Multi-Institutional Experience With the In-Office Potassium Titanyl Phosphate Laser for Laryngeal Lesions

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Summary: Objective/Hypothesis. To determine the efficacy of the potassium titanyl phosphate (KTP) laser in lesion reduction, as well as preservation of mucosal wave and glottic closure in a cohort of patients with benign laryngeal pathology across multiple institutions.

Study Design. Multi-institutional and retrospective.

Methods. One hundred two patients who underwent in-office KTP procedures at multiple academic laryngology practices with at least a single follow-up visit were included. Image analysis was used to quantify vocal fold lesion size before and after treatment. A subset of images was analyzed by expert reviewers to determine the impact of this treatment on glottic closure and mucosal wave.

Results. Statistically, when considering all lesions, KTP induced a significant reduction in lesion size. Post hoc analyses revealed some lesion specificity; all lesions decreased in size, with the exception of vocal fold scar. Mucosal wave and glottic closure were improved or unchanged in more than 90% of the patients examined. The inter- and intrarater reliabilities of the lesion quantification method were excellent.

Conclusions. With great care and insight, the KTP laser appears to be a valuable tool for the treatment of various benign laryngeal lesions. Furthermore, KTP laser therapy appears to preserve or improve mucosal wave and glottic closure. The lesion measurement protocol previously described by our group appears to be reliable.

Key Words: Potassium titanyl phosphate–KTP–Vocal fold–Voice–Mucosal wave–Glottic closure.

INTRODUCTION

In laryngology, potassium titanyl phosphate (KTP) nonablative laser therapy continues to evolve since its introduction in 2006.[1] The fundamental treatment principle is based on the selective absorption of emitted radiation by oxyhemoglobin in red blood cells within vessels. This absorption, in theory, allows emitted radiation to effectively photothermally coagulate or photoablate vascular-based lesions while sparing the relatively nonvascular and normal epithelium and lamina propria from direct thermal injury, the so-called photoangiolytic effect. This selective ablation presumably makes the KTP advantageous in treating certain vocal fold lesions.

Several clinicians have championed the use of this and the similar wavelength pulse dye laser (PDL) for primary treatment of a variety of laryngeal lesions. In early investigations, Shapshay and colleagues[2,3] studied the effects of the PDL on recurrent respiratory papillomatosis (RRP), noting excellent disease control with little collateral mucosal injury. More recently, Zeitels and colleagues[4–6] reported on the utility of the PDL for RRP and glottal dysplasia. Other investigators have subsequently reported on the successful use of the PDL and KTP on a variety of different lesion types, including vocal process granulomas, Reinke's edema, and nonvascular vocal fold polyps.[7]

Early clinical investigators have postulated that the results were because of the effects of the laser on the microcirculation of the lesion.[3,4,6] Yet our data, and those of others,[7–9] indicate that nonvascular lesions seem to respond similar to vascular-based lesions. We, therefore, hypothesize that these effects are because of a nonspecific thermal injury surrounding target chromophores (ie, blood vessels), initiating a wound repair process that ultimately leads to lesion regression. Theoretically, because blood vessels primarily exist in the lamina propria, the injury and wound healing process after treatment with these lasers should occur in this layer, leaving the epithelium largely intact. However, as eloquently described by Ayala et al,[10] the angiolytic laser was shown to create a cleavage plane between the epithelium and basement membrane zone, in addition to increased intercellular spaces in the vocal folds associated with the destruction of epithelial cells and desmosomal damage. These apparently conflicting hypotheses further contribute to our limited understanding of the mechanism of clinically favorable outcomes.

Previously, we described the efficacy of in-office KTP treatment for the regression of benign vocal fold lesions using a novel technique to quantify vocal fold lesion size.[8] The present study expands on those previous findings by including data from two other major academic laryngology practices, but more importantly, the present study addresses two nontrivial experimental

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issues. First, although we described significant findings related to the reduction of vocal fold lesion size, we did not describe any functional properties of the treated tissue. To address this deficit, we sought to describe the impact of the KTP on mucosal wave and glottic closure. Anecdotally, vocal fold scarring after laser procedures does not appear to be a significant morbidity. However, in the present study, we sought to ensure that fibrosis resulting in aberrant mucosal wave and glottic closure did not accompany these procedures, in the context of improved lesion appearance.

The other major limitation regarding our previous work was more related to the lesion quantification technique. Objective quantification of vocal fold lesions is limited by the inability to directly measure abnormalities via two-dimensional endoscopic views. Variability in the distance from the laryngoscope tip to the lesion between examinations as well as variability in the angle of the laryngoscope tip to the superior surface of the vocal folds and interexaminer variability in the quality of the examination pose significant obstacles. We previously described a novel method of lesion size quantification, and we now sought to systematically investigate the inter-rater reliability of these measurements in hopes of more global utility. Ultimately, we hypothesize that the KTP is a reasonable tool for the treatment of diverse vocal fold disease, in the right hands. Furthermore, we hypothesize that our protocol for lesion size quantification is a reliable and relatively simple method for standardizing future work regarding lesion size and changes related to treatment.

MATERIALS AND METHODS

The present study was approved by the Institutional Review Boards at the New York University School of Medicine, Emory University School of Medicine, and the University of Texas Health Sciences Center and encompasses three retrospective lines of investigation. First, previously published data regarding the role of in-office KTP therapy for benign vocal fold lesions were promising, and we now included two additional academic laryngology practices to address issues related to sample size and interinstitutional variability. Second, one of the major criticisms of the previous work was the lack of functional data with regard to tissue pliability and glottal incompetence. We, therefore, sought to determine that mucosal wave and glottic closure were preserved in the context of the previously noted favorable data regarding lesion size reduction associated with the KTP. And finally, our previous work described a novel means to quantify vocal fold lesion size. Currently, we sought to further validate this method via multiple raters across multiple institutions to potentially confirm utility on a more broad scale.

Patient selection and data collection

Patients who were selected to undergo in-office 532-nm KTP laser treatment for benign laryngeal lesions from January 2007 to March 2011 from the New York University Voice Center, the Emory Voice Center, and the Voice Center at the University of Texas Health Sciences Center were considered for inclusion. Patients with RRP were excluded as this disease process has been previously studied, and the focus of the present study was the applicability to more common benign pathologic conditions. In addition, we felt that, given the variability in regrowth of these lesions, we could not affectively measure treatment efficacy in this group. Each patient in the cohort had undergone routine pre-KTP evaluation and treatment per the usual protocol at each individual institution.

Each patient was required to have at least one pretreatment and one follow-up videoendoscopic examination for inclusion. Furthermore, this imaging had to be of adequate quality for accurate lesion measurement, described in further detail in following sections. For the purposes of data analysis, up to two post-treatment examinations were included. Examinations beyond the second post-treatment visit were excluded. The specific laser settings and/or energy delivered were not used in the analysis for this study. Our previous work showed marked variability with regard to these variables, with little impact on clinical outcomes,[8] likely associated with variability in the laser-tissue interaction related to the characteristics of the lesion and the significant inconsistency in delivered fluence related to variability in the fiber-to-tissue distance. Voice rest after the procedures varied between institutions, ranging from 0 to 3 days.

Mucosal wave and glottic closure

A video-based survey was used to determine preservation of mucosal wave and glottic closure, before and after in-office KTP treatment. Eighteen pairs (six per institution) of videos collected via chip-tip flexible endoscopy were randomly selected across all study sites in a blinded manner. Each video pair included one pretreatment and one post-treatment video from initial follow-up (ie, approximately 1 month after the procedure). The 5-second videos clearly showed the entire length of the vocal folds during phonation at comfortable pitch and loudness, including audio. The video segments were presented in a consistent fashion—before and then after. This order was selected based on the specific experimental question and paired nature of the stimuli. These videos were sent along with a survey to six independent university-based laryngologists, who were not involved in the care of any of the patients included in the current cohort. Raters were not provided with any information regarding the clinical history of the patients. They were asked to rate the mucosal wave and glottal closure in each video pair as *Improved*, *Unchanged*, or *Worse* after KTP treatment. Four video pairs were repeated for a total of 22 videos to determine intrarater reliability. Descriptive statistics were used, and a Cronbach alpha coefficient was used to quantify intrarater reliability.

Measurement of lesion size

Quantification of lesion size was performed as described previously by our group.[8] Pre- and post-treatment, videoendoscopic examinations of each patient were reviewed, and still images were captured. Image analysis software, *ImageJ* (National Institutes of Health, Bethesda, MD), was used for all measurements. For each still image, vocal fold length measured from the anterior commissure to vocal process, lesion size (in pixels), and the angle between the vocal folds were acquired. Adjusted lesion size was then calculated by dividing the lesion size by