

Doctoral dissertation entitled

Evaluation of the effectiveness of local antiviral treatment in patients with recurrent laryngeal papillomatosis undergoing laser microsurgery.

Summary:

Recurrent respiratory papillomatosis (RRP) is a condition characterized by benign but recurrent growth of papillomas in the larynx, caused by chronic infection with non-oncogenic types of HPV (mainly types 6 and 11). Disease manifests with hoarseness, breathing difficulties, and in severe cases, life-threatening airway obstruction. RRP poses a clinical challenge due to its high tendency for recurrence.

Diagnosis relies on videostroboscopy combined with Narrow Band Imaging (NBI), which highlights lesion vascularization, as well as direct microlaryngoscopy with biopsy for histopathological confirmation. Treatment primarily involves microsurgical removal of lesions using CO₂ laser or other methods, aiming to maintain airway patency and preserve voice and swallowing function. Due to frequent recurrences, adjuvant therapies are used, including local administration of the antiviral drug Cidofovir, which inhibits viral replication and modulates immune response. Research is also exploring the use of bevacizumab, an anti-angiogenic agent, to limit disease progression.

Objective of the study:

The aim of the study was to evaluate the effectiveness of laser microsurgery of the larynx in patients with recurrent respiratory papillomatosis of the upper airway, combined with adjuvant local administration of the drug Cidofovir. Additionally, the study assessed the impact of the drug on immunomodulation and the cell cycle of epithelial and stromal cells in individuals with disease recurrence.

Materials and Methods:

The study included patients with recurrent respiratory papillomatosis (RRP) treated between 2019 and 2023 at the Department of Otolaryngology, Laryngological Oncology and

Maxillofacial Surgery, Dr. Jan Bziel University Hospital in Bydgoszcz. Two groups were analyzed: 24 patients who underwent immunohistochemical evaluation and 31 patients included in a prospective study. Preoperative qualification was based on a standard ENT examination, videostroboscopy, and endoscopy performed immediately prior to surgery.

The most common localization of lesions was the vocal cords, followed by the epiglottis and other laryngeal structures; in some patients, multifocal lesions were observed. Treatment involved microlaryngoscopic removal of papillomas using a CO₂ laser, while in recurrent cases, additional cidofovir injections (150–225 mg) were administered.

Tissue samples were subjected to immunohistochemical analysis using antibodies including CD4, CD8, p16, p53, p63, and Ki-67. Expression was assessed semi-quantitatively using the H-score method. Statistical analyses included nonparametric tests, correlation analysis, and Cox regression models, with $p < 0.05$ considered statistically significant.

Results:

In recurrent laryngeal papillomatosis, disease control and reduction of recurrence are crucial, especially since patients often require multiple procedures. Diagnostics should be complemented with NBI endoscopy, which allows precise assessment of vascularization and lesion margins.

In the studied group, 48% of patients required repeated interventions, and 33% underwent ≥ 3 procedures, highlighting the need for adjuvant therapies. CO₂ laser microsurgery combined with local administration of Cidofovir reduces recurrence risk by up to 50%. This therapy decreases inflammation (CD8+) and cell proliferation (p53, p63, Ki-67).

Smoking negatively affects disease course—smokers showed higher expression of p53 and p16. The combination of microsurgery with adjuvant Cidofovir prolongs intervals between procedures and improves patients' quality of life.

Conclusions:

1. Laser microsurgery of the larynx is an effective method for treating patients with recurrent laryngeal papillomatosis.

2. Simultaneous local administration of the drug Cidofovir during laryngeal microsurgery reduces the risk of disease recurrence in 50% of cases.
3. Local use of Cidofovir reduces inflammatory response in tissues and decreases epithelial cell proliferation, thereby lowering the risk of papilloma recurrence.
4. Tobacco smokers are at risk of a more aggressive course of the disease.