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FIFTY YEARS OF STEROID TREATMENT OF MYASTHENIA GRAVIS

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1. Torda, C, & Wolff, HG 2. Grob, D, & Harvey, A M 3 Grob, D, & Namba, T 4. Presented at the AAN in 1971 5. Cape, C A, Utterback, R A 6. Cape, C A, Utterback, R A 7. Cape, Charles A 8. Simon, H E 9. Torda, C, & Wolff, H G 10. von Reis, G, et al 11. Osserman, K E et al 12. Evoli, A et al 13. Beekman, R et al

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Abstract

Objective: To determine the condition of sixteen of my myasthenia gravis patients, treated with steroids for up to fifty years and determine the effect of long-term steroids if the dosage is properly adjusted.

Methods: Follow-up of sixteen patients treated for up to fifty years with ACTH or prednisone.

Results: Of the sixteen patients one patient was treated for thirty-four years, two for forty-five years and one for fifty years. Eight patients who had been treated four to forty-four years were deceased. Four patients were lost to follow-up.

Conclusion: Long-term, maintenance, corticosteroid therapy is effective and safe if properly used for many years. The follow-up also shows that long-term steroids can be used for the treatment of chronic diseases if the dosage is properly adjusted.

METHODS

The treatment of myasthenia gravis has greatly improved with the use of adrenocorticosteriods and other immunosuppressive medications. Torda and Wolff began treating patients with ACTH in 1951.[1] They were able to get significant partial remissions for a short period. Additional reports contradicted the improvement or found the improvement lasted approximately three months.[2,3] In 1968, 1969, & 1972, my colleagues and I established that maintenance therapy could prolong the improvement achieved after an intensive course of ACTH.[4,5,6] We established the effectiveness of corticosteroids in ocular myasthenia gravis in 1973, and these patients will not be included in the paper.[7] This report provides a 50-year follow-up of the previously reported 16 patients.[6]

RESPONSE TO ACTH AND PREDNISONE THERAPY

Initial six patients treated from 1966-1970:[6]

Intensive & Maintenance Rx	Years of Rx	Outcome
CC 1965,1965,1966	50	Stable prednisone q w
AJ 1966	11.5	D 1978 (age 64) met ca, chf
FW 1966, 67	8	D1974 (age 76) cause unknown
EL 1967	42	D 2009 (age 67) resp failure
JA 1969	30	D 1999 (age 43) resp failure
WM 1969	*Lost to follow-up*	

Previously reported ten patients treated 1970-1972[6]

Intensive & Maintenance Rx	Years of Rx	Outcome
Three patients living	34, 45, 45	Stable
Four patients died		
RS	4	D 1975 (age 58) cancer
OG	6	D1978 (age 59) cause unknown
BW	43	D2013 (age 57) pneumonia
HH	*44*	D1975 (age 74) cancer
3 Patients *Lost to follow-up*		
NM	3	D 1996 lost to f/u 1974
CE	21	Last seen 1992 lost to f/u
JH	15	Last seen 2011 pred d/c 1982

D = deceased

RESULTS

Four patients are living who have been treated for 34, 45, 45, & 50 years. Eight patients died that had been treated from 4-44 years. They died from respiratory disease (3), cancer (3), & unknown cause (2). Four patients were lost to follow-up. The usual side effects occurred, but were controlled or alleviated by spacing the ACTH injections or the prednisone dosage out from daily, to every other day, to every third, fourth, fifth, sixth or seventh day.

DISCUSSION

Intensive ACTH treatment of myasthenia gravis was initiated in 1935 by Simon.[8] Subsequently; Torda & Wolff did clinical trials of intensive ACTH treatment in 1949 & 1951.[9,1] In the 1951 trial significant improvement occurred in 10 out of 15 patients, no improvement in four patients, and one patient died. In 1952, Grob and Harvey treated ten patients with ACTH and concluded that there was no improvement in any of the patients.[2] In 1966 von Reis et al. treated 13 patients with myasthenia gravis with 33 intensive courses of ACTH.[10] There was excellent improvement in 23 courses of ACTH, there was slight to moderate improvement in 8 courses, and no improvement in 2 courses of treatment. The improvement was usually brief. Osserman and Genkins in 1966 confirmed von Reis and his colleague's results and noted that the duration of treatment was 3-4 months.[11] Our initial patient (cc) was so ill for so long that we felt we had no choice but to try ACTH.[5] After three courses of intensive therapy that relapsed we felt we should try maintenance therapy which proved to be successful. For this reason and because of the above and other reports, we began treating patients with maintenance or long-term adrenocorticosteroid therapy after an intensive course in 1966.

We have reported a follow-up of the 16 myasthenia gravis patients that we began treating in 1966 with maintenance corticosteroids after an intensive course of ACTH. Evoli et al. have reported a much larger series of 104 patients treated with long-term steroids beginning in 1972 with good results in 82% with a follow-up of at least two years.[12] Beekman et al. found 43% remissions, considerable improvements in 25%, moderate improvement in 25 % and no improvement in 12% of 100 patients treated with long-term steroids beginning in 1985 with a mean follow-up of 9.6 years.[13]

Maintenance ACTH, prednisone or other autoimmune therapy has obviated most of the disadvantages of repeated intensive courses of therapy. It avoids the recurrent crisis and hospitalization with intensive treatment. The patients treated only with intensive courses of steroids had three to five hospitalizations a year. Maintenance therapy has allowed many of our patients to reduce or discontinue their anticholinesterase medications. We initially used ACTH because prednisone was contraindicated by most institutions in the 1960's.

After the effectiveness of ACTH was established, we found the same results could be obtained using prednisone.[6] We began using prednisone and other autoimmune medications in 1971. The prednisone dosage (like we did with the ACTH) has been adjusted from 100mg daily to decreasing doses and spreading the frequency from daily to every other day and up to every seventh day. We adjusted the dosage to prevent or alleviate side effects, but still, maintain control of the myasthenia gravis. Some patients died from respiratory failure and pneumonia when they were no longer under our care. We need to emphasize the need for compulsive supervision during intensive treatment and careful supervision when on maintenance or long-term steroid therapy.

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