The Role of Indole 3 Carbinol in the Treatment of Adult Recurrent Respiratory Papillomatosis: A Retrospective Review

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ABSTRACT

Objectives: To determine the impact that indole-3-carbinol (I3C) has on videostroboscopy scores in patients with adult recurrent respiratory papillomatosis (RRP).

Study Design: Retrospective chart review

Methods: Patients in the treatment group were those who were placed on I3C therapy and those treated with standard surgical therapy alone represented the control group. In-office flexible videostroboscopy was used along with a standardized grading system to give a score for each patient's clinical progress. These scores were used to compare trends between patients in the treatment versus control group.

Results: Twenty patients met inclusion criteria in the study. Eight patients met criteria for the treatment group and twelve patients were placed in the control group. Mean follow up was 24.3 months and 30 months in the treatment and control groups, respectively. For patients in the treatment group, the mean videostroboscopy score at initial visit was 23.5 (n=6) and 16.6 (n=6) at the last recorded visit. These results show a 29.4% improvement in scores from the initial to final visit (p=0.04). The mean videostroboscopy score in the control group at the initial visit was 23.7 (n=7) and 20.6 (n=7) at the last recorded visit. This was a 13% improvement, however, not statistically significant (p=0.4).

Conclusions: This is the first study to assess the efficacy of I3C based on videostroboscopy score. Our results show that patients treated with I3C had a statistically significant improvement in videostroboscopy scores when compared to control patients. However, future prospective studies with a larger patient population are necessary.

INTRODUCTION

• Recurrent respiratory papillomatosis (RRP)
  • RRP is a disease that affects millions of adults worldwide with an incidence that is approximately 1.8/100,000 in the adult population.
  • RRP is predominately caused by the human papilloma virus types 6 and 11, and less commonly, HPV-11.
  • RRP is a benign disease, but has the potential to cause significant airway compromise due to its tendency to recur and spread in the respiratory tract.

• Indole-3-carbinol (I3C):
  • I3C is found in high concentrations in cruciferous vegetables and modulates estrogen metabolism resulting in a metabolite that promotes proliferation of epithelial cells.
  • Studies have shown the efficacy of I3C for treating cervical intraepithelial neoplasia, with significant regression of disease compared to patients receiving placebo.
  • A preliminary study conducted by Rosen et al., 2004 observed that I3C reduced the surgical intervals in adults with RRP.

METHODS AND MATERIALS

After protocol review and approval by the Institutional Review Board of Albany Medical Center, medical records of all patients who were treated for RRP by one attending otolaryngologist, S.S., from 2006-2013 were obtained and reviewed. A total of twenty patients were recovered from these records. Inclusion criteria included patients who were >18 years old, had an existing diagnosis of RRP, and had not been treated with I3C previously. Records were reviewed and information including patient age, gender, I3C use, number of surgeries for RRP before I3C use, number of surgeries for RRP during I3C use, surgical intervals for RRP during I3C use, length of I3C treatment, and noted side effects from I3C were obtained. All patients were treated with 300mg daily. The control group was designated as those patients treated with traditional surgery and not treated with I3C.

Videostroboscopy was used as the primary objective measure at each patient visit and was recorded for assessment of clinical progress. A grading system using a combination of both subjective and objective items was used to assess the clinical progress of all patients in the study. Severity numbers range from zero to four for five depending on the category. A higher number is associated with a more severe clinical picture. Each patient was then given a total score. These scores were used to compare trends between patients using I3C and those who were in the control group. The average score at initial and final visit for both experimental and control group were compared using a two-tailed t test to analyze statistical significance.

RESULTS

Figure 1: Average Videostroboscopy Scores

Average scores at Initial and Final visit are shown. Changes in average videostroboscopy score was significant for the I3C group (p=0.04) but not the control group (p=0.4).

Figure 2: Longitudinal videostroboscopy results (I3C Group)

Figure 3: Longitudinal videostroboscopy results (Control Group)

Table 1: Average Videostroboscopy Scores in Individual Categories of Grading System.

<table>
<thead>
<tr>
<th>Group</th>
<th>Voice Quality</th>
<th>Voice Range</th>
<th>Voice Intelligibility</th>
<th>Phonation</th>
<th>Breathiness</th>
<th>Patency</th>
<th>Tissue</th>
<th>Tissue Mass</th>
<th>Tissue Tone</th>
<th>Symmetry</th>
<th>Initial</th>
<th>Final</th>
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<td>3.2</td>
<td>2.1</td>
<td>2.5</td>
<td>2.5</td>
</tr>
<tr>
<td>Control</td>
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<td>3.1</td>
<td>2.3</td>
<td>2.1</td>
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<td>1.0</td>
<td>1.1</td>
<td>2.2</td>
<td>3.2</td>
<td>2.1</td>
<td>2.5</td>
<td>2.5</td>
</tr>
</tbody>
</table>

DISCUSSION

• I3C group:
  • 70% of RRP patients treated with I3C adjuvant treatment had complete or partial response
  • Determined by improvement in surgical intervals.
  • Did not evaluate treatment effect on patient’s individual examinations based on fiberoptic video examination.

• Our current study:
  • Treatment with I3C did significantly improve videostroboscopy scores at the final office visit compared to the start of I3C treatment.
  • Patients treated with I3C did have more improvement in videostroboscopy scores than the scores in the control group.
  • All categories of the videostroboscopy exam showed improvement in the I3C group.

• Other considerations:
  • The variability in response may be caused by differences in metabolism of I3C and estradiol in individual patients.
  • Studies have shown that HPV-11 may be more aggressive and have more malignant potential than HPV-6 related RRP when looking at duration disease activity and number of surgical procedures required.
  • HPV subtype was not known for the patients in this study and may have an influence on the results of the study.
  • We did not account for other adjuvant therapy, such as Cidofovir, in the control or I3C group.
  • It is not known if there are any additive or synergistic effects with the use of both I3C and Cidofovir, and we did not account for this.

CONCLUSION

This study demonstrated that treatment with I3C significantly improves videostroboscopy scores in patients with RRP compared to controls. Our data from individual patients also showed improvements in scores in all patients in the treatment group. Our study was limited by sample size and the retrospective nature of the study. In the future, a prospective, double-blinded randomized study would be beneficial.

REFERENCES