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Review

Primary, secondary and tertiary prevention of human papillomavirus-driven head and neck cancers

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Screening

Abstract Human papillomavirus (HPV)-driven oropharyngeal cancers (OPCs) represent an increasing proportion of head and neck cancers that could become, in the next few decades, a public health problem in certain western countries. This significant epidemiological change strongly calls for preventive measures. Prophylactic HPV vaccination and screening programmes for early identification and treatment of premalignant lesions are currently being used to reduce the incidence of uterine cervical cancer, which is the paradigm of HPV-driven malignancy. These strategies have proven to be efficient as the incidence of cervical cancer has dramatically dropped since the 1960s in most countries where they are properly applied. The success of cervical cancer prevention encourages the development of similar approaches to prevent HPV-driven OPCs. However, a number of important limitations impede their application to HPV-driven OPCs, and the development of innovative and specific strategies dedicated to this disease are urgently needed.

This article provides an overview on primary, secondary and tertiary prevention of HPV-driven OPC and discusses some directions for future research.

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1. Introduction

Head and neck squamous cell carcinoma (HNSCC) is the sixth most common cancer worldwide, with an annual incidence rate of 600,000 cases [1]. These cancers, which are traditionally caused by excessive tobacco and alcohol consumption, are decreasing in most western countries since the 1980s due to the success of public health campaigns [2]. However, this trend is not homogenous, as cancers arising from the tongue base and the tonsils are on the rise as highlighted by recent epidemiological data from several western countries [3–5]. This increase is attributed to high-risk human papillomaviruses (HR-HPVs) and particularly to HPV16 [3–6], whose aetiological role in anogenital cancer has been clearly acknowledged for several decades [7].

Oral HPV infection is a sexually transmitted affection [8–10]. In a recent American study, the prevalences of oral HR-HPV and HPV16 infections were respectively 3,7% and 1%, which is significantly less than that at the genital level [11]. HPV-driven oropharyngeal cancers (OPCs) have specific clinical, pathological and molecular features compared to their HPV-negative counterparts [9,10,12,13]. These emerging cancers already represent the dominant form of OPCs in North America and Northern Europe, where up to 80% of OPCs are HPV-driven [3–5]. These significant epidemiological changes strongly call for preventive measures. Primary and secondary strategies are currently being used to prevent uterine cervical cancer, which is the most frequent and best-known HPV-driven malignancy [14]. These measures have proven their efficiency as the incidence of uterine cervical cancer has dropped dramatically since the 1960s in most countries where they are correctly applied [15]. From a theoretical standpoint, these good outcomes prompt the use of similar approaches to prevent HPV-driven OPCs. However, a number of important obstacles impede their application to the prevention of HPV-driven OPC, and the development of strategies specifically dedicated to this disease are urgently needed.

This article provides an overview on primary, secondary and tertiary prevention of HPV-driven OPC and discusses some directions for future research (the literature search methodology is described in the Supplementary data).

2. Primary prevention

Primary prevention aims to reduce the incidence of a disease within a population (Fig. 1). It involves interventions that are applied before there is any evidence of disease. As such, prophylactic vaccination against HR-HPV has proven its effectiveness. Several large randomized phase III clinical trials have demonstrated a significant reduction in the incidence of HPV 16/18 anogenital infections, genital warts and cervical and anal precancerous lesions, and have resulted in licencing and implementation of these vaccines in numerous national immunization programmes [16–21]. These very encouraging results suggest that prophylactic vaccination should decrease the incidence of anogenital cancers. However, given the considerable time lag between HR-

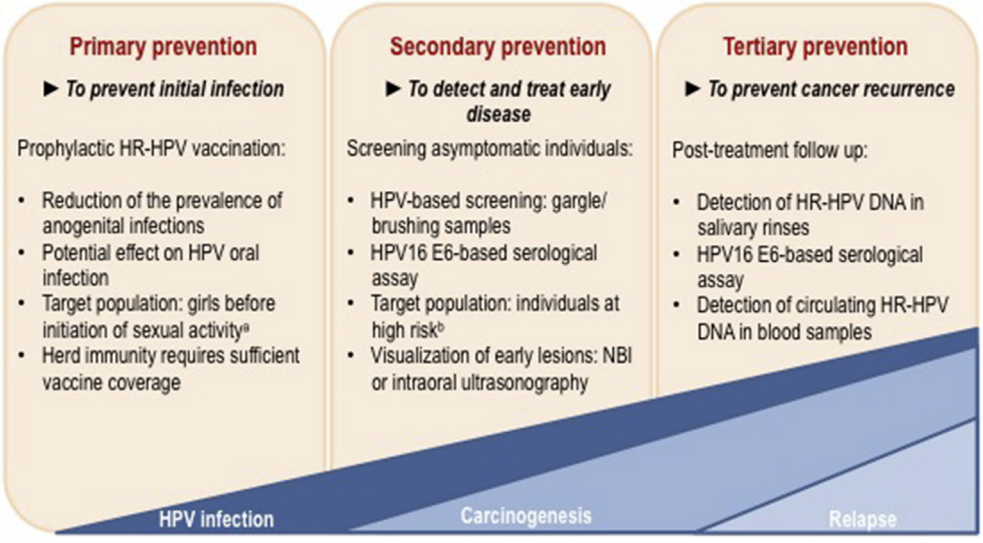

Fig. 1. Schematic representation of primary, secondary and tertiary strategies for the prevention of HPV-positive OPC and related morbidities. The consecutive occurrences of HPV primary infection, OPC development and post-treatment cancer relapse are represented as blue triangles. The different potential prevention methods/approaches, as well as relevant target populations are described. a – Most guidelines target adolescent girls (11–13 years of age) and some include a catch-up programme to varying degrees for older female age groups. Vaccine was also recommended for men in the USA, Canada and Australia but with different policies [16]. b – The concept of individuals at high-risk is discussed in section 3.2.1.