properties including biocompatibility, biodegradability, and immunomodulatory activity.[5,6] Recent botanical investigations have demonstrated that chitosan application induces specific cellular responses, including calcium-mediated signaling pathways and callose deposition in plant root hair systems.[7] These findings suggest potential mechanisms whereby chitosan may

From the *Medical Research Inc., Wonju; †SIORE Inc., Seoul, Republic of Korea; ‡ERHA Dermatology Clinic, Jakarta, Indonesia; §V Plastic Surgery Clinic, Daegu, Republic of Korea; ‖Namninforv Clinic, Bangkok, Thailand; ¶Dr. Soetomo General Hospital; #Rejuva Dental and Dermatology, Surabaya, Indonesia; **Preeyavej Medical Center, Phanom Sarakham, Chachoengsao, Thailand; ††CELV Dermatology Clinic, South Jakarta (Jakarta Selatan), Indonesia; and ‡‡Division in Anatomy and Developmental Biology, Department of Oral Biology, Human Identification Research Institute, BK21 FOUR Project, Yonsei University College of Dentistry, Seodaemun-gu, Seoul, Republic of Korea.

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Address correspondence and reprint requests to Kyu-Ho Yi, MD, PhD, Division of Anatomy and Developmental Biology, Department of Oral Biology, Yonsei University College of Dentistry, 50-1 Yonsei-ro, Seodaemun-gu, Seoul 03722, Republic of Korea; E-mail: kyuho90@daum.net

Informed consent was obtained from all participants, with full disclosure of the study's purpose, risks, and confidentiality.

J.W., N.N., P.H., A.I.P., P.C., R.P., and K.-H.Y.: conceptualization. J.W.: writing—original draft preparation. J.W., K.-H.Y., O.S., I.J., and W.C.: writing—review and editing. J.W., N.N., P.H., A.I.P., P.C., R.P., and K.-H.Y.: visualization. K.-H.Y.: supervision. All authors have reviewed and approved the article for submission.

This article does not contain any studies with animals performed by any of the authors. Informed consent was obtained from all patients for both the procedure and inclusion in this case series.

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influence cellular growth and repair processes in mammalian tissue.

The present controlled study evaluates the clinical efficacy of topical 2% chitosan applied after microneedling therapy, compared with 5% topical minoxidil and a no-treatment control, in patients presenting with androgenetic alopecia or diffuse hair loss.

METHODS

Patient Selection

A total of 81 patients presenting to our dermatology clinic between January 2024 and July 2024 were enrolled in this prospective, controlled clinical study. Patients were randomly assigned to one of three groups (n = 27 each):

Group A: Every 1 month, microneedling followed by topical 2% chitosan (Arche, Doum Inc, Korea) application.

Group B: Twice-daily application of 5% minoxidil.

Group C: Untreated control (no intervention).

Inclusion criteria comprised:

(1) Clinically diagnosed androgenetic alopecia or diffuse hair loss.
(2) Age between 18 and 65 years.
(3) No concurrent hair loss treatments for at least 3 months before enrollment.
(4) Agreement to maintain the current hair care regimen throughout the study.
(5) Signed informed consent.

Exclusion criteria included:

(1) Active scalp infection or inflammatory dermatosis.
(2) Known allergy to chitosan, minoxidil, or shellfish.
(3) Use of systemic immunosuppressive or anticoagulant medications.
(4) Pregnancy or lactation.
(5) Underlying autoimmune or endocrine disorders affecting hair growth.

Demographics

The study cohort consisted of 43 males (53.1%) and 38 females (46.9%), with a mean age of 37.9 years (range: 22–58 y). Androgenetic alopecia was diagnosed in 56 patients (69.1%), and diffuse hair loss was present in 25 patients (30.9%). Baseline demographics were statistically balanced across all 3 groups, with no significant differences in age, sex, or hair loss severity ($P > 0.05$ for all comparisons).

Statistical Analysis

Descriptive statistics were reported as means ± SDs for continuous variables and as frequencies and percentages for categorical variables. *One-way analysis of variance (ANOVA)* was used to compare continuous outcomes (hair density, shaft diameter, and satisfaction scores) among the 3 groups at baseline and at 6 months. Post hoc comparisons were performed using the *Tukey HSD test* to identify specific group differences. For within-group comparisons (baseline vs. 6-month outcomes), *paired t tests* were used. A 2-sided *P*-value of <0.05 was considered statistically significant. *Cohen's d* was calculated to assess effect size, and *95% confidence intervals* were reported where applicable. Statistical analyses were conducted using SPSS (IBM Corp., Armonk, NY).

Treatment Protocol

Group A: Microneedling + Chitosan

Following antiseptic preparation with chlorhexidine, the scalp was treated with a microneedle therapy system using a 1.5 mm needle depth. Overlapping passes were performed to ensure even coverage of affected regions. Immediately after microneedling, 4 mL of 2% chitosan (Arche, Doum Inc., Korea) solution (pharmaceutical grade, MW 50–190 kDa, 85% deacetylation) was applied topically to the scalp using gentle massage to enhance penetration. Treatments were performed monthly for 6 months.

Group B: Minoxidil 5%

Patients in the minoxidil group applied 1 mL of topical 5% minoxidil solution twice daily to affected scalp areas for 6 months. Patients were instructed to avoid additional hair products within 4 hours of application and to report any irritation or side effects.

Group C: Control

Patients assigned to the control group received no active intervention but underwent the same baseline and follow-up assessments at 6 months.

Assessment Parameters

Clinical evaluation was performed at baseline and after 6 months across all 3 groups using a standardized protocol. The following outcome measures were employed:

Photographic Documentation

Standardized high-resolution photographs were obtained using consistent lighting and positioning to assess visual improvement in scalp coverage.

Trichoscopic Hair Density

Hair density (hairs/cm^2) and shaft diameter (μm) were quantitatively measured using digital trichoscopy (×50 magnification). Three fixed anatomic scalp sites (frontal, vertex, occipital) were assessed per patient, and the mean of these values was used for analysis. Inter-rater reliability was confirmed with intraclass correlation coefficients > 0.85.

Patient-Reported Outcomes

Participants rated their satisfaction using a 10-point Likert scale (1 = very dissatisfied, 10 = very satisfied) and self-reported perceived hair improvement using a 5-point global assessment scale (much worse to much improved).

Hair Loss Severity

The Modified Hair Loss Assessment Scale (m-HLAS) was used by blinded evaluators to grade severity changes. Independent raters were blinded to treatment allocation to minimize assessment bias.

Histologic Evaluation (Chitosan subgroup only)

A representative scalp biopsy (4 mm punch) was obtained from one patient in the chitosan group for histologic evaluation using Picrosirius Red staining to assess follicular density and dermal collagen architecture.

RESULTS

Primary Outcomes

At 6 months, both the Minoxidil and Chitosan groups demonstrated statistically significant improvements in hair density compared with the Control group:

Minoxidil Group (n = 10):

Mean hair density increased from 66.2 ± 17.9 hairs/cm^2 at baseline to 86.4 ± 19.2 hairs/cm^2 at 6 months, representing a 30.5% improvement ($P = 0.018$ vs. control; 95% CI: 14.6–41.7; Cohen's $d = 1.28$).

Chitosan Group (n = 10):

Mean hair density increased from 65.8 ± 18.2 hairs/cm^2 to 80.5 ± 19.3 hairs/cm^2, a 22.3% improvement ($P = 0.043$ vs. control; 95% CI: 5.2–33.8; Cohen's $d = 1.04$) (Figs. 1 and 2).

Control Group (n = 10):

No statistically significant change was observed (baseline: 65.9 ± 19.1 hairs/cm^2; 6-month: 67.1 ± 19.5 hairs/cm^2; $P = 0.41$).

Secondary Outcomes

Hair Shaft Diameter

Both the Chitosan and Minoxidil groups demonstrated significant increases in mean hair shaft diameter after 6 months:

Chitosan Group (n = 10):

Increased from 55.4 ± 11.8 μm to 72.1 ± 14.9 μm, a 30.1% increase ($P < 0.001$; Cohen's $d = 1.38$).

Minoxidil Group (n = 10):

Increased from 56.1 ± 10.9 μm to 71.3 ± 13.6 μm, a 27.1% increase ($P < 0.001$; Cohen's $d = 1.31$).

Control Group (n = 10):

No statistically significant change was observed ($P = 0.47$).

There was no statistically significant difference between the Chitosan and Minoxidil groups in terms of hair shaft diameter improvement ($P = 0.69$).

Patient Satisfaction Scores

On a 10-point Likert scale, both active treatment groups showed marked increases in self-reported satisfaction:

Chitosan Group (n = 10):

Increased from 3.1 ± 1.7 to 7.9 ± 1.5 ($P < 0.001$).

Minoxidil Group (n = 10):

Increased from 3.2 ± 1.8 to 7.6 ± 1.4 ($P < 0.001$).

Control Group (n = 10):

Minimal change was observed, from 3.0 ± 1.6 to 3.4 ± 1.7 ($P = 0.35$).

Satisfaction scores were statistically similar between the Chitosan and Minoxidil groups at 6 months ($P = 0.58$).

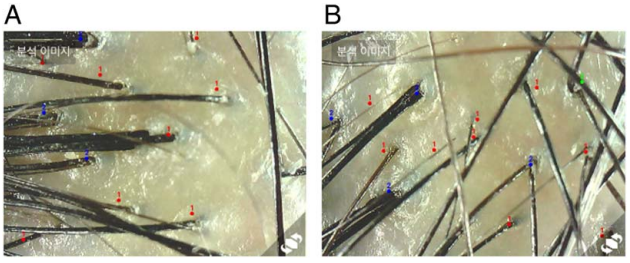

FIGURE 1. Trichoscopic analysis demonstrating baseline versus 6-month hair density measurements. Representative trichoscopic images showing (A) baseline hair density of 70 hairs/cm^2 with visible scalp and miniaturized hair shafts, and (B) 6-month posttreatment density of 100 hairs/cm^2 with improved hair caliber and reduced scalp visibility. Scale bar = 5 mm.

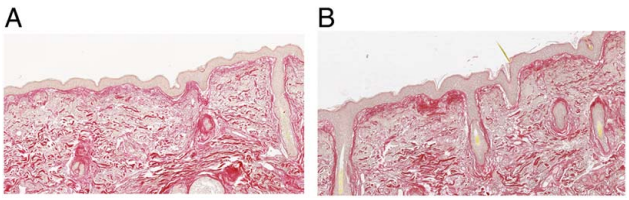

FIGURE 2. Histologic sections of scalp skin stained with Picrosirius Red (original magnification ×100). (A) Baseline biopsy showing sparse and irregularly distributed hair follicles with loosely organized dermal collagen. (B) Posttreatment biopsy from a patient in the chitosan + microneedling group at 6 months, demonstrating visibly increased hair follicle density with numerous closely packed follicles. Picrosirius Red staining highlights enhanced collagen fiber organization, reflecting improved dermal matrix structure and follicular support.

Temporal Response Patterns

Early clinical improvement was first observed between weeks 8 and 12 in both the chitosan and minoxidil groups, with progressive enhancement in hair density and shaft caliber throughout the 6-month treatment period. No perceptible changes were noted in the control group.

Safety Profile

All treatments were well tolerated, and no adverse events were reported in any of the study groups. No participants discontinued treatment, and no local, systemic, or serious side effects occurred during the 6-month study period.

DISCUSSION

The present controlled study demonstrates that microneedling followed by topical 2% chitosan application produces meaningful clinical improvements in patients with androgenetic alopecia and diffuse hair loss. While 5% topical minoxidil yielded a slightly greater increase in hair density, both treatment groups achieved comparable gains in hair shaft diameter and patient satisfaction scores compared with the untreated control. These findings suggest that chitosan, when applied after microneedling, may enhance transdermal absorption and stimulate local regenerative pathways contributing to follicular activation. The observed efficacy and favorable safety profile support the potential of chitosan as a non-hormonal adjunct or alternative to conventional therapies such as minoxidil in hair restoration strategies.

Recent botanical research has provided valuable insights into chitosan's cellular effects. Studies in plant root hair systems have demonstrated that chitosan induces calcium-mediated signaling pathways and promotes callose deposition at mild concentrations (0.001%). These findings suggest that chitosan may similarly influence cellular repair and growth processes in mammalian hair follicles.[8,9]

The microneedling component likely enhances chitosan penetration through temporary disruption of the stratum corneum barrier, while simultaneously inducing controlled inflammatory responses that may stimulate hair follicle regeneration.[10,11] The combination of enhanced penetration and bioactive chitosan effects may create a synergistic therapeutic environment promoting hair growth.

Interestingly, botanical research has shown that higher chitosan concentrations (0.01%) can disrupt cellular dynamics and growth processes.[7] This concentration-response relationship may explain the selection of 2% topical concentration in our protocol, which appears to optimize therapeutic benefit while avoiding potential growth inhibitory effects. The observed response rates compare favorably with established treatments

such as topical minoxidil (response rates 30–60%) and finasteride (response rates 65–80%), while offering potential advantages including minimal systemic absorption and absence of hormonal effects.[12,13]

While botanical studies have reported biological effects of chitosan at concentrations as low as 0.001% to 0.01%, these findings are based on plant cell models that differ significantly from human skin in both structure and barrier function. In mammalian systems—particularly following microneedling, which temporarily disrupts the stratum corneum—a higher concentration is likely required to achieve sufficient dermal exposure and sustained bioactivity. The 2% chitosan concentration used in this study was selected based on unpublished pilot data demonstrating favorable tolerability and early clinical response in human scalp applications. In addition, existing literature on topical chitosan formulations in dermatology has supported concentrations up to 2% as both safe and effective for enhancing wound healing and tissue regeneration. Given the limited enzymatic degradation time post-microneedling, we hypothesized that a higher concentration would optimize the therapeutic window without compromising safety, a rationale now supported by our observed efficacy and lack of adverse effects in the current trial.

This study has several important limitations. First, although 2% chitosan was selected based on preliminary human use and safety data, this concentration lacks formal dose-ranging validation, and its extrapolation from botanical studies may not fully reflect mammalian tissue dynamics. Second, the sample size was determined pragmatically without an a priori power calculation, limiting statistical power and generalizability. While significant differences were observed, the findings should be interpreted as exploratory, and larger, adequately powered trials are warranted. Third, treatment parameters such as microneedling depth and chitosan concentration were fixed across participants, precluding analysis of dose-response relationships. Future studies should explore these variables systematically to optimize therapeutic outcomes. Fourth, although baseline characteristics were balanced, the study did not control for potential confounders such as age, sex, hair loss duration, hormonal status, or concurrent use of hair-supportive agents, which may have influenced outcomes. Lastly, while proposed mechanisms draw on botanical models of chitosan-induced cellular signaling, their applicability to human scalp biology remains speculative and requires further investigation through histologic and molecular studies in human tissue.

CONCLUSIONS

This randomized controlled study demonstrates that microneedling followed by topical application of 2% chitosan (4 mL) is a safe and effective approach for treating androgenetic alopecia and diffuse hair loss. Although 5% topical minoxidil achieved a slightly greater improvement in hair density, both active treatments produced comparable gains in hair shaft diameter and patient satisfaction, with significantly better outcomes than the untreated control group. No adverse events were reported, underscoring the favorable safety profile of both interventions. These findings support the potential of chitosan, particularly when combined with microneedling, as a non-hormonal adjunct or alternative to standard therapies. Further large-scale, dose-optimized, and mechanistic studies are warranted to validate these preliminary results and to determine the long-term efficacy and durability of response.

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This study was conducted in compliance with the principles set forth in the Declaration of Helsinki.

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