A RANDOMIZED CLINICAL TRIAL STUDY OF NIOSOMAL MINOXIDIL VERSUS CONVENTIONAL MINOXIDIL IN TREATMENT OF MALE ANDROGENETIC ALOPECIA

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Introduction

• Androgenetic alopecia (AGA) is the most common cause of alopecia in male, affecting up to 50% of male until 50 years old and 95% of male during the life¹.

• Diagnosis and staging is clinical and according to Hamilton and Norwood classification²,³.

• Dermatoscop can be used to evaluate variability in hair diameter and decreasing in terminal hair follicles that extrudes from follicular unit at the beginning of the disease and in order to assess treatment response⁴.
• AGA can decrease quality of life and self esteem and change in psychological perception especially in youth, as treatment has an important role\textsuperscript{5}.

• Currently, only finasterid and minoxidil approved by FDA for the treatment of AGA\textsuperscript{6}.

• Minoxidil is a pyrimidine derived, promoting hair growth through proliferative and antiapoptotic effects on dermal papilla cells of the hair follicle, increases anagen to telogen ratio and inverses miniaturization of the hair follicle\textsuperscript{7-9}.
• Minoxidil has low skin penetration\textsuperscript{10}.

• In vitro studies, niosomal minoxidil led to more concentration in the skin and better drug release with more penetration to target organ (hair follicle) because of small size of drug particles\textsuperscript{11-13}.

• This is the first study to evaluate the efficacy of niosomal minoxidil in the treatment of AGA.
Lipid Based New Drug Delivery Systems

- Liposomes
- Ethosomes
- Niosomes
- ...
Niosome preparation

- In this method different amounts of Span, Tween, cholesterol and minoxidil were dissolved in chloroform. Organic solvent was evaporated by rotary evaporator and the dry lipid film was hydrated by normal saline.
Methods

• This is a randomized double blind clinical trial on 90 patients with AGA after signed written consent enrolled the study from dermatology clinic of Afzalipour hospital, Kerman, Iran.

• Inclusion criteria: Subjects affected to androgenetic alopecia according to clinical features and Hamilton classification and not received any treatment modalities for AGA in 3 months ago.

• Exclusion criteria: Diabetes mellitus, hormonal disorders such as thyroidal abnormalities, other systemic disease, chemotherapy and hypersensitivity to minoxidil.

• Participants randomized by mini tab 16 software (mini tab inc.) in two groups and information data recorded for each participant.

• Hair in target area 0.7 cm² clipped to 1-2 mm.
TREATMENT INTERVENTION

• GROUP A: niosomal minoxidil

• GROUP B: conventional minoxidil
twice a day for 6 months
TREATMENT EVALUATION

- Subject assessment
  - -3 : Significantly worsen
  - -2 : Moderately worsen
  - -1 : Mildly worsen
  - 0 : No change
  - +1 : Mildly improvement
  - +2 : Moderately improvement
  - +3 : Significantly improvement

- Physician assessment by dermatoscop
  - Significantly improvement (increase in hair count more than 50%),
  - Moderate improvement (increase in hair count 20-50%),
  - Mild improvement (increase in hair count less than 20%),
  - No change (without any changes in hair count),
  - Worsen (decrease in hair count)\textsuperscript{14}.
FOLLOW UP

- Patients evaluated with dermatoscop (VIDEO MICROSCOP BOMTEH – ELECTROCICS, LTD. Ko) and subject assessment every 4 weeks.
- Adverse effects as allergic and irritant contact dermatitis, dryness, hypotension, burning sensation were recorded.
Statistical Analysis

• This study approved by ethics committee in Kerman University of medical sciences by approval code K/92/49.
• Finally, collected data analyzed by SPSS version 20 (statistical package for social sciences, Chicago, IL).
• Descriptive tests such as frequency and analytical test was used for analysis.
• Comparison mean hair count and response rate between two groups was done by t independent test and chi-square test.
• P value less than 0.05 defined as statistically significant.
Results

• From 90 participants, 88 patients (43 in niosomal minoxidil, 45 in conventional minoxidil) July 2013-July 2014 completed the study.

• Two patients excluded from the study because of erythema and itching.

• Niosomal minoxidil was superior over conventional minoxidil especially from 3 to 7 visits (p=0.000), also, in each group during the time there was significant increase in hair count (p=0.000)
The number of counted hairs with dermatoscopy in 6 follow-up sessions

Covariates appearing in the model are evaluated at the following values: $N_{mohay1} = 52.8523$
Results

• Mean increased in hair count during the treatment in niosomal group and conventional group was 28.18±11 and 14.22 ±5.23, respectively.

• Thus, response rate in niosomal group was 2 times more than conventional group.

• Mean subject assessment in niosomal group was 8.7 (Vs 3.3 in conventional group) that was accomplish with more satisfaction than conventional group. (p=0.001)
Mean hair count change during the treatment

<table>
<thead>
<tr>
<th>Hair count</th>
<th>Niosomal Minoxidil</th>
<th>Conventional Minoxidil</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weak 4</td>
<td>48.7± 6.9</td>
<td>54.7± 9.6</td>
<td>0.911</td>
</tr>
<tr>
<td>Weak 8</td>
<td>52.5 ±7.8</td>
<td>57.4 ±10.2</td>
<td>0.003</td>
</tr>
<tr>
<td>Weak 12</td>
<td>56.9 ±9.1</td>
<td>60.6 ±10.6</td>
<td>0.000</td>
</tr>
<tr>
<td>Weak 16</td>
<td>62.3 ±10.8</td>
<td>64 ±10.8</td>
<td>0.000</td>
</tr>
<tr>
<td>Weak 20</td>
<td>68.3 ±10.8</td>
<td>67.6± 11.8</td>
<td>0.000</td>
</tr>
<tr>
<td>Weak 24</td>
<td>77.2 ±14.6</td>
<td>70.6 ±12.6</td>
<td>0.000</td>
</tr>
</tbody>
</table>
# Physician Assessment of Treatment Efficacy at final visit

<table>
<thead>
<tr>
<th>Score of treatment efficacy</th>
<th>Niosomal minoxidil N(%)</th>
<th>Conventional Minoxidil N(%)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 20% increase</td>
<td>3(7)</td>
<td>14(31.1)</td>
<td>0.000</td>
</tr>
<tr>
<td>Between 20% to 50% increase</td>
<td>18(41.9)</td>
<td>26(57.8)</td>
<td>0.000</td>
</tr>
<tr>
<td>More than 50% increase</td>
<td>22(51.2)</td>
<td>5(11.1)</td>
<td>0.000</td>
</tr>
</tbody>
</table>
## Subject Assessment of Treatment Efficacy

<table>
<thead>
<tr>
<th>Score of treatment efficacy</th>
<th>Niosomal minoxidil N(%)</th>
<th>Conventional minoxidil N(%)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>-3: Significantly worse</td>
<td>0(0)</td>
<td>0(0)</td>
<td>0.000</td>
</tr>
<tr>
<td>-2: Moderately worse</td>
<td>0(0)</td>
<td>0(0)</td>
<td>0.000</td>
</tr>
<tr>
<td>-1: Slightly worse</td>
<td>0(0)</td>
<td>0(0)</td>
<td>0.000</td>
</tr>
<tr>
<td>0: No change</td>
<td>2(4.7)</td>
<td>0(0)</td>
<td>0.000</td>
</tr>
<tr>
<td>+1: Slightly improved</td>
<td>1(2.3)</td>
<td>24(52.3)</td>
<td>0.000</td>
</tr>
<tr>
<td>+2: Moderately improved</td>
<td>17(39.5)</td>
<td>19(42.2)</td>
<td>0.000</td>
</tr>
<tr>
<td>+3: Significantly improved</td>
<td>23(53.5)</td>
<td>2(4.4)</td>
<td>0.000</td>
</tr>
</tbody>
</table>
Discussion:

- Androgentic alopecia affects men during the life\textsuperscript{15}. But, currently there is no approved drug with low adverse events and high efficacy\textsuperscript{16}.
- In two studies done by Olsen and colleagues in order to compare efficacy of 5\% and 2\% minoxidil, by global photography method showed response rate 60\% and 40\% respectively\textsuperscript{17,18}.
- In another study by Olsen et al in 2007, efficacy of 5\%minoxidil foam was evaluated in comparison with placebo and 13.4\% patients in foam (Vs 3.4\% in placebo) showed increased in hair count in physician assessment\textsuperscript{14}.
- In our study at 16 weeks, 99.9\% in niosomal vs 98.7\% in conventional, demonstrated increased hair count.
- In Olsen hair clipping method study target area was 2x2 cm, but our assessment was by dermatoskop.

•
Discussion:

• In a study by Price and colleagues in 2002 efficacy of 1 mg finasterid was evaluated in AGA\textsuperscript{19}.
• Mean increased hair count was 12.4\% in finasterid group vs 3.2\% in placebo at of 47 weeks by hair clipping method\textsuperscript{19}.
• In our study 51.2\% of patients showed increased hair count between 20\% to 50 percent in niosomal in 24 weeks that was considerable better than finasterid results.
• Except two patients with itching and erythema in niosomal group (4.4\%), no adverse effect was reported.
• In Olsen study adverse effects were seen in foam group as 7 \% vs 6.7\% in placebo, itching, erythema and skin dryness in decreasing order\textsuperscript{17-18}. 
Conclusion:

• Based on our results, increased hair count in niosomal group by physician and subject assessment was meaningfully greater than conventional group. But we had limitation and strength.

• Strength was randomization and assessment of response by dermatoscop instead of global photographic review (GPR).

• Limitation was small size of sampling, not using of hair weight method in order to evaluate treatment response, because this method in accordance to previous studies was more reliable method\textsuperscript{20}.

• Finally, Our study findings showed hoping results with niosomal minoxidil.

• It is recommended other studies with greater sample size and higher concentration of niosomal minoxidil.
Conventional minoxidil therapy

Before

After
Niosomal minoxidil therapy

Before

After
References


References


