Treatment Refractory Ocular Symptoms in Myasthenia Gravis: Clinical and Therapeutic Profile

CK Symposium

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Background

- Most MG patients develop ocular symptoms over the course of the disease
- Despite many therapeutic options available for management of MG, some patients remain resistant to standard therapies
- Limited literature is available regarding management of refractory ocular symptoms
Objectives:

To review clinical characteristics of patients with treatment resistant ocular symptoms in myasthenia gravis (MG)
Methods:

- Retrospective chart review after IRB approval
- Neuromuscular Research Database at KUMC
- Information on MG patients with ocular symptoms between January 2013 and December 2017 was obtained and reviewed
- Treatment resistance was defined as persistent diplopia or ptosis despite adequate trial of prednisone and at least one additional immunosuppressive agent
- Demographic, clinical, diagnostic and therapeutic information were extracted from the charts
Results: Demographics

Treatment resistant group

- Patients with treatment resistant ocular symptoms with acetylcholine receptor antibody positive MG: 5
- Gender: F:M=3:2
- Age at symptoms onset: Mean=32, Median=27

Treatment responsive group

- Patients with treatment responsive ocular symptoms: 36
- Gender: F:M=12:24
- Age at onset of symptoms: Mean=52, Median=59

**Age at onset of symptoms**
Results:
Symptoms

1) In the refractory group 3/5 patients had ocular symptoms at the onset of disease and 2 of these patients progressed to have generalized disease

2) In the responsive group 34/36 patients had ocular symptoms at onset of disease and 8 progressed to have generalized disease
Presence of other autoimmune diseases

Treatment refractory group:
- Two patients had positive thyroid peroxidase and thyroglobulin antibodies
- One patient was diagnosed with type 1 DM

Treatment responsive group:
- Two had psoriasis
- Two had mixed connective tissue disease
- One had Hashimoto’s thyroiditis
Results: Symptoms

The median time between the onset of symptoms and development of refractory ocular symptoms was 13 years (range of 3 to 25)
Results:
Diagnostic testing

1) In the refractory group all patients had positive AChR Ab

2) In the responsive group
   1) 21/36 had AChR Ab positive
   2) 1 MUSK positive
   3) Rest diagnosed with RNS and SFEMG
Results:
Interval between symptom onset and starting high dose steroids

- All patients in both groups were initially managed with pyridostigmine
- Most of these patients were started on high dose steroids within 6 months of the symptom onset

<table>
<thead>
<tr>
<th>Time after symptom onset</th>
<th>Treatment refractory group Total N: 5</th>
<th>Treatment responsive group Total N: 36</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soon after symptom onset</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>3-6 months after the onset</td>
<td>1</td>
<td>27</td>
</tr>
<tr>
<td>2-8 years after the onset</td>
<td>1</td>
<td>2</td>
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Results:

**Refractory group**
Other immunomodulators used in the refractory group were:

1) Cellcept (2 patients)  
2) Imuran (1 patient)  
3) Cyclosporine (1 patient)  
4) IVIG (4 patients)  
5) PLEX (3 patients)  
6) Thymectomy (1 patient)

- 3/5 patients in the refractory group required ICU admission for exacerbation

**Responsive group**
Patients in the treatment responsive group were treated with:

1) Cellcept (5 patients)  
2) Imuran (2 patients)  
3) Methotrexate (2 patients)  
4) IVIG (3 patients)  
5) PLEX (3 patients)  
6) Thymectomy (3 patients)

- 5/36 patients in the responsive group required hospital admission for exacerbation
Discussion – Ocular Symptoms Response to Treatment

- Benatar’s group showed that treatment failure for ocular MG was 17% in the prednisone group (1/6 patients).

- Kupersmith et al reported that 27% of OMG patients treated with steroids (13/48) had refractory ocular symptoms.

- Our study showed that ocular symptoms were refractory in 12% of the patients (5/41), all treated with prednisone and additional immunomodulatory therapy.
Discussion - Progression to Generalized MG

- Progression to generalized MG in myasthenia patients treated with prednisone was variable in the literature.

- Mittal et al showed that 38 patients with ocular myasthenia treated with prednisone and none of them progressed to generalized MG.

- Monsul et al reported that 3/27 (11%) patients with ocular MG treated with prednisone developed generalized MG.

- In our study, 27% of the patients with ocular onset developed generalized MG in spite of prednisone treatment.
Conclusion

- MG patients with treatment refractory ocular symptoms were mostly younger at symptom onset

- Duration between the onset of MG to the development of refractory ocular symptoms was variable

- Starting steroid therapy early was effective in resolving the ocular symptoms in most patients but a subgroup progressed to have refractory ocular symptoms

- More patients in the refractory group generalized compared to the responsive group
Questions & Discussion

THANKS
References


7- Michael Benatar, Henry J. Kaminski; The medical treatment of ocular myasthenia (an evidence-based review; Neurology Jun 2007, 68 (24) 2144-2149; DOI: 10.1212/01.wnl.0000263481.14289.90
References


