IMMUNOSUPPRESSION WITH CORTICOSTEROIDS AND THYMECTOMY IN MYASTHENIA GRAVIS

AN EVALUATION OF IMMEDIATE AND SHORT TERM RESULTS IN 20 PATIENTS

J. LAMARTINE DE ASSIS *
P. PAULO E. MARCHIORI **
ANTONIO A. ZAMBON **
NAGIB CURI ***
LUIZ TARCISIO BRITO FILOMENO **
MILBERTO SCAFF ****

Management of the severe form of myasthenia gravis (MG), by immunosuppression with oral corticosteroids gained impetus during the seventies, with the research carried out in most medical centers that treat this disease.1-13,15,16. Because with rare exceptions, controlled trials are few, controversies abound.14 In preparation for thymectomy, immunosuppression with corticosteroids has recently been used, even though there is no certainty that this improves the results.13

We report the immediate and short-term effects of this management before, during and after thymectomy.

MATERIAL AND METHODS

Forty patients of both sexes were submitted to thymectomy, but 20 of them received prednisone preoperatively. Characteristics of the disease and other factors were kept as similar as possible in both groups. The immediate and short term results of both groups were compared. By short term is meant the immediate postoperative period and the following two or three weeks. The long term result is up to 6 months after surgery. The age of the group receiving prednisone therapy varied from 9 to 35 years. An average of 22.7 years and standard deviation (sd) of 6.97. Duration of the disease was from 3 months to 13 years with a mean of 3.05 and a sd of 3.69 years. The group without previous prednisone therapy varied in age from 16 to 37 years, with an average of 25.25 and sd of 5.12 years. The length of illness was from 6 months to 13 years with an average of 3.52 and sd of 3.16 years.

From the Department of Surgery and the Department of Neuropsychiatry, University of São Paulo Medical School: * Professor Adjunto; ** Médico Assistente; *** Professor Assistente Doutor; **** Professor Livre-Docente.
Both groups had the generalized form of MG and responded little to medical management. The immunosuppressive regimen was begun with 80 mg daily and progressive reduction after the 10th or 15th day. Three patients began the treatment with 100 and three with 60 mg. The mean preoperative dose of prednisone was 45.5 mg with a sd of 22.05 mg. All patients needed to be kept on anticholinesterase up to the time of surgery. Pyridostigmine bromide was used routinely in oral daily doses varying from 60 to 1,560 mg, with most patients receiving 60 to 180 mg. The mean dose of preoperative pyridostigmine was 402 mg with a sd of 418.64 mg and of 184.23 mg with sd of 104.53 mg at surgery. The doses were always reduced to a minimum. Thymectomy was always done via a median sternotomy and the cervical region examined for possible ectopic thymus tissue.

During the immediate postoperative period, the same doses of prednisone were maintained in most, were reduced in 5 and increased in 1 patient. The anticholinesterase dose remained unchanged in 6, was reduced in 4 and increased in two cases. Two patients who were not on anticholinesterase preoperatively, were given small doses during the immediate postoperative period. The anticholinesterase had been suspended preoperatively in 5 patients and they continued so during the immediate postoperative period. It was also discontinued in the immediate postoperative period in 1 patient. The mean postoperative dose of pyridostigmine was 94.60 mg with a sd of 98.79 mg. All but one patient in the thymectomized group which did not receive prednisone preoperatively, received anticholinesterase in the immediate and short term period.

RESULTS

The group of patients with preoperative prednisone therapy showed very favorable immediate postoperative recovery. Thirteen of them (65%) showed complete remission or marked improvement. Four patients reported significant improvement, while one showed slight, slow but progressive relief. Two patients got worse so that one sustained a cholinergic crisis postoperatively requiring a respirator for 20 days. Usually improvement was quick, early and significant with complete remission in 8 patients. The latter were on prednisone therapy when submitted to thymectomy and during the immediate postoperative period (10-80 mg). Two of them got worse over a short period, one of them had an abrupt relapse six months after complete remission. Suppuration of the surgical wound developed in one patient and the infection lasted for a long time even though there was a remission of the myasthenic symptoms. Eight months postoperatively this patient continues asymptomatic with 10 mg/day of prednisone and 180 mg/day of pyridostigmine bromide. The progress during the immediate postoperative period in the group without preoperative prednisone therapy was very favorable in 14 patients (70%). One patient showed significant improvement and 13 complete remission. There was one death, one patient worsened and 4 showed slight improvement.

In the group receiving preoperative prednisone, the following complications occurred in 4 patients: slight surgical complications in two with prolonged suppuration of the wound, a myasthenic crisis in one, and a cholinergic crisis in another. There were complications in 8 patients in the group not receiving preoperative prednisone: minor surgical complications in 4 and myasthenic crisis in 4 others.
Most of the patients in the thymectomized group with preoperative prednisone continued in remission or marked improvement, in spite of progressive reduction of the doses of prednisone and anticholinesterase during a short term period. Six patients remained without anticholinesterase after thymectomy. However, two patients resumed using the drug although in small doses, one thirty days and the other 3 months later. The remainder were maintained on a combination of prednisone-anticholinesterase. Significant improvement or remission during the short term period was shown by most of the patients in the thymectomized group without preoperative prednisone therapy. Both groups showed the same proportion of significant improvement and complete remission during the short term period.

Histologic examination of the thymus done on 19 patients receiving prednisone showed 12 with hyperplasia (63%), 4 normal (21%), and 3 with atrophy (15.7%).

**COMMENTS**

The results of thymectomy on patients previously submitted to steroid therapy are reported. As stated in the introduction, there are few such reports and the value of this management is still controversial. The results were apparently very good, since 65% of the patients receiving preoperative immunosuppressive drugs reported complete remission or marked improvement. This occurred without a significant increase in postoperative complications caused by intensive and prolonged use of steroids. There were really only 4 complications. Only one was due to myasthenic crisis and two were minimal; namely, infection of the incision. The infection was prolonged in one of these two cases but there was remission of the myasthenic symptoms. The fourth patient, who immediately after thymectomy was receiving a double dose of anticholinesterase, entered a cholinergic crisis requiring the prolonged use of a respirator.

Considering the patients with complete remission and marked or significant improvement, 65% improved with this management over a short period of time. One improved slowly and slightly but progressively and 4 (25%) showed slight improvement. A high proportion, 90% sustained remission or improvement over a short term period in spite of the progressive reduction of prednisone and anticholinesterase. It is notable, that 6 patients (30%), discontinued the anticholinesterase postoperatively but after a short time, two of them resumed using the drug but in very small doses. The combination of prednisone-anticholinesterase medications was maintained for a short and mid-term basis in 70% of the cases. There were no deaths over a short term period, although 2 patients were doing poorly.

Seventy percent in the group not receiving immunosuppressive drugs reported complete remission or marked improvement on a short and mid-term basis. One patient got worse and another succumbed. Postoperative complications developed in 4 and a myasthenic crisis in 4 during the immediate postoperative period. No infection of the incision was reported. It is noteworthy that only
one patient reported complete remission without anticholinesterase drugs on a short and mid-term basis after thymectomy.

No significant difference was found on comparing the results of thymectomy in both groups, i.e., the group receiving immunosuppressive agents and the control group. However, the statistical analysis of the postoperative complications in both groups revealed a significant difference in favor of the group receiving preoperative immunosuppressive medication. These results led to the conclusion that preoperative use of prednisone for patients undergoing thymectomy is beneficial.

The excised thymus was hyperplastic in the majority of patients in the group managed by immunosuppression. This was mainly true in young females under 23 and in a 9 year old child. The three cases with atrophic thymus were 27, 31 and 35 years old. Their disease had begun respectively three, eighteen months and 8 years previously. As a matter of fact, they responded very well to the operation. The 4 with histologically normal thymus, varied in age from 16 to 32 and their illness from 15 days to 10 years. They responded very well to treatment and only one worsened. These data suggest that the histologic condition of the thymus does not influence the result of treatment and that hyperplasia predominates in younger female patients.

SUMMARY

A comparative study was conducted on two groups of patients with the generalized severe form of myasthenia gravis. The first group of 20 patients received oral daily doses of 60-100 mg of prednisone prior to thymectomy. The control group of 20 were submitted to surgery without prior corticosteroid treatment. The study included statistical analysis of the clinical results and surgical complications for both groups. The author concluded that the use of steroids preoperatively is beneficial.

RESUMO

Imunossupressão com corticosteróides e timectomia na miastenia grave: avaliação dos resultados em 20 pacientes a curto e médio prazos.

São apresentados os resultados da timectomia em 20 pacientes com miastenia grave generalizada, a maioria severa, e tratados previamente com prednisona em doses altas (60-100mg, diariamente) por via oral. Os resultados foram comparados aos de um grupo de 20 pacientes muito semelhantes aos primeiros quanto à idade, sexo e forma clínica da doença, mas sem preparo prévio com prednisona. Os autores concluem que os resultados da timectomia nos pacientes tratados ou não com prednisona são semelhantes. Entretanto, aqueles submetidos ao preparo prévio com o corticóide tiveram menos complicações no pós-operatório imediato e mediato do que os do grupo controle. As diferenças foram estatisticamente significantes.
REFERENCES


Clínica Neurológica, FMUSP — Caixa Postal 3461 — 01000, São Paulo, SP — Brasil.