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SPECIAL ARTICLE

Is The "See and Treat" Approach Appropriate for Management of Women with Abnormal Cervical Cytology in Thailand?

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ABSTRACT

At present, the "see and treat" approach for women with abnormal cervical cytology is widely accepted. It has been proven to be more cost-effectiveness than conventional management, making it particularly attractive for many regions in Thailand where resources are limited and poor patients' compliance is expected. However, the main disadvantage of the "see and treat" approach is the risk of overtreatment. National Health Service (NHS) guidelines recommend that the overtreatment rate in the "see and treat" approach must be less than 10%. The overtreatment rate appears to be acceptable if the "see and treat" approach is carried out in women with high-grade squamous intraepithelial lesion (HSIL) cytology or in women with lesser grades of smear abnormality whose colposcopic findings suggest high-grade disease.

Key words: see and treat, cervical cytology, overtreatment, colposcopy

Introduction

Cervical cancer screening is one of the most successful preventive strategies in clinical practice. This is due to the advancements in knowledge about cervical carcinogenesis and its natural course[1-4]. Cervical cancer is usually preceded by a considerably long pre-invasive stage, which permits repeated screening.

An adequate scale of screening could remarkably reduce morbidity and mortality from cervical cancer as has been observed in Europe and North America. However, cervical cancer remains a major health burden in many developing countries due to a lack of well-organized cervical prevention programs. In Thailand, cervical cancer is the most common female cancer. When stratified by the region, the highest age-standardized incidence rate (ASR) is in Chiang Mai (28.9), followed by Bangkok (20.9), Songkla (17.8), and Khon Kean (16.5)[5]. So, an effective strategy for cervical cancer prevention should be health public priority.

Although several screening strategies have been proposed, cervical cytology is still the principal method. Management of abnormal cervical cytology depends on various factors including severity of abnormal results, availability of laboratory i.e. human papillomavirus (HPV) testing, and patients' compliance and desire.

In previous reports from the authors' institute, an extraordinary high prevalence of underlying high-grade histology particularly invasive lesions were noted across

all grades of abnormial cervical cytology (Table 1)[6-10]. Immediate colposcopy therefore is the first choice offered to all women with abnormal cervical cytology at the Colposcopy Clinic of Chiang Mai University Hospital. Immediate colposcopy allows these significant lesions to be detected and treated in a timely manner.

Conventional approach in women with abnormal cervical cytology

The conventional approach in women with abnormal cervical cytology requiring colposcopy consists of several steps as follows:

1. Making an appointment for colposcopy

On the first visit, women with abnormal cervical cytology have to undergo pelvic examination and make an appointment for colposcopy. The waiting time from referral to colposcopy varies from only a couple of days to months depending on volume of cases in each setting. In Chiang Mai University Hospital, mean waiting period from referral to colposcopy is approximately 4 weeks[11].

2. Colposcopic examination

Colposcopy is helpful for determining the severity, size, and extent of lesions. At the same time, colposcopy can guide colposcopists the site of the most abnormal appearing lesion for taking a biopsy.

3. Discussing histologic results and treatment planning

Patients will be scheduled back to the clinic again for discussion about their histological results and treatment planning. The time frame in this step varies between hospitals. In Chiang Mai University Hospital, histologic results will be reported within 2 weeks after taking biopsy. However, attention must be paid to the fact that several hospitals in Thailand have no pathologists which means that biopsy tissue must be sent to other centers for histologic examination. The waiting time for histologic assessment therefore will inevitably be longer.

4. Making an appointment for diagnostic excision or definite treatment

If histologic results reveal high-grade disease or low-grade disease in some clinical settings i.e. persistent lesion or those preceded by high-grade cytology, a further appointment is scheduled for diagnostic excision or definite treatment.

Based on the flow pattern of the conventional approach, multiple visits are required, resulting in time-consuming and costly care. Additionally, completion of management is a major concern of this multiple visit care particularly in areas which lack an effective patient tracking system or where poor patients' compliance can be expected.

In the literature, default from the evaluation and treatment schedules among women with abnormal cervical cytology is not uncommon[12, 13]. In Chiang Mai University Hospital, approximately 16% of women with abnormal cervical cytology and 25% of women with cervical intraepithelial neoplasia (CIN) 2-3 are lost to appointments[11, 14].

The "see and treat" approach in women with abnormal cervical cytology

The "see and treat" approach, the so-called "single visit" is an alternative for managing women with abnormal cervical cytology. In this approach, although there are no intervening histologic diagnoses, women are immediately treated after colposcopic examination.

The clinical feasibility of the "see and treat "approach is mainly due to the introduction of loop electrosurgical excision procedure (LEEP), which is safe, has short operative time, and requires only local anesthesia; thus, LEEP can be performed in an outpatient setting[15-17]. Additionally, the treatment efficacy of LEEP is comparable to other treatment methods when carried out appropriately[18]. Unsurprisingly, LEEP is the most common method for diagnosis and treatment of cervical intraepithelial lesions in Chiang Mai University Hospital and probably in other hospitals in Thailand.

The first published article regarding the feasibility of the "see and treat" approach in women with abnormal cervical cytology was reported by Bigrigg et al[19] in 1990. In this study, 1000 women with satisfactory colposcopic examination underwent outpatient LEEP at the time of colposcopy regardless of the severity of preceding cervical cytology. An interesting result is that approximately 90% of women were successfully

managed and did not require additional treatment appointments, and severe peri-operative complications of outpatient LEEP were extremely low. This paper first raised the possibility of the "see and treat" approach in women with abnormal cervical cytology.

Advantages of the "see and treat" approach

1. Reducing number of hospital visits and treatment time

Due to requiring no intervening tissue diagnosis before definitive treatment, the underlying cervical lesions among women undergoing the "see and treat" LEEP are diagnosed and treated at the same time, resulting in fewer hospital visits. The time between referral to definite treatment is then shorter[20-23].

In a previous study from Chiang Mai University Hospital, time interval from colposcopy to definite histologic diagnoses in women undergoing the "see and treat" approach was significantly shorter than that in those who underwent conventional management. This advantage is substantially observed among women who are finally found to have underlying high-grade cervical lesions[21].

An improvement in patient's compliance when using the "see and treat" approach was confirmed by previous studies which showed a lower default rate among women undergoing the "see and treat" approach than those in the conventional group[20, 24].

2. Cost reduction

As mentioned earlier, the "see and treat" approach does not require intervening tissue diagnoses before LEEP. Costs related to the process of intervening biopsy are therefore diminished. Moreover, because of fewer hospital visits, costs related to traveling and lost wages are also reduced.

In resource utilization analysis conducted by Holschneider et al[25], the "see and treat" LEEP in the management of HSIL cytology was the most cost-effective algorithm, offering an approximately 40% cost reduction compared to the conventional approach. In addition, Dunn et al[24] observed that the "see and treat" approach in women with HSIL cytology saved an approximately 30% of total costs compared to the conventional approach.

3. Reducing patients' anxiety

Generally, the level of anxiety among women with abnormal cervical screening tests is closely related to the extent of time used during evaluation and treatment[26-28]. Unsurprisingly, Balasubramani et al[29] reported that the "see and treat" approach had psychological benefits. Women who underwent the "see and treat" approach reported a significantly lower anxiety level than women in the conventional group.

4. More accuracy in diagnosis of high-grade disease

Several reports noted that the diagnostic accuracy of cervical biopsy, although taking from the worst lesion under colposcopic vision or the so-called colposcopically-directed biopsy (CDB), is less than those obtained from cervical conization or hysterectomized specimens, particularly among women whose colposcopic examinations are unsatisfactory or who are of advanced age[30-35].

The deficiency in the diagnostic accuracy of CDB is reaffirmed by the recent study from Zuchna et al[36] In this study, although more than 90% of women had satisfactory colposcopic examination, 69 of 107 women (64.5%) who had CDB revealing CIN 1 or less were subsequently found to have CIN 2-3 on cone specimens. Moreover, this study also showed that women with HSIL cytology whose CDB showed CIN 1 or less missed approximately two-thirds of CIN 2-3 on cone specimens.

Because most "see and treat" approach in women with abnormal cervical cytology uses LEEP as the treatment option, the risk of under-diagnosis of severe lesions including CIN 2-3 and occult invasive cancer among women undergoing this approach is accordingly kept as low as possible, which makes it more appealing, especially in Chiang Mai University Hospital and probably other hospitals in Thailand where the prevalence of invasive cancer is considerably high across all grades of cervical smear abnormality (Table 1).

Table 1 Histopathologic findings among women with abnormal cervical cytology attending Colposcopy Clinic, Chiang Mai University Hospital stratified by type of cytologic results

Cytology	Histopathologic results, n (%)				
	No lesion	CIN 1	CIN 2-3	AIS	Cancer
ASC-US (n=208)[6]	153 (73.6)	5 (2.4)	21 (10.1)	3 (1.4)	5 (2.4)
ASC-H (n=85)[7]	20 (23.5)	6 (7.1)	52 (61.2)	0 (0)	7 (8.2)
LSIL (n=208)[8]	79 (38.0)	62 (29.8)	63 (30.3)	0 (0)	4 (1.9)
HSIL (n=282) [7]	18 (6.4)	9 (3.2)	195 (69.2)	3 (1.1)	57 (20.2)
SCCA (n=48)[9]	0 (0)	1 (2.1)	31 (64.6)	0 (0)	15 (31.3)
AGC* (n=63)[10]	49 (77.8)	0 (0)	5 (7.9)	3 (4.8)	2 (3.2)

*The remaining 4 cases had endometrial hyperplasia (1) and endometrial carcinoma (3)
CIN, cervical intraepithelial neoplasia; AIS, adenocarcinoma in situ; ASC-US, atypical squamous cell of undetermined significance; ASC-H, atypical squamous cell cannot exclude high-grade squamous intraepithelial lesion; LSIL, low-grade squamous intraepithelial lesion; HSIL, high-grade squamous intraepithelial lesion; SCCA, squamous cell carcinoma; AGC; atypical glandular cells

Disadvantages of the "see and treat" approach

The main disadvantage of the "see and treat" approach in women with abnormal cervical cytology is the risks of receiving an unnecessary treatment, the so-called "overtreatment". In US National Cancer Institute (NCI) and American Society for Colposcopy and Cervical Pathology (ASCCP) recommendations, overtreatment means the excised specimen contained CIN 1 or lesser[37].

The National Health Service (NHS) of the United Kingdom in collaboration with the British Society for Colposcopy and Cervical Pathology (BSCCP) has launched a set of standards for quality assurance of effective cervical cancer screening entitled "The Colposcopy and Programme Management: Guidelines for the NHS Cervical Screening Programme (NHSCSP)." The first edition was published in 2004 and covered various aspects regarding cervical cancer prevention including standard performances of the "see and treat" approach in women with abnormal cervical cytology. In the NHSCSP 2004 guidelines, overtreatment rate in women undergoing the "see and treat" approach was defined as the proportion of women whose excised specimens revealed no CIN of any grade.

The NHSCSP guidelines were recently updated and were launched in May 2010[38]. The fundamental change regarding to the "see and treat" approach is the revision of the definition of an overtreatment. In the NHSCSP 2010, women with CIN 1 on excised specimens were also considered as receiving overtreatment. Women with excised specimens containing CIN 2-3 or cervical glandular intraepithelial neoplasia (cGIN) were classified as receiving appropriate management. This revision was based on the fact that the majority of CIN 1 cases could spontaneously regress. The current definition of overtreatment given by the NHCSCP 2010 guidelines is similar to that used in the US NCI recommendations[37, 38].

Table 2 shows the results of literature review of the underlying cervical pathology among women with abnormal cervical cytology who underwent the "see and treat approach" including the reports from Chiang Mai University Hospital[8, 19-22, 24, 39-50].

Table 2 Overtreatment rate of the "see and treat" approach as per types of cervical cytology

Type	Authors (ref)	Year	No. of patients	Colposcopic diagnosis	Histologic results	
					No lesion	CIN 1 or lesser
LSIL‡	Bigrigg et al[19]	1990	247	Any	6.1	49.8
	Keijser et al[39]	1991	20	Any	25.0	60.0
	Chia et al[50]	1994	127	Any	31.5	74.0
	Ferris et al[40]	1996	27	Any	40.7	81.5
	Smith et al[41]	2001	62	Any	16.1	33.9
			54	HGL	11.1	29.6
	TOMBOLA Group[42]	2009	432	Any	31.0	59.0
	Kiatiyosnusorn et al†[8]	2010	29	HGL	3.4	27.6
ASC-H	Kietpeerakool et al†[21]	2008	58	Any	24.1	27.5
			40	HGL	7.5	10.0
HSIL	Bigrigg et al[19]	1990	412	Any	3.4	22.6
	Keijser et al[39]	1991	393	Any	6.1	11.2
	Chia et al[50]	1994	110	Any	11.8	30.0
	Ferris et al[40]	1996	14	Any	7.1	14.3
	Smith et al[41]	2001	385	Any	10.0	13.5
			380	HGL	10.0	13.7
	Irvin et al[43]	2002	50	HGL	4.0	18.0
	Szurkus et al[44]	2003	104	Any	25.9	39.4
			34	HGL	23.5	29.4
	Dunn et al[24]	2003	100	HGL	1.0	3.0
	Charoenkwan et al†[45]	2004	55	Any	0	3.6
	Numnum et al[46]	2005	51	Any	8.0	15.7
	Errington et al[47]	2006	378	HGL	3.4	15.6
	Sadan et al[22]	2007	81	HGL	8.6	28.4
	Kietpeerakool et al†[48]	2007	446	Any	5.8	7.8
	Kietpeerakool et al†[49]	2009	247	Any	7.3	9.3
	Monteiro et al[20]	2009	298	HGL	2.0	8.7

‡ Or equivalent

† Study from Chiang Mai University Hospital

CIN, cervical intraepithelial neoplasia; LSIL, low-grade squamous intraepithelial lesion; ASC-H, atypical squamous cell, cannot exclude high-grade squamous intraepithelial lesion; HSIL, high-grade squamous intraepithelial lesion; HGL, high-grade lesion

The data shown in Table 2 suggest important practical considerations, in that the overtreatment rate is low when the "see and treat" approach is carried out in women with HSIL cytology, regardless of their colposcopic findings. However, among women with a lesser degree of cytologic abnormality such as low-grade squamous intraepithelial lesion (LSIL) or atypical squamous cells cannot exclude high-grade squamous intraepithelial lesion (ASC-H), the overtreatment rate seems to be acceptable if the "see and treat" approach is solely carried out in women whose colposcopic findings suggest high-grade disease. So, expertise of the colposcopist regarding an accurate differentiation between low-grade and high-grade disease is important in order to reduce the overtreatment rate.

In the ASCCP 2006 consensus guidelines for the management of women with abnormal cervical cancer screening, the "see and treat" approach was accepted as an alternative option for managing women with HSIL cytology[51]. However, in order to avoid adverse obstetrics complications[52, 53], the "see and treat" approach should be meticulously considered in women who still desire their future fertility.

Factors predicting an overtreatment

Generally, the most important factor that can predict overtreatment in women with abnormal cervical cytology is the type of preceding cytology. The overtreatment rate appears to be acceptably low when the "see and treat" approach is strictly carried out in women with HSIL cytology[54].

In a prospective study from Numnum et al[46], parity status has been noted to be an independent predictor for overtreatment among women with HSIL cytology. Nulliparous women are approximately 12 times more likely than multiparous women to receive overtreatment after undergoing the "see and treat" approach.

In the authors' experience, an overtreatment rate among postmenopausal women with HSIL cytology who underwent the "see and treat" approach was slightly higher than that of premenopausal women (10.0% and 4.0%, respectively)[48]. Theoretically, the higher rate of overtreatment among postmenopausal women may be partly due to the higher false positive rate of HSIL cytology. Cytomorphologies of exfoliated atrophic cells found in postmenopausal women (i.e. cellular immaturity and atypical nuclear patterns) frequently resemble high-grade abnormality cells. The difficulty in distinguishing atrophy-related cells in postmenopausal women from HSIL cells is therefore expected[55, 56].

Audit of the "see and treat" approach

Due to the fact that variations in clinical practice are inevitable, quality control is therefore needed in patient care. Audits of routine medical practice are strongly recommended to evaluate and ensure the practice quality[57].

The "see and treat" approach for women with abnormal cervical cytology is no exception for audit. The main indicator used for auditing its performance is the rate of overtreatment. The NHSCSP 2010 guidelines state that the rate of overtreatment must be less than 10%[38]. The 10% threshold for overtreatment rate given by NHSCSP 2010 is consistent with the recommendation of the Cochrane Colposcopy and Cervical Cytopathology Collaborative[58].

Although LEEP is generally safe, it is not a complication-free surgical procedure. Concerning the safety of women undergoing treatment of CIN, the NHSCSP 2010 guidelines state that the incidence of primary hemorrhagic complication must be less that 5% and the admission rate owing to treatment complication should be less than 2%[38].

The "see and treat" approach is a common strategy for evaluating women with abnormal cervical cytology at Colposcopy Clinic of Chiang Mai University Hospital, particularly in women with HSIL cytology. An audit of standards of the "see and treat" approach in women with HSIL cytology using NHSCSP guidelines in our institute revealed that the overtreatment rate was 9.3% of the cases. Primary hemorrhage was noted in 5.3% of the cases but only 1.6% experienced severe LEEP complications requiring admission for inpatient treatment[49].

Conclusion

The "see and treat" approach for managing women with abnormal cervical cytology has become internationally accepted. This approach has been proven to be more cost-effective than conventional management because it decreases the number of hospital visits, the necessity of intervening tissue diagnoses before definite treatment, and the patients' anxiety. Thus, it is worth of considering, particularly in Thailand where the resources are limited and poor patients' compliance is expected. However, the performances of the "see and treat" approach, including its overtreatment rate and peri-operative LEEP complications, should be periodically audited to ensure that it is practiced according to the standard requirements.

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