Abstract

Background and Objectives: To analyze vocal fold vibration following PHOTOFRIN-mediated photodynamic therapy (PDT) for the treatment of Tis and T1N0M0 squamous cell carcinoma (SqCCa) tumors of the larynx.

Study Design/Materials and Methods: This is a prospective study of 10 patients with Tis-T1N0M0 SqCCa tumors of the larynx treated with PHOTOFRIN-mediated PDT. Videostroboscopy examination was performed prior to and following PDT therapy. Videostroboscopy exams were randomized and were analyzed by a speech language pathologist and laryngologist specializing in voice disorders for vocal fold vibratory characteristics. The exams were scored based on glottic closure, supraglottic activity, vertical level approximation, vocal fold edge, amplitude, non-vibrating portion, phase closure, and phase symmetry.

Results: There was significant worsening in the non-vibrating portion of the affected vocal fold in the first 5 weeks following treatment with PDT, which is expected. Ten weeks following PDT therapy, there was notable improvement from the baseline in the amplitude, mucosal wave, and non-vibrating portion of the affected vocal fold but the changes were not statistically significant. Comparing the appearance to the immediate post treatment period there was notable significance when looking at amplitude, non-vibrating portion, and mucosal wave.

Conclusion: PHOTOFRIN mediated photodynamic therapy has been used as a primary modality to treat Tis-T1N0M0 tumors of the larynx and for treatment that has failed prior surgery and/or radiation therapy. PDT allows for preservation of function and structure to maintain voice with absence of systemic toxicity.

Introduction

It is estimated that this year there will be 12,290 new cases of laryngeal cancer in the United States. Many individuals will undergo surgical excision (cordectomy, partial laryngectomy, hemilaryngectomy, total laryngectomy), radiation therapy or a combination for tumor control.

Materials and Methods

Patients

Following IRB approval through the Henry Ford Health System, patients were selected if they had early stage laryngeal cancers (Tis-T1N0M0) and were treated with PDT-mediated photodynamic therapy. They were offered, but did not desire or receive alternate therapy such as cold knife surgery aside from biopsy, radiation therapy, or CO2 laser therapy and were not receiving concurrent alternate therapy with PDT. Tumor size was limited to 1 cm in depth or less, which is the optimal depth for Photofrin treatment (QuantaLogic Technologies, Inc., Vancouver, British Columbia, Canada). Patients were not able to undergo photodynamic therapy if they (1) were pregnant, (2) had hypotension to porphyrins, or (3) had impaired hepatic or renal function. Administration of PDT was performed as described in Schweitzer et al. publication.

Patients were included in this study if they had preoperative and postoperative videostroboscopy exams. Patients who met these criteria were treated between February 2003 to October 2008. Some patients had multiple post treatment videostroboscopy exams. The time variable of the post treatment videostroboscopy exam was divided into 5 distinct intervals as follows: Time 1 (baseline), Time 2 (greater than 0 but less than 5 weeks), Time 3 (greater than or equal to 5 but less than 10 weeks), Time 4 (greater than or equal to 10 but less than 20 weeks), and Time 5 (greater than or equal to 20 weeks).

Videostroboscopy

Videostroboscopy exams were performed with the Olympus flexible video endoscope (OMV2) (Olympus America Inc., Madison, NJ) or with the Kay rigid endoscope model 9106 or were recorded with the Kay Pentax RLS 9100B Rhinolaryngoscope (Koe Elemtics Inc., Lincoln Park, NJ). The video clips were saved and were randomized without patient identifying information. They were analyzed by a laryngologist and speech language pathologist using the Henry Ford Health System Videostroboscopy Interpretation chart in blinded fashion (Figure 1).

Statistical Analysis

The total scores for the videostroboscopy interpretation and perceptual voice analysis for the pre and post treatment videostroboscopy exams were examined using a mixed model analysis of variance approach (ANOVA). The overall analysis indicated a significant interaction with tumor side and a subsequent mixed model ANOVA showed a primary interaction. The primary interest in these analyses was the pairwise comparisons of the 4 subsequent time intervals back to the baseline evaluation. These analyses were evaluated for significance using Hochberg’s method to adjust the p-values of 0.05 was maintained. As our expectation was for an initial worsening followed by recovery we also examined the set of three pairwise comparisons of time intervals 1, 3, and 5 compared to time interval 2. A Hochberg’s approach was used here as well.

Discussion

Photodynamic therapy has been shown to be an effective treatment for early stage laryngeal squamous cell carcinoma. Biel et al demonstrated an 89% complete response rate while looking at 171 laryngeal squamous cell carcinoma patients with a 16 year follow up. A more recent prospective trial demonstrated 5 out of 6 patients demonstrating a complete response in Tis and T1 laryngeal squamous cell carcinoma patients. The only minor disadvantage of PDT compared to other modalities is that patients are photosensitive for a minimum of 4 weeks following the procedure, without systemic toxicities.

There is not a consensus in the literature as to which therapy (surgery, radiation therapy, or photodynamic therapy) is the best treatment for laryngeal tumors for voice conservation. Hall-Peltier et al examined 54 patients that underwent radiation therapy for treatment of early stage glottic carcinomas. When compared to controls, the patients who received radiation therapy were more likely to have abnormalities of vocal fold vibration during videostroboscopy.

Results

Table 1. On the tumor side the variables amplitude (AMP), mucosal wave (MUC) and vocal fold edge (FOLD) all showed a significant difference in the Time 2 to Time 1 (baseline) comparisons. With all three variables, the mean responses increased. This was also observed for the same comparisons on the tumor side for the non-vibrating portion (VIB). This same comparison of baseline to the initial period was borderline significant for amplitude (AMP) in the tumor side and non-vibrating portion (VIB) on the non-tumor side.

Table 2. The results indicate a significant change for the tumor side amplitude (AMP), at times 4 and 5, mucosal wave (MUC) at time 5, and non-vibrating portion (VIB), at times 3, 4 and 5. The non-tumor side had significant results for amplitude (AMP) at times 4 and 5, mucosal wave (MUC) at times 4 and 5, and non-vibrating portion (VIB) at time 5, and vocal fold edge (FOLD) at times 3, 4 and 5. With all variables the mean responses decreased.

Conclusion

In our study, patients undergoing PDT demonstrated initial significant impairment in the vocal fold vibratory parameters of mucosal wave, non-vibrating vocal fold and amplitude of vibration as well as appearance of vocal fold edge for both the tumor and non-tumor side. However, over a few weeks and months, consistent trends toward normal vibration occurred. Future studies should be aimed at a prospective comparison of photodynamic therapy to surgery and radiation and subsequent voice production results.

Bibliography