Medical treatment for patients with generalized dystonia (GD) is often ineffective, and therefore it is important to consider alternative treatment modalities for this difficult disease. Although thalamotomy has been partially effective in patients with GD, there is risk of complications, particularly dysarthria and dysphonia if the surgery is bilateral.1,2

The study of Andrew et al.1 reported that whereas Chinese Medic J (Taipei) 2001;64:231-238

Original

Treatment of Intractable Generalized Dystonia by Bilateral Posteroventral Pallidotomy — One-Year Results

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Key Words: dystonia; pallidotomy; surgical treatment

Background. Recent study has revealed that bilateral posteroventral pallidotomy (PVP) significantly improves dystonic movements and improves motor function of those patients with generalized dystonia (GD). However, there is only a limited number of patients who have been reported so far.

Methods. This study was conducted to evaluate the clinical efficacy of surgical treatment with bilateral PVP on patients with intractable GD. All the studied patients were regularly rated with standardized scales (Burke-Fahn-Marsden Evaluation Scale for Dystonia) for dystonic movement and living disability before and after surgery.

Results. There were 18 patients, 8 males and 10 females with an average age of 24.8 years, included in the study. Postoperatively, there were slow, partial, but steady improvements of the dystonic movement and daily living function. Maximal effects were noted at the sixth month and the clinical benefits were sustained one year after the surgical treatment when there were statistically significant improvements in 13% of total dystonia movement score and 9% of the total disability score (p < 0.05). Upon further analysis, improvements of dystonic movements were statistically significant in the regions of mouth (50%), speech/swallowing (19%), and neck (43%), and daily living functions in speech (14%) and eating/swallowing (29%).

Conclusions. Bilateral posteroventral pallidotomy was only partially effective for the treatment of GD, and it produced clinical improvement in the dystonic movement limited to the craniocervical region. We therefore suggest that patients with GD should be carefully selected for the treatment of bilateral posteroventral pallidotomy, despite the surgery having a partially beneficial effect on this kind of movement.

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Dysarthria occurred in 11% of patients following unilateral thalamotomy, it occurred in up to 56% of patients after bilateral thalamotomy. Stereotactic surgery on the posteroverental portion of the inner segment of the globus pallidus (GPi) called posteroverental pallidotomy (PVP) to control parkinsonian symptoms was initially performed by Leksell in the late 1950s. However, further development of this approach was halted due to the introduction of medical treatment with levodopa. In the early 1990s, Laitinen and his colleagues began to reevaluate the therapeutic effect of PVP in patients with Parkinson disease (PD).

Since then, PVP has been proven to effectively improve response fluctuations, hypokinesia, rigidity and levodopa-induced dyskinesia in patients with PD. More over, the surgery was also found to be effective in relieving muscular pain and dystonia.

Recently, bilateral PVP has been investigated as a treatment modality for patients with intractable GD as well. The results showed that the surgical treatment could significantly improve dystonic movements and improve motor function of those patients with PD. Be cause of the limited number of patients studied, the potential effect of this surgical therapy on GD needs to be further studied.

This study was conducted to evaluate the clinical efficacy of surgical treatment with bilateral PVP on 18 patients with intractable GD.

**Methods**

This study included 18 patients with secondary GD from diverse etiologies; 2 patients of this series have been reported previously. The etiologies of the dystonia in these patients included 8 patients with cerebral palsy, 6 with hypoxia, 2 with car bon monoxide (CO) in toxication, 1 with post infectious encephalopathy, and 1 with encephalitis. There were 8 males and 10 females with an average age of 24.8 years (ranging from 14 to 36 years). All these patients had received rehabilitation therapy and medications that included trihexyphenidyl, baclofen, diazepam, clonazepam, levodopa, and dantrolene, but all with out benefit. Be fore operation, 11 out of the 18 patients were completely dependent, 4 were partially dependent, and 3 were in dependent in their daily living activities. Pa tients gave in formed consent prior to the procedure, and the pro tocol was reviewed and approved by the the Human Subjects Research Ethics Committee of Tri-Service General Hospital, Taipei.

**Clinical assessment**

The dystonic move ment and dis ability scales of Burke-Fahn-Marsden Evaluation Scale for Dystonia (BFMDS) were evaluated by two neurologists (J.J.L. and D.C.C.) one week before surgery and at regular intervals (1 week, 1, 3, 6, 9, 12 months). To ensure the objective evaluation of this study, video-taped segments were also randomized and scored by a neurologist experienced in the use of the dystonic movement and disability scales of BFMDS and who had not been involved in the patients' preoperative and postoperative care. Be side being evaluated by a standard protocol, patients were also video taped at the time of each evaluation. For this report, we have reviewed our first 18 patients completing 12 months of follow-up.

**Surgical procedures**

PVP was carried out as described in the paper of Laitinen et al. Be fore operation, all patients underwent brain MRI (Siemens 1.5 Tesla Scanner, Siemens, Magnetom, Erlangen, Germany). The detailed anatomy of the basal ganglia was visualized using inversion recovery sequences with long acquisition times to provide high resolution images. The relation between the posteroverental portion of GPi and the anterior and posterior commissures (AC/PC) of the third ventricle were calculated, and the predicted lesion volume was defined for each side. A Leksell mode (G) stereotactic frame (Elekta Instruments, Stockholm, Sweden) was secured to the patient's head under local anesthesia. Biopsies were taken from the hippocampus and the amygdala, and then the patient was trans ferred to the MRI scanner where the coordinates of the AC/PC were established. The tenative target was cho sen at the center of the posteroverental portion of GPi. It was 2-3 mm an te rior to the midcommissural points and 19-21 mm lateral and 4-6 mm inferior to the inter-
commissural line. Under local anes the sia, a small burr hole was made in the fron tal skull at a point 2.5 cm away from the midline and near the co ro nal su ture. A thermocoagulation bi po lar probe (2 mm in di am e ter and 4 mm un in su lat ed sep a ra tion be tween the an ode and the cath ode [Elekta Intruments]) was placed to the tar get of the posterover nal por tion of GPi through the burr hole. Microelectrode recording was not done. Elec tric stim u la tion test was done with an elec trode with low-frequency (8 Hz, 300 µ sec, up to 10 amp) and high-frequency (80Hz, 200 µ sec, up to 10 amp) stim u la tion. The aim of the stim u la tion was to de term ine the prox im ity of the in ter nal cap sule and the optic tract. If there was no sign of mus cu lar con trac tion of contralateral limbs or eye flush ing, a re vers ible le sion was made by thermocoagulating the tar get at 60 °C for 60 sec onds. When the pres er vation of mo tor function of the contralateral extremities was con firmed, a per ma nent le sion (80 °C for 80 sec onds) was car ried out. Each pallidotomy com prised three over lapping in di vid ual le sions and a typ i cally cy lin dri cal le sion about 6 × 6 × 10 cm³ was made. Pa tients had ei ther si mul ta neous or se quen tial lesioning (sep a rated by 2 weeks) de pend ing on their gen er al neu ro log i cal per for man ce. Post oper a tively, rou tine MRI was ob tained con firm ing ac cu rate place ment of the thermo coagulated le sion and check ing for pos si ble com pli ca tions, es pe cially ce re bral hem or rhage.

Analysis

Sta tis ti cal anal y sis of the per for man ce be fore and af ter sur gery was ob tained on the ba sis of Wilcoxon Signed Rank Test. A p < 0.05 was con sid ered sig ni ficant.

Results

Fourteen pa tients un der went si mul ta neous bi lat eral PVP, and four un der went se quen tial bi lat eral PVP. Postoperatively, there was im med i ate re duc tion of mus cu lar hyperton us in all pa tients. How ever, the im prove ment of dystonic move ment and dis abil ity were not noted un til the first month af ter the sur gi cal treat ment. There af ter, the im prove ment oc curred slowly

![Graph showing improvement in dystonia scale and disability scale over time.](image)
Fig. 2. Dystonic movement of Burke-Farhn-Masden Evaluation Scale for Dystonia on the different regions of 18 patients with generalized dystonia before and after bilateral posteroventral pallidotomy (*p < 0.05, **p < 0.01, by Wilcoxon Signed Rank Test).

Fig. 3. Disability scale of Burke-Farhn-Masden Evaluation Scale for the different daily living functions of 18 patients with generalized dystonia before and after bilateral posteroventral pallidotomy (*p < 0.05, by Wilcoxon Signed Rank Test).
but steadily, and max i mal ef fects were noted at sixth month af ter op er a tion (Fig. 1). These clin i cal ef fects per sisted for at least one year af ter the treat ment.

Com paring the rat ing scale be fore and one year af ter the treat ment, there were only 13% im prove ment of dystonic move ment (im prove ment of BMFDS dystonia move ment score from 58.03 ± 20.89 to 50.50 ± 17.60) and 9% of daily liv ing func tions (im prove ment of BMFDS dis abil ity score from 17.28 ± 6.61 to 15.72 ± 6.76). Al though the im prove ments were lim ited, they both reached sta tis ti cal sig nif i cance as per Wilcoxon Signed Rank Test (p = 0.013 and 0.010, re -spec tively). Fur ther anal y sis of those dystonia on the dif fer ent re gions showed that the clin i cal ef fects were sta ti cally sig nif i cant in the re gions of mouth (50%, p = 0.015), speech/swal low ing (19%, p = 0.040) and neck (43%, p = 0.008) (Fig. 2). Sim i larly, the sur gi cal treat ment im proved sig nif i cantly the daily liv ing func -tions, par tic u larly in speech (14%, p = 0.034) and eat -ing/swal low ing (29%, p = 0.027) (Fig. 3). Com par ison of the clin i cal ef fects of the sur gi cal treat ment and sex of these dystonia pa tients re vealed no sta tis ti cal dif fer -ences. More over, there were no sig nif i cant dif fer -ences in the im prove ments of the dystonic move ment and daily liv ing func tions be tween those who were treated by the si mul ta neous PVP and those who were treated by the se quen tial PVP.

Post oper a tively, ad verse ef fects de vel oped in 7 out of 18 pa tients. How ever, these com pli ca tions were all tem porary and spontane ously re solved within one month of sur gery. There were 5 pa tients with som no -lence, 2 with uri nary in con ti nence, 2 with vi su al field def i cit, 2 with hem iparesis, 1 with un steady gait and 1 with fe ver. There was no ce re bral hem or rhage found in the post oper a tive MRI.

**Discussion**

The lit er a ture re ports ap pli ca tions of bi lat eral PVP in the treat ment of pa tients with GD (Ta ble 1) and shows re mark able and sig nif i cant ef fects on the dystonia.9,12-15 These re ports show more than 60% im -prove ments of the dystonic move ment and/or func -tional dis abil ity in fol low-up pe riod of 3-12 months af ter the sur gi cal treat ment. How ever, re sults of our study re vealed less dra matic re sponses over all, that bi lat eral PVP treat ment of pa tients with GD pro duced some but not very re mark able im prove ment of dystonic move ment. There was only 13% im prove ment on dystonic move ments and 9% on the daily liv ing func -tions in this study. The un der ly ing dis ease pro cesses could prob a bly ex plain to this dis crep ancy.

Most pa tients re por ted in lit er a ture were pri mary id io -pathic dystonia, but pa tients in our study were sec ond ary eti -o lo gies. There fore, we may con clude that pa -tients with pri mary gen er al ized dystonia treated by the bi lat eral PVP im prove more ro bustly than those with sec ond ary dystonia. Within the spec trum of sec ond ary

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BMFDS = Burke-Fahn-Masden Evaluation Scale for Dystonia. *Average duration of follow-up after surgery.

Table 1. Summary of benefits of pallidotomy in patients with generalized dystonia

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dystonias, the association of other abnormalities (spasticity, ataxia, and others) further reduced the chances for significant functional improvement.

A re view of available reports in di cates that bi lateral pallidotomy could produce a max i mal func tional improve ment of gen er alized dystonia.17,18 De spite this gen er al con cord ance with re gard to the ef fective ness of bi lateral pallidotomy, our ob serv a tion of re stricted area of im prove ment, i.e., re duc tion of dystonia lim ited to the craniocervical re gion, is dis tinctly dif fer ent from that re ported by Iacono et al.9 and Lozano et al.,12 who ob served im prove ments in gen er al ized dys tonia in volv ing not only ax ial but appendi cular muscu la tures as well af ter bi lateral pallidotomy. The rea son for these dif fer en ts out comes comes from the same treat ment re mains un clear. Based on our re sults, we ad vo cate care ful se lec tion of pa tients, prefer ably those with marked dystonia in the craniocervical re gion, for the application of bi lateral PVP pro ced ure.

The pathogenesis of the ma jor symp toms of PD has been gen er ally thought to be re lated to the over ac tivity of in hib i tory GABAergic out put of GPi.4,8,19 It is possible, there fore, that the ef fective ness of PVP in re vers ing akinesia and elim i nating dyskinesias is re lated to its ab il ity to di rectly re duce the ac tiv ity of GPi in pa tients with PD. The pathophysiology of symp toms in id io pathic dystonia, how ever, may be dif fer ent from that of PD since there is ev i dence from re cent re ports sug gest ing that the fun da men tal dis tur bance of ac tiv ity in the basal gan glia of pa tients with idiopathic dystonia is dif fer ent from that of PD. For ex am ple, Hashimoto and Yanagisawa were able to show that over ac tiv ity of the pre mo tor cor ti ces, as a re sult of under ac tiv ity of basal gan glia, oc curred both at rest and on mo vement in pa tients with idiopathic dys to nia.20 In ad di tion, us ing mi croelec trode re cord ing dur ing PVP, re cent stud ies have shown that the fir ing rate of GPi neu rons in those pa tients with GD was lower than that in pa tients with PD and nor mal pri mates.12,21 Evi dent ly, by dis ru p ting the al tered neu ronal ac tiv ity of the GPi, PVP could re mark ably im prove the mo tor func tion of pa tients with dystonia. In light of this, our ob serv a tion of the ab il ity of PVP treat ment to pro duce sig nif i cant im prove ment in the ab nor mal move ment of pa tients with dystonia is also sup port ive of a mecha nism wherein the neu ronal ac tiv ity in the GPi play an im por tant role in the gen es is of dystonia; by re duc ing the al tered neu ronal ac tiv ity in GPi, the mo tor func tion in pa tient with dystonia can be im proved.

With re gard to the post op er a tive course, it is also of in ter est to note that the clin ical im prove ment ob tained from the bi lat eral ePVP treat ment, as noted in this study, was not im me di ate, but had a la tent pe riod. Sim i lar ly, de layed on set of the clin ical im prove ment may be re ported by Lozano et al.12,13 Sterio et al.14 and Ondo et al.15 Such find ings are in dis tinct con trast with the im me di ate symp tomatic im prove ment of pa tients with PD fol low ing treat ment with PVP.4,8 Fur thermore, it should be also noted that in pa tients with GD, rapid al le vi a tion of dystonic symp toms was achieved fol low ing treat ment with bi lateral PVP, as re ported by Iacono et al.9 and Vitek et al.15 The rea son for these dis crepan cies is pre sently un clear.

In con clu sion, the pres ent study showed that PVP is a par tially ef fective ther apy for pa tients with GD. We showed that the sur gi cal treat ment could pro duce a cer tain de gre e of sig nif i cant im prove ment in ab nor mal mo tor func tion and qual ity of life for pa tients with GD. Com plica tions such as weak ness, som no lence, uri nary in con ti nence and vi sual field def i cit, how ever, were not un com mon, but they were all tem por a ry. In con trast to the bi lat eral thalamotomy, requently com plicated by dysarthria and dysphagia, treat ment of gen er alized GD by bi lat eral PVP could also im prove the speech, eat ing and swal low ing. Al though the cli nical ef fects ob served in this study were re stricted to the craniocervical re gions, the en cour ag ing re sults have led us now to ad vise bi lat eral PVP as an al ter na tive ther apy in med i cally re frac tory cases of GD.

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