International Journal of Pediatric Otorhinolaryngology (2006) 70, 1911—1917

ELSEVIER

International Journal of Pediatric Otorhinolaryngology

www.elsevier.com/locate/ijporl

3.5-Year follow-up of intralesional cidofovir protocol for pediatric recurrent respiratory papillomatosis☆

Brian J. Chung[a,*], **Lee M. Akst**[a], **Peter J. Koltai**[b]

[a] *Head & Neck Institute, Cleveland Clinic Foundation, Desk A71, 9500 Euclid Avenue, Cleveland, OH 44195, United States*
[b] *Division of Pediatric Otolaryngology, Department of Otolaryngology/Head & Neck Surgery, Stanford University, Palo Alto, CA, United States*

Received 1 March 2006; received in revised form 19 June 2006; accepted 27 June 2006

KEYWORDS
Recurrent respiratory papillomatosis;
HPV;
Papilloma;
Cidofovir

Summary

Objectives: Intralesional injection of cidofovir has been described as an adjunctive treatment for pediatric recurrent respiratory papillomatosis (RRP). However, questions remain regarding the optimal dosing schedule and side-effect profile. The objective of this study was to describe patient outcomes following a standardized cidofovir protocol.
Methods: Eleven pediatric patients originally treated with a standardized stepped-dose protocol of intralesional cidofovir for RRP were followed for an extended observational period. Additional interventions, disease severity, and adverse outcomes were recorded.
Results: Five of 11 patients have required no further treatments following the original cidofovir protocol. Two patients initially achieved remission but have subsequently required additional treatment for recurrent disease. Four patients never achieved remission and have undergone multiple additional interventions. Mean follow-up time for all patients from the conclusion of the original study was 30.2 months (10—45). No adverse outcomes were noted.
Conclusions: Intralesional injection of cidofovir may have some potential as an adjunct in the treatment of RRP. Response to cidofovir is unpredictable. Further study of cidofovir is necessary to more clearly define whether the favorable responses observed represent a true treatment effect or simply reflect the natural history of the disease. Perhaps as important is to refine treatment protocols and informed consents that reflect the concern about the carcinogenic potential of cidofovir and to better characterize the drug's side-effect profile.
© 2006 Elsevier Ireland Ltd. All rights reserved.

☆ Work presented at the AAO-HNSF Annual Meeting as a podium presentation on 22 September 2004 in New York, NY.

* Corresponding author. Tel.: +1 216 444 4949; fax: +1 216 445 9409.
E-mail address: chungb@ccf.org (B.J. Chung).

0165-5876/$ — see front matter © 2006 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.ijporl.2006.06.018

1. Introduction

Recurrent respiratory papillomatosis is a relatively uncommon disease characterized by warty exophytic growths preferentially affecting the larynx. The disease is viral in origin and is caused most often by subtypes 6 and 11 of the human papilloma virus (HPV). Additional subtypes, such as 16 and 18, have been identified in RRP and are thought to pose a greater risk for malignant degeneration. The incidence of pediatric RRP in the US is estimated at 4.3 cases per 100,000 with an estimated cost between $40 and $123 million per year [1,2].

RRP is the most common benign neoplasm of the larynx in the pediatric population [3]. Although benign, the disease can be difficult to manage due to its recurrent nature and its ability to spread throughout the aerodigestive tract. Many patients require repeated operative debulking procedures to maintain a patent upper airway.

The recurrent nature of the disease and the need for repeated operative interventions has spurred interest in adjuvant therapies for RRP. Numerous agents, including interferon alpha, indole-3-carbinol, ribavirin, acyclovir, methotrexate, and isotretinoin have been tried. Unfortunately none of these agents has gained widespread acceptance as a useful adjunct in the management of RRP. Furthermore, questions related to systemic toxicity and appropriate dosing schedules persist for most of these agents.

Cidofovir ((*S*)-1-(3-hydroxy-2-phosphenylmethoxypropyl) cytosine) is an antiviral agent which was first approved for cytomegalovirus (CMV)-related retinitis in patients infected with human immunodeficiency virus (HIV). Cidofovir is a cytosine nucleoside analogue of deoxycytidine monophosphate which has demonstrated antiviral activity against a number of DNA viruses such as herpes simplex virus or CMV [4]. The active metabolite, cidofovir diphosphate, becomes incorporated into viral DNA and acts as a competitive inhibitor to viral DNA polymerase preventing viral replicates [5,6]. However, the antiviral activity in the setting of HPV infectivity is not clearly understood. HPV lacks DNA polymerase and therefore relies on the host DNA polymerase for DNA replication. The antiviral activity of cidofovir may be explained by the induction of apoptosis or activation of the host immune response [7—9].

Van Cutsem et al. [10] were the first to report on the successful use of intralesional cidofovir in an adult patient with squamous papilloma in the esophagus-hypopharynx. This was followed by data reported by Snoeck et al. [11] detailing favorable results using intralesional cidofovir for laryngeal papillomatosis. More recently Pransky et al. [12—14] published some favorable data using intralesional cidofovir as an adjunctive treatment for pediatric RRP. Despite these promising results, many questions still remain regarding the optimal number of treatments, concentration, and time interval between cidofovir treatments. Furthermore, there are legitimate concerns about the carcinogenic potential of cidofovir since the safety profile of this drug for this use has yet to be adequately elucidated.

Between 1 June 2000 and 31 December 2001 our institution enrolled 11 children in a prospective non-randomized case series in which adjunctive intralesional cidofovir was administered in conjunction with CO_2 laser treatments for RRP. Preliminary results have been previously published [15]. In this article we present an additional 3.5 years of follow-up data to further elucidate the role of adjuvant cidofovir in the treatment of pediatric RRP.

2. Methods

Between 1 June 2000 and 31 December 2001, 11 children diagnosed with RRP were enrolled in a prospective non-randomized study in which adjuvant intralesional cidofovir was administered in conjunction with CO_2 laser treatment (5 W, 0.2 s repeat). Treatments were performed under general anesthesia with suspension microlaryngoscopy. Patients initially underwent a series of four interventions at 1-month intervals, during which time the cidofovir concentration was maintained at 5 mg/mL. Disease severity was quantified based on the staging system described by Derkay et al. [16]. The extent of disease was considered mild for scores less than 5, and moderate for scores between 6 and 15. Severity and subsite scores were calculated 1 and 2 months after the fourth intervention. Patients demonstrating recurrent or recalcitrant disease were subject to another series of four interventions at 1-month intervals, again consisting of CO_2 laser treatment with adjuvant intralesional cidofovir administration. Patients were considered to have recurrent disease if the disease severity score reached 0 before returning, while recalcitrant disease was that which never completely resolved during treatment. For this second series of interventions cidofovir concentration was increased to 10 mg/mL. Patients were similarly reassessed 1 and 2 months following the fourth intervention using the higher cidofovir concentration. Parents were informed that cidofovir was being used in an ''off-label'' manner. They were also informed of the carcinogenic potential noted in some animal experiments. All parents were given the option to have

Download English Version:

https://daneshyari.com/en/article/4115421

Download Persian Version:

https://daneshyari.com/article/4115421

Daneshyari.com