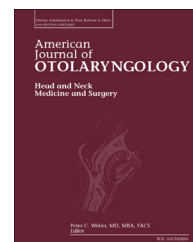


Available online at www.sciencedirect.com

ScienceDirect

www.elsevier.com/locate/amjoto

Original contributions

Positive therapy of andrographolide in vocal fold leukoplakia☆☆☆

Jue Xu, MD^{a,1}, Tao Xue, MD^{b,1}, Ying Bao, MD^c, Dong-hai Wang, MD^d, Bing-liang Ma^a, Chen-yi Yin^a, Guang-hui Yang^d, Gang Ren^a, Long-jiang Lan, MD^a, Jian-qiu Wang^a, Xiao-lan Zhang, MD^e, Yu-qin Zhao, PhD^{f,*}

^a Department of Otolaryngological Surgery, First People's Hospital Affiliated to Huzhou University, Huzhou, China

^b Laboratory of Molecular Medicine, First People's Hospital Affiliated to Huzhou University, Huzhou, China

^c Department of Hepatobiliary Surgery and Molecular Surgery, First People's Hospital Affiliated to Huzhou University, Huzhou, China

^d Department of Pharmacy, First People's Hospital Affiliated to Huzhou University, Huzhou, China

^e Department of Pathology, First People's Hospital Affiliated to Huzhou University, Huzhou, China

^f School of Food Science and Pharmacy, Zhejiang Ocean University, Zhoushan, China

ARTICLE INFO

Article history:

Received 19 August 2013

ABSTRACT

Purpose: Vocal fold leukoplakia is a premalignant precursor of squamous cell carcinoma. Although many efforts have been contributed to therapy of this disease, none exhibits a satisfactory result. The aims of this study were to investigate the effectiveness and feasibility of andrographolide therapy in vocal fold leukoplakia and to explore the preliminary mechanism underlying.

Materials and Methods: Forty-one eligible patients were enrolled in the study. The patients were treated for 10-minute exposures of 5 ml (25 mg/ml) andrographolide injection aerosols twice a day, and 2 weeks was considered as one treatment course. Electronic laryngoscope was used to observe the condition of vocal fold leukoplakia during the treatment. Every patient received one or two treatment courses, and the follow-up was carried out for 12 months. Toxic reactions of treatments were evaluated on the basis of the standards of the United States MD Anderson Cancer Center. Moreover, laryngeal carcinoma cell line Hep2 was applied to explore the mechanism of effect of andrographolide. Anti-proliferative effect on Hep2, cell nuclear morphology, express of mitogen-activated protein kinases (MAPK) and pro-apoptotic protein were detected after andrographolide treatment.

Results: We found that andrographolide exhibited significant curative effects on treatments, which were accompanied by thinning of the lesion of leukoplakia, reduction in the whitish surface area, and return of pink or red epithelium. A complete response up to 85% was observed, and no toxic side effect events occurred during the study. No patient with a complete response had a recurrence in the follow-up. Moreover, cellular experiments in

☆ Funding: Jue Xu MD is supported by Scientific Research Foundation of Huzhou University (Grant No. KX30072).

☆☆ No conflicts of interest are present.

* Corresponding author at: School of Food Science and Pharmacy, Zhejiang Provincial Key Engineering Technology Research Center of Marine Biomedical Products, Zhejiang Ocean University, Zhoushan 316002, China. Fax: +86 580 255478.

E-mail address: oceanow@163.com (Y. Zhao).

¹ Both Jue Xu MD and Tao Xue MD contributed equally to this work.

Hep2 indicated that andrographolide activated MAPK pathway and caspase cascade, and finally induced apoptosis in laryngeal carcinoma cell.

Conclusions: The advantages of andrographolide are connected with minimally invasive and localized character of the treatment and no damage of collagenous tissue structures, which are more convenient and less painful for patients. These results suggest that andrographolide treatment is a viable strategy for curing vocal fold leukoplakia.

© 2014 Elsevier Inc. All rights reserved.

1. Introduction

Vocal fold leukoplakia is the clinical term used to describe a white patch on the mucosa of vocal cords or larynx, which is related to tobacco smoking, excessive drinking or voice abuse [1]. Pathology of biopsy indicates that leukoplakia is attributed to epithelial dysplasia and hyperkeratosis [2]. Moreover, hyperkeratosis is considered as an important morphological feature in the process of cancerogenesis. It is reported that the presence of epithelial dysplasia can increase the risk of malignant transformation by up to 40% [3]. Although many efforts, such as surgery and laser ablation, have been contributed to treat the disease, results are still not satisfactory. Disadvantages of common treatments are revealed, including adverse effects, mucosa lesions and recurrences [4]. Therefore, studies on improvement in therapy of vocal fold leukoplakia are urgently needed.

Andrographolide (Fig. 1), a labdane diterpenoid, is the most active and important constituent of the medicinal plant *Andrographis paniculata*, which has long been used as a herbal medicine to prevent and treat upper respiratory tract infections, diarrhea, rheumatoid arthritis, and inflammation in Asia, Scandinavia and America [5-7]. It is reported that andrographolide could suppress IL-2 production and T-cell proliferation in a mixed lymphocyte reaction [8], and inhibit the activation of NF- κ B in asthma [9]. Recently, andrographolide shows activities in anticancer [10], including inhibition of cell growth of hepatocellular carcinoma [11], cervical carcinoma [12], prostatic adenocarcinoma [13], and breast carcinoma [14]. Meanwhile, more and more studies demonstrate that andrographolide has advantages of extensive pharmacological effects and less side effects in therapy. However, the curative efficacy of andrographis in vocal fold leukoplakia has not been investigated so far, and the mechanism is still not clear.

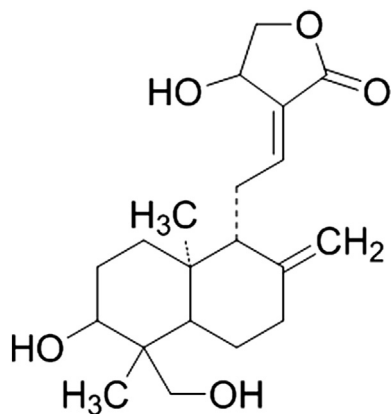


Fig. 1 – Structure of andrographolide.

It is known that aerosol inhalation is a direct method of drug administration for treatment of respiratory diseases. The great advantage lies in the fact that the drug deposited from inhalation results in a high concentration at the site of action [15]. In addition, a much lower concentration is produced in the systemic circulation following absorption, and it will reduce the possibility of adverse reactions.

In the present study, andrographolide-inhaled atomization was applied to cure vocal fold leukoplakia in the clinic, and laryngeal carcinoma cell line Hep2 was used as an in vitro model system to explore the mechanism underlying of andrographolide. Moreover, therapeutic toxicity was under strict monitor in order to evaluate whether andrographolide could be the candidate as a preventive agent for vocal fold leukoplakia.

2. Materials and methods

2.1. Patients

The study was performed at the Department of Otolaryngological Surgery of First People's Hospital Affiliated to Huzhou University. The study protocol complied with the Declaration of Helsinki and obtained approval from Ethical Committees. Candidates were identified in the head and neck oncology clinic. Patients, median age 46 years (range, 32-65 years), with at least one grossly visible leukoplakia lesion, with or without dysplasia, measuring 10 mm or more in diameter were included. Finally, 41 patients were enrolled in the study between January 2010 and June 2012. The detailed and important characteristics of patients were shown in Table 1.

Table 1 – Characteristics of patients treated with andrographolide for vocal fold leukoplakia.

Characteristics	Number of patients
Sex	
Male	34
Female	7
Histology	
Atypical hyperplasia	10
Moderate dysplasia	25
Severe dysplasia	3
Hyperkeratosis	3
History of risk factors	
Tobacco and alcohol	12
Tobacco only	9
Alcohol only	5
None identified	15

Download English Version:

<https://daneshyari.com/en/article/4103480>

Download Persian Version:

<https://daneshyari.com/article/4103480>

[Daneshyari.com](https://daneshyari.com)