AN INVESTIGATION CERVICAL CANCER, HUMAN PAPILLOMAVIRUS (HPV) INFECTION AND STEROID CONTRACEPTION

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ABSTRACT

PROJECT ONE

Introduction

HPV is detected in about 99.7% of cervical cancers. However, the HPV type distribution in South African women is unknown.

Objectives

To determine HPV-type distribution among women with cervical dysplasia in relation to oral contraceptive usage.

Methods

Prospective cross-sectional study of four groups of patients according to oral contraceptive usage: non-users, users of less than five years duration, users of between five years and ten years and users of more than ten years duration. Swabs of the cervix were analysed for HPV DNA using polymerase chain reaction method.

Results

A total of 124 women were recruited for the study. There were 75 HIV-infected patients (seroprevalence 61%). Of the 102(82%) HPV-positive patients, 79 patients had high-risk HPV DNA (78%). In terms of the four oral contraceptive groups, high-risk HPV DNA was detected in 70% (n=21), 79% (n=22), 90% (n=21) and 71% (n=15) of patients, respectively. The odds of having HPV DNA was six times higher for the combination of contraceptive users of less than 5 years duration/non-users (OR 5.9, 95% CI: 1.87 - 18.77).

There was no change when adjustment was made for age (OR 6.1, 95% CI: 1.9 - 19.4). HPV DNA types 16 and or 18 was present in a total of 21 patients (49%) (non-contraceptive users and users < 5years duration) versus 15 patients (42%) who used oral contraceptives of more than 5 years duration (p=0.524). HPV type 16 was the commonest HPV type detected (20.2%) and HPV type 58 was the next commonest high-risk HPV type (16.1%). HPV types 58 and 33 was detected in a much greater percentage of our population and HPV 16 in a much smaller percentage of our population compared with a non-South African population.

Conclusion

The findings of this study demonstrate an interesting distribution of HPV types in a South African population.

PROJECT TWO

Introduction

Various risk factors have been implicated in the causation of cervical cancer including human papillomavirus (HPV), the early genes (*E6* and *E7*) of which encode the main transforming proteins. Studies have suggested that steroid hormones may enhance the expression of these genes leading to loss of p53 gene-mediated cell apoptosis.

Methods

A total of 120 cervical tissue samples were obtained from patients with proven cervical cancer. Patients who used depo-medroxyprogesterone acetate steroid contraception were recruited as part of the study arm. Only HPV DNA type 16 samples were used for the study. Controls included three cell lines (CaSki, SiHa, & C33A) and glyceraldehyde-3-phosphate dehydrogenase (GAPDH) was used as an internal housekeeping gene. Of 120 patients, there were 111 patients with HPV type 16 identified. Of this number, RNA was present in 63 samples. There were 30 women (30/63) who used steroid contraception. In relation to patients who used contraception, HPV 16 *E6* gene expression was present in 79% (n = 23) and 88% (n = 30) of steroid users compared to nonusers, respectively. In total there were 25 patients (40%) with expression of the HPV 16 *E6*I* gene and 30 patients with expression of the *E6*II* gene. There were 57% of steroid users (n = 17) who had expression of the *E6*I/E6*II* gene, compared to 52% (n = 17) of nonusers (P = 0.800).

Conclusion

From a molecular level, this study reflects almost similar distribution of the HPV 16 E6/E6*1 and E6*11 and does not confirm the role of injectable progesterones in cervical carcinogenesis. Further studies with larger patient numbers are needed.

DECLARATION

This study represents work done by the author.

The research described in this thesis was performed in the Department of Obstetrics and Gynaecology, Inkosi Albert Luthuli Central Hospital, Durban, South Africa.

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PRESENTATION ARISING FROM THE PROJECT

1. **ACADEMIC MEETING DEPARTMENT OBSTETRICS GYNAECOLOGY 2005**
2. **THE OBSTETRIC AND GYNAECOLOGY UPDATE, UNIVERSITY OF PRETORIA, MAY 2009.**
3. **SOUTH AFRICAN SOCIETY OBSTETRICIANS GYNAECOLOGISTS 2010**

PUBLICATIONS ARISING FROM THE STUDY

1. **An investigation into oral contraceptive use, human papilomavirus (HPV)-type distribution and cervical intraepithelial neoplasia, Durban, South Africa. Eur J Gynaecol Oncol 2009 (accepted for publication).**
2. **The interaction between steroid hormones, human papillomavirus type 16, *E6* oncogene expression and cervical cancer. Int J Gynecol Cancer 2003; 13: 1-9.**
3. **The role of steroid contraceptive hormones in the pathogenesis of invasive cervical cancer: a review. Int J Gynecol Cancer 2003; 13: 103-110.**
4. **Use of the nested reverse transcription-polymerase chain reaction for the detection of human papillomavirus 16 E6 transcriptional activity in cervical cancer: A technical perspective. Eur J Gynecol Oncol 2003; 25: 51 - 54**

TABLE OF CONTENTS