Safety for preoperative use of steroids for transsternal thymectomy in myasthenia gravis

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Abstract

Objective: Effects of preoperative steroids on morbidity and mortality after transsternal thymectomy are analyzed. Methods: There were 620 transsternal thymectomies for myasthenia gravis performed in the period 1973–2002. There were 547 patients with nonthymomatous myasthenia, including 17 patients submitted to repeated thymectomy (rethymectomy) and 46 patients with thymoma. There were 522 upper median sternotomies performed in the period 1973–1997 and 98 complete median sternotomies performed in the period 1998–2002 (74 patients without thymoma, 7 thymomas and 17 rethymectomies). One hundred and seventeen of these 620 patients were taking steroids preoperatively. The impact of steroids use on postoperative respiratory insufficiency (ventilator), need for tracheostomy, superficial wound dehiscence, superficial wound suppuration, sternal dehiscence and mortality was analyzed. Results: The rate of morbidity and mortality in the steroids and the no-steroids groups included respiratory insufficiency necessitating the use of a ventilator in 46/503 patients from the no-steroids group (9.1%) and 8/117 patients from the steroids group (6.8%; \( P = 0.4260 \)), need for tracheostomy in 14/503 patients from the no-steroids group (2.8%) and 3/117 patients from the steroids group (2.6%; \( P = 0.9054 \)). Complications with wound healing (including sternal dehiscence, superficial wound dehiscence and superficial wound suppuration) occurred in 47/503 (9.3%) patients from the no-steroids group and in 1/117 (0.9%) patient from the steroids group (\( P = 0.0023 \)). The overall complications rate was 30.6% (154/503) in the no-steroids group and 11.1% (13/117) in the steroids group (\( P = 0.0001 \)). Mortality rate in the no-steroids group was 0.4% (2/503 patients) and none in the steroids group. Morbidity in patients with complete sternotomy was low, respiratory insufficiency in three patients (3.1%), and superficial wound suppuration in one patient (1.0%), no other morbidity and no mortality. Changing morbidity in periods 1973–1980, 1981–1990 and 1991–2002 is analyzed. Conclusions: Preoperative use of steroids for transsternal thymectomy in patients with myasthenia gravis had no negative impact on morbidity and mortality, conversely, the results in patients taking steroids were better, with significant difference of results regarding the overall complication rates and the overall complication rates of wound healing.

Keywords: Myasthenia gravis; Steroids; Thymus; Thymectomy

1. Introduction

Thymectomy is an accepted method of treatment for myasthenia gravis [1,2]. Generally, patients with stable myasthenia gravis in stages IIA and IIB, and occasionally I, according to Osserman classification are candidates for thymectomy [3,4]. In patients presenting with myasthenic crisis and respiratory insufficiency an initial treatment should be conservative, with the use of a ventilator, plasmapheresis, intravenous immunoglobulins and immunosuppressive drugs, including steroids [5]. Some of these patients, when myasthenic crisis subsides, are subsequently offered thymectomy. Besides treatment of crisis, steroids are also used in some other severe cases of myasthenia [6]. There are, however, controversies in regard to the use of steroids in patients submitted to transsternal thymectomy and their potential to disturb the process of healing the wound after thymectomy, first of all with concern of healing of the sternum [7,8]. In this report we reviewed retrospectively

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medical records of all patients operated on during the period 1973–2002 in an attempt to evaluate safety and effectiveness of preoperative use of steroids in transsternal thymectomy.

2. Materials and methods

There were 620 transsternal thymectomies performed for myasthenia gravis in the period 1973–2002. There were 547 patients with nonthymomatous myasthenia, including 17 patients submitted to repeated thymectomy (rethymectomy) and 46 patients with thymoma. There were 522 upper median sternotomies performed in the period 1973–1997 and 98 complete median sternotomies performed in the period 1998–2002 (74 patients without thymoma, 7 thymomas and 17 rethymectomies). One hundred and seventeen of these 620 patients (78 from the upper median sternotomy group and 39 from the complete median sternotomy group) were taking steroids preoperatively. Characteristics of patients taking/not taking steroids with nonthymomatous myasthenia is shown in Table 1 (age, gender, duration of myasthenia gravis, Osserman stage). The impact of steroids use on postoperative respiratory insufficiency (ventilator), need for tracheostomy, superficial wound dehiscence, superficial wound suppuration, sternal dehiscence and mortality was analyzed. The results for subsequent periods 1973–1980, 1981–1990 and 1991–2002 are analyzed separately because major changes in preoperative and postoperative treatments of myasthenia gravis occurred in these periods, affecting the postoperative morbidity. Patients submitted to the extended thymectomy through the complete longitudinal sternotomy approach for nonthymomatous myasthenia, thymoma and rethymectomy are also analyzed separately due to potentially higher risk of complications than in the basic thymectomy group performed through upper median sternotomy approach.

Twenty-eight patients taking high doses of steroids (prednisone, >1 mg/kg per day) preoperatively were considered a high risk group, especially regarding wound healing and problems with sternal dehiscence. The results in this group of patients were analyzed separately.

Statistical analysis was performed with STATISTICA software package. Probability values were generated with the \(\chi^2\)-test and the Student \(t\)-test or the Mann–Whitney test. Probability values \(P < 0.05\) were considered to be statistically significant.

3. Results

There were no differences regarding sex, age and duration of symptoms of myasthenia between both groups (Table 1). There was a significant difference in Osserman score \((P = 0.00002)\) reflecting more severe myasthenia in steroids group. Five patients died in the postoperative period, all in the no-steroids group (mortality 5/620, 0.8%). Complications of thymectomy in both groups are shown in Table 2. There were only two cases of sternal dehiscence (0.3%), both in the no-steroids group with a basic thymectomy performed through the upper median sternotomy in nonthymomatous myasthenic patients. Superficial wound dehiscence, superficial wound suppuration and sternal dehiscence and mortality was analyzed. The postoperative morbidity rate was decreasing in the periods 1973–1980, 1981–1990 and 1991–2002 (Fig. 1). In the years 1973–1980 the postoperative morbidity was 45.46% in the no-steroids group and 33.33% in the steroids group. In the years 1981–1990 the postoperative morbidity was 20.24% in the no-steroids group and 18.75% in the steroids group. In the years 1991–2003 the postoperative morbidity was 45.46% in the no-steroids group and 33.33% in the steroids group.

The postoperative morbidity rate was decreasing in the periods 1973–1980, 1981–1990 and 1991–2002 (Fig. 1). In the years 1973–1980 the postoperative morbidity was 45.46% in the no-steroids group and 33.33% in the steroids group. In the years 1981–1990 the postoperative morbidity was 20.24% in the no-steroids group and 18.75% in the steroids group. In the years 1991–2003 the postoperative morbidity was 7.11% in the no-steroids group and 6.58% in the steroids group. During the same periods the rate of preoperative use of steroids was increasing (7.69% in the period 1973–1980, 16.0% in the period 1981–1990 and 25.25% in the period 1991–2002).

In 28 patients high doses of steroids (prednisone, >1 mg/kg per day) were used. In this group, complications

Table 1

<table>
<thead>
<tr>
<th>Group</th>
<th>The steroids group (N = 117)</th>
<th>The no-steroids group (N = 503)</th>
<th>Statistical significance ((P))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex Male (%)</td>
<td>18 (15.38)</td>
<td>117 (23.26)</td>
<td>0.0633</td>
</tr>
<tr>
<td>Female (%)</td>
<td>99 (84.62)</td>
<td>386 (76.74)</td>
<td>0.0633</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>32.91 ± 12.02</td>
<td>30.86 ± 11.19</td>
<td>0.1819^a</td>
</tr>
<tr>
<td>Mean duration of MG (months)</td>
<td>109.76 ± 6.52</td>
<td>109.56 ± 10.51</td>
<td>0.8021^a</td>
</tr>
<tr>
<td>Osserman score</td>
<td></td>
<td></td>
<td>0.00002^b</td>
</tr>
</tbody>
</table>

\(^a\) Mann–Whitney test.
\(^b\) \(\chi^2\) test.
occurred in 10 patients (35.7%). The complications are listed in Table 3. All complications in this group occurred before 1990. In none of the 18 patients taking high doses of steroids operated on after 1990 was any complication noted. Postoperative morbidity in the group of 89 patients taking low doses of steroids (prednisone, <1 mg/kg per day) was 3.4% (3/89) and significantly lower than in patients taking high doses of steroids ($P = 0.0001$)

Postoperative morbidity in 98 patients operated on through the complete median sternotomy approach was low, respiratory insufficiency in three patients (3.1%), and superficial wound suppuration in one patient (1.0%), no other morbidity and no mortality (Table 4). All these operations were performed in the years 1991–2002.

### 4. Comment

Patients with severe myasthenia are at a higher risk of respiratory insufficiency with subsequent morbidity and mortality. It is widely believed, that especially a transsternal approach was responsible for most postoperative morbidity and mortality. The postoperative mortality was reported to be as high as 20–30% before the 2nd World War. At present, due to improved methods of preoperative and postoperative treatments many postoperative complications can be avoided. One of these methods is the preoperative use of steroids, leading to improvement of the clinical state of patients and, therefore, decreasing the risk of respiratory insufficiency and subsequent complications. Steroids have been a standard type of therapy in patients with severe myasthenia gravis since 1970 [3,6,9].

Immunosuppression caused by corticosteroids is nonspecific and affects antigen presenting cells in the thymus, the activation of lymphocytes B and T, secretion of autoantibodies and destruction of acetylcholine receptors at end-plates of the skeletal muscle receptor [9,10]. Steroids intake may induce reversible involution of the thymus [11]. Antineoplastic activity against thymoma was also reported, leading to the regression of a tumor [6]. There are, however, significant adverse effects complicating steroid intake, especially when long-term therapy is undertaken [12–15]. Preoperative use of steroids before thymectomy in patients with myasthenia gravis has been started at our hospital in 1973, therefore, the patients operated on for myasthenia gravis before this date were not included from the analysis. The use of steroids became the sole method of stabilization of severe myasthenia before thymectomy in patients operated on in our department. No other method, such as plasmapheresis or intravenous immunoglobulins has been used in the presented group of patients. Before 1973 no special method of preoperative amelioration of myasthenia was used, except anticholinesterase drugs.

In the presented series, the incidence of respiratory insufficiency was relatively high in the period 1973–1980 and was greatly reduced in the later decades, mostly due to the improvement of the preoperative treatment of myasthenia. Currently, the rate of postoperative respiratory insufficiency with the need of ventilator is 5.2% in patients who underwent the extended transsternal thymectomy at our department [16].

### Table 2

Mortality and morbidity rates after transsternal thymectomy for myasthenia gravis—comparison of steroids and no steroids groups

<table>
<thead>
<tr>
<th>Complication</th>
<th>The no-steroids group (503 patients)</th>
<th>The steroids group (117 patients)</th>
<th>Statistical significance ($P$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory insufficiency (ventilator)</td>
<td>46/503 (9.1)</td>
<td>8/117 (6.8)</td>
<td>0.4260</td>
</tr>
<tr>
<td>Need for tracheostomy</td>
<td>14/503 (2.8)</td>
<td>3/117 (2.6)</td>
<td>0.9054</td>
</tr>
<tr>
<td>Superficial wound dehiscence</td>
<td>32/503 (6.4)</td>
<td>0/117 (0)</td>
<td></td>
</tr>
<tr>
<td>Superficial wound suppuration</td>
<td>13/503 (2.6)</td>
<td>1/117 (0.9)</td>
<td>0.2675</td>
</tr>
<tr>
<td>Sternal dehiscence</td>
<td>2/503 (0.4)</td>
<td>0/117 (0)</td>
<td></td>
</tr>
<tr>
<td>Wound complications, overall</td>
<td>47/503 (9.3)</td>
<td>1/117 (0.9)</td>
<td>0.0023</td>
</tr>
<tr>
<td>Complications, overall</td>
<td>154/503 (30.6)</td>
<td>13/117 (11.1)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Mortality</td>
<td>2/503 (0.4)</td>
<td>0/117 (0)</td>
<td></td>
</tr>
</tbody>
</table>

Table 3
The complications in 28 patients treated preoperatively with high doses of steroids (>1 mg/kg of prednison/day)

<table>
<thead>
<tr>
<th>Type of complication</th>
<th>No. (%) of complications in a group of 28 patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory insufficiency (ventilator)</td>
<td>5 (17.85)</td>
</tr>
<tr>
<td>Need for tracheostomy</td>
<td>4 (14.28)</td>
</tr>
<tr>
<td>Wound dehiscence</td>
<td>1 (3.57)</td>
</tr>
<tr>
<td>Overall</td>
<td>10 (35.71)</td>
</tr>
</tbody>
</table>

Overall, complications occurred in 5/28 (17.85%) patients.

There is also a difference of results regarding the incidence of respiratory insufficiency and the need for tracheostomy in favour of the steroids group in comparison to the no-steroids group, although the level of significance was not reached. It is clearly seen that the rates of both complications was decreasing in periods 1973–1980, 1981–1990 and 1991–2002. During the same periods the rate of preoperative use of steroids was increasing.

The use of high doses of steroids before thymectomy is potentially associated with the problems of tissue healing, especially the sternum [17]. For the same reason total median sternotomy is avoided in fear of sternal dehiscence [7]. The risk and, especially, the consequences of this complication are relatively lower in cases of upper partial sternotomy because the danger of sternal instability is avoided.

In our series a vast majority of patients were operated on with the upper median sternotomy. There were only two cases of sternal dehiscence in these patients, with one patient treated conservatively and one patient with sternal resuture. The treatment was successful in both cases. There was a significant difference of results ($P = 0.0023$) regarding the incidence of all complications in wound healing (sternal dehiscence, superficial wound dehiscence or suppuration; $P = 0.00002$) and in the overall complications rate ($P = 0.0001$), both in favour of the steroids group, although myasthenia was more severe in the no-steroids group (Table 1). It may be hypothesized, that deterioration of the general state of the patients in the no-steroids group after thymectomy was more harmful for wound healing than potentially deleterious influence of steroids in the patients in steroids group.

The most important result of this study is a marked decrease of morbidity in patients taking steroids in the preoperative period. In our series this effect was most clearly visible in the period 1973–1980, when morbidity of the thymectomy was much higher than in subsequent decades. Even in this period, when the rate of wound complications was relatively high, there were only two sternal dehiscences, both treated successfully. There was also no single patient with sternal dehiscence in 98 complete longitudinal sternotomies including 39 patients who were treated with steroids preoperatively.

In the selected subgroup of patients treated with high doses of steroids (prednisone, >1 mg/kg per day) there was only one wound dehiscence (3.57%). Although the morbidity in this subgroup is considerable (35.71%), there were no complications in any of the 18 patients operated on after 1990. Nevertheless, there was a significant difference in complications rate between patients taking high and low doses of steroids preoperatively ($P = 0.0001$).

5. Conclusions

Preoperative use of steroids for transternal thymectomy in patients with myasthenia gravis had no negative impact on morbidity and mortality, conversely, the results in patients taking steroids were better, with significant difference of results regarding the overall complications rate and the overall wound complications rate. Steroids use cannot be, therefore, considered a contraindication for transternal thymectomy; however, in patients taking high doses of steroids preoperatively an increase of postoperative morbidity may be expected.

References
