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# Hemifacial Spasm Treated with Botulinum Toxin Injection : A Ten-Year Experience at Siriraj Hospital

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**Abstract : Background : Hemifacial spasm is a common movement disorder in Thailand. Botulinum toxin has been introduced as an advanced treatment for this condition recently.**
**Objective : To evaluate the efficacy and complication of botulinum toxin in the treatment of hemifacial spasm.**
**Method : We reviewed all files of patients with hemifacial spasm in the Movement Disorders Clinic at Siriraj Hospital, Mahidol University, who were treated with botulinum toxin injection from January, 1989 until September, 1999. Sex, age, duration of treatment, times of injection, treatment outcome, and complications were analysed.**
**Results : There were 913 patients of which 38 patients were excluded because they were loss to follow up. 875 patients were analysed, (269 males, 606 females sex ratio 1:2.25.) The mean age of all patients was 50.86±12.53 years with a range of 18 to 81 years. The follow up period ranged from 1-130 months (mean = 32.5±35.05 months). The outcome were classified as excellent (improvement >50%) in 58.9%, good (improvement >25%) in 37.3 %, fair (improvement <25 %) in 3.1 %, and no improvement in**

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**0.8%. Thus the efficacy of this treatment (improvement > 25%) was 96.2 percent. There were complications of mild facial paresis in 80 patients (9.1 %), ptosis in 39 patients (4.5%), excessive lacrimation in 7 patients (0.8%), and others (including pain and itching at the injection sites and double vision) in 7 patients (0.8%). All of the complications were transient.**

**Conclusion : Botulinum toxin A injection is a safe and effective way with no long term systemic complications (of treating patients with hemifacial spasm).**

**เรื่องย่อ :** **การรักษาผู้ป่วยใบหน้ากระตุกครึ่งซีกด้วยการฉีดสารเคมีชีวภาพโบทูลินัม : ประสบการณ์ของการรักษา 10 ปี ในโรงพยาบาลศิริราช**

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**ความรู้พื้นฐาน** : โรคใบหน้ากระตุกครึ่งซีกเป็นโรคที่พบบ่อยในประเทศไทย ซึ่งล่าสุดมีการใช้วิธีฉีดสารเคมีชีวภาพโบทูลินัมในการรักษาโรคนี้ได้ผลดี

**วัตถุประสงค์** : เพื่อประเมินประสิทธิผล และภาวะแทรกซ้อนของการรักษาโรคนี้ด้วยสารเคมีชีวภาพโบทูลินัม

**วิธีการศึกษา** : ได้วิเคราะห์ข้อมูลทั้งหมดจากแฟ้มประวัติผู้ป่วยโรคใบหน้ากระตุกครึ่งซีกที่มารับการรักษาในคลินิคโรคที่มีการเคลื่อนไหวผิดปรกติในโรงพยาบาลศิริราช ที่ได้รับการฉีดสารเคมีชีวภาพโบทูลินัม ตั้งแต่เดือนมกราคม พ.ศ. 2532 ถึงเดือนกันยายน 2542 การวิเคราะห์ข้อมูลด้านเพศ, อายุ, ระยะเวลาของการเป็นโรค, ระยะเวลาที่รักษา, ระยะห่างของการฉีดแต่ละครั้ง, ผลการรักษาและผลแทรกซ้อนต่างๆ ที่เกิดขึ้น

**ผล** : มีผู้ป่วยใบหน้ากระตุกครึ่งซีกทั้งสิ้นจำนวน 913 ราย ที่ได้มารับการรักษา โดยการฉีดสารเคมีชีวภาพโบทูลินัม แต่มีผู้ป่วย 38 ราย ที่ไม่ได้มาติดตามผลการรักษา ดังนั้นจึงวิเคราะห์ข้อมูลผู้ป่วยเพียง 875 ราย เป็นชาย 269 ราย, หญิง 606 ราย คิดเป็นสัดส่วนเพศชายต่อหญิง 1 : 2.25 อายุเฉลี่ยของผู้ป่วยเท่ากับ 50.86 ปี (ค่าเบี่ยงเบนมาตรฐาน 12.53 ปี) โดยมีค่าพิสัยระหว่าง 18-81 ปี. การติดตามการรักษาเฉลี่ยนาน 32.5 เดือน (ค่าเบี่ยงเบนมาตรฐาน 35.05 เดือน), ค่าพิสัยระหว่าง 1-130 เดือน ผลการรักษาพบว่ามีประสิทธิผลสูงถึงร้อยละ 96.2 โดยจำแนกเป็นผลดีเยี่ยม (อาการดีขึ้นมากกว่าร้อยละ 50) ร้อยละ 58.9, ผลดี (อาการดีขึ้นมากกว่าร้อยละ 25) ร้อยละ 37.3, ผลพอใช้ได้ (อาการดีขึ้นน้อยกว่าร้อยละ 25) ร้อยละ 3.1 และไม่ได้ผลร้อยละ 0.8 สำหรับผลแทรกซ้อนของการรักษาพบมีอาการปากเบี้ยวเล็กน้อย 80 ราย (ร้อยละ 9.1) หนังตาตก 39 ราย (ร้อยละ 4.5), น้ำตาไหลมาก 7 ราย (ร้อยละ 0.8) และอื่นๆ (เช่น คันหรือเจ็บบริเวณที่ฉีด, เห็นภาพซ้อน) พบ 7 ราย (ร้อยละ 0.8) สำหรับอาการแทรกซ้อนเหล่านี้พบว่าเกิดเป็นระยะเวลาสั้น และหายดีเป็นปรกติทุกราย

**สรุป** : การใช้สารเคมีชีวภาพโบทูลินัมในการรักษาผู้ป่วยในหน้ากระตุกครึ่งซีก พบว่าเป็นวิธีที่ดีมีประสิทธิผล โดยไม่มีผลแทรกซ้อนในระยะยาวใดๆ ทั้งสิ้น.

Hemifacial spasm, a condition characterised by involuntary unilateral contractions of the facial muscles, is a disabling disorder often resulting in patient irritation and social embarassment. It is usually attributed to compression of the facial nerve root exit zone by an abnormal vasculature in the posterior fossa[1]. Occasionally, the facial nerve is compressed by a cerebellopontine tumour. It may be treated by microvascular decompression with 80-90% success rate[2]. Nevertheless, many patients refuse surgery because it is a major procedure and has potentially serious complications such as cerebellar injury (0.45%), hearing loss (0.8%), and CSF leakage (1.85%)[3]. Anticonvulsants, such as phenytoin, carbamazepine, and clonazepam may benefit some patients. These medications are usually limitatied in their efficacy. Since 1990 after the American FDA approval of botulinum toxin injection for various movement disorders, several studies have shown that local injection of botulinum toxin is very effective in the treatment of hemifacial spasm but the number of patients in each study was too small. In Thailand botulinum toxin was first introduced in 1989 as in an experimental capacity initially and then The Thai FDA gave approval for trial of treatment in 1996.

Botulinum toxin is a neurotoxin produced by *Clostridium botulinum* bacteria. The toxin causes muscle paralysis by blocking the release of acetylcholine at the peripheral nerve endings (presynaptic location)[4,5]. The toxin has been approved for various movement disorders such as cervical dystonia, blepharospasm and hemifacial spasm[6].

There are few reports about the use, results and long term outcome of botulinum toxin in the treatment of hemifacial spasm. We present here ten-year experience in treating hemifacial spasm with botulinum toxin A injection. The objective of this study is to evaluate the efficacy and complications of botulinum toxin A in the long term treatment of hemifacial spasm.

## MATERIALS AND METHODS

**- Patients :**

Nine hundred and thirteen cases of hemifacial spasm attending the Movement Disorders Clinic at Siriraj Hospital, Mahidol University, Bangkok, Thailand from January 1989 to September 1999 were analysed for demographic data, sites of injection, amount of botulinum toxin given, clinical response, duration of response and complications.

**- Botulinum toxin A (Botox) :**

Botulinum toxin A was available initially from Smith-Kettlewell Eye Research Institute in San Francisco (1989-1992) and later from Allergan Inc., California (1992-1999). Vials of botulinum toxin A were kept in deep freeze at less than 20°C. The freeze-dried white powder toxin in each vial contains 100 international units. It was diluted with 1 ml of saline to a concentration of 100 IU/ml and was prepared half an hour prior to the injection and was not used more than six hours thereafter to ensure its efficacy.

**- Injection technique :**

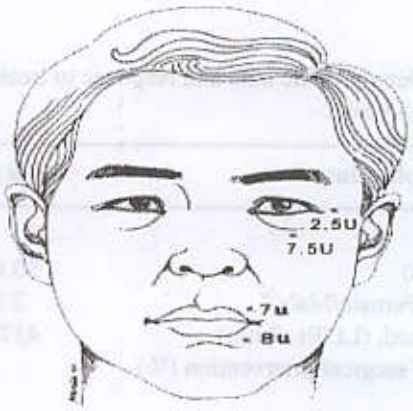


*Figure 1.* Demonstration of injection site and botulinum toxin dosage.

With the patient in a sitting position, the injection sites (as shown in Figure 1) were cleaned with 70% alcohol and the toxin was injected subcutaneously to a total amount of 25 IU.

**- Follow up and assessment :**

All patients were assessed after each treatment to determine clinical improvement and complications. By interview, the clinical outcome was classified as excellent (improvement >50%), good (improvement >25%), fair (improvement <25%), and no improvement. Complications were recorded and treated. Retiring of the next injection depended on the duration of clinical improvement which was approximately three to six months.

## RESULTS

There were 913 patients with hemifacial spasm in the Movement Disorders Clinic treated with botulinum toxin A during the ten-year period. Thirty-eight patients were excluded as they were lost to follow up after the first injection. Data from the remaining 875 patients were analysed (Table 1). There were 269 males (30.7%), the sex ratio of male to female was 1:2.25. The mean age of all patients was 50.86 ± 12.53 years with a range of 18-81 years. Of the 875 hemifacial spasm patients, 418 (47.8%) were on the right side. The mean duration of symptoms before receiving botulinum toxin was 2.57 ± 1.65 years. The mean follow up period was 32.52 ± 35.05 months ranging from 1-130 months. Almost all treatment were effective (at least 25% improvement) in 841 patients (96.2%)) which were excellent in 515 patients (58.9%), good in 326 patients (37.3%), fair in 27 patients (3.1%) and no improvement in 7 patients (0.8%). Complications were mild facial paresis in 80 patients (9.1%), ptosis in 39 patients (4.5%), excessive lacrimation in 7 patients (0.8%), facial palsy plus ptosis in 6 patients (0.7%), facial palsy plus excessive lacrimation in 2 patients(0.2%), ptosis and pain in 2 patients (0.2%) and others including pain, itching at the injection site, and double vision in 7 patients (0.8%). All of these complications were transient (Table 2).

**Table 1**. Demographic data and response to treatment in all patients compared with those patients treated for more than 5 years.

| Demographic data | All patients | Patients treated ≥ 5 years |
|---|---|---|
| Number | 875 | 164 |
| Age (years) | 50.86 ± 12.53 | 50.43 ± 12.33 |
| Sex ratio(Female/Male) | 2.25 (606/269) | 2.09 (111/53) |
| Side affected, (Lt./Rt. Ratio) | 457/417 (1.09) | 73/91 (0.80) |
| History of surgical intervention (%) | 26 (3%) | 4 (2.4%) |
| **Response to treatment** | | |
| Excellent | 515 (58.9%) | 108 (65.9%) |
| Good | 326 (37.3%) | 47 (28.7%) |
| Fair | 27 (3.1%) | 7 (4.3%) |
| No improvement | 7 (0.8%) | 2 (1.2%) |
| Duration of benefit (months) | 4.18 ± 2.92 | 4.66 ± 0.95 |

**Table 2.** Transient complications in patients during ten-year follow up period.

| Complication | All patients (N = 875) | Patients treated ≥ 5 years (N = 164) |
|---|---|---|
| Total | 143 | 40 |
| Facial paresis | 80 (9.1%) | 23 (14%) |
| Ptosis | 39 (4.5%) | 14 (8.5%) |
| Excessive lacrimation | 7 (0.8%) | 0 |
| Facial palsy + ptosis | 6 (0.7%) | 1 (0.6%) |
| Facial palsy + excessive lacrimation | 2 (0.2%) | 1 (0.6%) |
| Ptosis + pain | 2 (0.2%) | 0 |
| Others (pain, itching at the injection site) | 7 (0.8%) | 1 (0.6%) |

In the subgroup analysis of patients receiving treatment for more than five years, there were 164 patients who met this criteria. The mean follow up period was 94.40±20.95 months with a range of 61-130 months. Responses to treatment were considered as excellent in 108 patients (65.9%), good in 47 patients (28.7%), fair in 7 patients (4.3 %) and no improvement in 2 patients (1.2%). Complications were facial palsy in 23 patients (14%), ptosis in 14 patients (8.5%), facial palsy plus ptosis or excessive lacrimation in 2 patients (1.2%), excessive lacrimation in 1 patient (0.6%), pain and itching at the injection site in 1 patient (0.6%).

## DISCUSSION

Botulinum toxin A has been proven to be an effective and alternative treatment for patients with hemifacial spasm[6-9]. From most published studies, less than 5% of patients fail to respond to chemical denervation. In this report, we describe demographic data, response rate, duration of benefit and complications in patients who has been treated more than 5 years at Siriraj Hospital. This study is a descriptive analysis of 875 patients receiving a total 3,061 injections. There were only 4.2% of patients who were lost to follow up. Currently, this is the second report of long term botulinum toxin treatment in Thailand but the world's largest series.

The response rate of the whole group and long term treatment group are comparable to other series[10-16]. Our data showed a 98% improvement which is similar to the 97% reparted in the series by Jitpimolmard, et al[11]. The difference between the duration of improvement and the dose are attributed to different in type of botulinum toxin. (Dysport vs Botox). Sampaio C., et al.[17] performed a randomised parallel study to determine the difference in efficacy and found that the conversion factor for the chemical potency of Dysport and Botox is approximately 4:1 which is quite similar to the ratio of dose using in Jitpimolmard compared with our series (92/25 = 3.68:1). Inequalities in duration of improvement might be caused by the differences in injection site and technique between two studies. We do not use preinjection EMG to detect the injection site as we found it impractical and unneccessary because the facial muscles can easily be identified. The use of EMG guide is a necessity when treating conditions in which affected muscles are difficult to identify such as strabismus, spastic dysphonia, etc[18].

**Table 3.** Long term result in reported series of botulinum toxin treatment.

| Type of botulinim toxin | Authors | Fellow up (yrs) | Patients (n) | Stopped treat-ment | Treat-ments (n) | Pts complete Rx (n) | Mean dose (units) | Response rate (%) | Time of improve-ment (months) | Side effects (%) |
|---|---|---|---|---|---|---|---|---|---|---|
| Dysport | Jitpimolmard, et al[11] | 7 | 175 | 17 | 883 | 21 | 92 | 97 | 3.4 | 29 |
| | Bergh, et al[12] | 5 | 40 | 12 | 144 | - | 53 | 100 | 4.93 | 22 |
| | Elston[13] | 7 | 73 | - | - | - | 120–160 | 75 | 2.8-3.5 | 19–33 |
| Botox | Dutton, et al[14] | 4 | 60 | - | 148 | - | - | 96.8 | 3.60 | 23 |
| | Taylor, et al[15] | - | 130 | - | 336 | 7 | - | 98 | 4.23 | 32 |
| | Flanders, et al[16] | 8 | 65 | 14 | - | 9 | 34 | 100 | 4.06 | 8 |
| | Poungvarin, et al | ≥5 | 875 | - | 3,061 | 164 | 25 | 98 | 4.66 | 24.4 |

The mean duration of efficacy in the long term treatment group was 4.66±0.95 months which is slightly longer than the total group (4.18±2.92 months). The severity of the symptoms may lessen during the later treatment period. We did observe a decrease in the duration of benefit in a few patients who receive long term therapy but most of the patient have a sustained duration of benefit. Siatkowski, et al found that serum antibody to botulinum toxin A was presented in about 57% of patients[19]. Our observations seemed to agree with his study that antibody to botulinum toxin A has no direct effect on the patient's clinical response to treatment.

There were more complication rate in the group of patients treatment for more than 5 years which attributed to higher number of injection. All complications were transient. We did not find any adverse long term distant effects of botulinum toxin treatment although there have been some reports of brachial plexus neuropathy and Guillain-Barre syndrome[20-24]. We have no data concerning botulinum toxin treatment in pregnancy and lactation. We do not recommend botulinum toxin treatment in these patients although there have been some reports of healthy babies from at least 13 pregnant women using botulinum toxin[25].

## CONCLUSION

Botulinum toxin A injection is a simple, effective out-patient treatment for hemifacial spasm patients with few transient local side effects. The only drawback of this treatment is its high cost.

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