Original Research Paper Gynaecology

OVER EXPRESSION OF HPV E6/E7 ONCOPROTEINS IS A MARKER OF PROGRESSION TO CERVICAL CANCER

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ABSTRACT

AIM:-
For early detection and treatment of cancer cervix developing new molecular diagnosis method for screening and treating the patient on the E6 gene expression.

SUBJECTS & METHODS:-

STUDY DESIGN: Prospective Study
STUDY PERIOD: AUGUST 2015 to AUGUST 2016
PLACE OF STUDY: Department of Obstetrics & gynaecology, Government Kasturba Gandhi Hospital, Triplicane, Chennai.

METHODS:-Colposcopy guided blood material, mucus and inflammatory cells from cervix with help of plastic spatula and endocervical brush, this material into liquid fixative solution. The suspended cells are gently sucked on to filter membrane and filter pressed onto glass slide to form thin monolayer. The liquid is employed to test HPV infection making it a cost effective technique.

KEYWORDS : .

INTRODUCTION

HPV E6/E7 oncoproteins initial the development of cervical cancer. Their over expression, is associated with significantly increased risk of CIN and cervical cancer.

HPV-HR infection
PERSISTENT
↓
DNA-HPV
INTEGRATIVE
In cellular genome
↓
Celullar Cycle
Deregulation:
E6/E7
Over expression
↓

- Inactivation of P53 Tumour suppressor gene
- Blocking Celular Apoptosis
- Modulation of G Protein pathway
- Modulation of Immune System
- Induction of telomerase activity
- Modulation of Chromosomal Stability

↓
CANCER

SO E6/E7 MRNA oncoprotein test for early detection of cervical cancer.

Highly Specific molecular test

It has Highest positive predictive value, Correlates to disease with PPV above

90% vs DNA testing PPV of 43% in cells for CIN2 plus

No false negative cases as seen in LBC test

Methodology (Materials and Methods)

Setting:
This study will be carried out in the Institute of Social Obstetrics, Kasturba Gandhi Hospital, Madras Medical College, Chennai-3, in association with department of Pathology, Kasturba Gandhi Hospital, Madras Medical College, Chennai -3.

Method:
Those who are VIAVILI Positive cases, HPE report shows CINII & CIN III going to do this study under colposcopy guided with the help of plastic spatula / endocervical brush remove the blood material, mucus and inflammatory cells, This material into the liquid fixative Solution. The suspended cells are then gently sucked onto the filter membrane and the filter is pressed onto a glass slide to form a thin monolayer, and then it is stained. This liquid can also be employed to test HPV infection, making it a cost-effective technique. The cells wash off plastic device more than wooden one, and the fixation solution contains haemolytic and mucolytic agents.

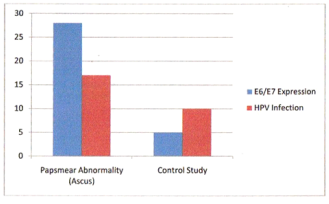
OVERVIEW OF LITERATURE

Major cause of cervical cancer is human papillomavirus which is as third most common cancer in women.

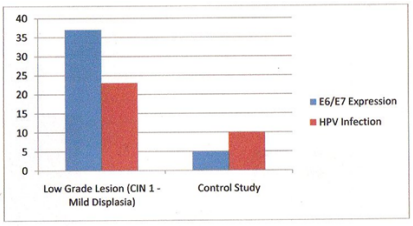
E6/E7 activities

- E6/E7 oncoproteins degrades the cellular tumour suppressor protein p53 and induces human telomerase reverse transcriptase activity that leads to progressive cervical carcino genesis.
- E6/E7 oncoproteins involve histone acetylation in cell extract.
- E6/E7 oncoprotein involve blocking the cellular apoptosis.
- E6/E7 oncoprotein that affects the chromosomal stability.
- E6/E7 changes the polarity adhesion and Gprotein modulation.
- E6/E7 oncoprotein become overexpressed in replication of basal and para basal cells of cervix.
- E6/E7 oncoprotein promotes the cellular proliferation.
- E6/E7 oncoprotein regulates the HTERT in Keratinocytes and fibroblast.

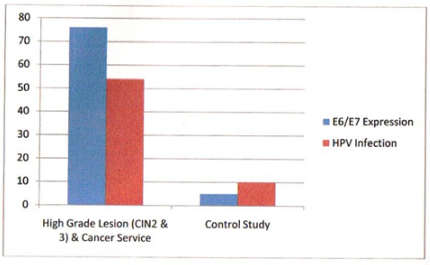
ANALYSIS OF STUDY



Bar Chart Showing: E6/E7 Expression in Pap smear Abnormality (ASCUS) and Control Study.



Bar Chart Showing: E6/E7 Expression in Low Grade Lesion (CIN 1 Mild Dysplasia).



Bar Chart Showing: E6/E7 Expression in High Grade Lesion (CIN2 & 3) & Cancer Service and Control Study.

RESULT

In this study deducted the E6/E7 oncoprotein expression positive in high grade cervical lesion shows around 75% to 80%, low grade cervical lesion shows 40% to 45% and Atypical squamous cell lesion shows around 20% to 25%.

CONCLUSION

This study has done in our hospital that over expression of HPV E6/E7 ONCOPROTEIN is a marker of progression to cervical cancer. The result were compared based on HPE grading of lesion, ca cervix and High Grade lesion gave 70 to 80% of expression of E6/E7 ONCOPROTEIN. According to my study there is earlier diagnostic / screening test for ca cervix, so identify the lesion earlier and to decide the modality of treatment earlier. My study findings are suggested that HPV E6/E7 ONCOPROTEIN expression could be used in diagnosing high grade cervical lesion and predictive tool for screening of low grade cervical lesion.

REVIEW OF LITERATURE

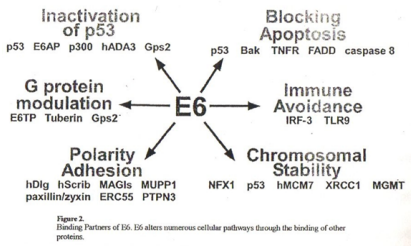


Figure 2.
Binding Partners of E6. E6 alters numerous cellular pathways through the binding of other proteins.

Papillomavirus E6 proteins

The papillomavirus are small DNA viruses that encode approximately eight genes, and require the host cell DNA replication machinery for their vital DNA replication. Thus papillomaviruses have evolved strategies to induce host cell DNA synthesis balanced with strategies to protect the cell from unscheduled replication. While the papillomavirus E1 and E2 genes are directly involved in vital replication by binding to and unwinding the origin or replication, the E6 and E7 proteins have auxiliary functions that promote proliferation. As a consequence of disrupting the normal cheek points that regular cell cycle and progression, the E6 and E7 proteins play a key role in the oncogenic properties of human papillomaviruses with a high risk of causing anogenital cancers. As a consequence E6 and E7 of HPVs are invariably expressed in cervical cancers. This article will focus on the E6 protein and its numerous activities including inactivating blocking apoptosis, activating telomerase, disrupting cell adhesion, polarity and epithelial differentiation, altering transcription and reducing immune recognition.

INACTIVATION OF p53

One of the most well studied interacting proteins of E6 is the p53 suppressor, a DNA site specific transcription factor, and one of the key signalling coordinators in the cell following genotoxic or cytotoxic stress. Normally present in low levels and transcriptionally inactive, cellular damage triggers an increase in p53 protein levels and activation via post translational modifications. Once activated, p53 functions to initiate pathways for DNA repair, cell cycle arrest and /or apoptosis, based upon the type and extent of damage. The importance of p53 in orchestrating the cellular response to cytotoxic agents is exemplified by the observation that approximately one-half of all human cancers harbour mutations in the p53 gene. These mutations impair the ability of p53 to trigger the appropriate signalling pathways to repair the damage or trigger cell death in cases where the damage is beyond repair. This in turn allows for replication of damaged DNA, and survival of cells with deleterious mutations that would normally be eliminated.

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