

A Case Report: Conservative Treatment Modalities as Loop Electrosurgical Excision Procedure (LEEP) Can Be Used to Treat Precancer Cervix Lesion High Grade Squamous Intraepithelial Lesion (HSIL) or Moderate and Severe Dysplasia (CIN II and III) with Post Coital Bleeding Disorders

Effectiveness of LEEP therapy in patients with cervical precancerous lesions of high grade squamous intraepithelial lesion (HSIL) or moderate and severe dysplasia (CIN II and III) with post-coital bleeding disorders.

Supriyono^{1, 2*}

1. Faculty of Medicine, Universitas Hang Tuah, Surabaya, Indonesia
2. Obstetry and Gynecology Departement, Rumah Sakit Pusat TNI Angkatan Laut
*corresponding author : supriyono.drspog@gmail.com

Abstract

Precancer cervix lesion High Grade Squamous Intraepithelial Lesion (HSIL) or moderate and severe Dysplasia (CIN II and III) is cervical Intraepithelial Neoplasia (CIN) which changes cervix epithelial cells without invasive to basal membrane cells. This change step cervical epithelial cells through high-risk Human Papilloma Virus (HPV) infection such are HPV 16, 18, 31, 33, 34, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68, and 70. Precancer cervix lesion HSIL could cause erosion of the cervix and cause post coital bleeding disorders. Loop Electrosurgical Excision Procedure (LEEP) treatment could cure HSIL or moderate and severe dysplasia (CIN II and III). Therefore, it relieves post coital bleeding disorders to the patients.

Cervical precancerous lesions High Grade Squamous Intraepithelial Lesion (HSIL) or moderate and severe dysplasia (CIN II and III) are Cervical Intraepithelial Neoplasia (NIS) or Cervical Intraepithelial Neoplasia (CIN) where changes in cervical epithelial cells occur without penetrating the basement membrane. The stages of normal cervical epithelial changes begin with high-risk Human Papilloma Virus (HPV) infection, namely HPV 16, 18, 31, 33, 34, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68, and 70. The HSIL cervical precancerous lesion could cause erosion of the cervix and cause complaints of post-coital bleeding disorders. Loop Electrosurgical Excision Procedure (LEEP) therapy could cure HSIL or moderate and severe dysplasia (CIN II and III) which could eliminate post-coitus bleeding disorders that suffered by patients.

Keywords: LEEP, HSIL pre-cancerous cervical lesions or moderate and severe dysplasia (CIN II and III), post-coitus bleeding.

1. Introduction

Cervical precancerous lesions are Cervical Intraepithelial Neoplasia (NIS) or Cervical Intraepithelial Neoplasia (CIN). Cervical epithelial cell changes occur without penetrating the basement membrane. Currently, cervical precancerous lesions are simply divided into low grade squamous intraepithelial lesions (LSIL) and high grade squamous intraepithelial lesions (HSIL) (Schifman et al., 2007).

Changes from a normal cervix to cervical cancer take a long time and those changes go through the stage of cervical precancerous lesions. Stages of normal cervical epithelial changes begin with high-risk human papilloma virus (HPV) infection, which consists of HPV 16, 18, 31, 33, 34, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68 and 70 (Burd, 2003). Research shows, about 90% of HPV will be eliminated in time 2 years and a small percentage who are persistent have a risk of cervical cancer (Gravitt et al., 2011).

There are 4 stages of progression to cervical cancer, namely: 1. High-risk HPV infection, 2. Persistent high-risk HPV infection, 3. Changes in cervical epithelial cells due to HPV and 4. progression to cervical cancer until it penetrates the basement membrane (Schffman et al., 2007).

Richardson et.al introduced the term CIN to describe pre-invasive cervical squamous cell abnormalities, there are 3 degrees of changes, which are: 1. CIN I (mild dysplasia), 2. CIN II (moderate dysplasia), and 3. CIN III (severe dysplasia/carcinoma in situ). This system is more consistent with the biological changes which occur in the cervix that describe the process of squamous cell carcinogenesis (Richardson et al.,2005)

HPV is found in 93% of cervical cancers (Schiffman et al, 2007). The most common high-risk HPV found in cervical cancer were HPV 16 (50%), HPV 18 (20%) and the rest were combined of HPV 31, 33, 45, 52, and 58. Research in China on cervical swab specimens showed that most were infected with 1 type of HPV (77.26%) only a small proportion were infected with several types of HPV. Multiple infections are more common in those under 30 years of age, while those infected with only one type of HPV are more in the 50-60 years age group (Ma et al, 2019).

When there is persistence of high-risk HPV infection, normal cervical epithelial cells can become LSIL, at this stage they can still regress or develop into HSIL. Of the 434 women with LSIL pap smear results and were observed for 5 years, it turned out that 7.4% developed HSIL and there was a correlation between HPV persistence and the risk of HSIL. If HPV infection persists for up to 2 years, the risk of LSIL becoming HSIL is high (Ma et al, 2019).

There are 2 possibilities for the development of LSIL, which are: experiencing regression or progressing to HSIL. Observation of LSIL for 5 years showed 10.7% progressed to HSIL, 55% experienced persistence and 34.2% regressed to normal (Saw et al., 2001). In the old pap smear reading system, there are 3 main categories of cervical precancerous lesions, namely CIN I, II and III. In the new reading system category, CIN I was categorized as LSIL and CIN II and III were categorized as HSIL. Women with CIN III have a cervical cancer risk 2 times greater than normal women and have a 7 times greater risk if CIN III occurs in women over 50 years (Loopik et al,2020)

Cervical precancerous lesions are diagnosed through a pap smear (cytology) or a biopsy (histopathology). Cytological examination is the initial screening examination. Currently cervical precancerous lesions are read according to the Bethesda system, which is simply divided into: normal, squamous disorders and glandular disorders (Perkins et al.,2020).

Squamous disorders are divided into:

1. Atypical squamous cell – of undetermined significance (ASC-US)- cannot exclude HSIL (ASC – H).
2. Low grade squamous intraepithelial lesion (LSIL) (encompassing: HPV/mild dysplasia/CIN I).
3. High grade squamous intraepithelial lesion (HSIL) (encompassing moderate and severe dysplasia, CIN II and III).
Squamous cell carcinoma (Perkins et al.,2020).

Glandular disorders are divided into:

1. Atypical - endocervical cells (not otherwise specified (NOS) or specify in comments), - endometrial cells (NOS or specify in comments), - glandular cells (NOS or specify in comments).
Atypical-endocervical cells, favour neoplastic – glandular cells, favour neoplastic
2. Endocervical adenocarcinoma in situ.
Adenocarcinoma: -endocervical - endometrial - extrauterine – not otherwise specified (NOS) (Perkins et al.,2020).

There are basically two categories of cervical precancerous lesion therapy: 1. Ablation therapy and 2. Excision therapy. Ablation therapy aims to destroy cells which undergo cervical precancerous changes and then grow new healthy cells after therapy. Excision therapy aims to remove cells that have precancerous changes. The main difference between the two procedures is specimens for histopathological examination, ablation therapy does not get specimens while excision therapy gets specimens for histopathological examination (Perkins et al.,2020).

Ablation therapy for cervical precancerous lesions consists of:

1. Cryotherapy.
 2. Cervical cautery with electrocautery.
- Cervical cautery with LASER (Perkins et al.,2020).

Excision therapy for cervical precancerous lesions consists of:

1. Conization (cold knife conization).
2. Laser conization.
3. Loop electrosurgical excision procedure (LEEP) (Perkins et al.,2020).

Treatment options for ASCUS are as follows:

1. HPV test.
If negative, observation and pap smear again 1 year.
If positive, performed colposcopy.
2. Pap smear again 4-6 months.
If 2x Pap smears are good, back to the routine pap smear schedule. If the pap smear still contains ASCUS □ A colposcopy is performed.
3. Colposcopy.
Direct colposcopy examination is carried out if there are facilities and further therapy in accordance with the results of the colposcopy (Perkins et al.,2020).

Treatment options for LSIL or CIN I are as follows:

As in some studies the risk of LSIL or CIN I being cervical cancer is very small, only 4% being HSIL, most of them will regress to normal. Therefore, in general, LSIL or CIN I therapy is an observation and pap smear repeats in 1 year. If the pap smear regresses to normal, there will be back to the routine screening schedule. However, if the pap smear test shows ASCUS or more severe than it, there will be a colposcopy examination as further examination. If LSIL persists within 2 years of observation, ablation or excision therapy can be performed (Mc Credie et al., 2008).

Therapy for HSIL or CIN II and III.

Basically, HSIL or CIN II and CIN III must be treated, observation only is not adequate, as in some studies the incidence rate of 20% becomes cervical cancer in 10 years of observation (Mc Credie et al., 2008). Treatment options are either ablation or excision.

Cervical precancerous lesions in pregnancy cervical examination is more difficult. As long as there is no suspicion of invasive cervical cancer, treatment of precancerous cervical lesions in pregnancy can be delayed until postpartum. Diagnostic excision therapy is only performed when there is suspicion of invasive cervical cancer. A cervical biopsy to confirm the diagnosis can be done if necessary. The progression of cervical precancerous lesions to invasive cervical cancer in pregnancy is similar to nonpregnancy. However, when cervical cancer is invasive, the stage development of cervical cancer becomes very progressive because of the high influence of the hormone oestrogen in pregnancy.

General practitioners are required to be able to diagnose cervical precancerous lesions, while general practitioners

who are allowed to perform cervical precancerous lesions are general practitioners who have attended training organised by the Association of Gynaecological Oncologists (HOGI) under the auspices of POGI regarding the therapy of cervical precancerous lesions and have received certification.

2. Case Report

A woman, 35 years old, Javanese, married, 2 children, born normal, had an IUD contraception which has been removed since 2015 due to complaints of post-coital bleeding. Middle socioeconomic background, housewife profession. Patient examined and checked up at the gynaecological oncology poly RSPAL Dr. Ramelan Surabaya, with a history of the following diseases:

1. October 2015: complaints of post-coital bleeding and vaginal discharge. The ectocervix has erosion. pap smear confirmed, pap smear result CIN I. Conservative therapy, pap smear repeated 1 year.
2. June 2016: complaints of post coital bleeding and vaginal discharge. The ectocervix showed erosion and white epithelium. Pap smear done, CIN II results and Hemophilus infection. Cauterized LEEP therapy, and histopathological examination, the results were CIN I – II and HPV infection. Pap smear 1 year.
3. June 2017, December 2018 pap smear examination results were normal and there were no complaints.
4. Between 2019 to 2020 was never do medical check-up because of the covid 19 pandemic.
5. August 2021, checked-up to the clinic for post-coital bleeding complaints. A cervical biopsy was performed at Siti Hajar Hospital Sidoarjo on July 30, 2021. Histopathological results were HSIL or CIN II - III. LEEP therapy and histopathological examination were carried out. The result was CIN I -II.
6. 7 September 2021, medical checked-up post LEEP cautery. There are no post-coital bleeding complaints. Gynaecological examination showed no abnormalities, negative portion erosion.

3. Discussion

The results of LEEP therapy in this case is great. It proofs that it could heal cervical cancer lesions and could eliminate post-coital bleeding disorders since it is supported by obedient patients with doctor's recommendations for regular control and regular pap smear examinations.

Cauterized LEEP therapy has the following advantages:

1. Can obtain specimens for histopathological examination.
2. Easy implementation.
3. Diathermy tools and devices are inexpensive.
4. No complications.
5. Can be done without anaesthesia.

The disadvantage is that the histopathological examination results will be graded because the edges of the LEEP incision are burned by the heat of the cautery.

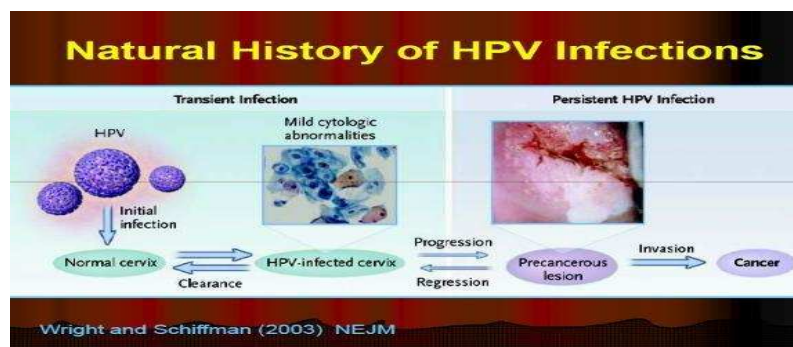


Figure 1.

Figure 1. Early infection with HPV triggers the appearance of mild cervical abnormalities, the infection can disappear, and conditions return to normal / if the body is able to inhibit the development of HPV, persistent infection will occur. Persistent HPV infection triggers progression to precancerous and cancerous lesions (Wright and Schiffman, 2003)

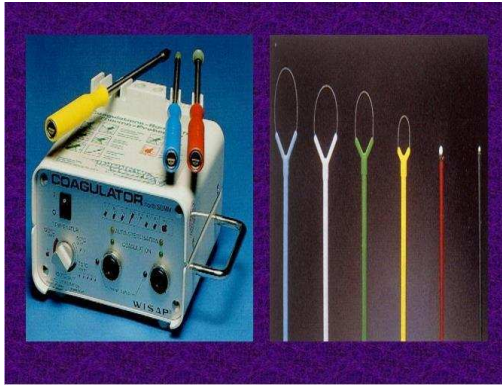


Figure 2. LEEP units consist of loops and electrosurgery unit

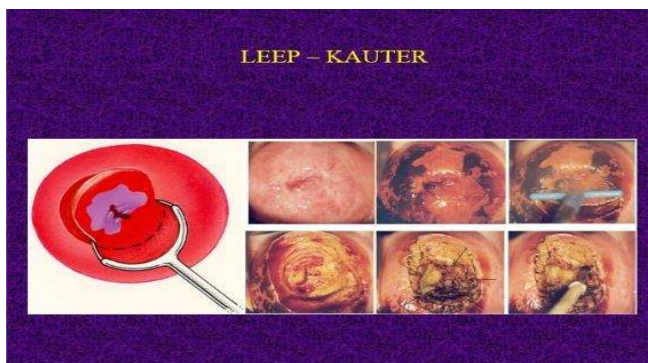


Figure 3. Cervical precancer lesion after using LEEP

4. Conclusion

1. Cervical precancerous lesions can be treated with great results using an excision therapy modality, namely Loop Electrosurgical Excision Procedure (LEEP).
2. With LEEP therapy cervical precancerous lesions can be prevented from developing into invasive cervical cancer.
3. LEEP therapy is easy to implement and can be carried out by Sp. OG doctors, not consultants for Gynecological Oncology or by general practitioners who have attended training in cervical precancerous lesion therapy and are certified.

5. References

- Bansal, N., Wright, J. D., Cohen, C.J. & Herzog, T.J. 2008. Natural history of established low grade cervical intraepithelial (CIN 1) lesions. *Anticancer Res*, 28, 1763-6.

- Burd, E. M. 2003. Human papilloma virus and cervical cancer. *Clinical microbiology review*, 16, 1-17.
- Brahmana Askandar, Indra Yuliati. Lesi Prakanker Serviks. 2020. *Buku Ginekologi Praktis Komprehensif*.
- Campion MJ. Preinvasive disorder. In: Berek JS, Hacker NF, eds. 2005. *Practical Gynecology Oncology* 4th Ed. Philadelphia: Lippincott Williams & Wilkins, 265-336
- Clifford GM, Gallus S, Herrero R, Munoz N, Snijders PJF, Vaccarella S, dkk. 2005. Worldwide distribution of human papillomavirus types in cytologically normal women in the International Agency for Research on Cancer HPV prevalence surveys: a pooled analysis. *Lancet*, 366: 991-8
- Gravitt, P. E. 2011. The known unknowns of HPV natural history. *The Journal of Clinical Investigation*, 121, 4593-4599.
- Loopik, D. L., Inthout, J., Ebisch, R. M. F., Melchers, W. J. G., Massuger, L. F. A. G., Siebers, A. G. & Bekkers, R. L. M. 2020. The risk of cervical cancer after cervical intraepithelial neoplasia grade 3: A population-based cohort study with 80,442 women. *Gynecologic Oncology*, 157, 195-201.
- Ma, L., Lei, J., Ma, L., Cong, X., Wang, N., Yang, H., Liu, Q., Yu, Y. & Cao, Y. 2019. Characteristics of women infected with human papillomavirus in a tertiary hospital in Beijing China, 2014-2018. *BMC Infectious Diseases*, 19, 670.
- Mc Credie, M. R., Sharples, K. J., Paul, C., Baranyai, J., Medley, G., Jones, R. W. & Skegg, D. C. 2008. Natural history of cervical neoplasia and risk of invasive cancer in women with cervical intraepithelial neoplasia 3: a retrospective cohort study, *Lancet Oncol* 9,425-34.
- Perkins, R. B., Guido, R. S., Castle, P. E., Chelmow, D., Einstein, M. H., Garcia, F., Huh, W. K., Kim, J. J., Moscicki, A. B., Nayar, R., Saraiya, M., Sawaya, G. F., Wentzensen, N. & Schiffman, M. 2020. 2019 ASCCP Risk-Based Management Consensus Guidelines for Abnormal Cervical Cancer Screening Tests and Cancer Precursors. *J Low Genit Tract Dis*, 24, 102-131.
- Richardson CD. Viruses and cancer. In: Tannock IF, Hill RP, Bristow RG, Harrington L. 2005. *The Basic Science of Oncology*, 4th ed. Singapore: McGraw Hill; 100-122
- Saw, H. S., Lee, J. K., Lee, H. L., Jee, H. J. & Hyun, J. J. 2001. Natural history of low-grade squamous intraepithelial lesion. *J Low Genit Tract Dis*, 5, 153-8.
- Schiffman, M., Castle, P. E., Jeronimo, J., Rodriguez, A. C. & Wacholder. 2007. Papillomavirus and cervical cancer. *Lancet*, 370, 890-907.
- Wright Thomas C & Schiffman Mark, 2003. Adding a Test for Human Papillomavirus DNA to Cervical-Cancer Screening. *The New England Journal of Medicine*, 348:6, 489-490.