OHTAC Recommendation

Anal Dysplasia Screening

July 2007

This recommendation summary has been prepared by the Medical Advisory Secretariat of the Ministry of Health and Long Term Care on behalf of the Ontario Health Technology Advisory Committee.

OHTAC Ontario Health Technology Advisory Committee

Anal Dysplasia Screening

Issue Background

The Ontario Health Technology Advisory Committee (OHTAC) met on June 22, 2007 and reviewed the role of anal dysplasia screening in those at high risk. The review was at the request of the MOHLTC AIDS Bureau and the Director of the Immunodeficiency Clinic at University Health Network (UHN). A previous review on this subject performed by the Medical Advisory Secretariat (MAS) in 2003 at the request of MOHLTC Laboratory Services Branch resulted in a recommendation that screening anal pap testing not be reimbursed at that time due to limited information on disease aetiology, screening test performance and effectiveness of treatment of early stage disease.

Anal cancer, like cervical cancer is one of a broader group of anogenital cancers known to be associated with sexually transmitted viral infection. The human papillomavirus (HPV) is extremely prevalent, particularly in young sexually active populations and sexual practices involving receptive anal intercourse lead to significantly elevated risk for anal dysplasia and cancer, particularly in those with immune dysfunctions.

Anal cancer is rare occurring at a rate of about 1-2 per 100,000 in the general population. It is the least common (about 4%) of the lower gastrointestinal cancers in contrast to colorectal cancers which remain the third most commonly diagnosed malignancy. Certain segments of the population, however, such as men who have sex with men (MSM), HIV positive men and women, women with genital dysplasia / cancer, transplant and other chronic immune suppressed patients have a high susceptibility to anal cancer.

The risk for anal cancer has been reported to be increasing in HIV positive males and females particularly since the introduction of effective antiretroviral therapy (HAART) in the mid 1990's. In San Francisco, one of the areas reporting the highest rates - anal cancer rates were reported to increase in men aged 40 to 64 years from 3.7 to 20.6 per 100,000 between 1996 and 1999. The introduction of effective viral therapy has been said to transform the AIDS epidemic in developed countries essentially into a chronic disease state of long term immunosupression.

In Ontario there are about 25, 000 people living with HIV infection – over 6,000 of them are women. In 2005, approximately 1,670 were newly diagnosed with HIV infection, 28% of these infections are in women, a doubling since 1999. It has also been estimated that 1 out of 3 people living with HIV are unaware of their infection.

Screening is a two step process with an initial pap test to collect cells for cytological examination followed by a referral of those with abnormal cytology for an anoscopic examination, similar to colposcopy, and possible biopsy. Anal cytology is classified by the same standardized classification system used for cervical cytology. Several HPV DNA detection technologies, Hybrid 11 Capture and the polymerase chain reaction (PCR) are currently available to detect and differentiate HPV viral strains.

Unlike cervical cancer there are no universally accepted guidelines or standards of care for anal pre cancer lesions and at present, there are no formal screening programs provincially, nationally or internationally. The New York State Department of Health AIDS Institute just released recommendations (June 2007) for the routine use of anal Pap testing in high risk groups. In Ontario, reimbursement currently exists only for Pap tests for cervical cancer screening. There is no reimbursement for anal Pap testing in men or women and HPV screening tests for cervical or anal cancer are also not reimbursed.

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The current request was to consider the use of anal Pap test as a screening test for anal dysplasia in patients at high risk of anal cancer. The scientific evidence base was evaluated through a systematic literature review. Assessments of current practices were obtained through consultations with various agencies and individuals including: the MOHLTC AIDS Bureau; Public Health Infectious Diseases Branch MOHLTC; Cancer Care Ontario; HIV/AIDS researchers; pathology experts and HIV/AIDS clinical program directors.

OHTAC Findings

- No direct evidence exists to support the effectiveness of an anal Pap test screening program on anal cancer mortality or morbidity. However there are several parallels with cervical pap testing for cervical cancer.

- Sexually transmitted infection with the human papillomavirus (HPV) is currently the acknowledged common causative agent for both anal and cervical cancer (International Association Research Cancer 2005, 2007 monographs).

- Anal cancer rates in high risk populations are approaching those of cervical cancer before the implementation of Pap testing.
    - High risk groups have been identified including HIV positive MSM (RR=59.5), HIV negative MSM (RR=37.9), HIV positive women (RR=7.2), women with prior anogenital disease (RR=6.3), transplant (RR=10) and other immunosuppressed patients.
    - The increasing rates of anal cancer in Ontario (0.26/100,000 in 1971 to 1.06/100,000 in 2001) are following the reported trends of increasing rates in other jurisdictions.
    - The epidemiology of HPV infection and anal precursor lesions, however, differs from cervical cancer in that the prevalence of anal HPV infection and pre cancer lesions in the MSM population are age independent and consistently high across a wide age range.
    - The rates of disease progression for both cervical and anal high grade lesions are not known because high grade lesions are generally treated in both regions and studies to follow their progression would be unethical because high grade lesions are the presumed pre cancer state for both cancers.

- The anal Pap test has similar operating characteristics as the cervical Pap test and testing in both regions is dependent on the assessment of morphology based technology.
    - Despite identifying a diverse group of patients at risk for anal cancer, the Pap test was mainly evaluated only in HIV positive males.
    - The variability and low sensitivity [range 46% (95%CI; 35%-56%) – 93% (95%CI; 87%-97%)] for the anal Pap test was also reported for the cervical Pap (range 30% - 80%) in several systematic reviews.
    - The specificity of the anal Pap test ranging from 33% (95%CI; 18-52) to 81% (95%CI; 76%-85%), however, was generally lower than that for the cervical Pap (range 86%-100%), particularly for the HIV patients and would yield a higher rate of false positives resulting in over referrals for anoscopic follow up.

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- No studies were found on the use of HPV DNA testing in the screening or diagnostic setting for anal dysplasia.
    - The reported prevalence HPV infection in high risk groups, particularly for HIV positive MSM, however, was sufficiently high to preclude any utility of HPV testing as an adjunct to anal Pap testing.

- Unlike for cervical precancer lesions there is no widely practiced standard of care.
    - The treatment options for lesions in the two genital regions are similar but options involving a definitive surgical resection in the anus are more limited than in the cervix because of the higher risk of complications.
    - A range of ablative therapies has been applied in this region with variable tolerance, success and recurrence particularly in the HIV positive MSM.
    - There is limited data available on the effectiveness of available treatment options.
    - New approaches involving topical immune stimulants, antiviral agents and therapeutic HPV vaccines are under investigation.

OHTAC Recommendations:

- OHTAC does not recommend screening of high risk individuals at this time based on the low specificity for cytological screening, inadequate evidence of effectiveness for current treatment of precancerous lesions, high recurrence rates, and no evidence that cytological screening reduces the risk of developing anal cancer

- This recommendation should be reviewed annually to assess new studies that report refinement of diagnostic and treatment modalities or larger sample sizes and/or longer follow-up periods

- The annual review should include consultation with the MOHLTC AIDS Bureau sponsored anal dysplasia working group and the physician researchers from UHN and Sunnybrook who are leaders in the field of anal cancer screening.

- OHTAC recognized the international excellence of research being undertaken in the province that includes cohort studies to evaluate the effectiveness of treatments for anal precancerous lesions. This clinical research will likely be greatly beneficial to people at high risk of developing anal cancer. OHTAC wishes to be kept appraised of new published information from this initiative in particular.