

RESEARCH ARTICLE

See-and-Treat Approach to Cervical Intraepithelial Lesions in HRH Princess Maha Chakri Sirindhorn Medical Center

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Abstract

Background: To evaluate the overtreatment rate with the see and treat approach in the management of women with abnormal cervical cytology. **Materials and Methods:** A retrospective review of patients with abnormal cervical cytology who underwent S&T at MSMC between January 2008 and December 2012 was conducted. Loop electrosurgical excision procedure (LEEP), histological results, cytology and colposcopic impression were analyzed to evaluate overtreatment rate, cyto-histologic correlation and related factors. **Results:** Average age of S&T cases was 42 years. Ninety seven percents were referred from affiliated health care providers. The study revealed 83.2% patients had HSIL or higher from cervical cytology. Correlation between HSIL and final histology was relatively low at 75% compared to other studies. Overtreatment rate was 28%. **Conclusions:** S&T was done in 197 patients in a tertiary care health facility with patient satisfaction. Overtreatment occurred, but the rate can be reduced with appropriate recommendations. HSIL Pap smears should be reexamined before S&T while low grade and lesser colposcopic impression groups should obtain conventional colposcopic approach for patient future reproductive benefit.

Keywords: High grade squamous intraepithelial lesion - overtreatment - see and treat

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Introduction

Cervical cancer is the most common gynecologic cancer worldwide. It is the second most common cancer among women in Thailand. The common age group of patients was 45-55 year (Wilailak, 2009). Pap smear was the principle method for cervical cancer screening. In standard practice women who had abnormal Pap smears were appointed for immediately colposcopic directed biopsy (CDB). In case of cervical intraepithelial neoplasia (CIN) 2⁺, most physician do cervical conization or ablation per guideline from 2006 consensus guidelines for the management of women with abnormal cervical cancer screening tests (Wright et al., 2007). In the conventional setting colposcopic directed cervical biopsy will be made for histopathology report. The CIN 1 or lesser will be conservatively managed. The CIN 2⁺ pathology are usually managed by cervical conization for more histopathology report. To reduce redundancy, see and treat protocol (S&T) is a sequence of actions designed to perform LEEP immediately when CIN 2⁺ is suspected from colposcopy without biopsy, as recommended by American Society for Colposcopy and Cervical Pathology (ASCCP) since

2006 (Wright et al., 2007). S&T has been introduced and used in HRH Princess Maha Chakri Sirindhorn Medical Center (MSMC) Srinakharinwirot University, Ongkharak Campus, Nakornnayok, Thailand since 2008. Patients welcomed the practice because it decreased patient's anxiety as they received the treatment right away (Chigbu et al., 2014). S&T cuts down on the number of medical visits, saves hospital trip, travel cost and prevents the dropout before treatment (Monteiro et al., 2009). It provides specimens for histologic diagnosis to rule out undetected invasive cancer (Emam et al., 2009). This study was a five years retrospective evaluation of S&T protocol in MSMC. Overtreatment and treatment affected factors were evaluated.

Materials and Methods

This study was approved from the Research Ethics Committee, Faculty of Medicine Srinakharinwirot University, Ongkharak Campus, Nakornnayok. Medical records of women who underwent colposcopic examinations and received LEEP during the same visit (S&T) at MSMC between January 2008 to December

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2012 were reviewed. The inclusion criteria were women who previously had abnormal Pap smear of atypical squamous cells of undetermined significance (ASC-US), atypical squamous cells favor neoplasia (ASC-H), low grade squamous intraepithelial lesion (LSIL), high grade squamous intraepithelial lesion (HSIL), and squamous cell carcinoma (SCC) types (Bethesda, 2000) and or suspicious lesions that were later subjected to colposcopic evaluation and later received LEEP. CIN 2⁺ was defined as CIN 2-3, adenocarcinoma in situ (AIS) and invasive lesion. In the S&T group approach, histopathological specimen from LEEP was obtained from initial colposcopy without biopsy when CIN 2⁺ was suspected. Overtreatment was defined as CIN 1 or less from LEEP specimen as per the National Health Services of Cervical Screening Programme (NHSCSP) 2010 Guidelines (Luesley and Leeson, 2010). The exclusion criteria were those with incomplete medical records. The pathological report of the LEEP specimen was collected, normally, low grade lesion (CIN 1), high grade lesion (CIN 2-3), invasive cancer, patient demographic data, contraceptive method, parity, menopausal status, reason for colposcopy, initial result Pap smear, satisfactory rating of colposcopy, colposcopic impression and histology of LEEP were collected. Descriptive statistics were used for demographic baseline. Correlation between cytology/histology, colposcopic impression/histology and overtreatment rate was calculated. Statistical analysis was performed using SPSS IBM Singapore Pte Ltd (Registration No 1975-01566-C). Chi-square was used at $p < 0.05$.

Results

Three hundred and twenty eight patient records were reviewed during the period between January 2008 to December 2012. Out of that group, 197 patients from Colposcope followed by LEEP were included in this study. Most of the patients were between 17-75 year old. Average age was 42. Nulliparous and postmenopausal groups were 17.7 and 17.8%, respectively. Ninety seven percent of colposcopic cases came from abnormal Pap smear. Among these groups, 57.8 percents had satisfactory

Table 1. Demographic Characteristics of Subjects in This Study

| Characteristics | No. (%) |
|-----------------------------|------------|
| Age (years) | |
| ≤50 | 160 (81.2) |
| >50 | 37 (18.8) |
| Parity | |
| Multipara | 116 (58.9) |
| Primigravida | 43 (21.8) |
| Nulliparous | 35 (17.7) |
| Unknown | 3 (1.5) |
| Menopausal status | |
| Premenopause | 162 (82.2) |
| Menopause | 35 (17.8) |
| Indication for colposcopy | |
| Abnormal Pap | 191 (96.9) |
| Unknown | 6 (3.0) |
| Satisfactory of colposcopy* | |
| Type 1 | 114 (57.8) |
| Type 2 | 59 (29.9) |
| Type 3 | 24 (12.2) |
| Total | 197 (100) |

*Type 1: entire visualized squamocolumnar junction and margin of visible lesion; Type 2: partial visualized squamocolumnar junction and margin of visible lesion; Type 3: not visualized squamocolumnar junction and visible lesion

colposcopy (Table 1). Indication for colposcopic referral in this investigation is shown in Table 2. HSIL was the majority of initial Pap smear result at 74.1 percents, cancer, ASC-H, LSIL and Atypical smear are 9.1, 9.1, 3 and 1.5 percents, respectively. MSMC is a regional tertiary medical care in the north Bangkok area. As a result, some patients were referred to our colposcopic unit without any cervical cytology reports from various gynecological physicians from small hospitals in the nearby area. Correlation between colposcopic impression and histological diagnosis of LSIL, HSIL, Cancer, normal/noCIN were 32, 78.46, 71.42 and 80.95 percents respectively as Table 3 Definition of overtreatment was the patients who undergone S&T with final CIN 1 or less histopathologic report. In this study the overtreatment rate was 28 percents and decreased to 11.2% if the “see and treat” approach was strictly carried out in women whose either preceding cervical smears or colposcopic impressions revealed high grade abnormalities.

Characteristic of patient histology who received overtreatment rate which compose with no CIN 70% (39/56), CIN 1 30% (17/56) as Table 5.

Table 2. Indication for Colposcopy

| Initial Pap smear result | No. (%) |
|------------------------------------------------------------------|------------|
| High grade squamous intraepithelial lesion (HSIL) | 146 (74.1) |
| Atypical squamous cell can not exclude high grade lesion (ASC-H) | 18 (9.1) |
| Squamous cell carcinoma (SCC) | 3 (1.5) |
| Low grade squamous intraepithelial lesion (LSIL) | 6 (3.0) |
| Atypical smear (ASC-US & AGC-NOS)* | 3 (1.5) |
| Unknown | 6 (3.0) |
| Total | 197 (100) |

*ASC-US: atypical squamous cell of undetermined significance; AGC-NOS: atypical glandular cells of undetermined significance

Table 3. Correlation between Colposcopic Impression and LEEP Histologic Diagnosis

| Colposcopic impression | LEEP histologic diagnosis (%) | | | | Total |
|------------------------|-------------------------------|----------|-------------|------------|-----------|
| | Normal/noCIN | LSIL | HSIL | Invasive | |
| Normal/noCIN | 17 (80.95) | 2 (9.52) | 1 (4.76) | 1 (4.76) | 21 (100) |
| LSIL | 12 (48) | 8(32) | 5 (20) | 0 | 25 (100) |
| HSIL | 10 (7.69) | 6 (4.61) | 102 (78.46) | 12 (9.23) | 130 (100) |
| Invasive | 0 | 1 (4.76) | 5 (23.8) | 15 (71.42) | 21 (100) |
| Total | 39 | 17 | 113 | 28 | 197 |

*CIN: cervical intraepithelial neoplasia, LEEP: loop electrosurgical procedure; LSIL: low grade squamous intraepithelial lesion, HSIL: high grade squamous intraepithelial lesion

Table 4. Literature Review of the Overtreatment Rate in Women Who Had HSIL on Preceding Smear

| Author (year) | Correlation | | Overtreatment (%) | |
|----------------------|--------------------------|----------------------------|-------------------|------------|
| | Cytology & Histology (%) | Colposcope & Histology (%) | | |
| | | LGL | HGL | |
| Charoenkwan, 2004 | 55 (76) | 0/4 | 96 | 3.6 |
| Suntornlinsiri, 2004 | 178 (87) | 17/27(63) | 104/130(80) | 12.35 |
| Sadan, 2007 | 82 (70.13) | - | - | 28.39 |
| Kietpeerakool, 2007 | 446 (92.2) | - | - | 5.8* |
| Kietpeerakool, 2009 | 247 (NA) | - | - | 9.3 |
| Monteiro, 2009 | 298 (NA) | - | - | 8.84 |
| Emam, 2009 | 31 (VIA)** | - | - | 16 |
| Aue-Aungkul, 2011 | 192 (89.47) | 19/42(45.23) | 125/150(83.33) | 10.5/7* |
| Nogara, 2012 | 117 (72.64) | 4/7(57) | 79/81(97.5) | 24 |
| Ingkapiroj, 2012 | 108 (74.1) | - | - | 52.8 |
| Srisuwan, 2014 | 197 (75) | 8/25(48) | 134/151(88.7) | 24.2/11.2* |

*Overtreatment rate in both HSIL and higher preceding Pap smear & colposcopic impression high grade lesion; **VIA: visual inspection acetic acid, NA: not available; LGL: low grade lesion, HGL: high grade lesion, HSIL: high grade squamous intraepithelial lesion

Table 5. Characteristic of Overtreatment vs Proper Treatment Patient Group

| | | Treatment | | p value |
|--------------------------|----------------|-----------------|--------------------|---------|
| | | Over (n=56)* | Proper (n=141)* | |
| Initial Pap result* | LGL | 16(28.6) | 17(12.0) | <0.01 |
| | HGL | 40(71.4) | 124(88) | |
| Parity* | Nulliparous | 15(26.8) | 20(14.2) | 0.06 |
| | Multiparous | 41(73.2) | 121(85.8) | |
| Menopausal status* | Premenopause | 43(76.8) | 120(85.1) | 0.2 |
| | Postmenopause | 13(23.2) | 21(14.9) | |
| Satisfactory colposcopy* | Satisfactory | 31(55.4) | 83(58.9) | 0.75 |
| | Unsatisfactory | 25(44.6) | 58(41.1) | |
| Colposcopic impression* | Normal/LGL | 39(69.6) | 7 (5) | <0.01 |
| | HGL/Invasive | 17(30.4) | 134(95) | |

*N (%); HGL: high grade lesion; LGL: low grade lesion

Discussion

LEEP is an effective and safe technique in the treatment of CIN when the eradication of the abnormal epithelium is required. For a common procedure, a colposcopic examination should be carried out, and the biopsy result seen to determine the treatment before the excision treatment. At our university health center it takes two weeks to receive the histopathological result. The LEEP appointment is done within two weeks interval. S&T was introduced to provide patients with faster service. Patients who came to the colposcopic investigation know that they were suspected of carrying malignant tissue and normally were stressed out by worry. Our S&T patients verbally stated that they felt relieved that the problem tissues were removed from their bodies in a timely manner. Kjellberg et al. (2007) describe in his literature that both of these methods (cytology and cervical directed biopsy) yielded almost the same detection rate (78.5 vs. 73.2%). The question arises if cervical biopsy is still needed to confirm the Pap smear result or can we skip the biopsy and go on with see and treat strategy (Kjellberg et al., 2007). A total of 75 percents of our patients with HSIL or higher on Pap smear had a corresponding diagnosis at LEEP specimen. In the published literature, correlation between cytology and histology values varies between 70-92 percent (Table 4). The studies between the correlation rate of colposcopy and histology since 2004 range from 80-97.5 percents in HSIL and invasive lesion (Table 4). At 88.7 percent, our correlation between colposcopic impression and histological diagnosis was within the range of other study (Charoenkwan et al., 2004; Suntornlimsiri, 2004; Aue-Aungkul et al., 2011; Nogara et al., 2012).

A see-and-treat protocol should be selected for use in patients with HSIL cytology if colposcopic impression suggests of cervical intraepithelial neoplasia (CIN) 2 or 3 lesions (Numnum et al., 2005; Cho et al., 2009). S&T should be avoiding in low grade cytology because overtreatment rate higher to 60% (Guldeniz, 2014). Colposcopic prediction from current investigation was a good predictive histological reading especially in high grade lesion and cancer cases. As a result, S&T was a proper recommendation in this situation. When S&T was applied in high grade both preceding cytology and colposcopic impression, overtreatment rate was decreased

from 28 to 11.2%. British Society for Colposcopy and Cervical Pathology (BSCCP) definition of overtreatment (missed diagnosis) rate was pathological report equal or less than CIN1. Overtreatment should not more than 10% per BSCCP recommendation (Wright et al., 2007; Luesley and Leeson, 2010). Selected S&T use in patients with HSIL cytology and high grade colposcopic impression overtreatment rate of our investigation was higher than 10 percent. The overtreatment in other local studies were between 3.6-7 percent if the preceding cytology and colposcopic impression revealed high grade abnormality (Table 4). Our investigation showed 75 percent correlation rate between cytology and histology compared to 70.1-92.2 percents in other local works (Charoenkwan et al., 2004; Suntornlimsiri., 2004; Sadan et al., 2007; Kietpeerakool et al., 2007; Aue-Aungkul et al., 2011; Nogara et al., 2012; Ingkapairoj et al., 2012). Majority of Pap smear reports in this study (97 percents) came from affiliated health care providers who were a part of our health consortium. To curb down the overtreatment rate, Pap smear report should be requested for a review by a second opinion before colposcopic examination.

Some studies found higher overtreatment rate among women with HSIL cytology in nulliparous and postmenopausal women (Numnum et al., 2005; Kietpeerakool et al., 2009; Navakorn et al., 2012; Yenrudee et al., 2013). Relatively high overtreatment groups in this current study were only found in High grade Pap smear and normal or low grade colposcopic finding group (Table 5). HSIL Pap smear reports were usually led the colposcopists to perform a more aggressive procedure. High grade Pap smear and normal or low grade colposcopic finding characteristic of overtreatment group were commonly found in referral patients. As agree with previous study (Molpen et al., 2014) this patient group should be evaluated carefully before LEEP. Conventional or three step approach are considered, because they are still in their reproductive years. The present study was limited by the use of retrospective data.

In conclusion, the study suggested that in order to reduce overtreatment incidence, First, HSIL Pap smear should be reexamined again before S&T is considered, especially Pap smears that were referred from the affiliated health care provider. Second, our study show overtreatment rate was higher in high grade and lesser colposcopic patient. So, patients with HSIL Pap smear and low grade colposcopic result should obtain conventional colposcopic approach than see and treat. Third, S&T is suitable approach for patients who got referral from a distance location who were less likely to follow up.

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