Association between Human Papillomavirus Infection and Risk of Prostate Cancer

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ABSTRACT

Human papillomavirus (HPV) is one of the most common causes of sexually transmitted diseases worldwide and is the etiological agent of cervical and other anogenital malignancies. Since HPVs have been shown to possess oncogenic potential, an association between HPV infection and prostatic cancer (PCa) has been suggested. There are conflicting reports on the impact of HPV infection on the development of prostate cancer. The aim of this article is to review the studies that investigated the association between HPV and PCa. The results of this review demonstrated the divergent frequencies of HPV positivity in PCa in different geographic areas.

Key words: Human Papillomavirus, Prostatic Cancer

Introduction

Prostate cancer (PCa) is the most common neoplasm of men and the second most common cause of cancer-related death in them (1). Risk factors for prostate cancer include older age, African American race, family history and probably diet and occupational exposures (2, 3).

Identification of an infectious agent for PCa would be an important issue. Human papillomavirus (HPV) is one of the most common causes of sexually transmitted diseases (STDs) of viral etiology worldwide (4). HPV is also associated with the development of several epithelial cancers such as cervical, anal, penile, esophageal, and vaginal cancers (5-7). Both HPV-16 and 18 have been associated with the development of these cancers, and HPV-16 is responsible for approximately 50% of these malignancies. The association of HPV-18 varies geographically and is stronger for adenocarcinoma of the cervix (8).

In 1990, McNicol and Dodd reported that HPV type 16 and 18 are present in normal and cancer tissues of human prostate (9, 10). Since that time, a growing number of studies had reported HPV in prostate carcinoma tissues by different methods (9-20).

Inflammation, regardless of etiology, can initiate carcinogenesis by 1) cell and genome damage, 2) promoting cellular replacement and 3) secretion of...
cytokines and growth factors, which can enhance cell replication, angiogenesis, and tissue repair (21, 22). The carcinogenesis of HPV depends on the expression of viral E6 and E7 oncogenes, which inhibit tumor suppressor proteins p53 and pRb, respectively (23). The various somatic genetic abnormalities associated with prostate cancer suggest that there is not a single dominant molecular pathway required for prostate carcinogenesis. To date, numerous germline mutations as well as somatic genome alterations (like mutations, rearrangements, amplifications, deletions and DNA methylation) have been identified for prostate cancer susceptibility (22, 24, 25).

HPV is capable of in vivo replication in the prostate and therefore may play a role in the transmission of this virus to sexual partners (4). The association of HPV infection, as a sexually transmitted disease, with the risk of prostate cancer may be explained by the role of chronic inflammation and genomic oxidative damage to prostate epithelium (22).

In this review, we described the findings of studies on the association between HPV and PCa.

Methods

Literature Search Strategy

An initial search was done using Medline from 1990 to July 2010. The search was restricted to studies published in the English language. The terms of prostatic cancer and human papillomavirus were used for the search. In addition, the references from the identified studies were reviewed to help ensure that all published papers had been reviewed. The literature search identified 30 studies that have investigated the relationship between HPV and prostate cancer.

Studies investigating the association between HPV and prostate cancer

Since 1990, approximately 30 surveys investigated the HPV presence in prostate cancer samples. These studies were conducted in different countries and mainly were case-control studies (4, 9-20, and 26-44). Some studies reported that HPV infection was related to prostate carcinoma. They showed that HPV prevalence varies from 2% to 100% in PCa samples. The most reported types of HPVs in prostate cancers were HPV types 16, 18, 33 and 31 (9-13, and 29-31). Some studies showed that HPV was equally prevalent in PCa and BPH and even in normal prostate tissue (16, 18, 20) and some investigations revealed that HPVs could not be detected in normal and cancer prostate tissues (33-39).

In 1990, McNicol and Dodd reported that HPV type 16 and 18 are present in normal and cancerous tissues of human prostate by PCR and southern blot (9, 10). Again, in 1991 they studied HPV presence in PCa cases and BPH controls by PCR and found the same results (31).

In a study by Masood et al. (32) HPV was not detected in PCa and BPH samples by ISH method. Another case-control study of prostate cancer patients also found no HPV-DNA in cancers or benign prostatic tissues and reported no difference in seropositivity to HPV-16 or 11 in case patients and control subjects (4). In other studies by Effert (33), Serfling (34), Gherdovich (35), Saad (36), Gazzaz (37), Bergh (38) and Noda et al. (39) also HPV was not detected in cancerous prostate tissues.

In a study by Anwar et al. (11), HPV-16, 18 and 33 were present in 41% of PCa cases and none of the controls. Leiros et al. (29) also found HPV-16 and 11 in 41.5% of PCa and none of the BPH samples. Balis et al. (30) showed HPVs in 4.8% of prostate cancers and Tu et al. (17) showed HPV-16 and 18 in 2% of PCa cases and 6% of metastasis but in none of the controls. Sarkar et al. (12) detected HPV-16 in 13% of PCa and PIN case and Suzuki et al. (19) found HPV-16 in 16% of PCa subjects. In Dillner et al. (43) study, seropositivity to HPV-18, the HPV type that most strongly associated with cervical adenocarcinoma, was associated with increased risk of subsequent development of prostate cancer.

Other studies by Ibrahim (16), Moyert-Lalle (18), Wideroff (20), Rosenblott (26), Carozzi (27), Korodi (28) Serth (40), Hisada (41), Adami (42) and Aghakhani et al. (44) showed that HPV detection rates were not significantly different in PCa and normal prostate tissues.

These divergent frequencies of HPV positivity...
in prostate cancer samples may be due to populational, environmental, geographical, and genetic heterogeneities, beyond methodological detection differences.

**Summary and conclusion:**
Epidemiological studies suggested a role of HPV in the etiology of PCa. These studies had examined the relation between HPV infection and prostate cancer and had shown conflicting results. If an association of HPV with prostate cancer have confirmed, it is good news for cancer prevention prospects; so the role of HPV in prostate carcinogenesis should be clarified. Due to the availability of HPV vaccines, these data may provide preventive measures against the one of the most frequent malignancies.

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**References:**


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