ORAL MEGA PULSE METHYLPREDNISOLONE FOR SEVERE FORMS OF ALOPECIA AREATA

E-POSTER (FP2011-02638)

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CONFLICT OF INTEREST:
-NONE OF THE AUTHORS HAS FINANCIAL SUPPORT FROM ANY PHARMACEUTICAL COMPANY OR OTHER COMMERCIAL SOURCE.
The treatment of severe forms of alopecia areata (AA) is difficult and no treatment, modifies the course of the disease.

Systemic Glucocorticosteroids (GC) are effective short term but carry the risk of severe side effects long term. (Ref. 1-4)
Studies in which pulse GC was used in AA were inconsistent with regards to type, dosage, frequency or duration of therapy, which made it difficult to conclude with certainty on the efficacy and safety of this therapy. (Ref. 2-12)
We used fixed more frequent and higher mega doses of oral methylprednisolone succinate (MPS) in the treatment of alopecia universalis (AU), totalis (AT) and ophiasis (OPH) to find the safest and most effective regimen for inducing as well as maintaining adequate scalp hair regrowth.
Methods

Patients were randomly allocated to one of 3 treatment groups. We planned to enroll 25 patients in each group.

Group A: received 3 consecutive daily pulses every 2 weeks.
Group B: received 2 consecutive daily pulses every 3 weeks.
Group C: received 3 consecutive daily pulses every 3 weeks.
Each pulse consisted of 15mg MPS/Kg body weight.
Labwork

- ECG, PPD test, TSH and thyroid antibodies at start of treatment.
- CBC, Urinalysis, FBS, Lipids. LFT, RP and Bone profile before & every 12 wks.
- Chest and Sinuses x-rays and ophthalmic exam before treatment and every 24 wks.
- Short synactin test before and one week after first treatment cycle.
Bone mineral density (DEXA Scan) before and on the last visit.
- Scalp biopsies before and at the end of treatment.
- ECG during and 2 hours after drug administration
- Serum electrolytes 2 hours after each drug administration
Efficacy Analysis

Photographs of scalp were taken before treatment and at every other visit.

Primary efficacy measure was the proportion of responders at 24 weeks, and was categorized as:

- **Adequate responders (AR):** ≥75% regrowth of terminal hair in the affected areas
- **Inadequate responders (IR):** 25-74% regrowth
- **Poor responders (PR):** <25% regrowth
If regrowth of terminal hair in scalp was <50%, treatment was discontinued.

If regrowth was 50% to 74%, treatment was continued for another 12 weeks.

If regrowth was 75% or more after 24 to 36 weeks of treatment, the intervals between pulses were increased gradually by 2 weeks increments until patients maintained their hair for 24 weeks off treatment.
Responses were analyzed in relation to:

- AA pattern and Status (stable vs. progressive)
- Age of onset and age of treatment
- Gender
- Duration of disease
- Personal history of atopy and autoimmune disease
- Family history of AA and autoimmune disease
- Response to previous treatment
- Presence of nail involvement
- Presence of subclinical hypothyroidism, thyroid antibodies, positive ANA and ferritin and IgE levels.
- Presence and severity of dermal fibrosis, inflammation and epidermal follicular plugging.
Data Analysis and statistical methods

All data were analyzed using the statistical package for social sciences (SPSS) version 16. Fisher exact test and Chi-square test were performed. P values <0.05 were considered statistically significant.
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**Results**

A total of 42 patients were analyzed at the end of the study.

27 patients were in Group C, 6 patients in Group A and 9 in Group B.

No more Pts enrolled in Group A after 2 Pts developed extensive striae and one pneumonia. No more Pts in Group B due to inadequate response at 24 wks.

Figure: 1 summarizes the outcome at 12, 24 and 36 weeks.
At 36 weeks
12 (28.6%) patients were AR
9 (21.4%) were IR
21 (50%) PR

- Among AU (32 patients)
  10 (31%) were AR, 7 (22%) IR and 15 (47%) PR.

- Among AT (4 patients)
  2 (50%) IR and 2 (50%) PR.

- Among OPH (6 patients)
  2 (33.3%) AR and 4 (66.6%) PR.
Figure 1: Percentage of Hair regrowth in the affected areas at 12, 24 and 36 weeks of treatment with different regimens of pulse steroid
- Found statistically significant differences between AR, IR and PR in 4 parameters:

  • Age of onset: AR were older (16.81±5.69 vs 11.18±7.07yrs, P=0.019)
  • Duration of disease: AR shorter (5.3±3.2yrs vs 8.7±4.6yrs, P=0.023)
  • Subclinical hypothyroidism: AR less (P=0.011)
  • Epidermal follicular plugging: AR less (P=0.046)
Relapse

Among 34 patients (8 patients had zero growth) followed up for 1-4 years.

- 7 (20.1%) maintained their growth
- 13 (38.2%) relapsed (>50% of hair lost)
- 5 (14.7%) developed moderate hair fall (25-50% of hair lost)
- 3 (8.8%) mild hair fall (<25% of hair lost)
- 6 (17.6%) lost to follow up

The time to relapse on or off treatment varied and was unpredictable. Some relapsed shortly after induction phase (24 weeks), other kept their regrowth for 4 years off treatment.
Adverse events

- Treatment was well tolerated
- Two moderately severe side effects (extensive striae x2 and pneumonia x1) occurred in Group A; probably due to higher total dose.
- Most common side effects were fatigue (64%), wt. gain (45%), steroid acne (36%), sleep disturbance (33%), irritability and heartburn (21% each).
Discussion

- Our study showed that oral mega pulses MP (15mg/Kg BW/day) given for 2-3 days every 2-3 weeks led to >75% hair regrowth in 28.6% of patients within 6-9 months.

- This is comparable with topical diphenylcyclopropenone in a prospective trial by Sotiriadis (Ref.13).

- Therapy was more effective in patients with later onset, shorter duration and normal thyroid function.
In previous studies of mega pulse steroid in AU, AT, and OPH less than 10% of patients responded adequately. (Ref.14,15,6-8)

- 38% of our patients relapsed at one year off treatment, and 20% maintained their growth. The rest had variable degrees of hair fall.

- Consistent with previous reports, pulsed GC does not influence long term outcome in severe AA, which necessitate long term maintenance. (Ref.16)
- No significant abnormalities detected in ECG, chest and sinuses x-ray, DEXA scan and synactin test.
- One case each of the following adverse effects: pneumonia, early cataract, hyperlipidemia and DM and six cases of striae.
- Otherwise well tolerated.
References