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Original article

Role of Lugol's iodine (VILI) in detection of pre-cancerous lesions of cervix

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ABSTRACT:

Introduction: Carcinoma of the cervix is the most common gynaecological malignancy, due to its slow progression, gives us ample opportunity for early detection and thus considerably improves prognosis. Visual inspection of cervix after application of Lugol's iodine (VILI) which is based on the ability of the trained Healthcare personnel to detect yellow, non-iodine uptake areas in the cervical transformation zone are currently being evaluated in experimental settings as an alternative to cervical cytology.

Aims & Objective: to promote the concept of visual inspection of the cervix after application of Lugol's iodine (VILI) can be applied as a screening method for the detection of precancerous lesions of the cervix.

Material & Method: A study of 100 women was from various cancer detection camps and 100 women from outpatient department cases. A pap smear was taken followed by VILI. If results of VILI test was positive or pap smear was suggestive of squamous intraepithelial neoplasia (SIL) then colposcopy of the patients was done and biopsy from different suspicious areas were taken for histopathological examination. According the results patients were treated.

Results: In outpatient departments patients shows that sensitivity, specificity, positive predictive value, and negative predictive value of VILI at G.C.R.I. was 90%, 90%, 50% and 98.7% respectively and at community level sensitivity, specificity, positive predictive value, and negative predictive value of VILI at community level was 88.8%, 86.8%, 40% and 98.7% respectively.

Conclusion: As compared to conventional cytology, VILI test is preferable because cytology is multiple step procedure and VILI is a single visit procedure.

Keywords: VILI, lugol's iodine, pre-cancerous cervical lesions

INTRODUCTION

Carcinoma of the cervix is the most common gynaecological malignancy in developing countries and the third most frequently diagnosed cancer.[1] in Indian women 1 lakh, new cases of cervical cancer occur and nearly 75000 women die annually from the disease.In many developing countries, an estimated 3/4 of the world's burden occurs, it is the most common cancer among women and the most common cause of death among middle-aged women, who is needed most in the family.[2] despite its public health importance, there is no effective prevention program in most developing countries; hence, the risk of disease and death from cervical cancer remains largely uncontrolled. Carcinoma of the cervix, due to its slow progression from a precancerous lesion to malignancy and easy accessibility to examination, gives us ample opportunity for early detection and thus considerably improves prognosis. Early Detection may be through opportunistic examination of women attending outpatient clinics or through a systematic program of screening.[3]

Screening is based on the concept that there is a detectable preclinical phase of the disease being screened and detection at this stage markedly alters disease prognosis. Cytology-based screening is effective but beyond the capacity of the health services in many of these countries. [3] Visual inspection of cervix After application of Lugol's iodine (VILI) is a simple, new technology screening test, which is based on the ability of the trained Healthcare personnel to detect yellow, non-iodine uptake areas in the cervical transformation

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zone are currently being evaluated in experimental settings as an alternative to cervical cytology.[4] With these goals in mind, this discussion reviews the role of Visual inspection of the cervix after the application of Lugol's iodine (VILI) in the detection of precancerous lesions of the cervix at the community level and activity cancer Institute in low-resource countries like India.[5]

AIMS AND OBJECTIVES

An aim to promote the concept that visual inspection of the cervix after application of Lugol's iodine (VILI) can be applied as a screening method for the detection of precancerous lesions of the cervix.

MATERIAL AND METHODS

A study was carried out of 200 women, out of 100 were from various cancer detection camps and 100 from outpatient department cases of gynaecology department. The study participants were apparently healthy, ambulant, women who were aged 20 to 65 years with an intact uterus and with no past history of cervical neoplasia. Women with obvious survival growth and women who had unsatisfactory colposcopy with no biopsy were excluded from the study at community level . Subsequently the study purpose and intervention including the need for biopsy were explained to the women to obtain their consent and participation in the study.

Detailed history of participants including menstrual history, sexual history, obstetrical history, marital history and educational history were taken in detail. A brief general examination was carried out. In all patients, pap smear was taken followed by VILI. If results of VILI test was positive or pap smear was suggestive of squamous intraepithelial neoplasia (SIL) then colposcopy of the patients was done and biopsy from different suspicious areas were taken and sent for histopathological examination. The patient was treated according to the results of biopsy and/or colposcopy.

Criteria for categorizing VILI test results

Results	Criteria
Negative	➢ Normal cervix where squamo-columnar junction stains mahogany brown or black and the columnar epithelium does not change colour. ➢ Patchy, indistinct, ill defined, colourless or partially brown areas in transformation zone. ➢ Scattered, irregular, ill-defined, non-iodine uptake areas on cervix. ➢ Thin, yellow, non-iodine uptake areas with angular or digitizing margins, resembling geographical areas located far away from squamo columnar junction.
Positive	➢ Well defined, dense, thick, bright mustard yellow or saffron yellow, iodine non-uptake areas touching the squamo columnar junction. ➢ Circumferential, well defined, thick, dense, yellow lesion occupying large portion of cervix. ➢ Growth on cervix turns yellow

Present study had been done by adhering to these criteria.

OBSERVATION

In outpatient department patients, commonest age group was 30-39 years (38%). Most of the women were having high school education (45%) and more than half women had coitage after 20 years (55%). 52% of the women had 3 or more children.

Most of the patients came with the complaint of excessive vaginal discharge (71%) followed by lower abdominal pain (14%). Study showed that most of the women attending community camps had come with the complaint of excessive vaginal discharge (33%) followed by inter menstrual bleeding(10%) and 65% of the women squamo-columnar junction was fully seen, followed by cervicitis (11%)

71% of the women attending the community camps, squamo-columnar junction were fully seen, followed by cervicitis (12%) and erosion (11%) .Conventional cytology (Pap smear) results showed ASCUS, AGUS, LSIL, HSIL and carcinoma were considered positive. Out of 100 women, 9 women tested positive for cytology results (ASCUS-1, LSIL-2, HSIL-5 and AGUS-1) and 91 women tested negative for the cytology results. One woman was reported ASCUS, which on histology turned out to be negative for pre-malignant lesion or malignancy. Two women were reported as smear

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repost negative for intra-epithelial lesion or malignancy, which on biopsy showed C1N1 and C1N2/C1N3 respectively, 8 women which were reported as having premalignant lesion or malignancy by conventional cytology were later on confirmed on histology. Study showed that the sensitivity, specificity, positive predictive value and negative predictive value of conventional cytology at G.C.R.I was 80%, 98.9%,88.8% and 97.8% respectively.

Out of 100 women, 6 women were reported as having abnormal smear (ASCUS-1, LSIL-1, HSIL-4). Out of these 6 women, the women having ASCUS smear turned out to be negative for premalignant lesion or malignancy on histological examination. Out of 100 women, 94 women did not show any evidence of malignancy on histological examination. Out of 94 negative results, 3 women showed evidence of malignancy on histological examination, 2 had C1N1 lesion and one woman had C1N2/C1N3 lesion. Study shows that the sensitivity, specificity, positive predictive value and negative predictive value of conventional cytology at community level was 62.5%, 98.9%, 83.8% and 96.8% respectively.

In outpatient departments patients, out of 100 women 18 women came out to be VILI test positive, 82 women were VILI negative. Out of 18 women tested positive for VILI 9 women were having false positive test. False positive results were due to false interpretation of erosion, cervicitis, infection with trichomonas vaginalis (TV) as VILI positive. One woman tested false negative because of post-menopausal women squamo columnar junction ascends into cervical canal, leading to false negative test. 81 women had true negative test as their conventional cytology reports were negative. shows that sensitivity, specificity, positive predictive value, and negative predictive value of VILI at G.C.R.I. was 90%, 90%, 50% and 98.7% respectively. At community level, out of 100 women, 20 women tested positive for VILI test, 80 women tested negative for VILI test. 12 women tested false positive due to false interpretation of erosion, cervicitis, infection with trichomonas vaginalis (TV) as VILI positive which later proved false on colposcopy examination or histology results. One woman was reportedly falsely as VILI test negative, because that woman was post-menopausal and in post-menopausal squamo-columnar junction ascends into endocervical canal giving test falsely negative. 8 tested women came out to be truly positive for VILI test as results were confirmed on colposcopies examination or histology. 79 women turned out to be true negative for VILI test. shows that sensitivity, specificity, positive predictive value and negative predictive value of VILI at community level was 88.8%, 86.8%, 40% and 98.7% respectively.

DISCUSSION

It showed that 94% of the women were in the pre-menopausal age group where VILI test was effective because these women had oestrogenised squamous epithelium. In post-menopausal women due to hypoestrogenism, sensitivity of VILI test decreases. In community camps, the commonest age group was 30-39 years (49%). 43% of the women were having high school education (43%) and more than half women (54%) had coitage before 20 years. 62% of women had 3 or more children. In the study done by Sankaranarayanan et al[6,7,8,9,10], in Trivandrum, Kerala, most of the women were between the age group of 30-39 years(34.7%). Most of the women were having primary grade education (56.6%) and more than half of the women had coitage before 20 years (79.9%). 75.5% of the women were having 3 or more children. Study corelated with the study done by Sankaranarayanan et al.[6,11- 15]

It shows that most of the women will have normal smear. In the study 5% of the women shows conventional cytology report of HSIL. In Samira Khan et al[8-11] study 9.7% of the women showed HSIL smear report. In Samira Khan et al[8-11] study, LSIL is present in 19.4% of women as compared to 2% in present study. The difference between present study and study done by Samira Khan et al[8-11] may be due to larger sample size in study by Samira Khan et al. [8-11] Pathologists are more conversant in reading LSIL results which is significantly different in two studies.

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Place	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Outpatient department	80	98.9	88.8	97.8
Community Camps	62.5	98.9	83.8	96.8

Table 1: Comparison of conventional cytology results outpatient department and at community level

Study	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Present study	90	90	50	98.7
Bhatla et al	87.5	58.7	15.6	98.2
Samira Khan et al	78.9	74.4	57.7	88.9

Table 2: Comparison of test performance of VILI in hospital set up

Sensitivity, specificity, positive predictive value and negative predictive value for VILI test are 90%, 90%, 50% and 98.7% respectively. The corresponding values for Bhatla et al study was 87.5%, 58.7%, 15.6% and 98.2% respectively. Corresponding values for Samira Khan et al[12] study was 78.9%, 74.4%, 57.7% and 88.9% respectively. The difference of specificity and positive predictive values between present study and studies by Bhatia et al and Samira Khan et al are because in present study VILI test is done by resident doctors and fellows pursuing training in gynaecological oncology .The studies done by Bhatia et al[16] and Samira Khan et al[17] are conducted in general hospital. So, the incidence of false positive results increases giving lower values of specificity and positive predictive values in studies done by Bhatla et al[16] and Samira Khan et al.[17]

The study Is comfortable with the study done by Bhatla et al[3] and Samira Khan et al. except positive predictive value specificity.

Study	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Present study	88.8	86.8	40	98.7
Sankarnarayanan et al	87.2	84.7	16.6	99.5
Bhatla et al	87.5	58.7	15.6	98.2

Table 3: Comparison of test performance of VILI at community level

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Corresponding values for studies done by Sankarnarayanan et al[19] were 87.2%, 84.7%, 16.6% and 99.5% respectively. Corresponding values for studies done by Bhatla et al[3] were 87.5%, 58.7%, 15.6% and 98.2% respectively.

The difference between specificity and positive predictive value between present study and studies by Sankarnarayanan et al[19] and Bhatla et al[3] are because in present study, VILI test is done by resident doctors and fellows pursuing training in gynaecological oncology. In studies done by Sankarnarayanan et al[10] and Bhatla et al[3], VILI test is done by health workers, so the number of false positive increases. So, the specificity and positive predictive values of their studies decreases.

But still the study correlates with the studies by Sankarnarayanan et al[19] and Bhatla et al.[3] except positive predictive value and specificity.

Place	Sensitivity (%)	specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Outpatient Department	90	90	50	98.7
Community Camp	88.8	86.8	40	98.7

Table 4: Comparison of VILI test results at Gujarat Cancer and Research Institute and at community level

CONCLUSION

Carcinoma of cervix is 100% curable when detected in pre-invasive state. Visual inspection techniques like visual inspection of cervix after application of Lugol's iodine (VILI) can be used as an alternative to conventional cytology for early detection of cervical cancer in low resource countries like INDIA. VILI test is preferable to VIA test as colour contrast is better in VILI, shelf life is more for Lugol's iodine which is considerably lower for acetic acid. Alsip VILI is easy to teach even to para medical, results are available immediately and recall period for patient's id 5 years which is very important in countries like India where most of the patients are lost to follow-up. As compared to conventional cytology, VILI test is preferable because cytology is multiple step procedure and VILI is a single visit procedure. Reading of VILI test is dependent upon the clinical acumen of the clinician. Thus, VILI can be used effectively for detection of pre-cancerous lesion of cervix at hospital set up as well as at community level.

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