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I, Michelle Kunkler,

hereby submit this as part of the requirements for the degree of:

Master of Arts

in Communication Sciences and Disorders

It is entitled Objective Analysis of the Effects of Botulinum Toxin on Adductor Spasmodic Dysphonia.

Approved by:

OBJECTIVE ANALYSIS OF THE EFFECTS OF BOTULINUM TOXIN ON ADDUCTOR SPASMODIC DYSPHONIA

A thesis submitted to the

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by

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Abstract

The present study examined acoustic, aerodynamic, and videostroboscopic measures of voice production following BOTOX injections in 4 patients with Adductor Spasmodic Dysphonia. Videostroboscopic measures showed a return to some normal aspects of vocal fold vibration 1 month post-injection. Several subjects exhibited suggested meaningful differences both one week and one month post-injection for acoustic and aerodynamic measures; however, results were highly variable and often did not bring the subjects' values into the normal range.

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INTRODUCTION

Adductor spasmodic dysphonia (ASD) has been defined as a "vocal fold movement disorder with excessive vocal fold closure on initiation of and during speech" (Ludlow, Naunton, Sedory, Schulz, and Hallett, 1988, p. 1220). The major related vocal symptoms found in ASD include tremor, harshness, and intermittent voice stoppages with uncontrolled pitch and phonatory breaks (Blitzer, Brin, Fahn, and Lovelace, 1988). The etiology of ASD is unclear as to whether it is neurologic or psychogenic (Colton and Casper, 1990), though recent evidence compares it with other laryngeal dystonias and points damage in the area of the brain stem (Schaefer, 1983).

Treatments of ASD have included a variety of methods from multiple disciplines such as laryngeal framework surgery, laryngeal nerve crush, and phonatory tasks; however, many of these methods have not been considered highly effective (Tucker, 1989). Two treatments have recently been utilized in order to reduce the symptoms of ASD. The first method, laryngeal nerve section, has been considered temporarily effective in reducing the symptoms of ASD (Brin, Fahn, Blitzer, Ramig, and Stewart, 1991; Dedo and Behlau, 1991). However, research indicates that nearly two-thirds of persons with ASD experienced recurrence of the symptoms three years after laryngeal nerve sections (Aronson and DeSanto, 1983). Some researchers consider laryngeal nerve section to be and extreme form of treatment due to the

permanent paralysis of the vocal folds that occurs after execution (Blitzer, Brin, Fahn, Lange, and Lovelace, 1986). The second method, which involves injection of the vocal folds with Botulinum Toxin (BOTOX), has been reported to be a successful form of treatment in recent years (Blitzer, Brin, Sasaki, Fahn, and Harris, 1989).

Studies exist on the subjective analysis of the effects of BOTOX on the voice mechanism (Blitzer and Brin, 1991; Blitzer, et al., 1988; Janovik, Schwartz, and Donovan, 1990, Truong, Rontal, Rolnick, Aronson, and Mistura, 1991). Researchers noted subjectively positive results (Blitzer and Brin, 1991; Blitzer, et al., 1988; Janovik, et al., 1990; Truong, et al., 1991).

Only two published studies report on the objective analysis of the effects of BOTOX on the vocal mechanism (Truong, et al., 1991; Zwirner, Murry, Swenson, and Woodson, 1992). Positive results were noted in each of these studies. The results in Zwirner, et al., (1992) indicated improvement in the subjects' acoustic, aerodynamic, and videoendoscopic parameters after a unilateral administration of BOTOX through an electromyographic (EMG) procedure. However, additional information is needed about the injection procedure that produces the most optimal results. Consistent with this need, this present investigation was designed to be a comparative study to Zwirner, et al. (1992). In this study, a bilateral, rather than unilateral, BOTOX injection occurred. Also, a transoral injection

occurred in substitution for EMG placement of the needle. This present investigation merely measured objectively the effects of the BOTOX injection on the vocal mechanism through acoustic, aerodynamic, and videostroboscopic measurements. The results of this investigation provided otolaryngologists with more complete information about injection procedures. In addition, patients with ASD may also be more likely to seek this type of treatment as a way of alleviating the negative vocal quality. Persons with ASD may also find greater ease in using their vocal mechanism, thus improving the quality of their life.

Chapter I - REVIEW OF THE LITERATURE

ETIOLOGY OF ADDUCTOR SPASMODIC DYSPHONIA

Adductor spasmodic dysphonia (ASD) is a relatively rare disorder claiming 30,000 Americans in which the voice perceptually sounds strained or strangled due to hyperadduction of the true and false vocal folds (Blitzer, et al., 1988; Colton and Casper, 1990; Friedman, Toriumi, Brybauskas, and Applebaum, 1987). The specified etiology of ASD is presently unknown. Two differing schools of thought exist in regards to the etiology of this disorder. ASD was originally considered to be psychogenic in origin and often classified as a conversion disorder (Parnes, Lavorato, and Myers, 1978). However, several recent researchers feel that ASD has a neurological basis to its occurrence (Aronson, Brown, and Litin, 1968; Dedo, Townsend, and Izdebski, 1978; Robe, Brumlik, and Moore, 1960). In cases in which the disorder is considered neurogenic, the site of lesion appears to be somewhere in the brainstem (Colton and Casper, 1990; Schaefer, 1983). Blitzer, et al. (1988) considered ASD to be a type of laryngeal dystonia which may be present with other movement disorders. Dystonia is a "neurological disorder of central motor processing characterized by abnormal, often action-induced, involuntary movements of uncontrolled spasms" (Blitzer, et al., 1988 p.193). If no etiologic factor can be identified, then ASD is considered idiopathic (Aronson and DeSanto, 1983; Friedman, et al., 1987).

SYMPTOMS OF ADDUCTOR SPASMODIC DYSPHONIA

Tremor, harshness, and intermittent voice stoppages are the main adverse effects on the voice in ASD. The vocal production in a person with ASD often involves effortful speech in which uncontrolled pitch and phonatory breaks are present. These are the symptoms which patients hope to eliminate or reduce with treatment (Cannito and Kondraske, 1990; Hartman, Abbs, and Vishwanat, 1988; and Watson, Schaefer, Freeman, Dembowski, Kondraske, and Roark, 1991) . Other symptoms often present in ASD include segmented vowels, prolonged vowels, difficulty with loudness control, glottal fry, glottal spasms, syllable repetitions, whispered speech, and hard glottal initiation (Blitzer, et al., 1988).

TREATMENT OF ADDUCTOR SPASMODIC DYSPHONIA

The efforts to relieve the symptoms of ASD have resulted in an evolution of numerous methods and treatment techniques from multiple disciplines (Aronson and DeSanto, 1983; Biller, Some and Lawson, 1979; Blitzer, et al., 1988; Brin, Fahn, Blitzer, Ranig, and Stewart, 1991; Hirano and Gould, 1985; Izdebski, Dedo, Shipp and Flower, 1981; Truong, et al., 1991; and Tucker, 1989). Types of treatment such as laryngeal framework surgery, laryngeal nerve crush, and phonatory tasks have been conducted on individuals with ASD (Biller, et al., 1979; Bloch, Hirano, and Gould, 1985; and Tucker, 1989), but none have been widely accepted or utilized. As individuals with ASD

approach the medical field for relief of the symptoms, two main types of treatment have been considered effective: laryngeal nerve section and Botulinum Toxin injections (Dedo and Behlau, 1991).

LARYNGEAL NERVE SECTION AS A TREATMENT FOR ASD

Early attempts to reduce the symptoms of ASD such as voice therapy, psychotherapy, tranquilizers, and biofeedback were unsuccessful due to the lack of direct treatment of the vocal folds (Blitzer and Brin, 1991; Dedo and Behlau, 1991; Dedo and Izdebski, 1983). However, in 1976, recurrent nerve section (RNS) became the first reliable treatment for ASD (Netterville, Stone, Rainey, Zealear, and Ossoff, 1991). The procedure for RNS involves the paralysis of one vocal fold in order to alleviate the force of vocal fold hyperadduction (Aronson and DeSanto, 1983).

Research has found that with RNS, temporary relief of the ASD symptoms results (Brin, et al., 1989). Studies have also found that a weak, breathy voice as well as a recurrence of the ASD symptoms may occur for some patients within 3 to 6 months after surgery (Aronson and DeSanto, 1981; Biller et al., 1979; and Levine, Wood and Batza, 1979). In addition, Aronson and Desanto (1983) indicated that sixty-four percent of their subjects experienced spasticity recurrence three years after their RNS. Of this sixty-four percent with failed voices at three years, forty-eight percent experienced more severe ASD symptoms

than before RNS (Aronson and DeSanto, 1983). This surgical management has undergone criticism by researchers due to the permanent paralysis of the vocal fold as well as the presence of a weakened and more spastic voice after the execution of a RNS procedure (Blitzer, et al., 1986; Blitzer, et al, 1988; Chollar, 1992).

BOTULINUM TOXIN INJECTION AS A TREATMENT OF ASD

While the benefits of laryngeal nerve section is questionable, temporary relief of the symptoms of ASD may be acquired through injections of botulinum toxin (BOTOX) (Blitzer, et al., 1989). Many researchers have discussed the benefits and advantages of this treatment for ASD and other focal dystonias (Blitzer, et al., 1986; Blitzer, et al., 1988; Blitzer and Brin, 1991; Jankovic et al., 1990; and Truong, et al., 1991).

Botulism, according to Kao, Drachman, and Price (1976, p.1256), is considered "the most potent biological poison known"; however, minute doses of this drug inhibit the calcium-dependent release of acetylcholine, thus causing a flaccid paralysis in muscles (Blitzer, et al., 1988; Brin, et al., 1991; Janovic, et al., 1990). Typically, there is a twenty-four to seventy-two hour delay between the administration of BOTOX and the onset of clinical effect (Brin, et al., 1991).

ADMINISTRATION OF BOTOX

The administrators of BOTOX closely monitor and adjust the dosage levels in response to the benefits versus

adverse effects of the injection (Blitzer and Brin, 1991; Brin, et al., 1991). The administration of BOTOX for ASD involves the injection of the drug into the vocalis-thyroarytenoid muscle using electromyography in predicting the localization of appropriate muscles (Blitzer, et al., 1988; Brin, et al., 1991). Another technique has also been practiced in which the drug is injected through indirect laryngoscopy, rather than electromyography (EMG) (Ford, Bless, and Lowery, 1990). Benefits of indirect laryngoscopy, according to Ford, et.al, included the following: no special EMG equipment or expertise is required; greater visualization when injecting causes a higher degree of precision in needle placement; and the BOTOX dosage is "titrated to the minimal effective dose for each patient" (Ford, et.al, 1990, p. 756).

EFFECTS OF BOTOX IN VOICE PRODUCTION

Some researchers have found that bilateral injections produce more positive effects on the voice of a person with ASD than unilateral injections (Blitzer, et al., 1986; Blitzer, et.al, 1988; Blitzer and Brin, 1991); however, others have found the opposite to be true (Ludlow, et al., 1988). According to Ludlow, et al., (1992) injections of BOTOX unilaterally avoided aphonia and aspiration in a majority of subjects while simultaneously reducing speech symptoms in all patients.

Blitzer, et al. (1988) conducted a study on the effects of BOTOX for the treatment of ASD and examined

improvements of the voice subjectively as well as through fiberoptic and indirect laryngoscopy. The results of this study indicated that all patients had the toxin effect within the first twenty-four to seventy-two hours (Blitzer, et al., 1988). This improvement or reduction of ASD symptoms lasted for three to six months (Blitzer, et al., 1988). Another researcher (Janovik et al., 1990) also found similar results for the time span of improvement. Breathiness and the experience of choking on fluids were exhibited by some of the subjects within the first few days after treatment (Blitzer, et al., 1988; Blitzer and Brin, 1991). Fiberoptic examination revealed no lesions prior to injection and following injection; indirect laryngoscopy revealed weak, but normal functioning vocal folds after treatment in some of the subjects (Blitzer, et al., 1988).

A study by Truong, et al. (1991) compared objective and subjective measures of the voice after four days in persons who received a BOTOX injection and those who received a placebo. Results found that there was no difference in either group's fundamental frequency and phonation time (Truong, et al., 1991). However, the perturbation scores and spectrographic analysis of the BOTOX treated group improved significantly (Truong, et al., 1991). Subjectively, the BOTOX treated group noticed improvement in their voice, whereas the placebo group had noticed none (Truong, et al. 1991). Research has found that persons with ASD prefer the BOTOX procedure over other

methods to help eliminate their symptoms and promote normal speech productions (Blitzer and Brin, 1991; Blitzer, et al., 1988).

Zwirner, Murry, Swenson, and Woodson (1992) recently conducted a study examining the effects of BOTOX therapy in patients with ASD through acoustic, aerodynamic, and videoendoscopic methods. Their study included 11 newly diagnosed patients with ASD (10 women, 1 man) who received unilateral treatment of BOTOX in the thyroarytenoid muscle. The mean age for the women in this study was 48 years, while the man was 59 years old. A control group consisting of 11 subjects (7 women and 4 men) was also created for comparison to the patient group. The format of the study included acoustic measures, airflow rates/aerodynamic measures, and videoendoscopy which were examined objectively one week prior to the treatment, followed by further objective analysis both one week and one month post-injection. Subjects were given the BOTOX injection through "a monopolar 27-guage 30-mm Teflon-coated hollow electromyographic needle percutaneously into the left thyroarytenoid muscle" (Zwirner, et al., 1992, pg. 401). Individual dosages, ranging from 5 to 30 units, were administered to each patient depending on the severity of the subject's symptoms.

The results found in Zwirner, et al., (1992) indicated significant improvement in the subjects' acoustic, aerodynamic, and videoendoscopic parameters after the

unilateral administration of BOTOX. Significant improvements were demonstrated 1 week after the BOTOX injection in both acoustic and videoendoscopic measures with additional improvement after 1 month. Acoustic analysis indicated that both jitter and shimmer measurements improved (not significantly) after 1 month in comparison to 1 week post-injection. Videoendoscopic data revealed that intrinsic laryngeal muscle hyperfunction was more effectively reduced than extrinsic muscle activity. Airflow/aerodynamic measurements indicated a significant increase 1 week post-injection, followed by a significant decrease to the normal range after 1 month. The two-phase effect of BOTOX on the phonatory system in persons with ASD is best supported by the aerodynamic observations.

STATEMENT OF THE PROBLEM

The BOTOX injection has become the desired "reliever" for many ASD patient's symptoms due to its safety and its availability in varying doses to meet the subject's needs. Researchers have examined subjectively the changes caused by BOTOX injections upon the vocal mechanism and have found positive findings (Blitzer, et al., 1988; Blitzer and Brin, 1991; Jankovic, et al., 1990; Truong, et al., 1991). In addition to this, objective analysis of the effects of BOTOX upon the laryngeal structure and function have occurred in research (Truong, et al., 1991; Zwirner, et al.) and again, data suggests that the drug has a positive effect on the vocal mechanism. In order to gain more

complete knowledge and to accumulate further data on the effects of BOTOX, more objective analysis is necessary. Zwirner, et al. (1992) provided valuable groundwork in the instrumental analysis of BOTOX on the vocal mechanism as a relief of ASD symptoms. In the present investigation, a comparative study to Zwirner, et al. (1992) was conducted. However, a bilateral, rather than unilateral, BOTOX injection occurred. Also, a transoral injection was performed instead of EMG placement of the needle. No research exists on controlling the two constraints described above (bilateral injections, transoral injections) for objective analysis on the effects of BOTOX for ASD. Due to this fact, this study was designed to expand knowledge of the effects of the BOTOX injection in persons with ASD on aerodynamic, acoustic, and videostroboscopic measures of voice production over a specified time period.

RESEARCH HYPOTHESES:

1. Acoustic analysis

a. There will be a difference greater than 3 standard deviations in fundamental frequency during sustained vowels collected 1 day prior to the BOTOX injection, 1 week post-injection, and 1 month post-injection, and this difference is greater than expected by chance.

b. There will be a difference greater than 3 standard deviations in jitter during sustained vowels

collected 1 day prior to the BOTOX injection, 1 week post-injection, and 1 month post-injection, and this difference is greater than expected by chance.

c. There will be a difference greater than 3 standard deviations in the average reading fundamental frequencies collected 1 day prior to the BOTOX injection, 1 week post-injection, and 1 month post-injection, and this difference is greater than expected by chance.

d. There will be a difference greater than 3 standard deviations in frequency ranges collected 1 day prior to the BOTOX injection, 1 week post-injection, and 1 month post-injection, and this difference is greater than expected by chance.

2. Aerodynamic Analysis

a. There will be a difference greater than 3 standard deviations in the phonation volume measures collected 1 day prior to the BOTOX injection, 1 week post-injection, and 1 month post-injection, and this difference is greater than expected by chance.

b. There will be a difference greater than 3 standard deviations in the flow rate measures collected 1 day prior to the BOTOX injection, 1 week post-injection, and 1 month post-injection, and this difference is greater than expected by chance.

c. There will be a difference greater than 3 standard deviations in the maximum phonation times collected 1 day prior to the BOTOX injection, 1 week post-

injection, and 1 month post-injection, and this difference is greater than expected by chance.

3. Videostroboscopic Analysis

There will be a difference greater than 3 standard deviations in the vibratory patterns of the vocal folds collected 1 day prior to the BOTOX injection, 1 week post-injection, and 1 month post-injection, and this difference is greater than expected by chance.

CHAPTER II - METHODS

SUBJECTS

Four female subjects diagnosed with adductor spasmodic dysphonia received their first BOTOX treatments for this disorder. Prerequisites for all subjects included no history of other voice disorders. Each subject received both verbal and written explanations of the procedures and methods to be utilized.

BOTOX INJECTION PROCEDURE

Each subject received two dosages of Botulinum Toxin injection of 1.25 units into each vocal fold. The toxin was injected transorally in order to assist in providing accurate placement for the injection into the vocal folds. The injection procedure itself was administered by a licensed otolaryngologist.

DATA COLLECTION

Before being tested, all subjects completed a brief case history pertaining to the onset, duration, and symptoms of the disorder, as well as any history of laryngeal pathology and vocal abuse.

All subjects were administered an objective voice evaluation on three of the following occasions: one-day prior to injection, one-week post-injection, and one-month post-injection. These objective evaluations included videostroboscopic, aerodynamic, and acoustic analyses. All of the testing procedures were performed in the offices of an otolaryngologist and a speech-language pathologist

specializing in voice disorders.

AERODYNAMIC AND ACOUSTIC ANALYSIS

The Nagshima Phonatory Analyzer (Model PS77H) was utilized in order to determine and evaluate aerodynamic measurements, which included phonation volume, air flow rate, and maximum phonation time. Acoustic measurements, which included fundamental frequency, jitter, and frequency range was determined by a Kay Elemetrics Model 6097 Visi-Pitch. A microphone was placed 4 inches in front of the subject's mouth during acoustic analysis.

Both aerodynamic and acoustic analyses were performed simultaneously by requesting each subject to sustain the vowels /a/, /i/, and /u/ at high, comfortable, and low pitch levels. Models were provided and trials were repeated if inappropriate pitch levels were produced. Reading fundamental frequency was obtained while the patients read a standard paragraph.

VIDEOSTROBOSCOPIC ANALYSIS

For stroboscopy, a rigid scope (R. Wolf 4450.47) was inserted into the back of the subject' oral cavity. With the use of stroboscopic lighting (Bruel and Kjaer 4914) and an R. Wolf Saticon Tube Camera, a videotape of laryngeal function was recorded during production of the sustained vowel /i/. A Panasonic Recorder (AG-630 MD) and Panasonic Color Monitor (BT S1990N) were used to record and monitor the images. A topical anesthetic (Cetacaine) was applied if any subject became sensitive to the presence of the scope in

the oral cavity.

DATA ANALYSIS

Acoustic and aerodynamic measures. Measures of fundamental frequency, jitter, maximum phonation time, phonation volume, and flow rate obtained during the voice analyses were averaged across three vowels for each subject. Means and standard deviations were computed across these measures. Pre- and posttests difference scores were calculated for each of the five measures. The differences between pretest versus posttest 1 (1 week), pretest versus posttest 2 (1 month), and posttest 1 (1 week) versus posttest 2 (1 month) were analyzed through the use of descriptive statistics. Any differences 3 times or more the standard deviation value of the compared baseline were considered and noted as a suspected meaningful change. Other forms of statistical testing (F-test, for example) would be considered an invalid measure due to the small number (N) of subjects.

Pre- and posttests difference scores were calculated for the lowest and highest frequencies in the frequency range. The three measures were compared separately (rather than calculating the total frequency range), to determine whether or not a suspected meaningful change occurred at either posttests. Pre- and posttests difference scores were also calculated for the reading fundamental frequency. The difference scores for the three pitch levels, the reading Fo and reading jitter values, were descriptively analyzed in order to determine any suspected meaningful change.

Videostroboscopic measures.

The videotapes of the stroboscopic analyses were evaluated by 2 speech-language pathologists with over 15 years experience in the area of voice disorders and expertise in videostroboscopy. Phonatory function analyzed in six dimensions were rated in the following areas: the configuration of glottic closure, the condition of the vocal fold edge, the amplitude of the vocal fold movement, the mucosal wave, phase closure and phase symmetry. A 6-point, equal-appearing interval scale was utilized for all measures except glottic closure, with 0 representing normal vibration and 5 representing a severe deviation from normal.

The examiners independently rated the videotapes. The examiners reviewed the tape together in cases of disagreement until a consensus was achieved. By rating the videostroboscopic evaluations of 2 randomly chosen subjects a second time, the intrajudge reliability could be determined.

An analysis comparing the pretest value to the posttests difference scores as well as the difference between posttests scores 1 and 2 is presented descriptively.

CHAPTER 3 - RESULTS

Subject 1

Means and standard deviations for the pre- and 2 posttests of Subject 1 are contained in Table 1. Results that represent at least 3 standard deviations (S.D.) between the pretest and 2 posttests are represented by a *.

Fundamental frequency

Comfort level. For Subject 1, the fundamental frequency for sustained tones /a, i, u/ changed from a mean of 182.0 Hz (pretest) to 203.8 Hz (posttest 1) and 200.3 Hz (posttest 2). Results indicated that the change after 1 week and 1 month versus pretest values were 9.1 times the pretest standard deviation (S.D.) value of 2.39 and 7.7 times the pretest standard deviation value for posttest 2. These calculations suggested meaningful change in the mean speaking frequency with both posttest mean values rising to lie within the normal range. The greatest change in fundamental frequency existed one week post-injection. The difference between posttests did not reach criterion (< 3 S.D.).

High level. For Subject 1, the fundamental frequency for sustained tones /a, i, u/ changed from a mean of 360.4 Hz (pretest) to 369.6 Hz (posttest 1) and 362.0 Hz (posttest 2). Results indicated that the change after 1 week and 1 month were 9.2 Hz and 1.6 Hz, respectively. There were no suspected meaningful difference in either post-test versus pretest, nor between the two posttests.

Low level. For Subject 1, the fundamental frequency for sustained tones /a, i, u/ changed from a mean of 166.1 Hz (pretest) to 162.5 Hz (posttest 1) and 162.4 Hz (posttest 2). There were no suspected meaningful differences in either posttest versus pretest, nor between the two posttests.

Jitter

Comfort level. For Subject 1, the jitter level for sustained tones /a, i, u/ changed from a mean of 3.26 (pretest) to .45 (posttest 1) and 1.47 (posttest 2). These differences between either pretest and posttests did not reach criterion. The difference between posttest one and two was 5.4 times the posttest one S.D. value of .19 and did reach criterion.

High level. For Subject 1, the jitter level for /a, i, u/ changed from a mean of .40 (pretest) to .47 (posttest 1) and 1.07 (posttest 2). Results indicated that the change in frequency perturbation after 1 week did not reach criterion. The pretest versus posttest 2 difference was 3.7 times the pretest S.D. value of .18 and reach criterion. The greatest change in jitter scores existed 1 month after the BOTOX injection administration and indicated a jitter score slightly outside the normal range. The difference between posttests was 6.7 times the posttest one S.D. value of .09 and did reach criterion.

Low level. For Subject 1, the jitter level for sustained tones /a, i, u/ changed from a mean of 4.66

(pretest) to .45 (posttest 1) and 1.47 (posttest 2). The difference between pretest and posttest 1 was 3.2 times the pretest S.D. value of 1.34 and did reach criterion. There was no suspected meaningful change between pretest and posttest 2. The difference between posttest one and two was 5.5 times the posttest one S.D. value of .14 and did reach criterion.

Phonation volume

Comfort level. For Subject 1, the phonation volume for sustained tones /a, i, u/ changed from a mean of 2550 ml (pretest) to 2520 ml (posttest 1) and 2653 ml (posttest 2). There were no suspected meaningful differences in either posttest versus pretest, nor between the two posttests.

High level. For Subject 1, the phonation volume for sustained tones /a, i, u/ changed from a mean of 2513 ml (pretest) to 2477 ml (posttest 1) and 2697 ml (posttest 2). Results indicated that the change after 1 month was 7.9 times the pretest S.D. value of 23.09 and did reach criterion. There were no suspected meaningful differences between pretest versus posttest one nor between the posttests.

Low level. For Subject 1, the phonation volume for sustained tones /a, i, u/ changed from a mean of 2363 ml (pretest) to 2440 ml (posttest 1) and 2457 ml (posttest 2). There were no suggested meaningful differences in either posttest versus pretest, nor between the two posttests.

Flow rate

Comfort level. For Subject 1, the flow rate for sustained tones /a, i, u/ changed from an average mean of 295 ml/sec (pretest) to 111 ml/sec (posttest 1) and 202 ml/sec (posttest 2). The decline in flow rate after 1 week indicated a difference 6.3 times the pretest S.D. value of 29.14. The posttest 2 difference was 3.2 times the pretest S.D. value. Both differences (pre- to posttests) appeared significant. These values indicated that the greatest change toward normal flow rate existed one week after the injection. The difference between posttest one and two was 17.5 times the posttest one S.D. value of 5.20 and did reach criterion.

High level. For Subject 1, the flow rate for sustained tones /a, i, u/ changed from a mean of 264 ml/sec (pretest) to 191 ml/sec (posttest 1) and 296 ml/sec (posttest 2). The decline in flow rate after 1 week was 6.7 times the pretest S.D. value (10.97) and did reach criterion. The difference in posttest 2 was 4.8 times the pretest S.D. value and did reach criterion. These calculations indicated the greatest change toward normal rate levels existed 1 week after the injection of BOTOX. The difference between posttests did not reach criterion.

Low level. For Subject 1, the flow rate for sustained tones /a, i, u/ changed from a mean of 191 ml/sec (pretest) to 107 ml/sec (posttest 1) and 113 ml/sec (posttest 2). There was no suggested meaningful difference in either

posttests versus pretest, nor between the posttests.

Maximum phonation time (MPT)

Comfort level. For Subject 1, the MPT changed from a mean of 8.7 seconds (pretest) to 22.8 seconds (posttest 1) and 13.8 seconds (posttest 2). The increase after 1 week was 17.8 times the pretest S.D. value of .79 and did reach criterion. The posttest 2 difference was 6.5 times the pretest S.D. value and did reach criterion. These results indicated the greatest increase in phonation time existed 1 week after the BOTOX injection. The difference between between posttest one and two was 4.5 times the posttest one S.D. value of 2.1 and did reach criterion.

High level. For Subject 1, the MPT for sustained tones /a, i, u/ changed from a mean of 9.5 seconds (pretest) to 14.5 seconds (posttest 1) and 9.2 seconds (posttest 2). The difference 1 week post-injection was 16 times the pretest S.D. value of .30 and did reach criterion. There was no suggested meaningful difference between posttest two versus pretest values, nor between the posttests.

Low level. For Subject 1, the MPT for sustained tones /a, i, u/ changed from a mean of 13.3 seconds (pretest) to 23.1 seconds (posttest 1) and 22.2 seconds (posttest 2). No apparent significance was calculated in either posttest versus pretest nor between the two posttests.

Frequency Range

For Subject 1, the frequency range changed from 143 Hz - 588 Hz (pretest) to 117 Hz - 477 Hz (posttest 1)

and 131 Hz - 651 Hz (posttest 2). The frequency range after 1 week increased by 1/8th of an octave to the pretest range of 2 octaves. Results indicated that the range after 1 month increased by 1/4th of an octave in comparison to the pretest range. These values indicated that the greatest increase in frequency range existed 1 month after the injection of BOTOX with both posttest results below the normal limits.

Fundamental Frequency While Reading

For Subject 1, the fundamental frequency while reading changed from 179 Hz (pretest) to 168 Hz (posttest 1) and 187 Hz (posttest 2). Results indicated that the changes after 1 week and 1 month were -9 Hz and +8 Hz, respectively. These values indicated the greatest change in fundamental frequency while reading existed 1 week post-injection with neither posttest within normal limits.

Videostrobscopic Findings

Pretest. For Subject 1, glottic closure was a spindle shape with a presence of slight compression of the ventricular folds (rating of 1). The following data were within normal limits (rated a zero): vertical level approximation; vocal fold edge; and non-vibrating portion. The amplitude and mucosal wave of vocal fold movement were moderately decreased. Phase closure was rated mildly impaired (rating of 2) and the closed phase predominated. Phase symmetry was rated moderately impaired (rating of 3) with irregularities in vocal fold movements occurring during

50% or more of the time.

Posttest 1 (1 week post-injection). For Subject 1, glottic closure was again a spindle shape with a presence of slight increased compression of the ventricular folds to a rating of 2. The following data were again within normal limits: vertical level approximation; vocal fold edge; and non-vibrating portion. No change was noted in mucosal wave. Amplitude improved to a rating of 1 and was slightly decreased in the right vocal fold, while the left vocal fold deviated to a rating of 4 in which amplitude was barely perceptible. Phase closure changed from a closed phase predominance to a open phase predominance (rating of -2). Phase symmetry remained constant with the pretest results.

Posttest 2 (1 month post-injection). For Subject 1, glottic closure was again a spindle shape with a presence of a decreased rating in the slight compression of the ventricular folds to a rating of 1. The following data were within normal limits (rated a zero): vertical level approximation; vocal fold edge; non-vibrating portion; and phase symmetry. Phase symmetry improved up to normal limits in comparison to pretest and posttest 1 scores. The amplitude remained a constant with the posttest 1 score with the right vocal fold, while the left vocal fold improved to a rating of 1 (slightly decreased amplitude). The mucosal wave of vocal fold movement improved to a rating of 1 (slightly decreased). Phase closure improved to a rating of -1 in which the open phase predominated minimally.

SUBJECT 2

Means and standard deviations for the pre and 2 posttests of Subject 2 are contained in Table 2. Results that represent at least 3 standard deviations (S.D.) between the pretest and 2 posttests are represented by a *.

Fundamental Frequency.

Comfort level. For Subject 2, the fundamental frequency for sustained tones /a, i, u/ changed from a mean of 227.9 Hz (pretest) to 175.7 Hz (posttest 1) and 194.4 Hz (posttest 2). The difference after 1 week was 9 times the pretest S.D. value of 5.76. The posttest 2 value is 5.8 times the pretest S.D. value. Both differences did reach criterion with the greatest change existing 1 week post-injection. The difference between posttest one and two was 16.1 times the posttest one S.D. value of 1.16 and did reach criterion (> 3 S.D.).

High level. For Subject 2, the fundamental frequency for sustained tones /a, i, u/ changed from a mean of 409.7 Hz (pretest) to 283.9 (posttest 1) and 410.5 Hz (posttest 2). The difference after 1 week was 139 times the pretest S.D. value of .90 and did reach criterion. There was no suggested meaningful difference between posttest 2 and the pretest. The difference between posttest one and two was 29 times the posttest one S.D. value of 4.36 and did reach criterion.

Low level. For Subject 2, the fundamental frequency for sustained tones /a, i, u/ changed from a mean of 155.0

Hz (pretest) to 139.9 Hz (posttest 1) and 155.5 Hz (posttest 2). There was no suggested meaningful change between the either posttest versus pretest. The difference between the posttests was 4.1 times the posttest one S.D. value of 3.82 and this difference did reach criterion.

Jitter

Comfort level. For Subject 2, the jitter score for sustained tones /a, i, u/ changed from a mean of .37 (pretest) to 1.30 (posttest 1) and .40 (posttest 2). The increase value after one week was 6.2 times the pretest S.D. value of .15 and did reach criterion. There was no suggested meaningful change between pretest versus posttest two. The greatest change existed 1 week after the BOTOX injection administration. The difference between posttest one and two was 5.3 times the posttest one S.D. value of .17 and did reach criterion.

High level. For Subject 2, the jitter level for sustained tones /a, i, u/ changed from a mean of .61 (pretest) to 1.31 (posttest 1) and .37 (posttest 2). There were no suggestive meaningful difference in either posttest versus pretest. The difference between posttest one and two was 4.1 times the posttest one S.D. value of .23 and did reach criterion.

Low level. For Subject 2, the jitter score for sustained tones /a, i, u/ changed from a mean of 2.64 (pretest) to 1.91 (posttest 1) and .53 (posttest 2). There were no suggested meaningful differences in either posttests

versus pretest, nor between the posttests.

Phonation volume

Comfort level. For Subject 2, the phonation volume for sustained tones /a, i, u/ changed from a mean of 2447 ml (pretest) to 2587 ml (posttest 1) and 2490 ml (posttest 2). There were no suspected meaningful differences in either posttest versus pretest, nor between the two posttests.

High level. For Subject 2, the phonation volume for sustained tones /a, i, u/ changed from a mean of 2210 ml (pretest) to 2607 ml (posttest 1) and 2707 ml (posttest 2). No suspected meaningful difference was observed between pretest and posttest 1. The posttest two value was 3.3 times the pretest S.D. value of 151.33 and did reach criterion. These values indicated the greatest change existing 1 month after the injection of BOTOX. The difference between posttest one to posttest two did not reach criterion.

Low level. For Subject 2, the phonation volume for sustained tones /a, i, u/ could not be tested on the pretest. Mean phonation volume changed from 2477 ml (posttest 1) to 2620 ml (posttest 2). The difference between posttest one to posttest two did not reach criterion.

Flow rate

Comfort level. For Subject 2, the flow rate levels for sustained tones /a, i, u/ changed from an average mean of 113 ml/sec (pretest) to 417 ml/sec (posttest 1) and 192

ml/sec (posttest 2). The mean rate increase after 1 week was 17.1 times the pretest S.D. values of 17.79. The mean rate for posttest two decreased and its difference was 4.4 times the pretest S.D. value. Both differences appeared to be significant. These values indicated the change in flow rate after 1 week was out of the normal range. The flow rate after one month was in the normal range as in the pretest value. The difference between posttest one and two was 5.3 times the posttest one S.D. value of 42.34 and did reach criterion.

High level. For Subject 2, the flow rate for sustained tones /a, i, u/ changed from a mean of 74 ml/sec (pretest) to 540 ml/sec (posttest 1) and 315 ml/sec (posttest 2). The flow rate after 1 week increased by 75.9 times the pretest S.D. value of 5.86. The flow rate decreased in posttest two and the difference was 13.0 times the pretest S.D. value. Both differences between posttests and pretest did reach criterion. These values indicated the greatest change in flow rate existed 1 week after the injection of BOTOX with both posttest scores lying outside the normal range for flow rate. The difference between posttest one and two was 9.5 times the posttest one S.D. value of 23.71 and did reach criterion.

Low level. For Subject 2, the flow rate for sustained tones /a, i, u/ at the pretest level could not be tested. However, posttest scores indicated flow rate levels of 361 ml/sec (posttest 1) and 136 ml/sec (posttest 2). The

decline in flow rate indicated an improvement 9.5 times the posttest one S.D. value of 23.63 and did reach criterion. The flow rate level in posttest 2 was within the normal range of flow rate.

Maximum Phonation Time (MPT)

Comfort level. For Subject 2, the MPT for sustained tones /a, i, u/ changed from a mean of 22.1 seconds (pretest) to 6.23 seconds (posttest 1) and 13.2 (posttest 2) seconds. The decreased phonation times after 1 week was 4.1 times the pretest S.D. value of 3.91 and did reach criterion. The difference between the pretest and posttest two did not reach criterion. These results indicated the greatest change in phonation time existed 1 week after the BOTOX injection. The difference between posttests was 12.0 times the posttest one S.D. value of .58 and did reach criterion.

High level. For Subject 2, the MPT for sustained tones /a, i, u/ changed from a mean of 29.8 seconds (pretest) to 4.83 seconds (posttest 1) and 8.7 seconds (posttest 2). The decrease after 1 week was 8.6 times the S.D. value of 2.89 and did reach criterion. The posttest two difference was 7.3 times the S.D. value and did reach criterion. These values indicated a decrease in phonation time after 1 week and 1 month versus pretest values with the greatest change in phonation time existing 1 week after the injection of BOTOX. The difference between posttest one and two was 12.6 times the posttest one S.D. value of .31 and did reach

criterion.

Low level. For Subject 2, the MPT for sustained tones /a, i, u/ could not be tested during the pretest administration of objective measures. However, posttest measures of maximum phonation time were obtained and indicated an average mean of 6.87 seconds (posttest 1) and 20.0 seconds (posttest 2). The difference between posttests was 29.2 times the posttest one S.D. value of .45. and did reach criterion.

Frequency Range

For Subject 2, the frequency range changed from 70.3 Hz - 778.2 Hz (pretest) to 119.0 Hz - 360.4 Hz (posttest 1) and 129.8 Hz - 557.1 Hz (posttest 2). Results indicated that the change after 1 week was one and one-half octave lower than the pretest range of 3 octaves. The change after 1 month was one octave lower than the pretest range. These values indicated the greatest change toward the norm existed 1 month after the injection of BOTOX with both posttests out of the normal range.

Fundamental Frequency While Reading

For Subject 2, the fundamental frequency while reading changed from 357.1 Hz (strained - pretest) to 173.3 Hz (posttest 1) and 191.8 Hz (posttest 2). Results indicated that the changes after 1 week and 1 month were -183.8 Hz and -165.3 Hz, respectively. These values indicated the greatest change in fundamental frequency while reading existed 1 week after the injection of BOTOX.

Videostrobospic Findings

Pretest: For Subject 2, glottic closure was complete with a slight compression of ventricular folds (score of 1). The following data were within normal limits: vertical level approximation; vocal fold edge; and non-vibrating portion. The amplitude of the vocal fold movement was moderately decreased (rating of 3). The mucosal wave was slightly decreased and rated a 1. Phase closure was mildly impaired (rating of 2) and the closed phase predominated. Phase symmetry was moderately impaired (rating of 4) with a generally irregular pattern of vocal folds movement existing.

Posttest 1 (One week post-injection): For Subject 2, glottic closure changed from complete to incomplete closure with a slight compression of ventricular folds. The following data again was within the normal range: vertical level approximation, vocal fold edge, and non-vibrating portion. The amplitude score decreased to a score of 2 (moderately decreased) in comparison to the pretest. The mucosal wave increased from a score of 1 to a score of 2 (moderately decreased). In addition, the phase symmetry declined toward normal measures with irregularities existing only during extremes of pitch or loudness (rating of 2).

Posttest 2 (One month post-injection). For Subject 2, glottic closure showed a posterior chink with a slight compression of the ventricular folds. The following data was within the normal range: vertical level approximation;

vocal fold edge; amplitude; mucosal wave, non-vibrating portion; phase closure, and phase symmetry. An improvement toward the normal movement of the vocal folds was noted in the areas of amplitude, mucosal wave, phase closure and phase symmetry.

SUBJECT 3

Means and standard deviations for the pre and 2 posttests of Subject 3 are contained in Table 1. Results that represent at least 3 standard deviations (S.D.) between the pretest and 2 posttests are represented by a *.

Fundamental Frequency

Comfort level. For Subject 3, the fundamental frequency for sustained tone /a, i, u/ changed from a mean of 185.0 Hz (pretest) to 198.4 Hz (posttest 1) and 207.9 Hz (posttest 2). There was no suggested meaningful difference between the pretest and posttests. The difference between posttest one and two was 6.3 times the posttest one S.D. value of 1.52 and did reach criterion (>3 S.D.).

High level. For Subject 3, the fundamental frequency for sustained tones /a, i, u/ changed from a mean of 361.0 Hz (pretest) to 436.7 Hz (posttest 1) and 507.0 Hz (posttest 2). The difference after 1 week was 21.6 times the pretest S.D. value of 3.5. The posttest two difference was 41.7 times the pretest S.D. Both posttests vs. pretest differences did reach criterion. The greatest change was found one month post-injection. The difference between posttest one and two was 43.9 times the posttest one S.D.

value of 1.6 and did reach criterion.

Low level. For Subject 3, the fundamental frequency for sustained tones /a, i, u/ changed from a mean of 160.0 Hz (pretest) to 171.0 Hz (posttest 1) and 154.1 Hz (posttest 2). The posttest one difference was 7.3 times the pretest S.D. value of 1.5. The posttest two difference was 3.9 times the pretest S.D.. Both posttests versus pretest differences did reach criterion. The results showed that the greatest change existed after 1 week post-injection. The difference between posttest one and two was 7.0 times the posttest one S.D. value of 2.4 and did reach criterion.

Jitter

Comfort level. For Subject 3, the jitter score for sustained tones /a, i, u/ changed from a mean of .52 (pretest) to 1.00 (posttest 1) and .67 (posttest 2). There were no suggested meaningful differences between pretest and posttests. The difference between posttest one and two was 4.7 times the S.D. value of .07 and did reach criterion.

High level. For Subject 3, the jitter score for sustained tones /a, i, u/ changed from a mean of .79 (pretest) to .84 (posttest 1) and .46 (posttest 2). There were no suggested meaningful differences in either posttest versus pretest, nor between the posttests.

Low level. For Subject 3, the jitter score for sustained tones /a, i, u/ changed from a mean of .61 (pretest) to 1.09 (posttest 1) and .84 (posttest 2). There were no suspected meaningful differences in either posttest

versus pretest, nor between the two posttests.

Phonation volume.

Comfort level. For Subject 3, the phonation volume changed from an average mean of 1830 ml (pretest) to 3423 ml (posttest 1). Posttest 2 values were unattainable due to spasms/breaks in the voice causing a recycling effect in the instrument. Results indicated that the improvement after 1 week was 3.3 times the S.D. value of 484.5 (pretest) and did reach criterion.

High level. For Subject 3, the phonation volume for sustained tones /a, i, u/ changed from a mean of 2483 ml (pretest) to 3707 ml (posttest 1). Posttest 2 values were unattainable due to spasms/breaks in the voice which caused a recycling effect in the instrument. Results indicated that the change after 1 week was 5.7 times the S.D. value of 213.6 (pretest) and did reach criterion.

Low level. For Subject 3, the phonation volume for sustained tones /a, i, u/ changed from a mean of 1093 ml (pretest) to 3310 ml (posttest 1). Posttest 2 results were unattainable due to spasms/breaks in the voice which caused a recycling effect in the instrument. The results indicated a difference after 1 week that was 12.2 times the pretest S.D. value of 181.8 and did reach criterion.

Flow rate

Comfort level. For Subject 3, the flow rate levels for sustained tones /a, i, u/ changed from a mean of 132 ml/sec (pretest) to 153 ml/sec (posttest 1). Posttest 2 scores

were unattainable due to spasms/breaks in the voice which caused a recycling effect in the instrument. There was no suggested meaningful difference between pretest and posttest one.

High level. For Subject 3, the flow rate levels for sustained tones /a, i, u/ changed from a mean of 171 ml/sec (pretest) to 289 ml/sec (posttest 1). Posttest 2 scores were unattainable due to spasms/breaks in the voice which caused a recycling effect in the instrument. Results indicated that the change after 1 week was 5.0 times the pretest S.D. value of 23.4 and did reach criterion. The subject's flow rate was within normal limits during the pretest; however, one week post-injection, the subject's rate was beyond normal limits.

Low level. For Subject 3, the flow rate levels for sustained tones /a, i, u/ changed from a mean of 107 ml/sec (pretest) to 140 ml/sec (posttest 1). Posttest 2 values were unattainable due to spasms/breaks in the voice which caused a recycling effect in the instrument. The difference after 1 week was 7.5 times the pretest S.D. value of 4.4 and did reach criterion. Both values were within normal flow rate levels.

Maximum Phonation Time (MPT)

Comfort level. For Subject 3, the MPT for sustained tones /a, i, u/ changed from a mean of 14.0 seconds (pretest) to 23.7 seconds (posttest 1). Posttest 2 values were unattainable due to spasms/breaks in the voice which

caused a recycling effect in the instrument. The improvement after 1 week was 11.4 times the pretest S.D. value of .85 and did reach criterion.

High level. For Subject 3, the MPT for sustained tones /a, i, u/ changed from a mean of 14.6 seconds (pretest) to 12.9 seconds (posttest 1). Posttest 2 values were unattainable due to spasms/breaks in the voice which caused a recycling effect in the instrument. There was not suggested meaningful difference noted between pretest and posttest 1.

Low level. For Subject 3, the MPT for sustained tones /a, i, u/ changed from a mean of 10.3 seconds (pretest) to 23.7 seconds (posttest 1). Posttest 2 values were unattainable due to spasms/breaks in the voice which caused a recycling effect in the instrument. The improvement after 1 week was 6.7 times the pretest S.D. value of 2.01 and did reach criterion.

Frequency Range

For Subject 3, the frequency range changed from 145 Hz - 970 Hz (pretest) to 153.7 Hz - 706.7 Hz (posttest 1) and 140.3 Hz - 1026 Hz (posttest 2). Results indicated that the change after 1 week was one-half octave lower than the pretest range of 2 octaves. The result after 1 month increased by 3/4th an octave to the pretest range. These values indicated the greatest increase in frequency range existed 1 month after the injection of BOTOX and was within normal limits.

Fundamental Frequency While Reading

For Subject 3, the fundamental frequency while reading changed from 154 Hz (pretest) to 204.9 Hz (posttest 1) and 185 Hz (posttest 2). Results indicated that the changes after 1 week and 1 month were 50.9 Hz and 31 Hz, respectively. These values indicated the greatest change in fundamental frequency while reading existed 1 week after the injection of BOTOX and was within normal limits.

Videostroboscopic Measures

Pretest. For Subject 3, glottic closure revealed an anterior chink and there was a slight compression of the ventricular folds. Vertical level approximation, vocal fold edge, and non-vibrating portion were all within normal limits. Both the amplitude and mucosal wave were slightly decreased (rating of 1). Phase closure was also rated a 1 with the closed phase slightly predominating. Phase symmetry was rated a 3 and was irregular more than 50% of the time.

Posttest 1 (One week post-injection): For Subject 3, glottic closure was incomplete with no supraglottic activity. Vertical level approximation , vocal fold edge, and non-vibrating portion were, again, all within normal limits. The degree of amplitude decreased to a severe level and was rated a 3. The mucosal wave rating was 1, the same as pretest conditions (slightly decreased). Phase closure was rated a 4 with the open phase moderately predominating. The phase symmetry improved to a rating of 2 in which

irregularities existed only during extremes in pitch or loudness.

Posttest 2 (One month post-injection): For Subject 3, a posterior glottal chink with a slight compression of the ventricular folds was noted. Vertical level approximation, vocal fold edge, mucosal wave, non-vibrating portion were all within normal limits. Amplitude of the vocal folds movements improved to a rating a 1 (slightly decreased amplitude). Phase closure improved to a rating of -1 with a slight predominate open phase. The phase symmetry improved to a rating of 1 with irregularities existing only during the end or beginnings of tasks.

SUBJECT 4

Means and standard deviations for the pre and 2 posttests of Subject 4 are contained in Table 4. Results that represent at least 3 standard deviations (S.D.) between the pretest and 2 posttests are represented by a *.

Fundamental Frequency

Comfort level. For Subject 4, the fundamental frequency for sustained tones /a, i, u/ changed from a mean of 221.5 Hz (pretest) to 255.8 Hz (posttest 1) and 213.5 Hz (posttest 2). The difference after 1 week was 12.2 times the pretest S.D. value of 2.82 and did reach criterion. There was no suggested meaningful difference between pretest and posttest two. The greatest change occurred during one week post-injection. The difference between posttest one and two was 7.0 times the posttest one S.D. value of 6.04

which did reach criterion (>3 S.D.).

High level. For Subject 4, the fundamental frequency for sustained tones /a, i, u/ changed from a mean of 344.3 Hz (pretest) to 414.2 (posttest 1) and 481.4 Hz (posttest 2). The difference after 1 week was 1165 times the pretest S.D. value of .06. The posttest two difference was 2285 times the pretest S.D. value. Both posttest differences did reach criterion with the greatest change noted at 1 month post-injection. The difference between posttest one and two was 25.7 times the posttest one S.D. value of 2.61 and did reach criterion.

Low level. For Subject 4, the fundamental frequency for sustained tone /a, i, u/ changed from a mean of 197.6 Hz (pretest) to 214.5 Hz (posttest 1) and 171.6 Hz (posttest 2). The difference after 1 week was 14.4 times the pretest S.D. value of 1.17. The posttest two difference was 22.2 times the pretest S.D. value. Both posttest differences did reach criterion with the greatest difference one month post-injection. The difference between posttest one and two was 37.1 times the posttest S.D. value of 1.15 and did reach criterion.

Jitter Comfort level. For Subject 4, the jitter scores for sustained tones /a, i, u/ changed from a mean of 1.68 (pretest) to 1.11 (posttest 1) and .50 (posttest 2). There was no suspected meaningful difference in either posttest versus pretest, nor between the posttests.

High level. For Subject 4, the jitter scores for

sustained tones /a, i, u/ changed from a mean of .29 (pretest) to .90 (posttest 1) and .58 (posttest 2). The changes in frequency perturbation after 1 week was 10 times the pretest S.D. value of .06. The posttest two difference was 4.8 times the pretest S.D. value. Both values did reach criterion and indicated that jitter remained constant and within normal limits after 1 week and 1 month post-injection. There were no suspected meaningful difference in either posttest.

Low level. For Subject 4, the jitter scores for sustained tones /a, i, u/ changed from a mean of 1.65 (pretest) to 1.00 (posttest 1) and .56 (posttest 2). There was no suggestive meaningful difference in either posttest versus pretest, nor between the posttests.

Phonation volume

Comfort level. For Subject 4, the phonation volume for sustained tones /a, i, u/ changed from a mean of 2323 ml (pretest) to 2160 ml (posttest 1) and 2177 ml (posttest 2). There was no suggested meaningful difference in either posttests versus pretest, nor between the posttests.

High level. For Subject 4, the phonation volume for sustained tones /a, i, u/ changed from a mean of 2150 ml (pretest) to 2177 ml (posttest 1) and 2383 ml (posttest 2). There was no suggested meaningful difference in either posttests versus pretest, nor between the posttests.

Low level. For Subject 4, the phonation volume for

sustained tones /a, i, u/ changed from a mean of 2400 ml (pretest) to 2120 ml (posttest 1) and 2043 ml (posttest 2). The difference after 1 week was 3.9 times the pretest S.D. value of 72.11. The posttest two difference was 5.0 times the pretest S.D. value. Both of these values did reach criterion and indicated the greatest change existing 1 month after the BOTOX injection. There was no suspected meaningful difference between the posttests.

Flow rate

Comfort level. For Subject 4, the flow rate for sustained tones /a, i, u/ changed from an average mean of 277 ml/sec (pretest) to 285 ml/sec (posttest 1) and 105 ml/sec (posttest 2). Results indicated no suspected meaningful difference between pretest and posttest 1. The posttest two difference was 6.2 times the pretest S.D. value and did reach criterion. These values indicated the greatest change in flow rate existing 1 month after the BOTOX injection falling into the normal range. The difference between posttest one and two was 18.3 times the posttest one S.D. value of 9.85 and did reach criterion.

High level. For Subject 4, the flow rate for sustained tones /a, i, u/ changed from a mean of 97 ml/sec (pretest) to 457 ml/sec (posttest 1) and 272 ml/sec (posttest 2). Results indicated that the decline rate after 1 week was 235.3 times the pretest S.D. value of 1.53. The posttest two difference was 114.4 times the pretest S.D. value. Both differences did reach criterion with the greatest change in

flow rate existing 1 week post-injection. The difference between posttest one and two was was 6.5 times the posttest one S.D. value of 28.35 and did reach criterion.

Low level. For Subject 4, the flow rate for sustained tones /a, i, u/ changed from a mean of 261 ml/sec (pretest) to 198 ml/sec (posttest 1) and 115 ml/sec (posttest 2). There was no suggested meaningful change between pretest and posttest 1. Results indicated that the decreased flow rate measures in posttest 2 was 6.6 times the pretest S.D. value of 22.05. These values did reach criterion and indicated the greatest change in flow rate existing 1 month post-injection decreasing toward normal limits. The difference between posttest one and two was 7.0 times the posttest one S.D. value of 11.8 and did reach criterion.

Maximum Phonation Time (MPT)

Comfort level. For Subject 4, the MPT for sustained tones /a, i , u/ changed from a mean of 8.4 seconds (pretest) to 7.6 seconds (posttest 1) and 20.8 seconds (posttest 2). The changes after 1 week did not reach criterion. The posttest two difference was 14.9 times the pretest S.D. value and did reach criterion. These values indicated the greatest increase in phonation time existing 1 month post-injection. The difference between posttest one and two was 19.1 times the posttest one S.D. value of .69 and did reach criterion.

High level. For Subject 4, the MPT for sustained tones /a, i, u/ changed from a mean of 22.3 seconds (pretest) to

4.8 seconds (posttest 1) and 8.8 seconds (posttest 2). Results indicated that the improvement after 1 week was 12.1 times the pretest S.D. value of 1.45. The posttest two difference was 9.3 times the pretest S.D. value. Both of these differences did reach criterion with the greatest increase in phonation time existing 1 week post-injection. The difference between posttest one and two was 66 times the posttest S.D. value of .06 and did reach criterion.

Low level. For Subject 4, the MPT for sustained vowels /a, i, u/ changed from a mean of 9.2 seconds (pretest) to 10.7 seconds (posttest 1) and 19.7 seconds (posttest 2). Results indicated no suggested meaningful difference between pretest and posttest 1. The improvement over 1 month was 11.1 times the pretest S.D. value of .95 and did reach criterion. These values indicated the greatest increase in phonation time existing 1 month post-injection. The difference between posttest one and two was 9.9 times the posttest one S.D. value of .91 and did reach criterion.

Frequency Range

For Subject 4, the frequency range changed from 126 Hz - 506 Hz (pretest) to 164.6 Hz - 778.2 Hz (posttest 1) and 159.9 Hz - 956.9 Hz (posttest 2). Results indicated that the change after 1 week was constant to the pretest range of 2 octaves. The results after 1 month increased by one-half an octave to the pretest range. These values indicated the greatest increase in frequency range existed 1 month after the injection of BOTOX with the posttest 2

result within normal limits.

Fundamental Frequency While Reading

For Subject 4, the fundamental frequency while reading changed from 235 Hz (pretest) to 254 Hz (posttest 1) and 219 Hz (posttest 2). Results indicated that the changes after 1 week and 1 month were 19 Hz and -16 Hz, respectively. These values indicated the greatest increase and change in fundamental frequency while reading existed 1 week after the injection of BOTOX with both posttests within normal limits.

Videostroboscopic Measures

Pretest. For Subject 4, a posterior glottal chink with a slight compression of ventricular folds existed. Vertical level approximation, vocal fold edge, and non-vibrating portion were all within normal limits. The amplitude and mucosal wave of vocal fold movement was rated a 2 (moderately decreased. Phase closure was rated a 2 with the closed phase predominating. Phase symmetry was rated a 2 with irregularities existing only during extremes in pitch or loudness.

Posttest 1 (One week post-injection). For Subject 4, an incomplete glottic closure was found with a slight compression of ventricular folds. Vertical level approximation, vocal fold edge, and the non-vibrating portion were all within normal limits. In addition, an improvement in mucosal wave to normal limits was observed. The amplitude of the vocal fold movement remained a score of 2 (moderately decreased). Phase closure decreased in score

to a -4 in which the open phase was predominate. Phase symmetry was rated a 2 in which irregularities exist during extremes of pitch or loudness.

Posttest 2 (One month post-injection). For Subject 4, a posterior glottal chink existed with a slight compression of the ventricular folds. Vertical level approximation, vocal fold edge, mucosal wave and non-vibrating portion all remained within normal limits. The amplitude improved to a score of 1 (slightly decreased). Phase closure improved to a -2 in which the open phase was predominate. Phase symmetry was rated a 3 in which irregularities occurred during 50% or more of vocal fold movement.

CHAPTER 4 - DISCUSSION

The purpose of this study was to observe aerodynamic, acoustic, and videostroboscopic measures of voice in first time BOTOX-injected subjects with adductor spasmodic dysphonia. In order to indicate whether or not an improvement existed after the BOTOX injection in persons with ASD, a comparison of normative data with the results of this study needed to be explored.

Normative Data

Some normal objective measures of voice have been studied (Baken, 1987; Colton and Casper, 1990; and Hirano, 1981). Normative data on aerodynamic measures indicates that the mean phonation volume at comfortable pitch is 3.3 liters for males and 2.1 liters for females (Baken, 1987). Average values of mean flow rate (MFR) range from 89 to 141 ml/sec (Hirano, 1981) with no difference consistent between males and females. Hirano (1981) indicated that a MFR greater than 200 ml/sec or less than 40 ml/sec should be considered abnormal if phonation is at habitual pitch and loudness. The average phonation time is 25-35 seconds for males and 15-25 seconds for females. Any maximum phonation time values smaller than 10 seconds should be considered abnormal (Hirano, 1981).

Normative research on acoustic measures shows that the mean speaking frequency lies between 110 Hz and 130.8 Hz for males and between 196 Hz and 261.6 Hz for females

(Hirano, 1981). Normative data on frequency range indicates that there are large individual variations found between individuals. The average frequency range exists approximately three octaves for males and two and a half to three octaves for females (Hirano, 1981).

Normative data on videostroboscopic measures indicates that glottic closure normally is complete. When glottic closure is incomplete the shape of the glottis at maximum closing should be drawn (Hirano, 1981). Hirano (1981) also found that incomplete glottal closure has been observed in the normal larynges in cases of posterior chinks, which are common in females. The edge of the vocal fold (superior layer of the lamina propria) should be loose, pliable, and of a white, pearlish color. If the vocal fold is stiffened by a pathology, vibratory movements would be disturbed (Colton and Casper, 1990). Amplitude of vocal fold movement is defined as the displacement of the folds. Any differences existing in the amplitude of the two vocal folds should be described. The speed of the mucosal wave (wave traveling on the mucosa of a normal fold from the inferior to its superior surface during vibrations) is typically .5 to 1 m/sec. Phase closure measure refers to the duration of the closed phase relative to the duration of the total vibratory cycle. Phase symmetry refers to whether or not the moving vocal folds appear similar to each other. If the vocal folds are not symmetrical, the clinician should describe how asymmetrical they are. Any

asymmetry noted between the vocal folds indicates that their mechanical properties are different (Hirano, 1981).

Comparison of Results to Normative Data

The results of this study demonstrated that persons with ASD appeared to experience some meaningful differences in their acoustic, aerodynamic, and videostroboscopic parameters both 1 week and 1 month following a bilateral, transoral BOTOX injection. All parameters showed variability in the results.

Established norms for acoustic and aerodynamic data are based primarily on comfortable pitch levels. Therefore, this discussion will focus on comparison of data obtained at comfortable pitch level for subjects in the present investigation with published norms.

Acoustic Measures

Overall results in acoustic measures were variable.

Fundamental Frequency. Two subjects improved into the normal range 1 week post-injection, and 1 of the 2 subjects maintained normal status after 1 month. All other results that reached the 3 standard deviation (S.D.) criterion remained outside the norm.

Jitter. All results that reached the 3 S.D. criterion remained outside the norm.

Frequency Range. Two subjects showed improvement into the normal range 1 month post-injection. All other results that reached the 3 S.D. criterion remained outside the norm.

Fundamental frequency while reading. One subject showed changes within the normal range after 1 week and 1 month, while another subject exhibited improvement after 1 week into the normal range, but did not maintain it. All other results that reached the 3 S.D. criterion remained outside the norm.

Although there were changes greater than 3 S.D. in acoustic parameters pre-versus posttests as well as between posttests, these changes did not always occur in a positive direction and did not always bring the subject's values into the normal range.

Aerodynamic Measures

Overall results in aerodynamic measures were variable. Flow rate. One subject improved into the normal range 1 week post-injection (but did not maintain this improved value), while another subject exhibited improvement 1 month post-injection. It should be noted, however, that what may be considered normal flow rate measures for the average population may not be the case in a person with ASD. All other results that achieved the 3 S.D. criterion remained outside the norm.

Maximum Phonation Time. Two subjects improved into the normal range 1 week post-injection, and one of these two showed a slight decrease in phonation time within normal limits after 1 month. One subject improved into the normal range after 1 month only. It should be noted, however, that what may be considered normal maximum phonation time

spans for the average population may not be the case in a person with ASD. All other results that reached the 3 S.D. criterion remained outside the norm.

Although some aerodynamic parameters (flow rate and maximum phonation time) reached the 3 S.D. criterion in pre-versus posttests as well as between posttests, abnormal measures often remained.

Videostroboscopic Measures

In videostroboscopy, there was a general pattern of minimal improvement or deviation after 1 week followed by a larger improvement or constant positive results after 1 month. Mucosal wave scores deviated in 2 out of 4 subjects after 1 week, but improved in all 4 subjects after 1 month with 3 of those 4 in the normal range (rating of zero). The general pattern for phase closure went from a closed phase (pretest observation) to a predominantly open phase (posttest 1 observation) indicating reduction in tension in 4 out of 4 subjects. All subjects improved after 1 month in phase closure with one subject achieving a normal score. In analyzing phase symmetry, 2 out of 4 subjects improved after 1 week in comparison to pretest data. Three out of four subjects improved after 1 month in phase symmetry while 2 of these achieved a normal rating. In amplitude, 2 subjects during posttest 1 improved in score by 1 point, while one subject deviated by 1 and the other remained constant to pretest values. All four subjects improved in amplitude by at least one point; one of these subjects

improved into the normal range. In phase symmetry, two out of the four subjects improved by rating of 1. With glottic closure, 3 out of 4 subjects changed to incomplete closure after 1 week. These same three subjects then also exhibited posterior glottal chinks one month post-injection which according to Hirano (1981) is commonly found in females and can be considered normal. It should be noted, however, that what may be considered a normal glottic closures for the average population may not be the case in a person with ASD. Supraglottic involvement of the ventricular folds improved in 2 out of 4 subjects 1 week post-injection and deviated in 1 subject. Improvement after 1 month was noted in one subject, while 2 out of 4 subjects deviated from the norm and exhibited increased involvement of the ventricular folds. All four subjects essentially continued to exhibit some involvement of the ventricular folds after 1 month. Overall, a general improvement near or within normal range resulted in most of the subject's videotapes in most parameters.

Three subjects in this study exhibited incomplete glottic closure 1 week post-injection. Incomplete closure is more ideal in a person with ASD because the space between the two vocal folds may prevent hyperadduction and spasms from recurring. Due to this change into incomplete closure, two subjects also exhibited an increase in flow rate and a decrease in maximum phonation time after 1 week post-injection which was indicative of the BOTOX taking

effect on the phonatory system. However, it should be noted that the two subjects' glottic closure, flow rate, and maximum phonation time were positive changes, even though the results were out of the normal range. These same two subjects after 1 month achieved normal results in glottic closure (posterior chinks), with decreased flow rate scores and increased maximum phonation time spans into or near the normal range. However, the more complete the glottic closure, the more likely the spasms may return. Ideally then, the patient who has received the BOTOX injection, should eventually learn to sense when the voice is just returning to that patients "normal" state in order to get reinjected before the spasms entirely return.

Comparison of Results to Previous Research

When comparing the results explored in this study to other research, many similarities and differences appeared. When all pitch levels were considered, the fundamental frequency changes in the present study were most dramatic 1 week after injection, which was similarly found in Zwirner, et al. (1992). This present study also agreed with Zwirner et al. (1992) that jitter scores do not significantly change or reach the 3 standard deviation criterion after 1 week. Two subjects' mean airflow rates at comfort level appeared as a meaningful change 1 month post-injection with an exhibited increase in flow rate at 1 week followed by a decreased flow rate at 1 month. This occurrence correlated with the Zwirner, et al. (1992)

research which found that the effect of BOTOX was often a two-stage effect. Zwirner, et al. (1992) did not find any significance between posttests in maximum phonation time. In the present study, maximum phonation time appeared as a meaningful change in 8 out of 12 trials between all pitch levels and subjects, but only one subject exhibited improvement into the normal range.

Researchers have found that many persons with ASD exhibit supraglottic involvement of the ventricular folds (Davis, Boone, Carroll, Darveniza, and Harrison, 1988; Ford, Bless, and Lowry (1990) . All four subjects in this present study exhibited ventricular involvement in the pretest observation. One subject improved into the normal range with no supraglottic involvement; however, all 4 subjects exhibited supraglottic compression of the ventricular folds after 1 month.

Results from this study indicated that the greatest improvement occurred in videostroboscopic findings with a general pattern of greatest improvement within the norm occurring 1 month post-injection. With acoustic and aerodynamic measures at comfort level, a few subjects exhibited suggested meaningful changes which improved into normal ranges after 1 week and 1 month; however, most of the subjects' results remained outside the norm. Overall, a majority of the measures do not fall within the normal ranges even after one month post-injection in either the acoustic, aerodynamic, or videostroboscopic measures.

Implications of the Study

The objective results of this study have important implications for the treatment of symptoms exhibited in patients with ASD. The changes that occurred following BOTOX injections seemed to be highly variable. There appeared to be some improvement in vocal fold vibratory patterns after 1 month, but these improvements were not always reflected in acoustic and aerodynamic data. A probable cause for the variability in the results may have been due to all the patients being first time recipients of the BOTOX treatment. Due to this factor of variability after the first injection, the subjects in this study may need several trials of the BOTOX in order to establish an appropriate titration level and achieve greater effects of the drug after 1 week and 1 month. Also, many persons who receive BOTOX injections often need to get used to a new manner of speaking. The subjects in this study may have utilized an inefficient manner of speaking in which the phonatory system was overdriven. Overdriving the vocal mechanism could theoretically strengthen the system which could cause stronger spasms to return before their due time.

Because there were only 4 subjects in this study, generalization of the results to other speakers is limited. If further research proved that the variability seen in these patients is common, then counselling may be necessary. Counselling could center around discussions on

expected variability in voice changes after the first injection and that subsequent injections may trigger a more meaningful change within the normal range.

Due to the limited number of subjects participating in this study, further research is suggested in order to investigate additional acoustic, aerodynamic, and videostroboscopic measures of vocal function following a bilateral, transoral injection of BOTOX.

Table 1. Results of objective measures for pretest, posttest 1 (1 week), and posttest 2 (1 month) for Subject 1.

LEGEND

Pre = pretest
S.D. = Standard Deviation
P1 = Posttest 1 (1 week)
P2 = Posttest 2 (1 month)
C = Comfort pitch level
H = High pitch level
L = Low pitch level
Fo = Fundamental Frequency
J = Jitter
PV = Phonation Volume
FR = Flow Rate
MPT = Maximum Phonation Time
FREQ RANGE = Frequency Range
READ = Reading
* = Appeared significantly different pre to posttest 1 and posttest 2

Table 1

	Pre mean	S.D.	P1 mean	S.D.	P1-Pre	P2 mean	S.D.	P2-Pre	P2-P1
Fo(C)	182.0	2.39	*203.8	1.29	21.8	*200.3	1.80	18.3	3.5
Fo(H)	360.4	7.41	369.6	3.06	9.2	362.0	4.63	1.6	7.6
Fo(L)	166.1	5.11	162.5	3.80	3.6	162.4	2.42	3.7	.1
J(C)	3.26	1.61	.45	.19	2.81	1.47	.72	1.79	1.02
J(H)	.40	.18	.47	.09	.07	*1.07	1.31	.67	.60
J(L)	4.66	1.34	*.40	.14	4.26	1.17	.17	3.49	.77
PV(C)	2550	75.50	2520	105.4	30	2653.3	49.33	103	133.0
PV(H)	2513	23.09	2477	202.6	36	*2696.7	32.15	183.7	219.7
PV(L)	2363	333.82	2440	72.11	77	2456.7	113.7	93.7	16.7
FR(C)	295	29.14	*111	5.20	184	*202	60.5	93	91
FR(H)	264	10.97	*191	74.85	73	*296	37.1	32	105
FR(L)	191	70.38	107	15.50	84	113	18.7	78	6
MPT(C)	8.7	.79	*22.8	1.99	14.1	*13.8	3.43	5.1	9
MPT(H)	9.5	.31	*14.5	5.98	5.0	9.2	1.01	.3	5.3
MPT(L)	13.3	3.71	23.1	2.93	9.8	22.2	4.68	8.9	.9
FREQ RANGE	143 Hz to 588 Hz		117 Hz to 477 Hz			131 Hz to 651 Hz			
Fo READ	179		168			187			

Table 2. Results of objective measures for pretest, posttest 1 (1 week), and posttest 2 (1 month) for Subject 2.

LEGEND

Pre = pretest
S.D. = Standard Deviation
P1 = Posttest 1 (1 week)
P2 = Posttest 2 (1 month)
C = Comfort pitch level
H = High pitch level
L = Low pitch level
Fo = Fundamental Frequency
J = Jitter
PV = Phonation Volume
FR = Flow Rate
MPT = Maximum Phonation Time
FREQ RANGE = Frequency Range
READ = Reading
* = Appeared significantly different pre to posttest 1 and posttest 2

Table 2

	Pre mean	S.D.	P1 mean	S.D.	P1-Pre	P2 mean	S.D.	P2-Pre	P2-P1
Fo(C)	227.9	5.76	*175.7	1.16	52.2	*194.4	4.0	33.5	18.7
Fo(H)	409.7	.90	*283.9	4.36	125.8	410.5	24.9	.80	126.6
Fo(L)	155.0	15.44	139.9	3.82	15.1	155.5	1.69	.5	15.6
J(C)	.37	.15	*1.30	.17	.93	.40	.20	.03	.90
J(H)	.61	.27	1.31	.23	.70	.37	.12	.24	.94
J(L)	2.64	2.40	1.91	.92	.73	.53	.24	2.1	1.38
PV(C)	2447	243.4	2587	83.27	140	2490	153.9	43	97
PV(H)	2210	151.3	2607	80.83	397	*2707	149.8	497	100
PV(L)	-	-	2477	105.04	-	2620	96.4	-	143
FR(C)	113	17.79	*417	42.34	304	*192	31.4	79	225
FR(H)	74	5.86	*540	23.71	466	*315	30.1	241	225
FR(L)	-	-	361	23.63	-	*136	11.3	-	225
MPT(C)	22.1	3.91	*6.23	.58	15.87	13.2	2.2	8.9	6.97
MPT(H)	29.8	2.89	*4.83	.31	24.97	*8.7	1.2	21.1	3.9
MPT(L)	-	-	6.87	.45	-	20.0	.70	-	13.1
FREQ RANGE	70.3 Hz to 778.2 Hz		119.0 Hz to 360.4 Hz			129.8 Hz to 557.1 Hz			
Fo READ	357.1 (strained)		173.3			191.8			

Table 3. Results of objective measures for pretest, posttest 1 (1 week), and posttest 2 (1 month) for Subject 3.

LEGEND

Pre = pretest
S.D. = Standard Deviation
P1 = Posttest 1 (1 week)
P2 = Posttest 2 (1 month)
C = Comfort pitch level
H = High pitch level
L = Low pitch level
Fo = Fundamental Frequency
J = Jitter
PV = Phonation Volume
FR = Flow Rate
MPT = Maximum Phonation Time
FREQ RANGE = Frequency Range
READ = Reading
* = Appeared significantly different pre to posttest 1 and posttest 2

Table 3

	Pre mean	S.D.	P1 mean	S.D.	P1-Pre	P2 mean	S.D.	P2-Pre	P2-P1
Fo(C)	185	10.0	198.4	1.52	13.4	207.9	5.26	22.9	9.5
Fo(H)	361	3.5	*436.7	1.61	75.7	*507.0	3.34	146	70.3
Fo(L)	160	1.5	*171.0	2.42	11	*154.1	2.83	5.9	16.9
J(C)	.52	.18	1.00	.07	.48	.67	.22	.15	.33
J(H)	.79	.56	.84	.43	.05	.46	.29	.33	.38
J(L)	.61	.36	1.09	.57	.48	.84	.45	.23	.25
PV(C)	1830	484.5	*3423	90.74	1593	-	-	-	-
PV(H)	2483	213.6	*3707	72.34	1224	-	-	-	-
PV(L)	1093	181.8	*3310	79.37	2217	-	-	-	-
FR(C)	132	41.6	153	46.52	21	-	-	-	-
FR(H)	171	23.4	*299	22.05	118	-	-	-	-
FR(L)	107	4.4	*140	6.93	33	-	-	-	-
MPT(C)	14.0	.85	*23.7	6.98	9.7	-	-	-	-
MPT(H)	14.6	1.65	12.9	1.27	1.7	-	-	-	-
MPT(L)	10.3	2.01	*23.7	1.79	13.4	-	-	-	-
FREQ RANGE	145 Hz to 970 Hz		153.7 Hz to 706.7 Hz			140.3 Hz to 1026 Hz			
Fo READ	154		204.9			185.0			

Table 4. Results of objective measures for pretest, posttest 1 (1 week), and posttest 2 (1 month) for Subject 4.

LEGEND

Pre = pretest
S.D. = Standard Deviation
P1 = Posttest 1 (1 week)
P2 = Posttest 2 (1 month)
C = Comfort pitch level
H = High pitch level
L = Low pitch level
Fo = Fundamental Frequency
J = Jitter
PV = Phonation Volume
FR = Flow Rate
MPT = Maximum Phonation Time
FREQ RANGE = Frequency Range
READ = Reading
* = Appeared significantly different pre to posttest 1 and posttest 2

Table 4

	Pre mean	S.D.	P1 mean	S.D.	P1-Pre	P2 mean	S.D.	P2-Pre	P2-P1
Fo(C)	221.5	2.82	*255.8	2.42	34.3	*213.5	1.66	8	42.3
Fo(H)	344.3	.06	*414.2	2.61	69.9	*481.4	2.50	137.1	67.2
Fo(L)	197.6	1.17	*214.5	1.15	16.9	*171.6	2.24	26	42.9
J(C)	1.68	.76	1.11	.27	.57	.50	.28	1.18	.61
J(H)	.29	.06	*.90	.61	.61	*.58	.15	.29	.32
J(L)	1.65	.45	1.00	.63	.65	.56	.14	1.09	.44
PV(C)	2323	75.06	2160	122.88	163	2177	168.82	146	17
PV(H)	2150	101.49	2177	118.46	27	2383	55.08	233	206
PV(L)	2400	72.11	*2120	105.36	280	*2043	75.72	357	77
FR(C)	277	27.54	285	9.85	8	*105	12.50	172	180
FR(H)	97	1.53	*457	28.35	360	*272	27.30	175	185
FR(L)	261	22.05	198	11.79	63	*115	45.09	146	83
MPT(C)	8.4	.83	7.6	.69	.8	*20.8	2.63	12.4	13.2
MPT(H)	22.3	1.45	*4.8	.06	17.5	*8.8	.91	13.5	4
MPT(L)	9.2	.95	10.7	.91	1.5	19.7	7.62	10.5	9
FREQ RANGE	126 Hz to 506 Hz		164.6 Hz to 778.2 Hz			159.9 Hz to 956.9 Hz			
Fo READ	235		254			219			

CONSENT FORM

UNIVERSITY OF CINCINNATI MEDICAL CENTER

OBJECTIVE ANALYSIS OF THE EFFECTS OF BOTULINUM TOXIN ON ADDUCTOR SPASMODIC DYSPHONIA

I. **INTRODUCTORY PARAGRAPH**

Before agreeing to participate in this study, it is important that the following explanation of the proposed procedures be read and understood. It describes the purpose, procedures, benefits, risks discomforts and precautions of the study. It also describes alternative procedures available and the right to withdraw from the study at any time. It is important to understand that no guarantee or assurance can be made as to the results. It is also understood that refusal to participate in this study will not influence standard treatment for the subject.

II. **OBJECTIVES OF THE STUDY**

I _____, agree to participate in a research study, the purpose of which is to evaluate the effects of botulinum toxin (BOTOX) on various aspects of my breathing and voice production. I agree that the BOTOX injection I receive is a clinical treatment in alleviating symptoms in Adductor Spasmodic Dysphonia and is physician prescribed. I agree that this study merely measures objectively the effects of the BOTOX injection on my breathing and voice production.

III. **PROCEDURES**

As a participant in this study, I will be asked to:

1. Complete a case history related to my past and present health status, description of my voice problem, and my use of the voice.
2. Read a short passage while being recorded with a Panasonic tape recorder so that overall pitch, loudness, and quality levels can be subjectively evaluated.
3. Sustain three vowel sounds at my most comfortable pitch level, my highest pitch level, and at my lowest pitch level into a tube while a microphone is placed four inches in front of my mouth. The vowel sounds are /i/ (as in tree), /a/ (as in hot), and /u/ (as in boot).
4. Obtain my frequency range by gliding on the sound /o/ as high as I can go, and then gliding on the same sound as low as I can go.
5. Provide videostroboscopy of my vocal folds which involves inserting a scope into the back of my mouth in order for a videotape of the vocal folds to be made. Should I be overly sensitive to the presence of the scope, a topical anesthetic (Cetacaine) will be applied. In that case, I will be informed not to take anything by mouth for fifteen minutes. There is a potential risk of Cetacaine inducing a hypersensitivity reaction.

Since Cetacaine safety in early pregnancy has not be established, it will not be used on me if there is a possibility that I might be pregnant and a view of the vocal folds is not possible because of a hyperactive gag reflex.

One goal of the study is to expand the present evidence which suggests that BOTOX has positive effects on the vocal structure. Another goal is to investigate the effects of the drug on the vocal mechanism over a specified period of time.

The complete voice examination that I will be participating in typically cost approximately $336.00; however, I will be receiving this for free.

I will be participating in the protocol for approximately twenty to thirty minutes. If there is a significant variance from the stated time period, I will be notified.

IV. RISKS

I understand that there are no risks associated with the test protocol of videostroboscopy. There have been no hazards documented in conjunction with videostroboscopy using the rigid endoscope. It is a standard procedure performed by speech pathologists as part of objective voice analysis. There is a potential risk of Cetacaine inducing a hypersensitivity reaction.

Because Cetacaine safety in early pregnancy has not been established, it will not be used if there is a

possibility that I might be pregnant and a view of the vocal folds is not possible because of a hyperactive gag reflex.

V. **PREGNANCY**

Because Cetacaine safety in early pregnancy has not been established, it will not be used on females if there is a possibility that the subject might be pregnant and a view of the vocal folds is not possible because of a hyperactive gag reflex.

If I am a woman and I am or should become pregnant, there is no risk to me or my fetus by participation in any other aspect of this study.

VI. **CONFIDENTIALITY**

A number will be assigned to each subject in the analysis and reporting of data to assure participant confidentiality.

VII. **AVAILABILITY OF INFORMATION**

Any questions that I may have concerning any aspect of this investigation will be answered by Dr. Linda Lee (556-4491).

VIII. **COMPENSATION**

The University of Cincinnati Medical Center follows a policy of making all decisions concerning compensation and medical treatment for injuries occurring during or caused by participation in biomedical or behavioral research on an individual basis. If I believe I have been injured as a

result of research, I will contact Dr. Linda Lee (556-4491).

IX. **FISCAL RESPONSIBILITY**

Funds are not available to cover the costs of any ongoing medical care, and I remain responsible for the cost of non-research related care. Tests, procedures, or other costs incurred solely for purposes of research will not be my financial responsibility. If I have questions about my medical bill relative to research participation, I may contact Dr. Linda Lee (556-4491).

XI. **THE RIGHT TO WITHDRAW**

I am free to withdraw from this investigation at any time. Should I wish to withdraw, I have been assured that standard therapy for my condition will remain available to me. I have been informed of the probable consequences of my withdrawal from the study.

XII. **IS THE SUBJECT CURRENTLY PARTICIPATING IN ANOTHER STUDY?**

[ ] Yes. If yes, please provide the Principal Investigator's name and title of the study.

[ ] No.

XIII. **WITNESSING AND SIGNATURES**

I, the undersigned have understood the above explanations and given to my voluntary participation in:

_____

__ Subject's signature/legal representative Date

There is a possibility that I might be pregnant.
_____

There is no possibility that I might be pregnant.
_____

_____

Investigator Date

_____

Witness Date

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